ROUTLEDGE HANDBOOKS

Routledge Handbook of Medical Law and Ethics

Edited by Yann Joly and Bartha Maria Knoppers

Routledge Handbook of Medical Law and Ethics

This book explores the scope, application and role of medical law, regulatory norms and ethics, and addresses key challenges introduced by contemporary advances in biomedical research and healthcare. While mindful of national developments, the handbook supports a global perspective in its approach to medical law. Contributors include leading scholars in both medical law and ethics, who have developed specially commissioned pieces in order to present a critical overview and analysis of the current state of medical law and ethics. Each chapter offers comprehensive coverage of long-standing and traditional topics in medical law and ethics, and provides dynamic insights into contemporary and emerging issues in this heavily debated field. Topics covered include:

- bioethics, health and human rights;
- medical liability;
- law and emerging health technologies;
- public health law;
- personalized medicine;
- the law and ethics of access to medicines in developing countries;
- medical research in the genome era;
- emerging legal and ethical issues in reproductive technologies.

This advanced-level reference work will prove invaluable to legal practitioners, scholars, students, and researchers in the disciplines of law, medicine, genetics, dentistry, theology, and medical ethics.

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1
Introduction

Vasiliki Rahimzadeh, Yann Joly, and Bartha Maria Knoppers

The domains of medical law and ethics are distinct, yet inextricably connected. Whereas the law delimits the scope of activities permitted in a liberal society, ethics forms the basis whereby these activities subscribe to the values and moral principles society constructs. Social norms find their expression in ethics and often subsequently in the law (Posner 2000). Understanding the ways in which both shape the structure and function of the medical enterprise is the cornerstone of good professional practice, not to mention central to the humanitarian care of patients.

The societal and individual moral applications manifested in the law and ethics respectively, have together guided the practice of medicine since ancient times.[1] It would be naive to assume, however, that their relationship has always been a symbiotic one (Beauchamp 2004). Capron (1979) argues that law and ethics give rise to different forms of rights that can be used to make apparent a distinction between the two. He asserts that from the study of ethics in a medical context there emerge *moral* rights attributed to users of healthcare systems, which can be defended using philosophical paradigms such as Aristotelian virtue ethics, utilitarianism and Kantianism, to name a few, whereas from the law emerges *legal* rights, which assign enforceable duties and responsibilities 'among the competing, and often conflicting, interests of its citizens' within a legal system (Hodge and Gostin 2001).

Eras of rapidly evolving innovation within medicine – and within other scientific and technology disciplines to be sure – continue to underscore the immediacy of iterative reevaluation, reconceptualization and reform in the law in order to keep apace with medical progress. In this way, ethics provide a theoretical and conceptual framework for clarifying – but also problematizing – emergent laws that are both jurisdiction-specific and international in outlook in the wake of contemporary controversies. Such laws, therefore, become useful elements of scholarship and offer a methodology for contextualizing medical advancement in conversation with its ethical implications (DeGrazia 1999). This book enters into these discussions by exploring the application,

1 The first documented medical law was written in the Code of Hammurabi in 1772 BC, which read: 'If a physician make a large incision with the operating knife, and kill him, or open a tumor with the operating knife, and cut out the eye, his hands shall be cut off.' Discussions of ethics and value principles in medicine were largely coincident with the emergence of medical science itself, particularly in Ancient Greece (see Jones 1924).

scope and role of medical law and its regulatory norms in laying the groundwork for ethical policy and practice in healthcare. It attempts to find cohesion between medical law and ethics, debating new practical approaches to theoretical problems. Though the study of medical ethics is multidisciplinary by nature, this book unifies the otherwise incredibly diverse perspectives of interlocutors in the field under the auspices of medical law. It sets out to bring the complexities of this intersection to the fore of novel modalities and systems of care made possible by, *inter alia*, the genomic revolution and data-intensive sciences. Engaging with such themes is, we suggest, critical to navigating an increasingly data-driven healthcare system (Ozdemir *et al*. 2011), while preserving the ethos of rights-based medicine and optimizing health outcomes for populations globally. The Handbook, therefore, offers rich discussions of classical and novel ethical issues in medical jurisprudence from authors with a variety of theoretical perspectives, approaches and expertise. This diversity intentionally seeks to represent the key emerging domains of the field of medical law, and the breadth of ethical approaches purposefully addresses the many challenges of these new domains.

The authors of each chapter present the fundamental ethical and legal aspects, as well as discuss key international and national documents governing the activities in their field. Many offer an overview of the legal history and evolution of legal thinking, verifying their influence on the current legislative climate in which these issues are being examined. The chapters offer relevant case analyses, illustrating the practical applications of theoretical and normative ethics within a range of national and supra-national jurisdictions. The emergence of case law and precedence – as well as the formation of public opinion in response – alert us to the significance of legal processes in redefining socioethical norms and standards. Finally, each chapter carves a space for forward thinking and reflection. Authors provide critical commentary on some of the newest developments in their respective fields, elucidating the ways in which medical law governs advances in healthcare and clinical practice. It is called a Handbook not to put forth protocols or procedural guidance in deploying the law to resolve ethical conflicts. Rather it serves as a detailed compendium of legal instruments and ideas, both current and historical, in responding to matters of pressing ethical import in healthcare.

The Handbook takes up a number of these compelling issues and arranges them in four categories. *Rights of Persons* comprises chapters that interrogate the protections and freedoms of patients in their interaction with the healthcare system, including the traditionally more vulnerable categories of persons such as children (Chapter 5) and the mentally disabled (Chapter 7). It touches upon long-standing principles of bioethics, including consent (Chapter 3) and confidentiality (Chapter 4) and brings to light the contemporary challenges of preserving these traditional fixtures in the doctor–patient relationship. To this point, an entire category of the Handbook is dedicated to the *Professional Relationship*. Ries investigates the organizational infrastructures and healthcare mandates that guarantee adherence to, and maintenance of, professional standards of practice (Chapter 10). Moreover, the chapters in this section make clear that protecting patient safety is the focal point of professional standards. Khoury (Chapter 11), for example, puts into sharp relief the serious ethical and legal consequences when healthcare professionals fail to meet such standards in preventing nosocomial infections, and contextualizes the emergence of patient safety legislation in the aftermath of the tort frenzies that followed.

As its name suggests, *Medical Interventions and Emerging Technologies* highlights some of the frontiers of medical science, and the ways in which researchers and policymakers alike are attempting to chart their sociotechnical futures. From creating online clinical interfaces through telemedicine (Chapter 15), to developing high-precision techniques in assisted reproduction (Chapter 13), novel technologies and machines are transforming the landscape of healthcare delivery (Kahvejian *et al*. 2008). In turn, the law and regulatory mechanisms are challenged to evolve in parallel with

the technological sophistication witnessed in recent years. As life expectancies and quality of life are projected to increase with greater adoption of technology – though almost exclusively in countries able to invest in costly research and development – the need for international dialogue on access and policy harmonization has never been more immediate.

Likewise, multidisciplinary collaboration is required to translate research discoveries into routine medical practice. Our ethicolegal engagement with the increasingly genome-oriented objectives in research and care is reflected in *From Bench to Bedside*. In Chapter 17, Chalmers argues that the regulatory and legislative governance of medical research must adapt ethical frameworks better suited to preserve scientific freedom, and minimize risks unique to research participation in the 'genome era.' He underscores the fact that little more than a decade after completion of the Human Genome Project, diagnostics and treatment strategies are chiefly centering on a patient's genomic profile, most notably in rare genetic diseases (Ng *et al.* 2010; Bamshad *et al.* 2011) and cancer (Lander *et al.* 2001; Roychowdhury *et al.* 2011; Curtis *et al.* 2012). Sequencing techniques and an explosion in computational power have blossomed into entirely new research and clinical subfields, such as pharmacogenomics (Chapter 11), nutrigenetics (Fenech 2014; Mutch *et al.* 2005) and bioinformatics (Ouzounis 2012).

Where legal apparati purported to regulate new technologies often face issues of classification and applicability, the role of the law in safeguarding public health can raise questions of scope and competing notions of rights. 'The crux of public health,' Gostin maintains, 'is a public or governmental entity that harbors the power and responsibility to assure community well-being … perhaps the single most important feature of public health is that it strives to improve the functioning and longevity of populations' (2008). In *Public Health and International Health Systems*, authors provide an international take on models of public health law, and its purpose and permanence in augmenting a human right to health. Through a rights-based lens, Munyi canvasses the issue of access to essential medicines in the developing world (Chapter 22), where international instruments expand such access. Because public health *practice* is concerned with optimizing the health of populations, it is fitting that good public health *policy* recognizes the different sociocultural and regional constructions of health and wellbeing across the world. Kaan (Chapter 23) explores this complicated relationship by analyzing the protective capability of public health law between predominant medical traditions in the Global North and South.

Notwithstanding the plethora of legal structures and interpretations represented in this Handbook, a number of common motifs weave throughout the chapters. When examined together, they isolate the points of theoretical convergence that allow medical law and ethics discourse to complement each other toward the provision of effective and ethically sound healthcare.

1.1 Human rights and professional accountabilities in the law

Many contributors to this Handbook employ rights-based rhetoric to defend the vehicle of accountability espoused by medical law. December 10, 2013 marked the 65th anniversary of the 1948 Universal Declaration on Human Rights. An undoubtedly poignant moment in history, it was an opportunity to restore faith in humanity through collective agreement and codification of the inviolability of human life. For some, reference to human rights doctrines is implicit in the framing, formulation and protection the law offers its respective constituents. For others, these principles act as the starting point from which to assign legal accountability in facing ethical uncertainty. As was true at the time of its ratification, political will is necessary to actualize the Declaration's principles in national laws governing medicine and healthcare.

Annas (Chapter 2) describes this translational process in the context of leveraging the triad of bioethics, law and medicine to devise effective healthcare legislation. He argues that not to acknowledge how the three in fact coexist and inform each other is to create irresponsible law at best. Nowhere is this potential incongruity between the principles of human rights and the law starker than in drafting antidiscrimination legislation for communities of people with disabilities. Indeed, Hendriks (Chapter 6) affirms the frequent violations of human rights within this population, where patients are largely devalued and disregarded by the healthcare system.

Health professionals personify the actualization of rights through practice, and mediate the triangulated relationships Annas identifies. The role of the health professional, therefore, as both a specific technology user and care deliverer, is a centerpiece in ethics discourse on professionalism. Rothstein explores this theme in Chapter 4. He examines the unique transformations in the uptake and dissemination of health information through online networks and social media platforms such as Facebook and Twitter, and how the connectivity they allow are in fact reshaping standards of patient interaction. Moreover, with greater online presence comes enhanced privacy risks and the need to develop advanced information storage platforms. Others share this view, identifying the added ethical implications for healthcare professionals whose online presences have, more than ever, broadened their visibility and ready accessibility to patients (DeCamp *et al*. 2013).

Freckelton and Bennett's discussion of the migration of healthcare professionals and patients across national borders (Chapter 9) raises new questions in the way of redefining a professional ethic of care. They chronicle recent trends in the regulation of medical practice, charting a move from professional self-regulation through to contemporary (read external) models of oversight and accountability.

Similar transitions dare us to consider *quis custodiet ipsos custodes?* or, 'who will guard the guardians?'[2] Do our professional codes of ethics – like the law, purported to be reflections of the values and virtues society deems essential to the realm of professional practice – indeed protect healthcare users from abuses of the system or clarify legal accountability where ethical ambiguity dominates?

The authors in this Handbook do not resolve these pending questions *per se*. Perhaps more ambitiously, what resonates from their analyses is a demand for reconsidering the basic notions of professionalism and revisiting the fundamental purpose(s) of medicine. In doing so, the authors offer grounded perspectives on the extent to which the law ought to build on these foundational concepts so as to draw legal theory and clinical practice into healthier confines.

1.2 Reevaluating foundations

Implied above is how the law serves as a practical instrument to ground bioethical and human rights principles in the realities of healthcare delivery. It is from this practical standpoint that the conception of professionalism and a professional ethic of care emerge. In a healthcare context, there are three spheres of ethical priority setting that (ideally) converge on patients' best interests: that of the patient, the professional and the institution. Gastmans and Nys confirm this in Chapter 8. Through exploring the ethical tensions of end-of-life care in neonates, they validate

2 Though not directly quoted in his volumes, this question first appeared in Book Three of Plato's *Republic* before the Roman poet Juvenal includes it in his *Satires*. Plato's Socratic disciples ponder who will oversee the authority of those charged with overseeing everyone. It is often interpreted as musings on ending political corruption, but in the text it is deliberately referring to ensuring marital fidelity within the polis. They ultimately conclude, 'it would be absurd that a guardian should need a guard.' (See Besley and Robinson 2010; Book III, XII, 403E, p. 264 (Greek) and p. 265 (English), in Plato, *The Republic*, vol. 1, trans. P. Shorey. New York: G. P. Putnam's Sons 1930).

the true challenges in determining the moral permissibility of withdrawing care, at what point, and to what end. The authors contend that medical prognosis – and the courses of action it inspires – is but consideration as part of the ethical analysis that determines the child's best interest. Tensions arise when healthcare professionals find they must allow assessments on quality of life to become the province of, in the case of neonates, parental expertise. Oftentimes, these views can denounce Western medicine's obsession with curative rigor and rigid definitions of futile treatment.

That sophistication of medical technology, namely in genetics/genomics, can convert modalities of care and professional norms is key to Thorogood and Knoppers' thesis in Chapter 18. They argue how the notion of best interests can be problematic for healthcare professionals hoping to offer preventative care through genetic surveillance to pediatric patients and their families. Until recently, searching for particular biomarkers known to predispose patients to disease had been the hallmark and promise of genetic testing. Increasingly, the discovery of secondary or incidental findings using whole genome sequencing in clinical research (discussed in terms of professional duties to inform in Chapter 12) fuels widespread debate on the meaning and application of the respect for persons principle as it relates to a patient's or participant's best interest. The lack of professional guidance in disclosing such findings prompted a number of recent guidelines from the United States (Green *et al.* 2013; United States Presidential Commission for the Study of Bioethical Issues 2013) and abroad (Viberg *et al.* 2014).

The touristic undertone with which Sipp describes emerging stem cell therapies (Chapter 24) begs questioning whether medicine is in peril of becoming overly commoditized by for-profit entities. Patients in pursuit of the fountain of youth or a miracle cure need not look any further! Popular marketing campaigns boast the (dubious) regenerative promises of their stem cell products, many of which fall through the cracks of federal licensing and safety regulations. Stemming the tides of clinical and direct-to-consumer (Chapter 16) genetic testing likewise accentuates the law's dual responsibility for delimiting the availability of health services from private companies, and safeguarding autonomous rights to information concerning one's genetic material or health status. However, the difficulty of establishing clinical validity and utility for many of these new tests means that the information generated from them can sometimes cause more harm than good (Dickensen 2014; Cornel *et al.* 2014).

Beak and Isasi highlight similar challenges in product classification for new drugs and therapeutics in Chapter 14 on regenerative medicine. In a detailed examination of the regulatory pitfalls facing developers – including enormous time constraints and costs – they show how uncertainties in classification have a corresponding effect on the required scientific evidence to approve novel therapeutics for patient use. The failure of such classification schemes under current regulatory frameworks illustrates the dissymmetry between the law and new technologies, as the former 'attempts to govern [technologies] with an antiquated grasp of their meaning' (Askland 2011).

1.3 A brave new framework

The analyses presented in this Handbook mount increasing evidence of the need for more coherent legal frameworks that better reflect the ethical dimensions at the intersection of clinical research, healthcare and the law. Authors contend a more reflexive and versatile legal gaze is needed, one that takes into account history as either a cautionary tale – which Lobato de Faria and Cordeiro tell with respect to the public health initiatives and the economy in Chapter 20 – or an optimistic indication verifying the successes of anticipatory governance and 'norm entrepreneurship' that Aginam promotes in Chapter 21. Implicit in his arguments, and others, is the importance of regulatory harmonization and the interagency collaboration

among policymaking bodies (e.g. the World Health Organization (WHO)) that play a key role in its negotiation. Often, these bodies serve as collaborative grounds for the shared ideals and principles of the international community to inform jurisdiction-specific regulation. Thorogood and Knoppers make this connection in describing the ways in which micro and macro levels of governance frame the ethical issues that demand legal scrutiny. Indeed, online health information privacy presents us with one such realm where micro and macro governance must complement one another if patients are to receive equal protection under law. In Chapter 13, Ravitsky and Dupras-Leduc likewise cite reproductive tourism as an example of the possible consequences for maintaining varying levels of regulatory stringency between these micro and macro domains of governance.

1.4 Conclusion

The particular scope of legal frameworks established to respond to emerging issues in medicine and healthcare are a key focus for many chapters in the Handbook. It is through the use of effective yet nuanced and harmonized legal frameworks to justify legislation that we can ensure patients are cared for in an ethically responsible manner. Whether calling for the development of a new framework, or revisiting the foundational aspects of preexisting ones, the authors testify to the significance of frameworks for grounding medical law in normative ethical theory. Yet the law remains conceptually distinct from ethics. Healthcare professionals, institutions, and legal scholars need, therefore, to embrace opportunities for multidisciplinary collaboration on what constitutes ethical healthcare and research if for no other reason than to acknowledge the many facets and moving parts of providing it to patients, their families, and research participants. The sheer complexity and significance of the ethical issues identified through the various chapters of this Handbook speak to the need for building international consensus rather than working in jurisdictional silos.

In an increasingly globalized and connected world, the Internet has created a technological frontier for the masses that can be harnessed to improve healthcare delivery everywhere and enable mobilization around these efforts. Though the possibilities seem infinite, ethicolegal discourse is critical to constructing a morally permissible utilization path. This Handbook advocates that to better understand the role of medical law and ethics in the promotion of health, we must be able to recognize where our professional commonalities and differences lie. Only then can we begin to imagine a society that prioritizes public health as a global public good, for example, and ensure the continued relevance and legitimacy of international policymaking bodies. The array of ethical discussions that comprise this Handbook uniquely attest to the regulatory harmonization that is possible when efforts to enact legal reforms mirror the degrees of innovation and creativity witnessed in technology development.

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Part I
Rights of persons

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2

Bioethics, health law, and human rights

George J. Annas

Bioethics, health law, and human rights can be viewed either as distinct areas of study and advocacy, or as interrelated areas that not only overlap, but have synergistic energy that can be concentrated to produce social change and promote social justice. This chapter introduces a way to think about this interrelationship and applies it to real-world cases.

2.1 Theory

Bioethics, health law, and human rights are overlapping and interrelated in ways that are not always either articulated or understood. Rather than antagonistically competing for their own influence, these fields can most constructively be viewed as complementary and synergistic. Thus, for example, human rights strongly support the medical ethics principle of informed consent, and medical ethics supports the human rights concept of the right to health. Human rights are universal and as such apply to all humans; they also articulate governmental obligations, and as such, focus on states. Health law is jurisdictional, and is the result of a political process in a particular country – which may or may not be the result of a country signing a particular treaty, obligating it to implement certain domestic law. Bioethics, especially its subcategory of medical ethics, defines the obligations of physicians when treating patients, and can also define a physician's obligations when working for the state (usually seen as the domain of human rights).

Health law, bioethics, and human rights can be thought of as three different species of spiders that spin overlapping webs, the overlap becoming the strongest and most robust 'net.' The overlap of their webs can be observed with special clarity in the conduct of international research trials, especially those sponsored by rich countries and conducted in resource-poor countries. Other examples include the failure of the United Nations to take responsibility for introducing cholera in Haiti during their earthquake relief efforts, and the continued force-feeding of hunger strikers at the US military prison at Guantánamo. An even more striking example in the US is the abject failure of the government (and many physicians) to even acknowledge the internationally recognized 'right to health,' and to take effective steps to combat its components of hunger, homelessness, and lack of access to basic medical care (*Universal Declaration of Human Rights* 1948, article 25; UN Economic and Social Council 2000).

Physicians in the US and around the world have roundly condemned violations of medical ethics and human rights, including force-feeding at Guantánamo. That the practice nonetheless continues illustrates a major paradox with both medical ethics and human rights: both are widely supported in theory, but governments can (and do) ignore both when they think it is in their self-interest to do so. One reason often posited for the failure of governments to take human rights and medical ethics more seriously, and to incorporate them into their domestic law, is their inability to agree upon their origins and authority. It seems most reasonable to conclude that contemporary human rights and contemporary bioethics were born together in the aftermath of World War II (WWII). WWII produced the International Military Tribunal at Nuremberg (which articulated the *Principles of International Law Recognized in the Charter of the Nuremberg Tribunal and in the Judgment of the Tribunal* 1950 (*Nuremberg Principles*)), the subsequent *Trials of War Criminals before the Nuremberg Military Tribunals under Control Council Law No. 10* (which articulated the *Nuremberg Code* 1947 – and can be seen as the first bioethics trial), and the founding of the United Nations (UN). The UN quickly adopted the *Universal Declaration of Human Rights* (UDHR) in 1948, and soon thereafter the *Geneva Convention Relative to the Protection of Civilian Persons in Time of War (Fourth Geneva Convention)* 1949 (*Geneva Convention*).

2.1.1 Human rights and Nuremberg

There was a series of attempts to define and champion human rights before Nuremberg. Thomas Aquinas taught that human rights came from God, but that man could discover the content of this 'natural law' through reason. Kant grounded rights on the notion of human dignity and taught that they were universal (Robertson 2000: 33). The revolutions in the US and France were both based on concepts of human rights. In the case of the former, the *Declaration of Independence* 1776 proclaimed that 'all men are created equal and endowed by their creator with certain inalienable rights, including life, liberty, and the pursuit of happiness.' The *Bill of Rights* 1791 also defined areas of a citizen's life the government could not invade, including rights of free speech, religion, and the press. The French *Declaration of the Rights of Man and the Citizen* 1789 proclaimed 17 specific rights as 'the natural, inalienable and sacred rights of man' (preamble). Jeremy Bentham objected to the French list, arguing that there was no such thing as a natural right, but that they were all created by the law of the country (Robertson 2000: 11–12). Bentham's view that rights are created by governments through law, and thus can and do vary from country to country, continues to have adherents today. Nonetheless, it seems correct to say that the most common view is that humans are special. Human rights are seen as inherent in what it means to be human, and are thus sometimes described simply as the 'birthright' of a human newborn (Morsink 2009: 46).

The 'natural' versus government-defined (positive law) dichotomy could not survive World War II. The horrors of mass murders, the Holocaust, torture, slavery, and arbitrary detention, all 'legal' under the positive law of Germany, were universally condemned as violations of the customary/natural 'law of nations.' At Nuremberg, many acts were judged as war crimes and 'crimes against humanity,' crimes that no government could lawfully authorize, including murder, torture, slavery, and arbitrary detention (Alston and Goodman 2013: 126). All of these can be rightfully categorized as 'negative' human rights, as in the right not to be murdered, tortured, enslaved, or treated as a research subject without informed consent. The most important human rights documents, including the *Universal Declaration of Human Rights*, the *International Covenant on Civil and Political Rights* 1966 (ICCPR), and the *International Covenant on Economic, Social and Cultural Rights* 1966 (ICESCR) are all direct products of World War II. The same can be said about the most important humanitarian treaty, the *Geneva Convention* and the *Nuremberg*

Principles, which were established in the major war crimes trial (the International Military Tribunal) of the Nazi leaders after World War II. The *Nuremberg Principles* made it clear that there are such things as war crimes and crimes against humanity (including murder, torture, and slavery); that individuals and not just states can be held criminally accountable for committing these crimes; and that it is not a defense for an individual to claim he was 'just obeying orders' or following the law of his country (Principles I, IV, VI). The rapid growth of international human rights law in reaction to the horrors of World War II has been profound in both human rights law and humanitarian law.

2.1.2 Humanitarian law

Humanitarian law is the formal term used to denote the law of war, especially that which pertains to rules restraining the worst impulses of the armies of warring states. The law of war is generally divided into two parts: (1) laws relating to the prevention of war (primary prevention) by discouraging going to war in the first place (*jus ad bellum*); and (2) laws relating to what may be thought of as secondary prevention, rules for the conduct of war, especially rules to protect civilians (*jus in bello*) (Grodin *et al.* 2013: 264).

Because war is so terrible it has, at least since Roman times, required justification, usually set forth in a version of the just war doctrine. This doctrine requires that war be waged under a public authority, be instigated either for self-defense, or to punish a grievous injury, and be pursued only to achieve the just ends, not for vengeance (Grodin *et al.* 2013: 264). What constitutes self-defense has been open to some interpretation, but notions of 'preemptive war,' designed to respond to a future threat, have no just war pedigree. Nations need not wait until they are attacked to defend themselves, but an attack must be imminent and unstoppable by other means to justify initiating a self-defense war.

Jus in bello rules, rules that limit the destructiveness of an inherently destructive activity, may seem strange, even counterproductive, since they may make war appear less horrible than it is. Nonetheless, prohibiting the mass slaughter of civilians has been a central tenet of the laws of war at least since the Thirty Years War (1618–48) and the work of Dutch jurist Hugo Grotius. Before that time, murder, rape, and pillage were seen as acceptable, even necessary, consequences of war.

The *Convention (II) with Respect to the Laws and Customs of War on Land and Its Annex: Regulations Concerning the Laws and Customs of War on Land* 1899 and the *Convention (IV) Respecting the Laws and Customs of War on Land and Its Annex: Regulations Concerning the Laws and Customs of War on Land* 1907 (collectively referred to as the *Hague Conventions*), established before World War I, specifically apply to land warfare and prohibit, among other things, 'the attack or bombardment of towns, villages, habitation or buildings which are not defended' (*Convention (II)*, article 25). The post-World War I League of Nations was singularly ineffective in preventing World War II, and the *Hague Conventions* were systematically ignored during the war, which included both the slaughter of civilians by Germany and the Soviet Union, but also the firebombing of German and Japanese cities by the US, and even the use of atomic weapons on Hiroshima and Nagasaki.

The killing of millions of civilians during World War II, as well as the deaths of millions of prisoners of war, led to the *Geneva Conventions* of 1949 and their two additional protocols of 1977. Occupying powers are obliged to protect nonmilitary persons and places, and to make sure that the civilian population is provided with food and medical supplies as well as 'clothing, bedding, means of shelter, and other supplies essential to the survival of the civilian population' (*Protocol Additional to the Geneva Conventions of August 12 1949, and relating to the Protection of Victims of International Armed Conflicts (Protocol I)* 1977, article 69). Common article 3 of the

Geneva Conventions, common to all four of the conventions, sets the minimum standard for all conflicts, and prohibits not only torture, but also cruel, inhuman, or degrading treatment of all prisoners of war. Its operative section, which applies to all persons 'taking no active part in the hostilities' for whatever reason (including injury and detention), ensures that these persons 'shall in all circumstances be treated humanely,' by prohibiting the following acts at all times:

(a) violence to life and person, in particular murder of all kinds, mutilation, cruel treatment and torture;
(b) taking of hostages;
(c) outrages upon personal dignity, in particular, humiliating and degrading treatment.

(Geneva Conventions, article 3*)*

The results of these efforts to protect civilian populations and members of the armed forces who have been captured or have 'laid down their arms,' have, at best, been mixed, as can be seen in the wars in Iraq, Afghanistan, the Congo, and Syria over the past decade. The attempt to develop a 'permanent Nuremberg' tribunal, now known as the International Criminal Court – formally established in 2000 – has great potential. Unfortunately, the United States has not ratified the treaty that established it, due primarily to concerns about trying its own soldiers in an international court and post-9/11 politics.

2.1.3 Human rights law and the Universal Declaration of Human Rights

The *Charter of the United Nations*, signed by the 50 original member nations in 1945, spells out the goals of the UN. The first two are 'to save succeeding generations from the scourge of war … and to reaffirm faith in fundamental human rights, in the dignity and worth of the individual person, in the equal rights of men and women and of nations large and small' (*Charter of the United Nations*, preamble). After the *Charter* was signed, the adoption of an international bill of rights, complete with legal authority, proceeded in three steps: a declaration, two treaties, and an implementation measure (Alston and Goodman 2013: 139).

The *Universal Declaration of Human Rights* 'marked a new chapter in a history that began with the great charters of humanity's first rights moment in the seventeenth and eighteenth centuries' (Glendon 2001: xvii), notably the *British Bill of Rights* 1689, the US *Declaration of Independence*, and the French *Declaration of the Rights of Man and the Citizen*. In 1946, the UN established the Commission on Human Rights, which held its first meeting in January 1947 to create an international bill of rights. Eleanor Roosevelt was the chairperson. Other members included the head of the Chinese delegation, Peng Chun Chang, Lebanon's Charles Malik, France's René Cassin, Canada's John Humphrey, and India's Hansa Mehta. Altogether, 16 member states were represented on the Commission. The Commission had input both from its members and other groups. Perhaps most significantly, the United Nations Educational, Scientific and Cultural Organization (UNESCO) philosophers' committee gathered input from around the world on human rights, including perspectives from Chinese, Islamic, Hindu and other traditions. A remarkable consensus on what should be considered a human right emerged when people as diverse as Mohandas Gandhi, Pierre Teilhard de Chardin, Benedetto Croce, and Aldous Huxley (Glendon 2001: 51) were among those who provided input. But, as Mary Ann Glendon observed:

> … they harbored no illusions about how deep the agreement they had discovered went. Maritain liked to tell the story of how a visitor at one meeting expressed astonishment that

> champions of violently opposed ideologies had been able to agree on a list of fundamental rights. The man was told: 'Yes, we agree about the rights but on condition no one asks us why.' (2001: 77)

The rights listed in the *Universal Declaration of Human Rights* were seen as rights that in practice no one would oppose, rather than as growing out of any particular foundational philosophy of the world. The UDHR was adopted without dissent by the General Assembly of the United Nations on December 10, 1948. Some of its articles are noteworthy, as highlighted by Figure 2.1.

The status of the UDHR was very much like that of the US *Declaration of Independence*, i.e. it was a statement of what its signers believed should be included in the notion of human rights – a statement of belief and aspiration, with no enforcement mechanism or status as international human rights law. This took the development and ratification of a treaty, in this case two treaties (Donnelly 2003: 23). The names of the two subsequently developed treaties well describe their content, the *International Covenant on Civil and Political Rights* and the *International Covenant on Economic, Social and Cultural Rights*. The division of human rights into two treaties has been most persuasively attributed to the competing ideologies in the Cold War. The US and its allies were firmly in favor of the former, but not willing to adopt the latter; similarly, the Soviet Union was in favor of the latter, but not of the former. The treaties were promulgated in 1966, adopted in 1976, and by 2012 each of them had been ratified by 150 (of approximately 200) countries (Alston and Goodman 2013: 141–2 and 282).

More specifically, the rights articulated in articles 1 to 21 can be categorized as 'civil and political rights,' such as 'the right to life, liberty and security of person' (*Universal Declaration of Human Rights*). The rights articulated in articles 22 to 27 can be categorized as 'economic, social, and cultural,' such as rights to education, health, and social security (*Universal Declaration of Human Rights*). Article 25, of course, has special interest to public health and bioethics practitioners as it articulates the right to health (*Universal Declaration of Human Rights*). It also contains a recurring theme in international human rights that motherhood and childhood merit special care. Because the government must spend money to support political rights as well, such as protecting people's right to life and physical security, developing a judicial system, and treating people equally, the traditional distinction between negative and positive rights has lost much of its appeal. Most modern commentators discuss human rights in the context of state obligations instead. Specifically, when a country ratifies a treaty, including the two Covenants, the government undertakes the obligation or duty to 'respect, protect, and fulfill' the rights articulated in the treaty.

Respect requires that the government itself not violate the rights; protection requires that the government passes laws and otherwise prohibits private parties from violating the rights, and fulfillment requires the government to undertake an affirmative obligation to actualize the rights. This latter step can involve setting up a school system, a healthcare system, and an infrastructure system for food, shelter, sanitation, and clean water. Because many governments that adopted the two Covenants do not currently have the financial resources to implement all of the economic and social rights, the requirement is that they move in the direction of implementation by 'progressively realizing' the rights to the extent of their ability (Annas 2010: 191).

It should also be noted that since the development of the UDHR, almost 100 new countries have been formed, many of which have adopted at least some of the provisions of the two treaties into their own constitutions. In these countries, the treaties are not just a matter of international human rights law, but have the full force of the highest level of domestic law as well. In countries where the treaty provisions are part of their national constitutions, including India and South Africa, courts have consistently insisted they be enforced (Annas 2005: 59–67). Human rights

Universal Declaration of Human Rights

PREAMBLE

Whereas recognition of the inherent dignity and of the equal and inalienable rights of all members of the human family is the foundation of freedom, justice and peace in the world,

Whereas disregard and contempt for human rights have resulted in barbarous acts which have outraged the conscience of mankind, and the advent of a world in which human beings shall enjoy freedom of speech and belief and freedom from fear and want has been proclaimed as the highest aspiration of the common people . . .

ARTICLE 1

All human beings are born free and equal in dignity and rights. They are endowed with reason and conscience and should act towards one another in a spirit of brotherhood.

ARTICLE 2

Everyone is entitled to all the rights and freedoms set forth in this Declaration, without distinction of any kind, such as race, color, sex, language, religion, political or other opinion, national or social origin, property, birth or other status . . .

ARTICLE 3

Everyone has the right to life, liberty and security of person.

ARTICLE 4

No one shall be held in slavery or servitude; slavery and the slave trade shall be prohibited in all their forms.

ARTICLE 5

No one shall be subjected to torture or to cruel, inhuman or degrading treatment or punishment.

ARTICLE 6

Everyone has the right to recognition everywhere as a person before the law.

ARTICLE 7

All are equal before the law and are entitled without any discrimination to equal protection of the law. All are entitled to equal protection against any discrimination in violation of this Declaration and against any incitement to such discrimination.

ARTICLE 8

Everyone has the right to an effective remedy by the competent national tribunals for acts violating the fundamental rights granted him by the constitution or by law.

ARTICLE 9

No one shall be subjected to arbitrary arrest, detention or exile . . .

ARTICLE 18

Everyone has the right to freedom of thought, conscience and religion; this right includes freedom to change his religion or belief, and freedom, either alone or in community with others and in public or private, to manifest his religion or belief in teaching, practice, worship and observance.

ARTICLE 19

Everyone has the right to freedom of opinion and expression; this right includes freedom to hold opinions without interference and to seek, receive and impart information and ideas through any media and regardless of frontiers.

Figure 2.1 Extracts from the *Universal Declaration of Human Rights*

ARTICLE 20

(1) Everyone has the right to freedom of peaceful assembly and association.

(2) No one may be compelled to belong to an association.

ARTICLE 23

(1) Everyone has the right to work, to free choice of employment, to just and favourable conditions of work and to protection against unemployment.

(2) Everyone, without any discrimination, has the right to equal pay for equal work.

(3) Everyone who works has the right to just and favourable remuneration ensuring for himself and his family an existence worthy of human dignity, and supplemented, if necessary, by other means of social protection.

(4) Everyone has the right to form and to join trade unions for the protection of his interests.

ARTICLE 25

(1) Everyone has the right to a standard of living adequate for the health and well-being of himself and of his family, including food, clothing, housing and medical care, and necessary social services, and the right to security in the event of unemployment, sickness, disability, widowhood, old age or other lack of livelihood in circumstances beyond his control.

(2) Motherhood and childhood are entitled to special care and assistance. All children, whether born in or out of wedlock, shall enjoy the same social protection.

ARTICLE 26

(1) Everyone has the right to education . . .

ARTICLE 27

(1) Everyone has the right freely to participate in the cultural life of the community, to enjoy the arts and to share in scientific advancement and its benefits.

(2) Everyone has the right to the protection of the moral and material interests resulting from any scientific, literary or artistic production of which he is the author.

Figure 2.1 Continued

were codified in Europe following the UDHR with the adoption of the *European Convention on Human Rights* 1950, and equipped with its own enforcement mechanism, the European Court of Human Rights. The United States, on the other hand, adopted only the *International Covenant on Civil and Political Rights*. Even in this context, the US generally insists it can only be enforced by the courts in a way that is consistent with its *Constitution* 1787 – which remains the highest law in the US.

2.1.4 Bioethics and human rights

Contemporary bioethics can be usefully thought of as having been born at the Doctors' Trial in Nuremberg in which Nazi physicians were called to answer for crimes of murder and torture committed under the guise of human experimentation (Annas and Grodin 1992: 3). The US judges who presided over the first of 12 subsequent trials (i.e. following the International Military Tribunal which had judges not only from the US, but also from Britain, France, and the Soviet Union as well), articulated the *Nuremberg Code*, not only the first comprehensive code of

conduct regarding human experimentation, but also the first to clearly articulate the requirement of informed consent of the research subject (Annas and Grodin 1992: 2; Perley 1992: 151).

After adopting the *Universal Declaration on the Human Genome and Human Rights* 1997 (Lenoir 1997: 31), and the *International Declaration on Human Genetic Data* 2003, UNESCO took on the project of developing an international declaration on bioethics. This project, which involved 180 nations, eventually sought to combine human rights and bioethics into a single declaration, the *Universal Declaration on Bioethics and Human Rights*, adopted in 2005. The purpose of the *Declaration* is primarily to guide states, individuals, and corporations in dealing with issues of medicine and human research. Its principles are set forth in article 3:

1. Human dignity, human rights and fundamental freedoms are to be fully respected.
2. The interests and welfare of the individual should have priority over the sole interest of science or society.

(Universal Declaration on Bioethics and Human Rights)

The declaration is especially strong on consent, equality, privacy, and non-discrimination, and it has been praised for setting an international standard that applies basic human rights principles to bioethics (Adorno 2007: 152–3). On the other hand, it has been argued that many of the principles are overly vague and generalized (e.g. 'Appropriate assessment and adequate management of risk related to medicine, life sciences and associated technologies should be promoted' (*Universal Declaration on Bioethics and Human Rights*, article 20) (Macpherson 2007: 588). The World Health Organization (WHO) also objected to UNESCO's development and promulgation of the Declaration, arguing that health and health-related regulation should be left to the WHO. Of course, there are private organizations that have also promulgated ethical rules that can be seen as human rights declarations as well, perhaps, most notably, the World Medical Association's (WMA) *Declaration of Malta on Hunger Strikers* 1991 (*Declaration of Malta*) which, as noted at the beginning of this chapter, prohibits the force-feeding of hunger strikers by physicians, even when the physicians are working for the military or the prison. It is especially noteworthy to see private medical organizations, like the WMA, explicitly adopt human rights language in their declarations of medical ethics.

Today many healthcare and public health advocates use 'the right to health' to demand decent healthcare worldwide (Ruger 2010: 1). Likewise, human rights are almost always at the forefront of arguments about the wars in Iraq, Afghanistan, and Syria. Bearing witness to the slaughter in all of these (and other) countries, it is easy to become cynical and disenchanted with human rights. David Kennedy catalogs the major critiques of human rights, noting how they limit other emancipatory possibilities, frame problems and solutions too narrowly, overgeneralize and become unduly abstract, and express a Western liberalism; human rights promises more than it can deliver, and the UN human rights bureaucracy is itself part of the problem (2004). In his words:

> The generation that built the human rights movement focused its attention on the ways in which evil people in evil societies could be identified and restrained. More acute now is how good people, well-intentioned people in good societies, can go wrong, can entrench and support the very things they have learned to denounce.
>
> *(Kennedy 2004: 35)*

Philosophers both support and contest the existence of human rights (Sen 1985; Etzioni 2010). Allan Gewirth has, for example, argued that agency or action is the common subject of all morality and practice, and human rights are found in the basic freedom and wellbeing necessary for human agency (1978: 229; 1979: 1156). He also distinguishes three types of human rights: basic rights which safeguard one's very existence; nonsubtractive rights, which are required to fulfill the capacity for purposive agency; and additive rights which provide the requisites for developing one's capabilities (Gewirth 1985). Alasdair McIntyre, on the other hand, insists human rights do not exist in the real world any more than other mythological creatures such as unicorns and witches (MacIntyre 1988: 83; Walters 2003).

In the real world, however, the philosophical and legalistic debates are mostly beside the point. As Joseph Kunz observed more than 60 years ago in regard to the UDHR, '[i]n the field of human rights … it is necessary to avoid the Scylla of a pessimistic cynicism and the Charybdis of mere wishful thinking and superficial optimism' (1949: 320). With specific application to bioethics, 'no other language than rights language seems as suitable for global health advocacy. All people have (inherent) human rights by definition, and people with rights can demand change, not just beg for it' (Annas 2010: 191).

2.2 Illustrations from the US

2.2.1 Law and medicine

Medical care in 2013 is unrecognizable from what it was in 1813, and no nineteenth-century physician would be at home in a modern hospital. A nineteenth-century lawyer, however, would be completely at home in a contemporary courtroom, as would a present-day lawyer transported back to the early nineteenth century. Although slavery was still legal and women did not yet have the right to vote, the US Supreme Court was the highest court in the land, and the US *Constitution* and its *Bill of Rights* would be familiar, as would the jury and the common law system adopted from England.

Over the past two centuries, the discipline of medical jurisprudence – the application of medical knowledge to the needs of justice – has been renamed legal medicine (including forensic science), and applying the law to medicine has expanded from medical law to health law. Legal procedures and courtrooms have changed little, but there have been almost as many changes in the application of law to medicine over the past 200 years as there have been changes in the practice of medicine. Health law's intimate relationship with medical ethics also has a strong precedent. Thomas Percival's original title for his 1803 *Medical Ethics* text, which has been described as 'the most influential treatise on medical ethics in the past two centuries' (Beauchamp and Childress 2001: 31), was *Medical Jurisprudence* (Percival 1803). More than half of Percival's text specifically addresses 'professional duties … which require a knowledge of law' (Percival 1803: xiv and 61). Medicolegal expert David Paul Brown argued more than 100 years ago that both professions needed to understand the other, saying: '[a] doctor who knows nothing of law and a lawyer who knows nothing of medicine, are deficient in essential requisites of their respective professions' (Channing 1860: 233).

A court case from England in the mid-eighteenth century illustrates that the law's concern with human experimentation by physicians did not begin at Nuremberg. The celebrated case of *Slater* v. *Baker and Stapleton* was decided in England in 1767 (95 Eng. Rep. 860 (*Slater*)). Slater had broken his leg, it had not healed well, and he had sought treatment from another physician, a surgeon named Baker, and an apothecary named Stapleton. They broke the leg again and set

it in 'a heavy steel thing that had teeth' to stretch it, with a poor result. Slater sued them, and three surgeons testified that the 'steel thing' should not have been used. The jury awarded Slater £500 (approximately £60,000 today), and the defendants appealed. The appeals court affirmed the award, saying that a radical experiment could itself be considered malpractice, at least in the absence of the patient's consent. In the Court's words:

> This was the first experiment made with this new instrument; and although the defendants in general may be as skillful in their respective professions as any two gentlemen in England, yet the Court cannot help saying that in this particular case they have acted ignorantly and unskillfully, contrary to the known rule and usage of surgeons.
>
> *(Slater* 1767, p. 863*)*

Even this is not the first legal mention of consent in the context of experimentation. Rather it follows, as noted by medical historian and ethicist Robert Baker:

> It dates to the very first law regulating health professionals in the British colonies, the Duke of York's Law of 1665. The law states in relevant part, that 'no physician … [may engage in experimental surgery or medicine] … upon or toward the body of any … without the … consent of the patient or patients if they be mentis compotes, much less contrary to such consent.
>
> (2013: 233–4)

From these doctor–patient relationship cases, the law (and bioethics) expanded their reach and, following World War II, were often seen in each other's company. Of particular note is the increasing application of health law to the field of international human rights, including the right to health, the regulation of research on human subjects, and the physician's role in war and civil conflict. Physicians and lawyers now work together in US-based organizations such as Physicians for Human Rights and Global Lawyers and Physicians. When working separately, medical associations, including the British Medical Association and the WMA, rather than legal associations, deserve much of the credit for the growth of the international 'health and human rights' arena. Both law and medicine are critical tools for improving health and wellbeing on a global level, and each profession is more effective when the two work together.

2.2.2 The human right to health

The US healthcare system is not a model for any other country. Where in the world, for example, is there any country (other than the US) where its citizens have the distinct impression that all human beings as such are entitled to any and all treatments and services necessary for the maintenance of health and life, no matter what the cost? Where in the world (other than the US) do we experience a ceaselessly proliferating list of highly expensive, marginally effective treatments for diseases? Where in the world (other than the US) do we expect our health system to provide certain drugs, no matter how experimental or expensive, to forestall death and improve health? And where in the world (other than the US) do we expect, as a matter of right, (access to) the latest developments in open heart surgery, chemotherapy, and cosmetic psychopharmacology? Because American bioethics is grounded in a uniquely dysfunctional healthcare system, it does not travel well. That is why it is extremely unlikely that any country (other than the oil-rich UAE) would model their healthcare system on ours, or that any country would model their bioethics on ours.

We need a model other than the US, one which is dominated by a hyper-individualist market model that is fueled by an almost hysterical fear of death, to define the content of the right to health. In this regard we at least seem to agree on some fundamental points regarding the right to health: rights are not self-enforcing; rights require definition (and in the case of 'progressive realization' in resource-poor nations, benchmarks to measure progression); and an unbounded right to health care (which is part of the right to health), whether or not it includes a 'laundry list,' would be fiscally unsustainable, even in the US (Moses *et al*. 2013). It is worth reviewing a few characteristics of the international human right to health.

Rights are set forth in brief and general language in the UDHR and the treaties, though not restricted to these documents. Rights are explicated by the very bodies the treaties established, within which experts and special groups can be formed to do so. In terms of the 'right to health,' *General Comment No. 14* of the UN Committee on Economic, Social and Cultural Rights (the body set up to help implement the *International Covenant on Economic, Social and Cultural Rights*) explains a state's obligation to respect, protect, and fulfill the right to health:

> 34. … States are under obligation to *respect* the right to health by, *inter alia*, refraining from denying or limiting equal access for all persons …; and abstaining from imposing discriminatory practices as State policy …
> 35. Obligations to *protect* include, *inter alia*, the duties of States to adopt legislation or to take other measures to ensure equal access to health care and health-related services provided by third parties; …
> 36. The obligation to *fulfill* requires States parties, *inter alia*, to give sufficient recognition to the right to health in the national political and legal systems, preferably by way of legislative implementation, and to adopt a national health policy with a detailed plan for realizing the right to health. States must ensure provision of health care, including immunization programs against the major infectious diseases and ensure equal access for all to the underlying determinants of health, such as nutritiously safe food and potable drinking water, basic sanitation and adequate housing and living conditions … provide for sexual and reproductive health services.
>
> (UN Committee on Economic, Social and Cultural Rights 2000, paras 34–36)

American bioethicists, like American healthcare, have generally ignored the right to health. In the past three decades, for example, American bioethicists have learned virtually nothing about the right to health, and this is a major limitation of the field. A related problem is that in a US-centric bioethics, the right, when it is discussed, is most often referred to simply as a 'right to healthcare,' whereas in the human rights world, it is the 'right to health.' On the other hand, there are major issues involving resource allocation and identifying who gets to make allocation decisions (Fink 2013). There is no 'limitless right to health' or healthcare any more than there is a limitless right to anything, including liberty, free speech, religious freedom, or free press. As the South African nevirapine case illustrates, when a country adopts the right to health as a constitutional right, its courts have the ability to define and enforce it (Annas 2005: 60–1). Nonetheless, there are also major weaknesses in relying on courts to enforce health rights:

> [T]he focus in a courtroom struggle is likely to be narrow, involving specific medical interventions such as chronic kidney dialysis or nevirapine. Should nevirapine not turn out to be the drug of choice … the [court] opinion will not help HIV-positive patients to obtain care.

> The HIV/AIDS epidemic demands a comprehensive treatment and prevention strategy, including education, adequate nutrition, clean water, and gender equality.
>
> *(Annas* 2005: 67*)*

2.1.3 American bioethics and freedom from torture and inhuman treatment

That the US has consistently and openly violated the fundamental human right to be free from torture is remarkable. Freedom from torture is one of the most basic human rights of all. Identified by the International Military Tribunal in 1946 as a war crime and a crime against humanity, it was given prominence as a human right in the Nuremberg Doctors' Trial, the UDHR, the ICCPR, and the *Geneva Conventions*, and it carries its own federal criminal statute, as well as dedicated treaty, the *Convention Against Torture and Other Cruel, Inhuman or Degrading Treatment or Punishment* 1984 (UN General Assembly) (*Convention Against Torture*).

Since 9/11, US physicians have been implicated over and over again in torture, abusive interrogations, force-feeding prison hunger strikers, and falsifying death certificates of prisoners (Task Force 2013). Nonetheless, the premier US bioethics organization, the President's Council on Bioethics, has only once mentioned torture by physicians in the context of condemning the force-feeding of a political prisoner by physicians in a Soviet prison camp more than 30 years ago (Bukovsky 2003: 218–19). This failure is shameful, but helps explain why ending force-feeding by physicians (a violation of the *Geneva Conventions*' common article 3 and the *Declaration of Malta*) has so far been impossible (Annas *et al.* 2013).

2.3 Current controversies suggesting convergence

An ongoing dispute involving the United Nations (and the meaning of both accountability for harm caused in delivering disaster relief and the right to health) helps us appreciate the interrelationships among health law, bioethics, and human rights, and how, used together, they increase the chances of benefiting both individuals and populations.

Shortly after the devastating 2010 earthquake in Haiti, the region experienced a deadly cholera epidemic that afflicted more than 600,000 people, killing more than 8,000 of them. It is now well-documented that this epidemic was caused by infected United Nations peacekeeping forces who were deployed from Nepal to join other UN troops in Haiti to aid in the relief effort. These troops were based in Meye, near the capital of Port-au-Prince, on a tributary of Haiti's largest river, the Artibonite River, a major source of water for drinking and cooking. The troops from Nepal, an area in which cholera is endemic, brought the disease with them, and it spread quickly from their camp via the river. The United Nations denies any responsibility for the tragedy to this day, claiming, among other things, immunity based on its *Charter*. A 2013 report from the Yale Law School challenges the position of the UN, and uses health law, medical ethics, and human rights language to assert that the UN must take responsibility for the cholera epidemic and for preventing future epidemics of cholera in Haiti (Transnational Development Clinic *et al.* 2013).

First, the Yale researchers argue that the UN is in violation of the law. Specific language in the *UN Charter* and the *Convention on the Privileges and Immunities of the United Nations* 1946 limits immunity to those instances 'necessary for the exercise of its functions and the fulfillment of its purposes' (*UN Charter*, article 104). Moreover, even in these areas, article 29 of the *Convention on the Privileges and Immunities* provides that the UN 'shall make provisions for appropriate modes of settlement of disputes.' This has been interpreted as requiring the UN to establish a

'claims commission' to adjudicate claims for damages caused by UN personnel, including peacekeepers (Transnational Development Clinic *et al.* 2013: 5). The UN has yet to establish such a claims commission to hear the claims of the Haitian cholera victims.

Second, drawing from principles in the 'Code of Conduct for the International Red Cross and Red Crescent Movement and Non-Governmental Organizations (NGOs) in Disaster Relief' (International Federation of Red Cross and Red Crescent Societies and International Committee of the Red Cross (ICRC) 1994), the Yale Group notes the ICRC's incorporation of a fundamental principle of medical ethics into their Code: 'commitment to the "do no harm principle"' (Transnational Development Clinic *et al.* 2013: 4). In the Yale Group's view, this bioethics principle does not just apply to physicians, but to all humanitarian relief operations and personnel. In the report's words, the UN's 'introduction of cholera into Haiti violated the do no harm principle of humanitarian intervention. The do no harm principle includes an obligation to not expose individuals to physical hazards, violence, or other rights abuse, including disease' (Transnational Development Clinic *et al.* 2013: 47). This principle was violated 'by introducing an epidemic disease into a major waterway used by a vulnerable population, leading to severe illness and death for many Haitians' (Transnational Development Clinic *et al.* 2013: 47).

Third, and perhaps the strongest argument, the Yale report points out the UN failed to honor its own human rights obligations set forth in foundational UN treaties, including the ICCPR and the ICESCR. The report identifies the UN's failure to respect the right to water, which includes access to safe drinking water and sanitation. Safe drinking water is defined as water 'free from micro-organisms … that constitute a threat to a person's health' (Transnational Development Clinic *et al.* 2013: 38). Likewise, the UN fell short of respecting the right to health 'by failing to prevent the introduction of cholera into Haiti' (Transnational Development Clinic *et al.* 2013: 39). This created a public health crisis in Haiti, which directly interfered with the country's ability to 'comply with its own obligations under the human right to health' (Transnational Development Clinic *et al.* 2013: 38, 39, 51). Combining principles from law, ethics, and human rights makes the recommendations of the Yale Group much more compelling than had their report relied on any one of these sources alone. Nonetheless, debate continues and it is uncertain whether the UN will accept its moral and legal responsibilities for this incident.

Guantánamo Bay Prison provides a vastly different context for the convergence of law, ethics, and human rights. In 2013, Sondra Crosby and I commented on the ongoing hunger strike by at least 100 of the 166 remaining prisoners and the strategy of using military physicians to 'break' the hunger strike by force-feeding (Annas *et al.* 2013: 101–3).

As we noted, force-feeding competent hunger strikers is a violation of basic principles of medical ethics and is not a matter of serious dispute. The American Medical Association (AMA) has appropriately taken a leadership role on behalf of the profession, writing to the Secretary of Defense that 'forced feeding of [competent] detainees violates core ethical values of the medical profession' (Lazarus 2013). Similarly the US Constitution Project's bipartisan Task Force on Detainee Treatment concluded in April 2013 that 'forced feeding of detainees [at Guantánamo] is a form of abuse that must end,' and urged the US to 'adopt standards of care, policies, and procedures regarding detainees engaged in hunger strikes that are in keeping with established medical, professional and ethical care standards' (Constitution Project's Task Force on Detainee Treatment 2013: 36). Another report issued in 2013 also combined law, bioethics, and human rights to call for an end to physician participation in the interrogation and torture of prisoners at Guantánamo, terming such action 'a violation of medical ethics and international [human rights] conventions' (Task Force 2013: 1).

The medical ethics standard for physician involvement in hunger strikes has probably been best articulated by the World Medical Association in its *Declaration of Malta on Hunger Strikers*.

The *Declaration of Malta* is meant to have the same ethical effect as the *Declaration of Helsinki* 1964. Physicians can no more ethically force-feed competent hunger strikers than conduct research on competent human subjects without informed consent (Annas *et al.* 2013: 102). The *Declaration of Malta*'s bottom line couldn't be clearer: [f]orcible feeding [of competent hunger strikers] is never ethically acceptable' (WMA 1991).

Hunger striking is a political activity to protest against terms of detention or prison conditions, not a medical condition. The fact that hunger strikers develop medical problems that need attention and may worsen does not make hunger striking itself a medical problem. Nonetheless, at Guantánamo, prison officials consistently seek to medicalize hunger strikers by asserting that they are 'suicidal' and must be force-fed to prevent self-harm and 'save lives' (Annas *et al.* 2013: 102). The Department of Defense's (DOD) 2006 Medical 'Instruction' states specifically that '[i]n the case of a hunger strike, attempted suicide, or other attempted serious self-harm, medical treatment or intervention may be directed without the consent of the detainee to prevent death or serious harm' (DOD 2006: 5). This policy mistakenly conflates hunger striking with suicide. Hunger strikers are not attempting to commit suicide. Rather, they are willing to risk, or even accept, death if their demands are not met. Their goal is not to die, but to have perceived injustices addressed. The motivation is similar to that of a free living person who finds kidney dialysis intolerable and discontinues it knowing he will die. This refusal of treatment with the awareness that death will soon follow is not suicide according to both the US Supreme Court and international medical ethics (Annas *et al.* 2013: 102).

Law and medical ethics here are consistent with basic human rights, and examining all three simultaneously is much more likely to produce a reasonable and responsible policy than looking at any one of them in isolation. In this instance, using all three sources of guidance helps us to recognize that force feeding a competent person is not the practice of medicine, it is aggravated assault. Military physicians are no more entitled to betray medical ethics than military lawyers are entitled to betray the *US Constitution* or military chaplains are entitled to betray their religion.

2.4 Conclusion

Ongoing controversies at Guantánamo, the deadly continuing war in Syria with the slaughter and starvation of civilians, as well as wars across the globe caution us not to expect too much even from a synthesis and symbiotic activism fueled by a belief in law, ethics, and human rights working together. Nor is despair a credible strategy for human betterment. We should leverage bioethics, law, and human rights in creative ways in which the whole can be made greater than the sum of its parts. This will require active citizens putting pressure on their governments to honor human rights and the rule of law. But it will also require legal and medical professionals to take their professions seriously and to actively support their colleagues when they are pressured to abandon medical ethics in favor of short-term political or military gains. Transnational professions can benefit both themselves and humanity by fostering human rights. They are much more likely to do so if human rights are viewed as supportive of their own professional ethics, and their actions in fulfillment of their ethics are in turn supported by the law.

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3
Informed consent

Trudo Lemmens

3.1 Legal and ethical theory

3.1.1 Introduction

Obtaining 'informed consent' is now firmly established as a preeminent legal and ethical requirement in medical practice and research. The specialized health law, bioethics, and medical literature abound with discussions of its precise meaning and content, explorations of the various challenges to informed consent and, increasingly, empirical studies about informed consent practices. This contemporary literature does not question the value of informed consent, but rather generally focuses on how informed consent can best be obtained and promoted or, in specific circumstances, how it may need to be delayed or replaced by surrogate procedures that respect its underlying value. It is therefore hard to imagine that informed consent has become such a moral and legal mainstay only in recent decades.

This chapter first situates the development of the concept in its historical context. This is followed by a discussion of the normative basis of informed consent in bioethics and law. After an identification of some of the key features of informed consent in law and bioethics, the chapter then proceeds with an overview of the legal requirements to remedy violations of informed consent, focusing in particular on Canadian common law. A brief discussion of increasingly important statutory and guideline-based governance of informed consent completes this section. Finally, some brief comments are made about contemporary issues, focusing on two areas of research where commentators are increasingly calling for more flexible informed consent standards to facilitate public interest oriented research.

3.1.2 Historical development of the informed consent doctrine

Scholars disagree about the extent to which seeking consent based on some level of information-sharing was already recognized in professional practice prior to the twentieth century. The late Jay Katz always maintained that there was little trace of meaningful consent-seeking prior to the second half of the twentieth century (Katz 1984). Ruth R. Faden and Tom L. Beauchamp, who critically analyzed Katz's claims, historical medical records, and other historical research

on consent, suggest that there was some level of consent-seeking in medicine, but agree with Katz that the practice was different from what we now understand as 'informed consent' (1986: 56–60). They point out that consent-seeking was driven by a commitment to 'first, do no harm,' a key principle of medical ethics, rather than by the more modern and legal conceptualization of informed consent as an expression of self-determination.

The dominant attitude in the medical profession, even among those sensitive to truth-telling, was that patients ought not to be needlessly upset with worrisome news about their medical condition. Early twentieth-century versions of the Hippocratic Oath even explicitly prescribed hiding potentially troubling information from patients. The influential nineteenth-century English physician Thomas Percival stressed in his influential book *Medical Ethics* the importance of the 'delicate sense of veracity, which forms a characteristic excellence of the virtuous man' (1803: 166), but suggested at the same time that truth-telling yields to the important obligation to shield information that could be harmful to patients.

Jay Katz discussed how early ethical codes enacted by the American Medical Association directly took over – often verbatim – Percival's ethical stance on informed consent and that these views dominated English and American medical ethics until the mid-twentieth century (2004: 1256). Those who supported some level of information-sharing and consent-seeking did so with the idea that providing information offered therapeutic benefits or that deception had a pernicious effect on medical institutions (Beauchamp and Faden 1986: 1233), and not out of respect for autonomous decision-making.

Providing information and obtaining some level of agreement prior to intervening appeared more common in some areas of medical practice than in others. As Beauchamp and Faden suggest, consent in the context of surgery, for example, was understandably a somewhat 'pragmatic response' since '[i]t is at best physically difficult and interpersonally awkward to perform surgery on a patient without obtaining the patient's permission' (Beauchamp and Faden 1986: 1233).

In medical research, the 1947 *Nuremberg Code* is generally seen as the first strong affirmation of the need to obtain consent from research participants. Yet, the seeds of the informed consent requirement for research participation were also already planted at the end of the nineteenth century in Europe when critical accounts were published about outrageous research practices on the most vulnerable in society, such as the poor, (juvenile) prostitutes, and children (Katz *et al*. 1972: 284–92). Critical reports of the deliberate infection of patients with syphilis and gonorrhea in Russia and Germany not only illustrate that research often took place without or with only questionable consent, but also that some people within and outside the medical profession already felt morally troubled about this research practice. In the wake of public exposure of some of this research, we saw the development of the first guidelines and regulations on medical research. A Prussian regulation of 1900, enacted in the wake of the prosecution of a German physician for medical experiments without consent and probably the first regulation of its kind, explicitly required consent prior to experimentation, which had to be based on 'a proper explanation of the possible negative consequences of the intervention' (Vollman and Winnau 1996).

3.1.2.1 Development of the doctrine of informed consent in the twentieth century

The start of the legal doctrine of informed consent in Anglo-American law is associated with the US case of *Schloendorff* v. *New York Hospital* [1914] 211 NY 125, in which Justice Cardozo famously stated that '[e]very human being of adult years and sound mind has a right to determine

what shall be done to his own body; and a surgeon who performs an operation without his patient's consent commits an assault, for which he is liable in damages' (p. 126). In *Schloendorff*, the court found that the removal of a tumor from a woman who had only consented to an examination constituted battery. Although there are earlier cases that acknowledged a duty to obtain consent from patients (Beauchamp and Faden 1986: 116–23), its association with self-determination and the characterization of surgery without consent as battery set the stage for the twentieth-century legal developments. Cardozo's formulation became one of the key quotes in later informed consent cases around the world.

The term 'informed consent' itself was introduced only much later, in the 1957 case of *Salgo* v. *Leland Stanford Jr University Board of Trustees et al.* [1957] 154 Cal App2d 560, where the court emphasized that consent had to be based on sufficient information to make it 'intelligent.' But, as Jay Katz points out, in the very phrase in which the court introduced for the first time the term 'informed consent,' it also tried to reconcile this duty to some degree with the traditional practice of medicine by emphasizing that in providing risk information to patients, physicians had to exercise a certain degree of 'discretion' (Katz 2004: 1258). This reflected the more traditional stance that information-sharing could be restricted to avoid harm to the patient. The ambiguity about who determines what level of information patients should receive in order to make meaningful decisions would become in the subsequent years an important part of the legal debate. With its acceptance of some discretionary departure from information-sharing, the court also indicated that failure to provide informed consent was not necessarily an assault or battery. Later US cases, notably *Canterbury* v. *Spence* [1972] 464 F.2d 772, confirmed explicitly that most cases of failure to provide adequate informed consent could give rise to liability in negligence, while battery should be reserved for the most extreme departures from the informed consent standard. Other jurisdictions also applied this two-pronged approach to failures of informed consent.

Case law may have influenced professional thinking about informed consent, but a variety of interacting cultural and social changes were also taking place at the same time. In particular, legal decisions were influenced by a growing emphasis on individual and consumer rights and professional medical discourse was affected by awareness of legal and social developments and concern for litigation. Faden and Beauchamp suggest that 'case law has been extremely influential,' not only in coining the term 'informed consent,' but also by 'set[ting] others on the road to conceiving of the social institution of consent rules as a mechanism for the protection of autonomous decisionmaking' (Beauchamp and Faden 1986: 142), even if medical professionals took a longer time to embrace informed consent as a standard practice.

3.1.2.2 Development of informed consent standards in research post-World War II

In the research context, the post-World War II (WWII) period is also characterized by a steady development towards the imposition of detailed informed consent requirements, albeit not so much through the courts, but through guidelines and regulations. The first influential formulation of the need for informed consent in the international context was, as mentioned before, the *Nuremberg Code*. The *Nuremberg Code* consists of ten key ethical principles for research on humans, set out in the 1947 judgment of the international criminal court in the Nuremberg Doctor Trials (*Trials of War Criminals before the Nuremberg Military Tribunals under Control Council Law No. 10* 1949). As is well known, German doctors were prosecuted in this trial for some of the most horrific experiments on concentration camp prisoners. Experiments ranged from the recreation of battlefield conditions to find survival techniques and treatment for German

soldiers, to the testing of poison and other mass murder tools, to biological warfare, and to studies of twins aimed at confirming Nazi racial ideology. The most common element of these experiments was the blatant disregard for the wellbeing of human beings, but obviously also the absence of any form of consent. Consent thus became emphasized as one of the ten key ethical requirements for medical experimentation.

Some of the people involved in the prosecution became instrumental in developing research ethics standards in the US, in part as a result of their role as expert witnesses. When then Vice President of the University of Illinois, Andrew Ivy, was asked to testify about the disregard of the Nazi doctors for widely accepted ethical principles in research, he was faced with the fact that there were no explicit ethical standards for research in the US. Some research practices in allied countries, for example malaria research in Stateville Prison in Illinois (Advisory Committee on Human Radiation Experiments 1995: 272) and British research funded by the military on infants suffering from spina bifida (Schmidt 2004: 76–7), while not as horrific in nature and not based on a troubling racial ideology as some of the Nazi experiments, shared arguably some characteristics with the Nazi experiments. Recent revelations of US and Pan American Health Organization sponsored syphilis research in Guatemala now confirm even more explicitly how seriously problematic research continued to take place without, or with questionable, informed consent around the same time outside of Germany (Reverby 2012). Prior to testifying in Nuremberg, Ivy drafted a set of rules, including explicit informed consent requirements, which were quickly adopted by the American Medical Association, and sections of which were later verbatim integrated in the Nuremberg decision. When questioned by defense lawyers about the nature of these rules, Ivy alleged that they were a codification of common research practices (Advisory Committee on Human Radiation Experiments 1995).

The Nuremberg trial itself did not appear to have a huge impact outside of Germany. Katz suggests that the *Nuremberg Code* was seen as a code for 'barbarians' and therefore not really relevant outside of Germany (Katz 1992). Yet it did lead to appropriate reflection among leading figures in the medical profession. After all, Germany pre-WWII had one of the most sophisticated healthcare and medical research sectors. And, somewhat cynically, it had also been one of the few countries, if not the only country, that had introduced regulations for medical research. The 1932 'Richtlinien' (guidelines) for non-therapeutic research, which incongruously remained in place during the war, contained more detailed standards than those of the *Nuremberg Code* and included strong requirements for consent (Lederer 2007).

Following Nuremberg, pressure mounted worldwide to develop a more comprehensive set of rules for medical experimentation. The World Medical Association (WMA), a medical professional organization set up in the wake of WWII, started deliberating on ethical standards for medical research in 1953 (Lederer 2007: 150–60) and eleven years later adopted the *Declaration of Helsinki* (DOH) 1964. The DOH can be seen as an attempt by the medical community to keep control over research standards within the realm of professional self-regulation (Beauchamp and Faden 1986). But industry interests also influenced its development and approval process. Susan Lederer documents in detail how in the years prior to its adoption, the WMA became financially dependent on the American pharmaceutical industry (Lederer 2007: 157–70). The DOH was in part aimed at curtailing more drastic and detailed international legal rules about research. While Nuremberg's key requirement for informed consent found its way into the 1966 *International Covenant on Civil and Political Rights* (ICCPR), which reaffirms the need for informed consent as a human rights issue, no further firm international legal rules for research were developed.

George Annas has argued that the proposed changes to the US Food and Drug Administration (FDA) regulations, which introduced new clinical trials-based standards for drug regulatory approval, made the adoption of the DOH even more important (Annas 1991). The rules of

the DOH were more specific than the *Nuremberg Code*, but they clearly also introduced greater flexibility with respect to informed consent standards. Whereas Nuremberg (and later also the ICCPR) formulates 'prior informed consent' as a necessary condition for any form of experimentation, thus prohibiting research on incompetent people, the DOH permitted such research, albeit under specific conditions. Changes to the FDA rules and regulations resulted in a substantial increase in the need for clinical trials, even resulting over time in the development of an entire new clinical trials industry, and stimulated more widespread change in the procedures for informed consent in clinical research, including regulatory standards for informed consent.

Separate from this development in the context of clinical drug trials, exposure in the academic literature of unethical research practices also created pressure for reform within academic research more generally. In 1966, Henry Beecher published a seminal article in the *New England Journal of Medicine* in which he discussed in detail 22 published studies which, in his view, were ethically dubious, most of them also failing to identify clearly that informed consent was obtained from research subjects (Beecher 1966). Among the studies discussed were two that remain cited as paradigm cases of violations of informed consent in research: the Willowbrook State school study and the Jewish Chronic Disease Hospital study. In the Willowbrook study, parents were asked to consent to the inclusion of their children in an experimental research unit, but with incomplete information about the nature of the study (which involved testing deliberate infection with hepatitis as a possible prophylactic) and in a context of pressure, since it provided at one point preferential access to the overcrowded school. The Jewish Chronic Disease hospital study, for which researchers were subsequently sanctioned, involved the injection of live cancer cells in unconsenting terminally ill patients.

While these and other publications, including the popular press, evoked debate, it was the public exposure of the Tuskegee study in the *New York Times* in 1972 that had the biggest impact and resulted in firmer official initiatives which lie at the origin of the research ethics review systems that have since mushroomed all over the world (Beauchamp and Faden 1986: 157–67). The Tuskegee study originally started in the 1930s as an observational study comparing health and mortality rates of 400 African-American men infected with syphilis with those of a control group of 200 uninfected men. None of the research subjects were adequately informed that they were involved in research and investigators even presented invasive research procedures as treatments. When the study started, penicillin had not yet been invented, standard treatment for syphilis was both toxic and not very effective, and the disease was not well understood. Yet, the 'observational study' continued until its public exposure in 1972 and several papers in the medical literature reported on aspects of the study – long after effective treatment had become available.

In response to public criticism, the Department of Health and Human Services set up an *ad hoc* panel to review the study. This panel emphasized the need for stronger research guidance, including in the area of informed consent. It further recommended the establishment of a national board to look into the development of more appropriate research ethics procedures. Following this recommendation, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research was set up. In 1978, the Commission issued a seminal report, widely known as the Belmont Report, in which it formulated a set of key ethical principles for research involving humans, specifically respect for persons, beneficence, and justice (National Commission for the Protection of Human Subjects 1979). The report connected respect for persons explicitly with a need for the development of informed consent guidelines. This reflected a strong emphasis on autonomy and human dignity as the basis of the need for informed consent. In the years following the Belmont Report, the Department of Health and Human Services issued more specific regulations, clarifying in much more detail than ever

before various components of informed consent, exceptions to the strict rules, and also different procedural requirements, such as the exchange of a copy of the informed consent form. It moved the obtaining of informed consent in research into a new era, at least with respect to what officially became required in the context of research.

The move towards stricter research ethics review of informed consent forms and more detailed rules does not mean that no further serious violations occurred in the decades following these developments. In fact, several reports have emerged of serious violations of informed consent standards following the adoption of informed consent requirements. New Zealand, for example, was confronted with a Tuskegee-like research scandal involving 'observational studies' of women suffering from cervical cancer, which led to a public inquiry (Committee of Inquiry 1988). In the US, President Clinton set up in 1994 an Advisory Committee to investigate postwar research involving radiation that took place in the context of the Cold War, and which revealed numerous instances of research with no or questionable informed consent from research subjects (Advisory Committee on Human Radiation Experiments 1995). More recently, Canadian historian Ian Mosby unearthed nutritional research undertaken in the post-WWII period on aboriginal communities and aboriginal children residing in residential schools, which raises troubling questions about failures of, or serious problems with, informed consent and exposure of research subjects to harm (Mosby 2013).

In the wake of the US regulatory initiatives mentioned earlier, developments followed internationally. Informed consent became a key requirement in medical research, particularly also because of the internationalization of clinical research. International regulatory initiatives in the years following the adoption of the DOH also contributed to this. The regulatory agencies of the USA, Europe and Japan established, for example, the International Conference on Harmonization (ICH), aimed at harmonizing drug regulatory requirements of the industrialized countries. One of its key initiatives has been the development of the ICH Good Clinical Practice Guidelines (ICH GCP) in the 1990s. These guidelines reflect the key requirements of the US FDA rules and regulations, and include detailed informed consent requirements. The ICH GCP has been very influential around the world. As the DOH, they have often been integrated as soft-law requirements in the drug regulatory processes of various countries (Hirtle *et al.* 2000).

3.1.2.3 Normative basis of informed consent

The historical overview of the development of informed consent already hinted at different foundations of the concept. As mentioned, the first calls for consent were based on the idea that it was the best way of ensuring good healthcare outcomes. Moreover, patient benefit is still put forward as an important rationale for informed consent. Stephen Weir emphasizes how informed consent benefits the patient in several ways: it promotes better patient compliance and participation with current treatment; it may help patients to be more realistic about their prognosis and to plan their lives accordingly; and it can strengthen doctor–patient relations, which may be of benefit in future situations (2004: 72–6). Onora O'Neill also emphasizes the importance of safeguarding trust in the doctor and in healthcare institutions as an important element of informed consent (O'Neil 2002). O'Neil's identification of 'trust' as a foundation of informed consent moves informed consent beyond an issue of 'beneficence.' Trust in this context refers to the unique nature of the doctor–patient relation and implies the existence of unique moral duties that arise out of that relation and that help promote meaningful autonomy.

Framing informed consent merely as an issue of beneficence leaves much uncertainty about how the benefit of being informed will be weighed against other benefits or harms. As mentioned, those who first acknowledged that physicians should obtain consent recognized a wide

range of exceptions to avoid troubling the patient with potentially harmful information. This notion that too much information can cause harm is what some researchers also invoked as an excuse in some of the historical research studies discussed earlier. In the first court decisions that embraced the informed consent doctrine, a therapeutic exception was still quite prominent. In the 1972 US case of *Canterbury* v. *Spence*, for example, the court confirmed the importance of sharing relevant risk information with patients for the purpose of self-determination, but also stressed that it was up to the physician to determine whether some level of non-disclosure was therapeutically required. English courts, while recognizing the importance of information-sharing, left it, until very recently, entirely up to physicians to decide how this must be done and to what extent, according to the standards of the medical profession (*Sidaway* v. *Bethlem Royal Hospital Governors* [1985] AC 871). In fact, in *Sidaway*, the House of Lords even explicitly rejected the 'informed consent' doctrine espoused by *Canterbury* v. *Spence* as not in line with English law, holding instead that the degree of disclosure required to assist a patient in deciding whether or not to undergo a particular medical procedure was primarily a matter of clinical judgment. However, the idea that decisions about the sharing of information should entirely be left to a physician and based on a weighing of the benefits and harms of information-sharing, which is now rejected in most jurisdictions, is now also increasingly questioned in England.

Benefit fails to provide a solid basis for informed consent in, for example, non-therapeutic research, when the research really aims at generating generalizable knowledge. The patient has, in that case, no therapeutic benefit from being properly informed about the process, and yet we value informed consent in that situation. One could argue that the failure to provide information risks creating psychological harm to research subjects, or could reduce their and other people's interest in participating in future research projects. But, in theory, this type of harm could be avoided by perfect secrecy. Arguing that research subjects are harmed when not informed about research procedures thus requires some consideration of the impact of disclosure on the integrity or dignity of the person, hence some autonomy-related argument.

Autonomy is most frequently identified as the core value underlying informed consent (Grubb 1998: 110; Beauchamp and Faden 1986; Mclean 2010: 86–7). Informed consent is seen as a condition for proper self-governance. This idea of informed consent as the basis for self-governance is reflected in different ways in the context of medicine. At a most basic level, as in Cardozo's famous statement, it means that patients have a right to refuse any invasion of their physical integrity. Informed consent constitutes in that context a waiver, which allows health care providers to perform actions under conditions of explicit agreement that would otherwise be considered unacceptable. Informed consent in this sense reflects John Stuart Mill's view of a person's sovereignty over his or her own body and mind (2003).

A different, Kantian autonomy-based notion of consent is that it is an important tool to rational self-governance: patients are expected to be properly informed to enable them to opt for morally principled lives (O'Neill 2002: 73–95). Informed consent is, in this view, connected to the value of respect for persons and their dignity (National Commission for the Protection of Human Subjects 1979; Beauchamp and Faden 1986).

Whether informed consent is connected to autonomy or to some notion of beneficence has implications for how information has to be provided and what level of information has to be shared. Beneficence is hardly the only value underlying informed consent, since patients would only need as much information as required to make treatment more effective or the doctor–patient relation more fruitful. Informed consent grounded in autonomy requires more: it requires that patients receive all information they deem relevant to enable a meaningful autonomous choice. Yet, as will be discussed in the section on informed consent law, the practical implementation of that idea is not straightforward. In the healthcare context, we often deal with

highly technical and complex information that has to be translated by healthcare professionals so that it can be meaningfully used by patients. Legal systems have embraced different approaches with respect to who should decide what level and type of information must be disclosed to patients.

A detailed discussion of the nature of autonomy exceeds the contours of this chapter, but it is worth pointing out here that there is a rich literature questioning the atomistic notion of autonomy that underlies the dominantly liberal legal and bioethics literature around informed consent. Some authors argue for a situated contextual view of autonomy that calls for a more sophisticated analysis of whether particular decisions are contributing to a self-development that is not undermined by personal and contextual vulnerability and duress. They emphasize also that patients are inevitably connected to others and construct and reaffirm their autonomy through relationships with those around them (McLeod and Sherwin 2000). Those who defend these more complex views of autonomy will tend to pay greater attention to the possible impact of contextual factors on individual decision-making. While these views are widely discussed in the literature, and find to some degree their way into ethics codes and guidelines, for example in concepts such as 'undue inducement' and 'vulnerability,' courts tend to embrace a practical model of autonomy based on a presumption of autonomy when key conditions are met.

It is worth also noting that the overemphasis on autonomy and informed consent is often identified as a Western phenomenon. Many cultures place emphasis on the need to involve families and communities in healthcare decision-making. Yet promoting individual choice through informed consent clearly seems to have strong appeal, even in, for example, European countries which until recently also embraced more familial and communal involvement. Whether it is seen as a form of cultural imperialism or not, informed consent has clearly gained an important status around the world. The globalization of healthcare practices, and in particular the growing number of international clinical trials and, related to that, the influence of clearly Western-dominated international research ethics standards such as the *Declaration of Helsinki*, have undoubtedly contributed to its growing status.

3.2 Current understanding and legal remedies

3.2.1 Current content of informed consent: definition and defining features

It is difficult to provide an all-encompassing legal definition of informed consent as it is understood today. One way is to define it is as an authorization that healthcare providers have to obtain from patients or research subjects, prior to healthcare interventions or enrollment in research procedures, and based on sufficient information about the nature of the procedures, possible alternatives, and the risks and potential benefits of the various options. Yet the concept of informed consent is also widely applied in the context of health information where consent does not lead to any concrete intervention or physical participation in research. In that context, it refers to the agreement to allow confidential information to be used for specific purposes. Informed consent for the use of sensitive health information for research purposes involving the mutual signing by the research subject and researcher of 'informed consent forms' can be seen as both an agreement to allow the use of information as well as a pledge by the researcher to keep the information confidential (Lemmens *et al.* 2013).

Informed consent is more often described by emphasizing its core components: disclosure of information; comprehension; voluntariness; competency; and an agreement with the proposed procedure or intervention. Case law and various statutes dealing with healthcare consent have

identified the key elements to be disclosed. Healthcare providers have to provide information about the nature of the procedure, possible alternative options, the risks and benefits of the procedure and of alternative options, and the consequences of not undergoing a procedure (*Health Care Consent Act* 1996).

The need for comprehension seems obvious. If the goal of information-sharing is to enable people to make autonomous decisions, they have to grasp what they are being told and understand the consent forms they sign. In reality, though, the comprehension component is not always easy to fulfill. Technical information about the procedures involved and the nature of the risks can be hard to translate into accessible language. This is particularly challenging in the context of research, where complex procedures such as randomization, placebo controls, and stopping rules have to be explained, and where there is also inherently more uncertainty about the comparative risks and potential benefits. Funding and regulatory agencies often provide detailed guidelines about how to make information accessible. These guidelines tend to focus on consent forms, emphasizing that they need to be adjusted to the target population, avoid legalistic and highly technical language, and use language of 'a grade 6 to 8 reading level' (Health Canada 2010). The informed consent forms can thus contribute to meaningful comprehension. Consent forms also serve a legal purpose (i.e. they provide some level of evidence about the informed consent process). The formalization of consent in the signing of consent forms approved by hospital legal departments or by research ethics committees can, however, also obfuscate meaningful understanding and is often given disproportionate weight. Real informed consent requires more than the signing of a consent form. Healthcare providers and researchers have to ensure through direct communication that the information is understood by patients or research subjects. In this context, Jay Katz's view of informed consent as part of a process of 'shared decision-making' should be kept in mind (Katz 1984). Physicians and researchers have to engage in dialogue to address all relevant informational needs.

Voluntariness refers to the need to ensure that consent is obtained without influences that undermine autonomous choice. Clearly, not all influences do so. Influences can be explicit or implicit, and external or internal. Coercion, undue influence, and fraud or misrepresentation are factors which most commonly affect voluntariness. The term 'coercion' tends to be too easily used for all situations where people feel some form of pressure to consent. According to the Belmont Report (National Commission for the Protection of Human Subjects 1979), '[c]oercion occurs when an overt threat of harm is intentionally presented by one person to another in order to obtain compliance.' There is voluminous literature on coercion in healthcare, particularly in the context of research ethics, where Alan Wertheimer's analysis of coercion has been particularly influential (Hawkins and Emanuel 2005). Wertheimer suggests that coercion only exists when the refusal to comply with the threat would make a person worse off, and that is not present when resisting the threat would leave the person in the same position (Wertheimer 1987). For example, a physician would coerce a patient if he or she indicates that refusing to participate in research would result in withdrawal of all forms of medical care. However, in my view, 'coercion' could also be used to characterize an offer that is intentionally made to a person who is extremely vulnerable due to distress, need, or poverty, and who would, under the most basically fair conditions, never accept such an offer. In those circumstances of particular vulnerability, the recipients of the offer may feel that that they have no other option but to accept.

Undue influence is seen as impacting more subtly on voluntariness than coercion does. The concept has been particularly used in research ethics. Clearly, not all forms of influence are undue, since our decisions are inevitably shaped by various influences. Undue influence, according to the US Office for Human Research Protections, 'occurs through an offer of an excessive or inappropriate reward … in order to ensure compliance' (Department of Health and Human

Services 2013). But when is a reward excessive or inappropriate? The regulations provide no clear answer to that question. It has been suggested that influence is undue when it makes people act 'against their better judgment' – for example when payments are so structured that they push people to continue their participation in a clinical trial when they experience side effects and would normally want to withdraw, or when it leads to distortions of the risks and benefits of participation in research (Halpern *et al.* 2004). Rewards may also be seen as 'undue' when they risk undermining the core moral value attached to an activity. Large payments to research subjects can be seen as undermining what is often characterized as the altruistic nature of research participation, or research participation as a 'humanitarian enterprise' (Lemmens and Elliott 2001: 52), particularly in the context of research involving patients. Undue influence reflects in that context a concern about commodification. Commodification concerns are also widely debated in the context of organ transplants and assisted human reproduction, where commentators have expressed concern about the use of financial incentives to push people to sell their organs or ova (Radin 1996; Cohen 2002). In particular, in situations of extreme poverty, questions are asked about the possibility of meaningful consent. Some are critical of the use of concepts such as undue inducement and coercion in this context, pointing out that this raises concerns about 'exploitation' (Hawkins and Emanuel 2005). Yet it seems artificial to completely separate these different concepts as they are interrelated.

The use of the terms coercion and undue influence in research ethics should be distinguished from their use in legal contexts. In research ethics, reflections on what constitutes coercion or undue influence should make researchers and research ethics committees pause to reevaluate the informed consent practices that will be used in the future. Courts, in contrast, have to rule on whether informed consent was present in the past. The concepts of coercion and undue influence are only exceptionally used in legal cases about informed consent. The consequences of ruling that there was no consent are serious for the person who performed a medical procedure and courts tend to be reluctant to rule that no consent occurred. In law, the two terms are also not always clearly separated (*Norberg* v. *Wynrib* [1992] 2 SCR 226, p. 247). Coercion, the intentional use of psychological pressure, physical force, or threat, is more clearly deemed to vitiate consent. Undue influence is commonly used in testamentary law, where several conditions have been identified that relate to the vulnerability of the person, the relation of dependency, and the likelihood that the pressure may have had an effect. As Grubb puts it, in discussing the leading English case *Re T (Adult: Refusal of Medical Treatment)* [1992] 4 All ER 649 '"[u]ndue influence" is clearly a more insidious and subtle process than overt pressure and, therefore, calls for a closer examination of the facts' (Grubb 1998: 178). In the case of *Norberg* v. *Wynrib* (1992), an opinion supported by three of the six judges, the Canadian Supreme Court applied the contract law-based 'doctrines of duress, undue influence, and unconscionability [that] have arisen to protect the vulnerable when they are in a relationship of unequal power' to determine whether a drug-addicted patient could genuinely consent to sexual activity with a doctor who prescribed opioids in exchange. The Supreme Court held the doctor liable for battery, concluding the consent was not valid as a result of the patient's vulnerability and her dependency in the context of the unequal power relation.

Fraud and misrepresentation, on the other hand, are not often discussed in the bioethics literature on consent, but arise frequently in court. The reason is simple: research ethics committees do not speculate that an informed consent protocol will be fraudulently applied, and it seems clear, from an ethical perspective, that physicians ought not to fraudulently misrepresent information. In contrast, after problems occur, patients or research subjects may claim in court that their consent was affected by fraud. The Supreme Court of Canada indicated in *Reibl* v. *Hughes* [1980] 2 SCR 880 that only fraud or misrepresentation invalidates consent. The

consequences of fraud or misrepresentation depend on the level of fraud or misrepresentation. The key concern in English common law is whether the patient understood the nature and purpose of the procedure (Grubb 1998: 154–5). The Ontario Court of Appeal more recently found in *Gerula* v. *Flores* (1995) 126 DLR (4th) 506 that when a surgeon first operated on the wrong spinal vertebrae and then misrepresented why a new operation was needed, consent was absent for both procedures. But an alleged misrepresentation related to collateral issues, such as a physician's non-disclosure of his own epilepsy in the context of a surgery, is not considered fraud or misrepresentation (*Halkyard* v. *Mathew* [2001] WWR 26). As will be discussed further, whether the fraud or misrepresentation vitiates consent impacts the type of legal action that can be undertaken by the patient or research participant.

Competency is another key condition for informed consent. It refers to a person's ability to understand the relevant information and to appreciate the consequences of accepting or rejecting a treatment option or research participation. Competency is presumed in law in the case of adults (see Chapter 7 on mental health for a detailed discussion of competency issues). Questions of competency arise in the context of mental health, and healthcare or research involving children, to which common law jurisdictions generally apply the mature minor rule, which allows children and adolescents to provide consent when they are deemed mature enough to understand and appreciate the consequences of doing so. Competency is connected to comprehension: competency is treatment specific, so that a person with borderline competency can be competent to make one decision, but incompetent to decide in more complex situations.

The act of consenting can in many circumstances be explicit or implicit, verbal or written. Consent does not always have to be formalized and can be expressed in different ways. Written consent provides stronger – yet not conclusive – evidence that consent has been obtained and that specific information has been shared. Regulations often prescribe that a written consent form must be used, particularly in the research context. Written consent forms are also used for complex medical procedures, such as invasive surgeries, that involve more elevated levels of risk. Yet courts can still rule that notwithstanding the signed consent form, there was no informed consent (*Tremblay* v. *McLauchlan,* 2001 BCCA 444). Inversely, the absence of a written consent form should not be equated with the absence of consent. Rather, when regulations require written consent as a norm, they will often specify exceptions where written consent may be impractical or impossible to obtain.

It is sometimes suggested that consent can be 'presumed,' for example in an emergency context. However, using the term 'consent' for those situations seems questionable and unnecessary, as an emergency exception to informed consent, based on necessity, is widely accepted (Peppin 2011: 158–9). Obviously, informed consent procedures should be adjusted to the circumstances. Specific situations may require shorter informational exchanges, and in exceptional circumstances it will be impossible to obtain even the most minimal form of consent prior to a healthcare intervention. Providing information after the fact should then not be seen as obtaining 'informed consent' but as a proper debriefing in line with the standard of care. The exchange of information at that point may also be necessary for follow-up interventions.

A final note is warranted here about another another exception that is often mentioned and has strong historical roots: therapeutic privilege. As mentioned before, physicians were traditionally given much discretion about hiding information that could distress the patient. While the exception is still often mentioned, it is doubtful when physicians could still invoke it to justify a failure to disclose relevant information. Physicians have a duty of care in how they transfer information, and a patient may also express a desire not to receive further information, but the concept of therapeutic privilege clearly no longer allows physicians to make their own judgment about what to tell patients. In some situations, the inability of a patient to comprehend and deal

with information may be associated with competency issues. In that case, other protective measures apply based on substitute decision-making (see Chapter 7 on mental health).

3.2.2 Legal claims based on the informed consent doctrine

Different normative foundations of informed consent may result in different interpretations of its various components in law. Yet, even though courts and legislators often ground the need for informed consent with references to autonomy and the importance of self-determination, they do not engage in a detailed philosophical discussion of what type of autonomy or other ethical norm is the real basis for informed consent, or how various challenges to autonomy impact on meaningful consent. The legal notion of informed consent has its own meaning. For Jessica W. Berg and colleagues, the idea of consent as 'autonomous authorization' or as 'shared decision-making' and 'the legal and institutional rules and requirements the fulfillment of which constitutes the social practice of informed consent' are different but interrelated notions (2001: 16–17). The legal concept of informed consent is driven in part by pragmatic concerns about clarity, feasibility, and certainty. The legal rules surrounding the institutional practice of informed consent will often explicitly refer to the ideals discussed earlier. Common law and civil law jurisdictions generally start from the premise that a person has the right to make his or her own healthcare decisions, and that some level of information-sharing is needed to enable this (McLean 2010). But legal and institutional rules aim to clarify what level of information is to be provided; how it is to be provided (e.g. the use of informed consent forms); who determines what constitutes proper information-sharing; and what the consequences are of violating these rules. These rules vary among jurisdictions. The discussion here aims at offering a picture of some of the key legal concepts, questions, and tests that have emerged, with particular attention to Canadian common law. This will be followed by a brief discussion of the regulation of informed consent in various jurisdictions.

3.2.2.1 Informed consent: negligence or battery

When patients (or research subjects) feel that they have not been properly informed about a medical procedure or about the research project they were enrolled in and they feel harmed, what type of legal action is available to them at common law? Two common law actions can be used, depending on the nature of the violation: battery or negligence. Battery involves the intentional touching of a person without his or her consent. The action in battery, a form of trespass on the person, seemed a logical tool for courts, once it became accepted that the right to self-determination required medical professionals to obtain consent from patients prior to any physical interference with their body. As Katz points out (1997), battery offers a more robust protection of the concept of self-determination underlying informed consent: the mere fact of bodily intrusion suffices for a claim of battery. No physical or psychological harm has to be proven as the harm resides in the violation of the dignitary interest people have in the integrity of their body (Katz 1997: 165). Battery also offers the advantage that it is up to the defendant to provide evidence of consent (Peppin 2011: 162). Nonetheless, courts became hesitant to allow actions in battery, fearing the use of the action every time that there was a potential problem with the consent given for a medical procedure. Consequently, battery became restricted to cases where there was no disclosure as to the nature of the procedure, notably where patients consented to one operation and surgeons performed another (*Mulloy* v. *Hop Sang* [1935] 1 WWR 741; *Marshall* v. *Curry* (1993) 3 DLR 260; *Murray* v. *McMurchy* [1949] 2 DLR 442). Katz locates this development in the judicial and societal deference to the medical profession.

For McLean, other factors favored the introduction of a remedy based on negligence: some healthcare practices do not involve physical touching, such as the prescription of medication; and some failures to obtain informed consent, such as the failure to discuss alternatives, are hard to qualify as battery (2010: 71).

Other Canadian cases have broadened the scope of battery: the earlier mentioned Ontario case of *Gerula* v. *Flores* where a surgeon performed a second operation under a false pretext to correct an earlier mistake; *Malette* v. *Schulman et al.* (1990) 72 OR (2d) 417, where a doctor provided an emergency blood transfusion to a Jehovah's Witness even though he was aware of a prior expressed wish not to receive such transfusion; *Norberg* v. *Wynrib*, discussed above; *Nightingale* v. *Kaplovitch* [1989] OJ No 585, where the doctor continued an examination of a patient's colon after being asked to stop; and *Toews* v. *Weisner and South Fraser Health Region*, 2001 BCSC 15, involving the vaccination of a minor without parental consent, even though the nurse vaccinating the child believed the parents had consented.

3.2.2.2 Negligence: standard of disclosure

While battery protects the right of patients to be free from physical intrusion in extreme cases of failure to consent, negligence protects more widely the right of patients to have all relevant information before making healthcare decisions. Negligence has become the more common claim in cases of failure to provide adequate informed consent. To establish negligence, a plaintiff must overcome several hurdles associated with traditional tort claims. Patients must establish a duty of care, a breach of that duty, harm suffered, and causation between the breach and the harm. In the context of informational negligence, there are three key issues: the content of the informational duty of care, and particularly how the standard of care will be determined; the nature of the harm suffered; and causality between the failure to inform and the harm suffered.

3.2.2.3 Content of the informational duties

Courts have developed different standards to determine what constitutes sufficient information. As pointed out before, English common law has been more reluctant than other jurisdictions to fully embrace the doctrine of informed consent. Even though English courts have long recognized the importance of providing information to enable patients to make self-regarding decisions, how that information is to be provided and how much information should be shared is still largely measured according to the so-called professional standard (McLean 2010: 73–6). The 1985 *Sidaway* case and *Gold* v. *Haringey Health Authority* [1988] QB 481 both confirmed that the traditional test for negligence in medical practice from *Bolam* v. *Friern Hospital Management Committee* [1957] 1 WLR 583 also applied in cases about information-sharing. The duty of disclosure is seen as 'primarily … a matter of clinical judgment' (*Sidaway* v. *Bethlem Royal Hospital Governors et al.*), to be determined on the basis of what a reasonable physician would have done (i.e. disclosed) in those circumstances. Sheila McLean notes, however, that more recent cases, while not rejecting outright the *Bolam* test, move prudently away from mere reliance on professional judgment (2010: 79–81). In *Chester* v. *Afshar* [2004] UKHL 41, which dealt with a question of causation (see below), Lord Walker of Gestingthorpe emphasized that 'autonomy has been more and more widely recognized' in the time that elapsed since *Sidaway* (1985: 92). Lord Steyn stated even more explicitly that the traditional physician-centered approach is to be abandoned: '[i]n modern law medical paternalism no longer rules and a patient has a prima facie right to be informed' (*Chester* v. *Afshar* 2004, p. 16). Without explicitly abandoning *Sidaway*,

the English Lords promoted patient autonomy through a remarkable interpretation of the causation test.

Canadian, Australian, and US courts have since long adopted a test that appears more in line with the concept of self-determination underlying informed consent. As mentioned earlier, the US *Canterbury* case emphasized in 1972 that all information that is material to a patient's decision should be disclosed, thus recognizing that information-sharing should be approached from the perspective of the patient's informational needs. In Canada, a duo of 1980 Supreme Court cases, *Hopp* v. *Lepp* [1980] 2 SCR 192 and *Reibl* v. *Hughes*, rejected the professional standard and emphasized that the duty of disclosure has to be assessed from what a reasonable patient in the same position would want to know in order to make a properly informed decision. Physicians should not only inform patients about the nature of the procedure, but also about 'any material risk and any special or unusual risks' (*Hopp* v. *Lepp*, p. 210). In addition, the duty also extends to elements that 'the doctor knows or should know that the particular patient deems relevant to a decision' (*Reibl* v. *Hughes*, p. 894). The *Reibl* case is particularly interesting because the court recognized that information-sharing is not just about transferring medical evidence, but also about what particular risks mean to the person because of his or her particular circumstances. Mr Reibl had testified that had he known about a particular risk factor, he would have postponed the elective surgery until his lifetime retirement pension started and he would have been covered by disability insurance. Also noteworthy is the court's emphasis that the surgeon should have made sure that he was understood, considering the patient's difficulty with the English language (*Reibl* v. *Hughes*, p. 927). The Supreme Court thus emphasized that informed consent requires attentive interaction and not just the unilateral transfer of information. Australian decisions have also moved away from the English doctrine and towards the same recognition of a duty to disclose not only the type of material information patients generally need to make informed decisions, but also information that a doctor knew or should have known specific patients needed in order to make healthcare-related decisions (*Rogers* v. *Whitacker* (1992) 175 CLR 479; *Chappel* v. *Hart* (1998) 156 ALR 517). The information-sharing itself should be done according to proper professional standards.

Numerous decisions explore what type of information should have been provided pursuant to the patient-centered test. Even though courts will make decisions on the basis of the particular circumstances of each case, some illustrations are useful to show the possible consequences of the reasonable patient standard. There are some precedents indicating that patients reasonably prefer more detailed risk information when medical procedures are elective, as in plastic surgery, since detailed risk assessment appears more important than in medically necessary procedures (Peppin 2011: 168). In the same vein, research subjects can be expected to prefer more detailed risk information, particularly when they participate as healthy volunteers in a research project. Case law in the context of research is rare, but two Canadian precedents suggest that the disclosure obligation of researchers 'is at least as great as, if not greater than, the duty owed by the ordinary physician or surgeon to his patient' (*Halushka* v. *University of Saskatchewan* (1965) 53 DLR (2d) 436, pp. 443–4). The 1965 *Halushka* case from Saskatchewan was cited with approval in the 1989 case of *Weiss* v. *Solomon* [1989] AQ no. 312, decided under Quebec civil law. Michael Hadskis points out, however, that *Halushka* was decided prior to the affirmation of the patient-centered disclosure test in 1980, and can thus be situated as a reaction against the existing professional practice standard, which seems indeed even less appropriate in the context of non-therapeutic research on healthy subjects (2011: 471–2). He suggests that it was more important for the court in that context to indicate how the research standard was 'different.' It seems indeed logical that research subjects would generally want to engage in a fuller risk assessment in those circumstances. But this more detailed risk assessment would now also fit under the 'reasonable patient in the

same circumstances' standard, making this simply an application of the same test. The question of whether there is a higher standard of disclosure in the context of research, or whether this is simply an application of the reasonable person standard, is important in the context of new forms of research, particularly in the context of biobank research, where the highest possible standard of disclosure would be hard if not impossible to respect. A reasonable person standard, on the other hand, could make it possible to look at what people in similar circumstances would usually expect to receive as information.

Courts have emphasized that all reasonable alternatives, with their specific risks and comparative benefits, should be explained (*Van Dyke* v. *Grey Bruce Regional Health Centre* [2005] 197 OAC 336; *Van Mol (Guardian ad litem of)* v. *Ashmore*, 1999 BCCA 6). But what are 'reasonable alternative options'? Indirectly, professional standard components emerge again when it comes to determining the duty of physicians to provide information about alternatives outside of 'mainstream' medicine. A growing number of patients are interested in so-called complementary or alternative medicine, which includes a wide gamut of practices, some of which run counter to the standards of the medical profession and are firmly rejected by mainstream medicine (see Chapter 23 on traditional, complementary, and alternative medicine). Other alternative practices, such as acupuncture or naturopathy, have gained some level of acceptance in the context of medicine. Should physicians disclose these 'alternatives' and discuss their risks and potential benefits? It may depend on the level of professional and societal support for the practice, and whether physicians could be reasonably expected to have known about the patient's interest, for example because a patient asked questions that hinted at his or her interest.

3.2.2.4 Nature of the harm and causality

Another important hurdle to surmount in common law liability for negligence in informed consent is the causal link between the breach of the informational duty and the harm. The requirement to prove harm and causation make it much harder to obtain compensation for negligence than when courts find battery in cases where consent was absent or fraudulently obtained. In the latter cases, no questions of causation arise as the harm is the intentional violation of the person's physical integrity.

As discussed, the doctrine of negligence provided patients a remedy when physicians give incomplete or inadequate information, with less serious implications for physicians than battery-based claims. In negligence, patients still have to show that the procedure they inadequately consented to harmed them, and that the harm would have been avoided had they been properly informed (Peppin 2011). This means that two elements have to be proven: 'injury causation' and 'decision causation' (Tenenbaum 2012). In information negligence cases, a patient has to show that, had proper information been given, he or she would have made a different decision and the harm would thus not have occurred. This may seem relatively straightforward when the procedure is elective (e.g. plastic surgery), a serious risk factor was not disclosed, and the procedure clearly resulted in harm that could have been avoided by not having the procedure at all.

Proving on a balance of probabilities that harm was caused by a particular procedure or healthcare product (the injury-causation element), tends to be difficult in the context of healthcare because it is often unclear whether the harm was a result of the condition being treated or a result of the procedure/healthcare product. The provision of healthcare involves a multitude of interactions by many different people and complex chains of causation that have to be disentangled in court.

It is also difficult to reconstruct what patients would have done had they been properly informed, particularly when we are dealing with complex risk/benefit analyses. Risk assessment has inherently subjective components (Waring and Lemmens 2004). People's perception of risk inevitably changes in light of personal experiences, and people are obviously much more inclined to see themselves as risk averse once they have suffered harm. How do the courts establish – or better, hypothetically reconstruct – what patients would have done had they been properly informed? Different tests have been used by courts.

Some New Zealand and Australian courts have employed a so-called subjective standard to determine decision-causation (*Smith* v. *Auckland Hospital Board* [1964] NZLR 191; *Ellis* v. *Wallsend District Hospital* [1990] 2 Med LR 103). The Canadian Supreme Court, while rejecting this approach in ordinary medical malpractice cases, has explicitly endorsed this subjective test in the context of the relation between manufacturer of healthcare products and patients, specifically in *Hollis* v. *Dow Corning Corporation* [1995] 4 SCR 634). *Hollis* addressed the manufacturer's failure to inform patients of risks of rupture of breast implants. The Supreme Court of Canada explained that:

> In the case of a manufacturer … there is a greater likelihood that the value of a product will be overemphasized and the risk underemphasized. It is, therefore, highly desirable from a policy perspective to hold the manufacturer to a strict standard of warning consumers of dangerous side effects to these products.
>
> *(Hollis v. Dow Corning Corporation, para. 46)*

The Court emphasized the power imbalance between manufacturers, patients, and doctors with respect to the resources and the available information. One of the confounding factors was that the manufacturer had invoked the learned intermediary rule, which could have interrupted the chain of causation. The 'learned intermediary rule' refers to the role of physicians in providing detailed information to patients with respect to prescription drugs. The Court emphasized that this rule would only have applied if the company had fully informed the physician with clear, complete, and up-to-date information.

This subjective standard has frequently been described as 'open to the abuse of hindsight' (Mason and Laurie 2006: 408; Grubb 1998: 176), even by Canadian courts. This concern was acknowledged in *Hollis*, but Justice Laforest simply stated (for a majority of five judges) that that this 'can be adequately addressed at the trial level through cross-examination and through a proper weighing by the trial judge of the relevant testimony' (para. 46). This statement that cross-examination and the usual factual determination at the trial level can address problems of hindsight is significant. It is unclear why this would not be possible in standard information negligence cases. The rejection of the subjective test in those cases is as much a policy decision to facilitate judicial decision-making and limit the liability of physicians.

Nearly all US state statutes governing malpractice and most US case law embrace an objective standard of causation (Tenenbaum 2012: 709–20), arguably for the same policy reason. Under an objective standard, the question is not what the particular patient would have done, but whether the hypothetical reasonable patient would not have consented. The use of an objective standard has been criticized for conflicting with the underlying foundation of informed consent: respect for patient autonomy (Tenenbaum 2012: 718–19). Indeed, according to an objective standard, there is no inquiry into the values, preferences, or personal sensitivities of patients that are an essential component of individual decision-making. The objective standard makes it very difficult to obtain damages on the basis of informed consent claims alone (i.e. if there is no concurrent negligent practice) since it is easy to claim that the reasonable person in need of care

would have consented to a procedure offered by a healthcare provider. In a way, the objective causality standard facilitates the type of medical paternalism that was diminished through the rejection of the professional disclosure standard.

As mentioned, the Canadian Supreme Court also explicitly rejected the subjective test in standard information negligence cases because it would 'put a premium on hindsight' (*Reibl* v. *Hughes*, p. 898), and could threaten the medical system through an onslaught of 'liability claims from patients influenced by unreasonable fears and beliefs' (*Arndt* v. *Smith* [1997] 2 SCR 539, para. 15). Yet it recognized the problems of a 'reasonable person' standard. It introduced a middle-of-the-road test, or modified objective test. Under this test, the court asks whether the particular patient, appropriately informed of the risks and in those particular circumstances, would have accepted the treatment. The 'objective' component of the test lies in the requirement of the 'reasonableness' of the particular position of the patient. In the case of Mr Reibl, as pointed out earlier, the court took into consideration that he was close to retirement and could reasonably have decided to wait for the surgery. This appears somewhat similar to a 'hybrid test' that has been used in a few English cases (*Chatterton* v. *Gerson* [1981] 1 All ER 257) and which Grubb describes as a subjective test, followed by an objective appraisal (1998: 175).

In the 1997 case of *Arndt* v. *Smith*, a split Canadian Supreme Court confirmed the modified objective test but, according to Peppin, 'made the test somewhat more subjective both in emphasizing the *Reibl* elements of subjectivity and in making the "in the shoes of" test a more interior and particularized one' (2011: 182). A minority of justices (three out of nine) even argued that the subjective test should have been used. The case is an interesting illustration of the causality question. In *Arndt*, the court dealt with the claim that Ms Arndt, who developed chicken pox during pregnancy, was not adequately informed by her family physician about the reasonably remote risk of serious implications for the foetus. She gave birth to a seriously disabled child. The trial judge made reference to Ms Arndt's particular scepticism towards mainstream medicine, her interest in having a midwife, and her rejection of an ultrasound, and concluded from these factors that she would not have opted for an abortion (which was at that time in Canada also still subject to procedural limitations). Based on the factors mentioned in the lower court, the majority concluded that the reasonable person in the same circumstances as Ms Arndt, with her type of beliefs and expectations, would not have opted for an abortion. Commentators have rightly criticized the second-guessing that is reflected in the reasoning of the majority of the court with respect to such an intimate area of personal life, based on stereotypical presumptions of how people's belief in traditional medical procedures must also be reflected in how they feel about abortion (Peppin 2011: 179–84; Nelson and Caulfield 1999).

A final note in the causation context: English law has taken a most peculiar approach to causation in the earlier mentioned case of *Chester* v. *Afshar* (Mason and Laurie 2006: 409–11). In this case, the House of Lords had to decide on the case of a woman who underwent lumbar surgery and suffered from a rare serious adverse event. The trial judge found that the neurosurgeon had failed in his duty to warn Ms Afshar of this small, 1 to 2 per cent risk. The question to be decided by the House of Lords was one of causation between the failure to warn and the harm. Interestingly, there was no finding that Ms Afshar would not have undergone the surgery with the particular surgeon. Three of the Lords concluded that to establish causation, it was sufficient to find that had she been warned of the risk, she would not have decided to take the surgery '*at the time and place that she did*' (*Chester* v. *Afshar*, p. 8), and that it was thus very unlikely that the same adverse event would have happened. They referred to the Australian case of *Chappel* v. *Hart*, which shared some features with this case, but where the rationale was that the patient would have opted to have the operation performed by a more skilled surgeon, thus changing perhaps more substantially the risk profile of the operation.

One can conclude from this discussion of the legal components of negligence that most common law jurisdictions have struggled in trying to reconcile the practical requirements of judicial decision-making as well as policy considerations about the need for compensation, and the importance of avoiding significant costs to the healthcare system that could result from excessive litigation, with the important value underlying informed consent. Some jurisdictions have a longer history of recognizing the informed consent doctrine. England has until very recently resisted the doctrine of informed consent, but is now catching up in its own particular way, through, as it is stated in *Chester*, 'a narrow and modest departure from traditional causation principles' (p. 10).

3.2.2.5 Statutory, regulatory and guideline-based governance

The right to make one's own, well-informed healthcare decision is further reflected in various statutory provisions, regulations, and guidelines. As mentioned earlier, most US states, for example, have codified the common law rules in specific healthcare consent statutes, clarifying the requirements of informed consent and the rules about causation (Tenenbaum 2012). Many Canadian provinces also have healthcare consent legislation. Since 1994, several provisions in the *Civil Code of Quebec* 1991 section on personality rights grant specific decision-making authority to patients (Kouri and Philips-Nootens 2011). The same development is noticeable in other common law and civil law jurisdictions. New Zealand is an example of a jurisdiction which regulates informed consent in a specific patient rights code, part of a new trend towards the codification of such rights. The New Zealand *Code of Health and Disability Services Consumers' Rights* 1996 explicitly requires healthcare providers to give an 'informed choice' to patients and to obtain their 'informed consent' (basic provision right 7(1)).

In addition, many jurisdictions also have privacy statutes, some focusing specifically on health information, which contain rules about informed consent with respect to the use of personal information, often with specific rules about health information research (Lemmens and Austin 2009). It is worth noting here, even if a detailed discussion exceeds the scope of this chapter, that the concept of privacy is often interpreted as a component of other constitutionally protected rights, such as the right to liberty. Other privacy law remedies based on constitutional rights could thus be available in some jurisdictions.

As mentioned earlier, drug regulatory agencies, medical organizations, and funding agencies have historically played an important role in promoting better informed consent procedures for research. The legal status of the guidelines enacted by these agencies varies. Some, such as the historical *Nuremberg Code*, are part of international law. Others, such as the *Declaration of Helsinki*, are highly influential, but are enacted by organizations with no direct legal authority. Yet the *Declaration of Helsinki* has been integrated in many countries as a reference document in national guidelines or regulations (Sprumont *et al.* 2007). In many countries, including Canada, there are overlapping yet distinct research guidelines for clinical trials aimed at drug approval on the one hand, and for other forms of publicly funded research on the other. In Canada, both the *Declaration of Helsinki* and the ICH GCP are mentioned in guidance documents for clinical trials issued by the drug regulatory agency, Health Canada. The Canadian federal funding agencies have issued another research ethics document, the *Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans* (TCPS), which has to be respected in all federally funded institutions (Hadskis 2011). Both the ICH GCP and the TCPS require – with some exceptions – the signing of consent forms and provide a detailed list of elements that have to be disclosed, such as the nature of the research, the identity of the researchers, the procedures involved, the foreseeable risks, the potential benefits, the right to withdraw from the study, and the measures in place to

protect the confidentiality of the information provided. Hadskis emphasizes that the TCPS, but not the ICH GCP guidelines, also explicitly requires disclosure of commercialization plans and conflicts of interest issues (2011: 473). It is important to point out that research ethics committees prospectively review the appropriateness of the informed consent procedures and can thus impose additional requirements for specific studies.

Due to their status as 'soft' law in Canada, the ICH GCP guidelines and the TCPS are not directly enforceable. Violations of the ICH GCP can be seen as a violation of good clinical practices by the drug regulatory agencies and lead to an investigation and sanctions associated with drug approval. Funding agencies can indirectly enforce the TCPS through the withdrawal or suspension of research funding to the investigators or the institutions involved. Courts could also possibly use the ICH GCP and TCPS as sources to establish a common law standard of care in the context of research where participants take researchers to court for failure to obtain informed consent (Campbell and Glass 2001).

Courts could theoretically also refer to a gamut of international declarations and statements, as well as professional ethics codes that are not directly mentioned in the national research or clinical trials governance systems, and that emphasize the importance of informed consent. A discussion of all these other soft law-based mechanisms exceeds the scope of this chapter.

3.3 Emerging issues

As discussed in this chapter, informed consent has evolved from a concept imposed by early case law on a somewhat reluctant medical profession, to gradually being implemented – albeit not always respected – in the context of research through research ethics guidelines and regulations, and to finally becoming established as a crucial component of medical practice and research. Even if there is still much discussion about how to best meet the requirements of informed consent and to refine practices to achieve the ideal of the fully informed patient and research subject, there is now also a growing chorus of commentators questioning its feasibility or even its appropriateness in particular areas of medicine, particularly in the context of research.

One area where traditional approaches to informed consent are questioned is biobank-based research. Biobanks are research infrastructures (Kaye 2009) rather than one-dimensional research projects, which involve the long-term storage of biological samples, and constantly accumulate associated information, including clinical, familial, environmental, and social data. In the context of biobank research, many of the specific items that have traditionally been seen as essential elements of the duty to inform (e.g. nature of the research, risks and potential benefits, identity of the researcher) are not known at the time the samples and data are collected and stored. Many authors, including some in this book, have pointed out that traditional legal and ethical informed consent requirements are difficult if not impossible to respect in the context of biobanks (Kaye 2009; Deschênes *et al.* 2001; Caulfield and Knoppers 2010; Allen *et al.* 2013). Knoppers and Caulfield state that 'the existing law and ethics policies were not developed with … the large-scale biobanking in mind' (Knoppers and Caulfield 2010: 4). Many have therefore argued for different informed consent models for biobanking research. These models, several of which have overlapping elements, include the use of an option model, broad (or blanket) consent, and authorization.

Under the model of broad consent, biobank participants are given a set of core choices, which allows them to set parameters surrounding the use of their samples (Deschênes *et al.* 2001; National Bioethics Advisory Commission 1999; McGuire and Gibbs 2006). They can thus refuse some forms of future research, determine whether they want to be recontacted for specific purposes, or even allow general use with or without anonymization of samples. The 'authorization

model' recognizes that consent to the use of a sample is not exactly the same as consent for research participation (Caulfield *et al.* 2003). More recently, Kaye and colleagues have also advocated for a model of 'dynamic consent,' which involves the creation of communication structures and more detailed involvement of research subjects and patients in subsequent research practices. In this model, information technology is used to transform consent into a bidirectional, ongoing, interactive process between patients and researchers. Participants can express preferences about the use of their data and samples for research on a continuing basis (Kaye *et al.* 2011).

Are all of these models in line with the legal and ethical informed consent requirements? Some authors have gone as far as to suggest that biobank research may violate traditional legal consent requirements and recommended that a legislative framework be introduced for biobanks (Caulfield 2007) or that consent requirements be overhauled (Allen *et al.* 2013). Yet in many jurisdictions, including Canada, the difficulty of obtaining informed consent in this type of research involving stored samples and information is to some level already addressed through legislative provisions. Many Canadian privacy statutes, for example, contain a broad research exception that allows health information to be used for research purposes without consent under specific circumstances (Alberta *Health Information Act* 2000; Ontario *Personal Health Information Protection Act* 1996). Research ethics committees are given the task of evaluating these conditions and determining if appropriate privacy mechanisms and other measures are in place to protect research subjects. They have to evaluate whether obtaining consent is difficult or impossible (and Kaye's work on dynamic consent suggests that there are ways to promote ongoing patient involvement), whether appropriate privacy protection is in place, and whether the research serves a public interest. Although special legislation may therefore not always be needed, it could indeed provide clarity to have more detailed provisions that are adjusted to biobank research.

It seems appropriate to distinguish in the context of biobanks the procedures for the original consent to storage of a sample (which one could still appropriately call 'consent to storage') and those for the subsequent use of the sample for specific research-related procedures. With respect to the consent to storage, information can be provided about the nature of the biobank, the overall area of research, and some of the typical issues and concerns that can arise in the context of biobanks. The consent should also include agreement to submit one's personal information and biological sample to a specific 'governance system,' which should be surrounded by a publicly accountable governance system. Lisa Austin and I have argued elsewhere that focusing on informed consent obfuscates the fact that biobank research raises difficult legal and ethical issues that cannot be appropriately addressed by individual consent (Lemmens and Austin 2009). These issues include the familial nature of the information, the impact on communities and aboriginal peoples, and concerns about the commercialization of products developed on the basis of personal biological samples and associated research.

The commercialization issue, raising concerns about exploitation and questions of ownership of personal biological samples, has received much attention, and has also resulted in legal claims and compensation requests (*Moore* v. *Regents of the University of California* [1990] 51 Cal. 3d 120; *Greenberg et al.* v. *Miami Children's Hospital Research Institute* [2003] 264 2d 1064; *Washington University* v. *Catalona* [2007] 490 F.3d 667). Rather than pretending that informed consent procedures will help us to adequately deal with this, we suggest that the focus should be on the improvement of the often very weak governance structures surrounding research. This will be particularly challenging for research that increasingly traverses jurisdictional boundaries. Some private initiatives, such as the Public Population Project in Genomics and Society, are worth noting in this context, but further international initiatives appear needed to ensure accountable public interest-oriented governance. International organizations such as the World Health Organization could play a role in developing a proper governance framework for international

research (Gostin *et al.* 2013). There are precedents of international legal initiatives in this area. The *European Convention on Human Rights and Biomedicine* 1997, for example, has integrated several detailed provisions on the protection of human rights in the context of biomedicine, which provide remedies to individuals residing in states that ratified it.

Another related area where there has been much discussion lately is in the context of research that aims at evaluating different standards of care where, arguably, research subjects are subjected only to risks associated with the standard therapies. This issue recently came up in the controversy surrounding the SUPPORT study, a large National Institutes of Health funded international, multi-centre, randomized controlled trial, which aimed at determining the optimal oxygen saturation levels for premature newborns (SUPPORT Study Group 2010) by comparing two different levels that were routinely used in standard care. No one questioned the scientific rationale and the importance of the study since neonatologists have been struggling for decades with how much additional oxygen could be provided to premature newborns to reduce the risk of brain damage, while still avoiding the risk of blindness that has been associated with exposure to high oxygen levels. The Office of Human Research Protections (OHRP), an official US agency mandated with the protection of human research subjects and the enforcement of research regulations of the Department of Health and Human Services, criticized the research study for violations of informed consent procedures (Department of Health and Human Services 2013).

Commentators in the medical community, some of whom were directly involved in or provided institutional support for the study, accused the Office of overzealousness. They insisted that an elevated standard of informed consent was inappropriate and unnecessary for studies comparing different standards of care (Hudson *et al.* 2013; Modi 2013). Interestingly, a group of leading bioethics and research ethics scholars also promptly published a letter in support of the study and accusing the OHRP of overreach (Wilfond *et al.* 2013), which evoked in turn a similarly strong support letter for OHRP by other research ethics experts (Macklin *et al.* 2013). The OHRP, these research ethics commentators, and patient advocate Sydney Wolfe (Wolfe 2013) particularly criticized the failure to give detailed information to parents about the different types of risk associated with being included in a clearly defined high or low oxygen group in the context of this research study. Even if all of the oxygen levels were used in standard care, the inclusion in a small, clearly delineated group of either low or high oxygen did create, according to the critics, a different type of risk, which had to be explained to parents. It was also argued that not all consent forms explained well the procedures involved in creating the double blind, which involved the use of manipulated oximeters so that clinicians would not know the exact level of oxygen provided.

Interestingly, around the same time, several articles came out in the literature arguing for more flexible informed consent procedures for SUPPORT-like comparative research studies (Faden *et al.* 2013; Faden *et al.* 2014). Particularly noteworthy are the repeated calls by consent experts Faden, Beauchamp, and Kass to rethink our approach to informed consent for such studies: 'in a mature learning health care system with ethically robust oversight policies and practices,' they argue, 'some randomized CER studies may justifiably proceed with a streamlined consent process and others may not require patient consent at all' (Faden *et al.* 2014: 766). Their suggestion that facilitating consent procedures for minimal risk research could help ensure that 'higher-risk research gets the focused attention it deserves' rejoins increasing criticism on the unnecessary administrative burden imposed by research ethics review (Kim *et al.* 2009).

Faden and colleagues seem to take for granted, though, that one of their key conditions for more flexible consent procedures (i.e. the existence of robust oversight policies and practices) has been fulfilled. Yet this is certainly overstated in many jurisdictions (Lemmens and Austin 2009).

Even though the USA has one of the most extensive systems for research governance, ongoing concerns as expressed in the wake of the SUPPORT Study and recent controversies about highly questionable informed consent procedures in the context of research involving vulnerable psychiatric patients at the University of Minnesota add fuel to the fire of those arguing that oversight in the US is also seriously lacking and in need of reform (Lemmens 2014).

3.4 Conclusion

There is certainly something to be said about the fact that research ethics review now often focuses excessively on procedural requirements, particularly related to informed consent, and ignores much more difficult but key questions about appropriate levels of risk in research. Checking informed consent forms and imposing informed consent rituals is indeed not necessarily increasing research subject protection. At the same time, there is also reason to be concerned about heeding too quickly calls from the research community to lift informed consent requirements in order to facilitate research. Research efficiency is important, but the history laid out in the first part of this chapter should remind us how the rights of individuals to make autonomous choices in healthcare and research are all too easily trampled upon. Avoiding informed consent bureaucracy and promoting research efficacy are important, but it is equally important not to take the progress in the protection of research subjects and truly meaningful informed consent for granted.

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4

Privacy and confidentiality

Mark A. Rothstein

4.1 Legal and ethical theory

4.1.1 Background

Privacy and confidentiality are foundational principles in medicine and all of healthcare, but both terms are often used inconsistently and are difficult to define. Privacy is generally recognized as the broader concept, sometimes including confidentiality. Privacy has several dimensions – informational, physical, decisional, proprietary, and relational (Beauchamp and Childress 2013: 312). This chapter concentrates on the informational dimension of privacy. Accordingly, *privacy* is defined here as a condition of limited access to an individual or information about an individual. *Confidentiality* is defined as the condition under which information obtained or disclosed within a confidential relationship is not redisclosed without the permission of the individual. *Security* is defined as the personal and electronic measures granting access to personal health information to persons or entities authorized to receive it and denying access to others (National Committee on Vital and Health Statistics (NCVHS) 2006).

Another ethical principle related to informational health privacy is *autonomy*. As defined by Beauchamp and Childress (2013: 101), '[a]t a minimum, personal autonomy encompasses self-rule that is free from both controlling interference by others and limitations that prevent meaningful choice, such as inadequate understanding.' Many individuals believe that they ought to be able to control the uses and disclosures of their health information and biospecimens, even if their records and specimens are deidentified (Rothstein 2010b; Hull *et al.* 2008). In addition, many individuals believe a physicians' obligation to respect patient autonomy arises from the physician–patient relationship.

The obligation of physicians to safeguard the confidentiality of patient-derived information dates back at least to the fourth century BCE and the Oath of Hippocrates. The pertinent provision of the Oath reads:

> What I may see or hear in the course of treatment in regard to the life of men, which on no account must be spread abroad, I will keep to myself, holding such things shameful to be spoken about.
>
> *(See Reich 1995: 2632)*

Although the Oath had a somewhat different meaning in ancient Greece than is often ascribed to it today (Miles 2004: 150), modern conceptions of the Oath are perhaps more important than the actual wording (Rothstein 2010a). Today, the Hippocratic Oath is generally considered the original source of a physician's duty to maintain as confidential virtually all patient health information.

In the nineteenth century, medicine emerged as a scientifically based health profession (Starr 1982). Codes of medical ethics, beginning with Thomas Percival's code of medical ethics in 1803, incorporated confidentiality requirements. The American Medical Association's (AMA) first Code of Ethics in 1847 also expressed the physician's duty to maintain confidentiality. The current version of the AMA's Code of Medical Ethics provides that:

> The information disclosed to a physician by a patient should be held in confidence. The patient should feel free to make a full disclosure of information to the physician in order that the physician may most effectively provide needed services. The patient should be able to make this disclosure with the knowledge that the physician will respect the confidential nature of the communication.
>
> *(AMA 2011: section 5.05)*

The AMA's Code of Medical Ethics, like other such codes, links maintaining confidentiality with the ability to provide appropriate health services. Without assurances of confidentiality, patients would be reluctant to share intimate information about their health and lifestyle. Likewise, without accurate and detailed histories and symptoms from patients, it would be difficult to provide appropriate medical care.

Codes of ethics from around the world similarly place a high priority on protecting the confidentiality of patient information. The World Medical Association's International Code of Medical Ethics and Declaration of Geneva explicitly mention the duty of a physician to protect confidentiality:

> A physician shall respect a patient's right to confidentiality. It is ethical to disclose confidential information when the patient consents to it or when there is a real and imminent threat of harm to the patient or to others and this threat can only be removed by a breach of confidentiality.
>
> *(World Medical Association (WMA) 2013: 2)*

Similar provisions appear in the codes of ethics or ethical guidelines of various national medical associations, including the Australian Medical Association (2006: subsection 1.1(12)), the British Medical Association (2013), and the Canadian Medical Association (2013: paras 31–7).

4.1.2 Right to privacy

The legal right to privacy has relatively recent origins. In 1890, two young law partners from Boston, Samuel D. Warren and Louis D. Brandeis, published a groundbreaking article in the *Harvard Law Review* titled simply 'The Right to Privacy' (Warren and Brandeis 1890). Presumably motivated by the intrusive Boston press, Warren and Brandeis argued more broadly in favor of a comprehensive common law right of individuals to be free from unwanted intrusions. They proposed a general legal principle of protecting the 'privacy of private life' and urged creating a legal cause of action to redress 'the more flagrant breaches of decency and propriety' (Warren and Brandeis 1890: 215–16).

Despite its well-deserved acclaim in the academic literature, the Warren and Brandeis article did not immediately translate into a well-accepted legal theory permitting the redress of invasions of privacy. Beginning in the 1930s, however, several courts recognized some aspects of a common law right to privacy, but the right was not clearly defined. In 1960, that would change. William L. Prosser, the leading figure in the development of American tort law, published an even more simply titled article 'Privacy,' in which he proposed the common law right of privacy was actionable in four discrete situations: (1) intrusion upon the plaintiff's seclusion or solitude, or into his private affairs; (2) public disclosure of embarrassing private facts about the plaintiff; (3) publicity which places the plaintiff in a false light in the public eye; and (4) appropriation, for the defendant's advantage, of the plaintiff's name or likeness (Prosser 1960: 389).

All four categories of invasion of privacy could be violated in the context of health information and healthcare. The public disclosure of private facts represented one category most applicable to healthcare, and would be implicated whenever sensitive health information was wrongfully disclosed to the public. Although Prosser's classification scheme was criticized for being overly reductionist and restrictive (Bloustein 1964; Richards and Solove 2007), it was adopted by the *Restatement (Second) of Torts* (Prosser was the reporter) (Richards and Solove 2007). Since then, this categorical approach to invasion of privacy has been widely adopted by courts in the United States. Yet invasion of privacy cases have been difficult for plaintiffs to win due to the strict set of criteria imposed by the courts. Courts require that: (1) the publication of the information must be widespread; (2) the information disclosed must be of a private nature; (3) the disclosure must be highly offensive to a reasonable person; and (4) the matter must not be a legitimate concern of the public (Rothstein 2009).

4.1.3 Constitutional law (US)

The United States Constitution does not contain an express provision establishing or protecting the right to privacy. The Fourth Amendment to the Constitution prohibits unreasonable searches and seizures, and therefore, it has been the most widely invoked source of a constitutional right to privacy. Because the Constitution is designed to restrain the exercise of government powers, its provisions generally may not be invoked in purely private disputes. Thus a prerequisite to application of the Fourth Amendment is action by the federal, state, or local government. The fundamental legal question is whether the Supreme Court recognizes a constitutional right to informational health privacy in cases where the government is alleged to have violated an individual's privacy. In *Whalen* v. *Roe* (1977) 429 US 589, the plaintiffs challenged the constitutionality of a New York State law requiring the collection in a centralized database of the names and addresses of all persons who obtain, pursuant to a doctor's prescription, certain controlled drugs, including powerful analgesics. The Supreme Court stopped short of declaring an individual's constitutionally protected interest in informational health privacy, holding that even assuming there is such a right, the New York statute was a reasonable measure to prevent the unlawful diversion of controlled substances.

American courts have since followed the approach used in *Whalen*, assuming but not deciding there is a constitutional right to informational health privacy. Most recently, *National Aeronautics and Space Administration* v. *Nelson* (2011) 131 SCt 746 (*NASA*) involved a challenge to the intrusive background questionnaire mandated for employees working for a contractor at NASA's Jet Propulsion Laboratory. Among other things, the questionnaire asked employees if they had used, possessed, supplied, or manufactured illegal drugs in the last year. If so, they were required to explain and disclose any substance abuse treatment they received. Employees were also required to sign a release authorizing the government to obtain personal information from schools,

employers, and other sources during its investigation. The Supreme Court again assumed, without deciding, there was a constitutional right to informational privacy. Even assuming such a right, however, the Court upheld the questionnaire requirement as reasonable in light of the government's important interest in employee safety and probity, as well as the protections in place to prevent disclosure of the information to the public. Thus, as *NASA* and *Whalen* demonstrate, even if there is a constitutional right to informational health privacy, the courts have been so deferential to the government's interests that plaintiffs' claims are rarely sustained (Rothstein 2011).

4.1.4 Privacy Act *(US)*

In 1974, partly in response to the government abuses disclosed in the Watergate scandal, Congress enacted the *Privacy Act* 1974 (5 USC § 552a). The *Privacy Act* established a code of fair information practices that governs the collection, use, and dissemination of information about individuals maintained in 'systems of records' by federal executive branch agencies. The *Privacy Act* aims to: (1) restrict disclosure of personally identifiable records maintained by agencies; (2) grant individuals increased rights to access agency records maintained on themselves; (3) grant individuals the right to seek amendment of agency records upon a showing that the records are not accurate, relevant, timely, or complete; and (4) establish a code of fair information practices requiring the agencies to comply with statutory norms for collection, maintenance, and dissemination of records (US Department of Justice 2012).

The *Privacy Act* creates a default rule that individually identifiable information should not be disclosed unless one of the 12 statutory exceptions applies (5 USC § 552a(b)). Among these exceptions are disclosures for civil or criminal law enforcement activity, if (i) the activity is authorized by law; and (ii) the request is made in writing that specifies the portion of the records requested and the law enforcement activity for which the record is sought.

Each agency must keep an accurate accounting of the disclosures of records under its control (5 USC § 552a(c)), preserve an individual's right of access to his or her own records, and preserve an individual's right to request an amendment of his or her records (5 USC § 552a(d)). Furthermore, agencies must maintain only information that is relevant and necessary to accomplish their purpose, maintaining it in as complete, timely, and accurate a fashion as possible (5 USC § 552a(e)). Each agency must also provide public notice through publication in the Federal Register of the character and nature of the records it maintains, as well as the rules it follows in disclosing information.

The *Privacy Act* represents groundbreaking privacy legislation because it establishes a code of fair information practices – rules applicable across the federal government to limit disclosures and grant individuals rights with respect to their own information (Levin and Nicholson 2005) – rather than stating the specific information that will be protected from disclosure. However, its main limitation is that it applies only to information in the possession of the federal government (Schwartz and Solove 2013).

Another federal law, the *Freedom of Information Act* 1966 (5 USC § 552), prescribes rules for public access to documents in the possession of the federal government. An important exception to the disclosure requirement is for records protected by the *Privacy Act*, including individual health information.

4.1.5 Health Insurance Portability and Accountability Act Privacy Rule *(US)*

Despite having seriously considered enacting comprehensive privacy legislation in the 1970s, Congress took no action on privacy legislation, including health privacy legislation, until the 1990s. Although several states enacted health privacy legislation in the absence of federal action,

these laws were of limited scope, such as granting patients a right of access to their health records and requiring informed consent before making certain disclosures (Pritts 2002). Federal action in the realm of health privacy came about indirectly and in an unlikely legislative vehicle.

During the 1990s (as well as today), many Americans obtained their healthcare coverage from employer-sponsored group health plans. If an employee had a preexisting health condition or had a dependent with such a condition, the employee found it difficult, if not impossible, to maintain comparable coverage under an employer-sponsored group health plan if the employee changed jobs. Both insured and self-insured health plans were free to deny coverage, exclude certain conditions, charge higher rates, or take other actions when a new employee or a newly covered dependent had a preexisting health condition. Concerned about the unfairness of this loss of health coverage and the drag on the nation's economy by limiting occupational mobility due to 'job lock,' Congress took up the bipartisan Kennedy-Kassebaum Bill, the *Health Insurance Portability and Accountability Act* (HIPAA) 1996. HIPAA was designed to increase the portability of health coverage by prohibiting employer-sponsored group health plans from imposing certain burdensome conditions on new enrollees.

By prohibiting exclusionary practices, HIPAA imposed costs on the health insurance industry. During the legislative process, the health insurance industry indicated that it would not oppose the bill if the legislation also contained a provision, long favored by the industry, requiring all health claims submitted for payment to be in standard electronic formats. The bill's sponsors agreed, thereby adding the provisions to Title II of HIPAA, 'Administrative Simplification.' Before its final enactment, however, Congress realized that the electronic filing of millions of health claims created issues of privacy and security. Therefore it added a provision that if Congress did not enact privacy legislation within two years, the Secretary of Health and Human Services (HHS) was required to do so (Pub. L. 104–191). After Congress failed to enact privacy legislation, the HHS issued the controversial *HIPAA Privacy Rule* (45 CFR Parts 160, 164).

This detour into the origins of the *HIPAA Privacy Rule* is important because it explains why it was never intended to be a comprehensive health privacy law and, indeed, it is not. Because of its narrow mandate, it only applies to three classes of covered entities in the healthcare payment chain: health providers (e.g. hospitals, physicians), health plans (e.g. health insurance companies, employer-sponsored group health plans), and health clearinghouses (entities that put billing information into standard electronic formats). In its current form, the *Privacy Rule* is more of a 'notice and disclosure' rule than a privacy rule. For example, informed consent from a patient is not required before a covered entity may use and disclose individually identifiable health information for treatment, payment, or healthcare operations (e.g. quality assurance). Instead, covered entities are merely required to provide a notice of privacy practices to patients and, for healthcare providers with a direct treatment relationship, to make a good faith effort to obtain the patient's written acknowledgment of receipt of the notice.

The *Privacy Rule* also includes 12 categories of 'permissive' disclosures for public purposes, including disclosures for public health, law enforcement, and to avert an imminent harm. Any legal obligations for a covered entity to make one of these disclosures (e.g. reporting cases of suspected child abuse) are based on other laws. The *Privacy Rule* merely provides that disclosures for these purposes are permitted. Significantly, the *Privacy Rule* does not contain a private right of action. An aggrieved individual's only remedy is to file a complaint with the Office for Civil Rights of HHS. Violators are subject to civil monetary penalties, and for egregious cases, criminal prosecutions may be brought by the Department of Justice.

4.1.6 International data protection law

European data protection law is similar to the US *Privacy Act* in that it uses general principles of fair information practices rather than detailed rules for each type of data and disclosure.

The two foundational documents are the *European Convention on Human Rights* 1950 and the *Charter of Fundamental Rights of the European Union* 2000, which reiterates many of the same principles set forth a half-century earlier by the *European Convention on Human Rights* and those derived from shared constitutional traditions of EU member states. Both documents contain language guaranteeing privacy protection in one's private life (*European Convention on Human Rights* 1950: article 8; *Charter of Fundamental Rights of the European Union* 2000: article 7).

In response to the increased flow of information across borders, the European Parliament adopted Directive 95/46/EC. This Directive, along with Directive 2002/58/EC concerning personal data processing and privacy protections in the electronic communications sector, form the basis of modern data protection law in the European Union (Hiller *et al*. 2011). Directive 95/46/EC provides that:

> 1. In accordance with this Directive, Member States shall protect the fundamental rights and freedoms of natural persons, and in particular their right to privacy with respect to the processing of personal data.
>
> *(1995: article 1(1))*

To help achieve this goal, article 29 of the same Directive created the Data Protection Working Party, an independent advisory board on data protection and privacy (Directive 95/46/EC, 1995). The Working Party's responsibilities are described in article 30 of Directive 95/46/EC and article 15 of Directive 2002/58/EC and include examining the uniform application of EU data protection laws and advising the European Commission as to possible amendments or additional measures needed to safeguard privacy protections. In response to evolving technologies in healthcare that could implicate patient privacy protections, the Working Party issued a report in 2007 that provides guidance and recommended legal protection of individual health privacy in the use of electronic health records (see section 4.2.1 below) (Data Protection Working Party 2007). More recently, in 2012, the European Commission proposed the *General Data Protection Regulation*, which, if adopted, would substantially reform Directive 95/46/EC (see section 4.2.2 below).

As is the case in the US and Europe, other industrialized nations also try to preserve privacy by enacting data protection laws. For example, Australia enacted the *Privacy Act* 1988, essentially an analog to the US *Privacy Act*, to better protect how personal data is processed and collected (Atkinson *et al*. 2009). Likewise, although no general right to privacy exists in the *Canadian Charter of Rights and Freedoms*, Canadians are guaranteed a constitutional right comparable to the one provided by the American Fourth Amendment (Levin and Nicholson 2005). The Canadian government therefore enacted two major federal privacy laws, the *Privacy Act* 1983 and the *Personal Information Protection and Electronic Documents Act* (PIPEDA) 2000. In combination with the nation's aforementioned constitutional law, both strengthen personal data protection and quell privacy concerns in a manner that blends European and American privacy principles (Levin and Nicholson 2005; Office of the Privacy Commissioner of Canada 2009).

4.2 Current and emerging issues

4.2.1 Electronic health records and networks

New electronic technology is revolutionizing the way health information is collected, aggregated, analyzed, stored, used, and disclosed. As such, health information technology (HIT) also presents important challenges for health information privacy and security. In the 'old days' of paper records, healthcare was too often compromised by illegible, nonstandard, fragmented,

uncoordinated, and error-filled records. The disarray caused by paper-based health records, however, served to protect health privacy by making it virtually impossible to compile inclusive individual health information from numerous sources over long periods of time (Silversides 2010). Moreover, paper records allowed individuals to control access to their health information by simply changing healthcare providers and choosing what elements of their health histories to disclose to their new providers.

HIT holds the promise of interoperable, comprehensive, and longitudinal health records and networks, while offering greater safety, accuracy, efficiency, and effectiveness (Rynning 2007). At the same time, the consolidated and integrated health information never goes away (see section 4.2.2 below), raising questions about who should have access to sensitive information, especially when it has little or no current clinical utility (Rynning 2007). The following section is divided into two parts that discuss access to health information (1) within healthcare settings and (2) beyond healthcare settings.

4.2.1.1 Healthcare settings

Many hospitals and larger medical institutions have electronic health record (EHR) systems with role-based access controls. For example, food service or custodial employees are denied access to sensitive clinical information, while there are generally no limits on the scope of information available to physicians, nurses, pharmacists, various technicians, and other health professionals with direct patient care responsibilities. Security measures, such as password protected access, encryption, and audit trails are a necessary but insufficient means of limiting access to unauthorized personnel.

Although instances of lost laptops and hackers unlawfully breaking into EHRs garner great publicity, they are not the greatest threats to health privacy. The greatest privacy threat involves an authorized user accessing more information than is necessary to treat an immediate problem (Chalmers and Muir 2003). For example, a physician in an emergency department treating a woman for a sprained ankle is unlikely to need access to the woman's reproductive health history, but there is currently no operational way to limit the scope of this access. Even though, as a practical matter, busy physicians do not have the time to troll through exhaustive health records, as long as they *could* access this information many patients will be concerned that their sensitive information is not really confidential.

The lack of privacy controls on health information can lead to a variety of individual and societal harms. First, individuals may suffer embarrassment, stigma, discrimination, and other harms to their dignity if sensitive information is inappropriately disclosed. Second, quality healthcare may be undermined if individuals who fear widespread disclosure of their sensitive information forego timely treatment for stigmatizing conditions or engage in defensive practices, such as withholding or 'editing' the sensitive information they share with their healthcare providers. Third, public health harms may occur if individuals with infectious disease, mental illness, substance abuse, or other sensitive conditions delay or decline treatment because they fear a loss of privacy (Rothstein 2012; California Health Care Foundation 2005).

One of the most promising technologies for limiting unnecessarily broad access to health information is segmentation, permitting patients to designate entire fields of sensitive information as inaccessible unless they provide additional consent. Candidate classes of health information for segmentation include genetic information, domestic violence information, mental health information, sexuality and reproductive health information, substance abuse information, sexually transmitted disease information, and child and adolescent health information.

Many technical and policy issues need to be resolved before segmentation is operational. These issues prevent widespread implementation of EHR segmenting in the clinic by raising questions regarding whether there should be a 'break-the-glass' feature for emergency access to comprehensive health records; whether clinical decision support should operate on all health information, including segmented information; and whether the records should carry a notation that some information is being withheld at the request of the patient (Rothstein 2010a; NCVHS 2008).

4.2.1.2 Beyond healthcare

Many individuals and entities beyond healthcare (e.g. employers, insurers) have a legitimate need to access an individual's past or current health information, but there is little agreement on what information should be available or how to prevent overly broad access. Among the issues are the following: (1) Is it permissible for third parties to require individuals to sign authorizations giving access to their health information? (2) Is it possible to limit the amount of health information disclosed pursuant to an authorization? (3) How may the third-party recipients use the health information they obtain.

A variety of individuals and entities have economic leverage over other individuals, which can be used to compel them to sign an authorization to disclose their health information. For example, if an individual applies for a life insurance policy, the life insurer can require authorization for health information disclosure as a condition of applying for the policy. This is lawful and appropriate for an insurance product whose availability and pricing traditionally have been based on medical underwriting. The life insurance applicant need not sign the authorization, but if the applicant declines to do so, the insurer may not consider the individual's application (Rothstein and Talbott 2006). It is not known precisely how many of these 'compelled authorizations' are signed each year, but a conservative estimate is that there are at least 25 million compelled authorizations in the United States annually (Rothstein and Talbott 2007). The largest numbers of authorizations are for employment (10.2 million) and life insurance (6.8 million), but other forms of insurance and government benefits also generate numerous compelled authorizations.

Some statutes limit the permissible scope of disclosure. For example, workers' compensation laws in some states limit the health information disclosed to matters relevant to the workers' compensation claim (e.g. *Colorado Workers' Compensation Act,* Colo. Rev. Stat. § 8-47-203(1); *Louisiana Workers' Compensation Law*, La. Rev. Stat. Ann. § 23:1127(B)(1); *Minnesota Workers' Compensation Act*, Minn. Stat. § 176.138(b)). Similarly, federal law prohibits the disclosure of genetic information in the process of conducting preplacement medical examinations (see section 4.2.3 below). The main problem is, as noted above, there is no easy way to limit the scope of the disclosures. Consequently, it is common for the custodians of the health records simply to send the entire file, regardless of how broadly or narrowly the authorization is worded.

The most difficult and contentious issue regarding authorization is how health information may be used. Upon disclosure to a third party, use of the information is not a matter of privacy so much as it is a matter of how the information may inform health assessment or risk allocation. For example, when a long-term care insurer obtains the health records of an applicant for long-term care insurance, what information should the insurance company be able to use in underwriting? Certain genetic factors (along with prior head trauma, alcoholism, and other factors) are known to predispose individuals to Alzheimer's disease. Naturally, higher costs are associated with the care of affected individuals. Results of genetic tests and whole-genome sequencing information increasingly will be contained in EHRs. If insurers are permitted to use the results of a genetic test or to require their own genetic testing, an at-risk individual is likely to be denied

coverage or be charged higher premiums, a situation that some would call 'genetic discrimination.' On the other hand, if long-term care insurers were prohibited from using genetic information, there is likely to be an adverse selection of applicants (at-risk individuals are more likely to apply for insurance) who will be charged higher premiums for long-term care insurance. As more individuals are unable to afford private insurance policies, and will be forced to receive long-term care services (e.g. nursing home care) under the government's Medicaid program, higher tax revenues will need to be generated as a result (Rothstein 2001). Thus policies for health information uses and disclosures involve more complicated and contentious issues than merely informational health privacy.

4.2.2 Social media

Despite their very recent conception, social media have become ubiquitous in society and play an important role in the lives of many. The archetypal social media giant, Facebook, was launched from a college dormitory room in 2004. By 2012, it had over one billion active users. Twitter, created in 2006, boasted over 200 million users by 2013 who sent more than one billion tweets every three days. Similarly, YouTube, founded in 2005, features millions of videos uploaded for free by users across the world. The privacy issues surrounding these forms of social media, such as the broad disclosure of highly sensitive matters, are well known and often debated in contexts besides the health privacy issues of this chapter (Leary 2011; Swire 2012).

Like social media sites, health-based sites are becoming extremely important as health education portals and information dissemination centers. Some sites combine both social and health information media. PatientsLikeMe is a social network designed to provide a forum for patients and their families to share their experiences and stories for the benefit of other patients. In addition to being a valuable, online support network, PatientsLikeMe provides information about treatment options, research, and local support groups. Many patients freely upload their personal health information in the hope it will benefit others or aid research efforts. The Internet has enabled population-based health activities as well, including the Personal Genome Project, which aims to recruit 100,000 individuals interested in sequencing their genome for research (Personal Genome Project 2013).

Social networks can be very effective in sharing health information quickly and effectively (Terry 2010), and can also be used for less formal communications. Some physicians and other healthcare providers now use social network technology to establish patient groups based on diagnosis or affiliation with a specific provider. On this point, a number of issues surface. First, there is a concern about the propriety of physician interaction with patients in an informal domain to discuss health issues. Opinion 9.124 of the AMA, 'Professionalism in the Use of Social Media,' provides that '[i]f [physicians] interact with patients on the Internet, [they] must maintain appropriate boundaries of the patient–physician relationship in accordance with professional ethical guidelines just as they would in any other context' (AMA 2013: 1). Second, patient populations differ in their computer savviness and access to technology. Thus the 'digital divide' can be seen as exacerbating health disparities (Brodie *et al.* 2000; Chang *et al.* 2004). Third, there is concern about the security of sensitive health information contained on certain websites, which can be vulnerable to hacking, and the lack of protection against third-party disclosure. It is important to note that neither the *HIPAA Privacy Rule* nor any other federal health privacy rule applies to social media.

Both social media (located on public access websites) and EHRs (private repositories) present a major problem for individual privacy. The information, once posted, 'never goes away'

(Rosen 2010). Because privacy for social media sites is not regulated in the same ways as for EHRs, for example, they have not systematically addressed the issue of removing information. In comparison, many state laws prohibit deleting or removing information from a health record, electronic or not (Center on Medical Record Rights and Privacy 2013). Such laws were enacted to prevent the alteration of health information in contemplation of medical malpractice litigation. Restricting access at the request of the patient, however, would seem not to violate these statutes (see section 4.2.1 above).

In 2012, the European Commission proposed the *General Data Protection Regulation*, a comprehensive package aimed at amending the Data Protection Directive of 1995 (see section 4.1.6 above). Of particular relevance to this issue, article 17 of the proposal creates the 'right to be forgotten and erasure' on the Internet. At the request of the subject of the information, the controller of the data which has made it public (e.g. website) has an obligation to remove personal information and also to inform third parties to erase any links to or copies of the personal data (European Commission 2012). Other proposals are also being developed to promote the idea of online 'obscurity' (Hartzog and Stutzman 2013).

4.2.3 Genetic privacy

Genetic privacy, a subset of health privacy, has received a great deal of attention since the launch of the Human Genome Project in 1990 (Alpert 2003; Rothstein 1997). Genetic privacy raises the question of whether privacy law, ethics, and policy ought to focus on specific types of health concerns (e.g. genetic information, mental health information) or should be more general. Thomas Murray, borrowing terminology from the 'HIV exceptionalism' debates of the 1980s, coined the term 'genetic exceptionalism' to refer to the argument that genetics raises such unique ethical and legal issues that it ought to be addressed separately from other health conditions or information (Murray 1997). Among the reasons why genetics was said to be different is that it has implications for reproduction, family members, and members of the same ethnic group; the immutable nature of genetic inheritance; the predictive capacity of genetic information for future health; historical misuse of genetics; and the distinction afforded to genetic information by many members of the public.

Even though most scholars, including Murray, have concluded that genetic exceptionalism is unwarranted (Hellman 2003; Lemmens 2000; Suter 2001), virtually all genetic privacy and antidiscrimination laws in America, both at the federal and state levels, have been genetic-specific or 'exceptional' laws. The simple explanation is that genetic laws are narrower and therefore more politically feasible than legislation addressing broader social problems (Rothstein 2005; Suter 2001).

Numerous state laws address genetic privacy and the use of genetic information in health insurance and employment (National Conference of State Legislatures 2013). At the federal level, the most important law is the *Genetic Information Nondiscrimination Act* 2008 (GINA). GINA was not a response to a wave of genetic discrimination, but rather an attempt to 'allay [the public's] concerns about the potential for discrimination, thereby allowing individuals to take advantage of genetic testing, technologies, research, and new therapies' (GINA 2008, § 2(5)). GINA has several shortcomings, including the following: (1) GINA only applies to health insurance and employment and does not prohibit genetic discrimination in life insurance, disability insurance, long-term care insurance, or other potential uses of genetic information; (2) GINA prohibits discrimination based on genotype, but not phenotype, thereby extending protection only to individuals who are asymptomatic; and (3) GINA prohibits employers from requiring or requesting an individual to undergo genetic testing or to disclose the results of a genetic test as a condition

of employment. However, there is currently no feasible way to segment genetic from nongenetic information in health records, such that only nongenetic information is disclosed in determining whether an individual has the ability to perform essential job functions. Taking into account these limitations, it can be said that GINA has a limited though salutary aim, and it is unclear whether it has achieved even its modest goal.

Looking beyond genetic testing in the legislative context, a somewhat unusual feature of genetic testing is that, at least in the United States, it is widely promoted by direct-to-consumer (DTC) companies. There are different types of tests performed (e.g. ancestry, health risk assessment) and there are different motivations for obtaining them (e.g. family health history, curiosity). All DTC testing uses a home collection kit, modern genetic testing technology, proprietary analytics, and customer review of results via password-protected Internet access. In the United States, the legality of DTC genetic testing depends on the law of the state in which the consumer lives: it is lawful in about half the states (American Society of Human Genetics 2007). Typically, DTC testing companies have privacy policies indicating that individually identifiable results will not be given or sold to any other party. DTC companies, however, are not covered entities under the *HIPAA Privacy Rule* and there is little federal oversight of their practices with regard to quality as well as privacy (American Society of Human Genetics 2007). A ruling by the Food and Drug Administration in 2013 cast great doubt on the future of DTC genetic testing.

Another unregulated type of genetic testing is nonconsensual testing. Because of the rapid advances in genetic technologies, it is possible to perform a genetic analysis using small amounts of DNA. Consequently, genetic testing can be performed using residues of DNA (e.g. in blood, saliva) on commonly used items (e.g. sheets, drinking glasses) or abandoned property (e.g. used chewing gum, cigarette butts). Under American law, individuals generally have no legal rights in 'abandoned' property and no reasonable expectation of privacy in the DNA specimens left behind as a result of normal daily activities. Several commercial enterprises have seized on this opportunity to offer genetic testing services on a wide range of materials without any informed consent or verified chain of custody (Rothstein 2009; Joh 2011). One common use of this type of testing is surreptitious paternity testing. Although the results are not admissible in court because of the lack of a chain of custody, the testing is often the first step in challenging paternity.

In contrast to the United States, the United Kingdom enacted the *Human Tissue Act* 2004, section 45 of which makes it unlawful for any individual, without proper consent, to possess any 'bodily material' with the intent to have DNA testing performed. There are exceptions for medical treatment, law enforcement, research, and other uses. Persons found guilty of violating the Act are subject to a fine, imprisonment for up to three years, or both (*Human Tissue Act* 2004, § 45(3)).

Genetic privacy serves to illustrate the types of specialized concerns likely to be associated with informational discoveries related to many other new technologies. For example, the successful sequencing of the human genome spawned a series of large-scale research undertakings in proteomics, transcriptomics, matabanomics, toxicogenomics, pharmacogenomics, epigenomics, and microbiomics. Each new application raises the issue of whether information generated by novel research methods should be regulated separately or under more general laws applicable to health information.

4.3 Conclusion

Privacy and confidentiality are essential components of modern, patient-centered healthcare. Patients expect their physicians and other healthcare providers to safeguard the confidentiality

of their sensitive health information, and to obtain the patient's permission for any nonroutine uses and disclosures. Without a reasonable expectation of confidentiality, many patients would be reluctant to disclose personal, often-sensitive, health information vital to appropriate care.

Despite widespread public support for privacy and confidentiality principles, legal protection, especially in the United States, is fragmented and inadequate. The primary national law on informational health privacy, the *HIPAA Privacy Rule*, is not comprehensive in application, contains numerous exceptions, and does not provide adequate remedies for individuals whose privacy has been violated.

Internationally, data protection laws typically have wider applicability than privacy laws in the United States because they are broader and reach both the public and private sectors. General provisions for transparency, data collection, heightened standards for sensitive information, enforcement, and oversight are also part of the data protection framework. The European Commission's proposed *General Data Protection Regulation* is a comprehensive legislative package that, if adopted, will apply to all European Union member states and establish more uniform and stringent protections.

Even as legal and ethical standards are still attempting to keep pace with modern healthcare, new developments in science and technology race ahead. This chapter has addressed three contemporary challenges. First, the shift from paper-based to electronic health records and systems will result in individual health records that are interoperable, comprehensive, and longitudinal. Healthcare providers, privacy experts, computer scientists, and policymakers are struggling to balance privacy with safety and efficiency in regulating access to and use of sensitive, electronic health information. Second, social media platforms, virtually all developed in the last decade, have allowed users to post vast quantities of personal information, including health information, voluntarily online. Social media therefore raise issues concerning the transparency of the website's privacy rules, information security, secondary uses of the information, and procedures to remove personal information from sites. Third, new clinical and research topics and methods, exemplified in genomics, involve analyzing large data sets of sensitive information. Thoughtful, nuanced regulation has proven to be elusive in many countries.

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5
Children

Ellen Wright Clayton

Providing medical care for children has several distinguishing features. The first is that most children lack the capacity to make healthcare decisions for themselves. This means that others, typically parents in consultation with the child's healthcare provider, must decide. At the same time, children usually develop greater capacities for decision-making as they mature and so can play a greater role in deciding about their healthcare as they get older. Another feature is that the government, exercising its power of *parens patriae*, intervenes more frequently to protect the interests of children than it does to protect those of adults. The result is a set of dynamic interactions, among parents, clinicians, the government, and the child, which is unique to pediatrics.

This chapter proceeds by addressing the United Nations *Convention on the Rights of the Child* 1989 (CRC), which lays out two critical frameworks: (1) the importance of promoting children's best interests in decisions that affect them; and (2) the need to create opportunities for children's views to be informed, to be heard, and ultimately for their decisions to be honored. The second section outlines some of the challenges that arise when the child's best interests may be compromised by the interests of others or where stakeholders disagree about the child's interests. The next section is devoted to exploring the roles of parents, clinicians, the state, and the child in healthcare decision-making, addressing, in particular, situations in which the various participants conflict. This discussion focuses primarily on the law of the United States but considers at length the *Gillick* case from the United Kingdom. The fourth section illustrates ways in which advances in technologies can challenge understandings of how the child's interests are to be promoted, using the case of exome and genome sequencing.

5.1 The United Nations Convention on the Rights of the Child

5.1.1 The role of the best interests of the child

The best interests of the child (BIC) is the framework most commonly used for decision-making. This standard applies because, unlike many adults who become incompetent, children, particularly when they are younger, have never had an established set of values that can form the

basis of substituted judgment. In the international *Convention on the Rights of Child*, which is the most widely adopted international convention,[1] rights and responsibilities are shared between parents, the state, and the child.[2] While parents typically make decisions on behalf of their children, the Convention provides rights of the child that can be asserted against parents, typically by the state. Article 3 of the CRC, which sets forth a framework for allocating this decision-making authority, states that:

> In all actions concerning children, whether undertaken by public or private social welfare institutions, courts of law, administrative authorities or legislative bodies, the best interests of the child shall be a primary consideration.
>
> *(1989)*

Close attention reveals that this article leaves room for interpretation. The use of the term 'a primary' implies that the BIC principle is 'not the only factor to be considered in the actions of institutions, authorities and administration' (UN Committee on the Rights of the Child 2009: para. 71) or even the only important one. Exactly what weight is due is debated. Hammarberg, for example, writes the BIC should be 'among the first aspects to be considered and … given considerable weight in all decisions affecting children' (2008: 5). Some worry that the BIC gives inappropriate weight to the child, at times to the child's detriment, as well as to the interests of the parents and the family (Iltis 2010; Cherry 2010). By contrast, others, including the World Medical Association (WMA) in its *Declaration of Ottawa on Child Health*, state that the child's best interest is the primary consideration (2009: General Principle 3a).

The UN Committee on the Rights of the Child, the enforcement body for the CRC, expanded upon the BIC in its General Comment No. 15 on the right of the child to the enjoyment of the highest attainable standard of health (art. 24) (2013) in which it interpreted the child's right to health as:

> an inclusive right, extending not only to timely and appropriate prevention, health promotion, curative, rehabilitative and palliative services, but also to a right to grow and develop to their full potential and live in conditions that enable them to attain the highest standard of health through the implementation of programmes that address the underlying determinants of health.
>
> *(2013: para. 2)*

The Committee went on to 'underscore the importance of the best interests of the child as a basis for all decision-making with regard to providing, withholding or terminating treatment for all children' (2013: paras 12–14), and directed states to develop criteria to help healthcare providers to determine the child's best interests.

With regard to the responsibilities of parents, the Committee opined that:

> Parents should fulfil their responsibilities while always acting in the best interests of the child, if necessary with the support of the State. Taking the child's evolving capacity into

1 The United States has signed, but not ratified this Convention and so is not bound by it. For a recent consideration of the United States' position, see Bartholet (2011).

2 I am heavily indebted to Ma'n H. Zawati, David Parry and Bartha Maria Knoppers for their analysis of international law in 'The Best Interests of the Child and the Return of Research Results: International Comparative Perspectives,' submitted to *BMC Medical Ethics* for publication.

> account, parents and caregivers should nurture, protect and support children to grow and develop in a healthy manner …
>
> *(2013: para. 78)*

The Committee later discussed at length the many ways that parents can and should shape the child's health and development and urged states to assist parents in these endeavours (2013: para. 67).

5.1.2 The rights of the child to be heard, to be informed, and to make their own decisions

Complementing its discussion of BIC, the UN Committee on the Rights of the Child also addressed the role of the child, insisting on the right of children to be heard as a general principle (2009: para. 74). Article 12 of the Convention, which for the first time codified this right, reads:

> States Parties shall assure to the child who is capable of forming his or her own views the right to express those views freely in all matters affecting the child, the views of the child being given due weight in accordance with the age and maturity of the child … (1989)

The UN Committee insisted that children have the right to information (2013: para. 13) and should be presumed to have the capacity to form their own views (2009). The right of children to express their views, embodied in article 12, has three elements: they must be allowed to decide whether they want to speak (UN Committee on the Rights of the Child 2009: paras 35–42); if they do wish to speak, they must be free from undue pressure (Lücker-Babel 1995); and finally, according to the UN Committee on the Rights of the Child's statement in 2013, children's views should be 'seriously taken into account, according to age and maturity' (para. 19). As a result, sufficiently mature adolescents may be able to provide adequate consent for their own healthcare. The Committee expanded upon the state's obligation to honor the developing capacity of the child, explaining that:

> In accordance with their evolving capacities, children should have access to confidential counselling and advice without parental or legal guardian consent, where this is assessed by the professionals working with the child to be in the child's best interests … States should review and consider allowing children to consent to certain medical treatments and interventions without the permission of a parent, caregiver, or guardian, such as HIV testing, sexual and reproductive health services, including education and guidance on sexual health, contraception and safe abortion.
>
> *(2013: para. 31)*

The Committee has been more ambivalent about preserving adolescents' confidentiality. In a report focused on adolescent health, the Committee concluded that confidential 'information may only be disclosed with the consent of the adolescent, or in the same situations applying to the violations of the adult's confidentiality' (UN Committee on the Rights of the Child 2003: para. 7), but later stated that such information can be disclosed to parents if it is in the child's best interests (para. 28). Nonetheless, the picture that emerges from the discussion of BIC and of the child's participation in decision-making is child-centered, with the interests of parents playing a secondary role.

5.2 Challenges to the best interests of the child in clinical practice

The best interests of the child, while clearly elevated above those of the parents in the CRC, at times may be redefined or even subordinated in order to accommodate other interests. This conflict of interest is perhaps most obvious when one child is a potential donor of a kidney or bone marrow to his or her sibling, procedures that pose risks to the donor. The cases that most frequently reached court were those in which the potential donor is developmentally delayed or quite young. In many cases, courts in the United States objected to the procedure, concluding that it was not in the donor's best interest (see, for example, *Curran* v. *Bosze,* 566 NE 2d 1319 (1990)), or exceeded the court's authority (*In re Richardson*, 284 So.2d 185 (1973)). The few courts that permitted the donation did so specifically on the ground that the benefit to the *donor* from the survival of the sibling/organ recipient was so great that it outweighed the risks to the donor of the procedure to harvest the organ, recasting organ donation as a primary benefit to the donor. (See, for example, *Little* v. *Little*, 576 S.W.2d 493 (1979); *Hart* v. *Brown*, 289 A.2d 386 (1972)).

Another area where questions can arise about the BIC and from whose perspective it is assessed is childhood immunizations, which are required to protect the child and others from a wide array of communicable diseases. Some parents, however, feel that their children's best interests are compromised by state immunization requirements, reasoning that their child's risk of contracting the disease does not warrant exposure to the perceived risks of vaccines.[3] These differences in understanding of 'best interest' have led to enormous controversy.

In the discussion that follows, which will focus on US law while making some comparisons to the laws of other countries, we will examine the roles of parents, clinicians, the state and the child in making healthcare decisions for minors to address the extent to which legal systems protect the best interests of the child and their rights to health, to be heard, and to decide.

5.3 Who decides about the healthcare of children?

5.3.1 The role of parents

Parents are literally the primary care providers for their children. Parents decide, after all, whether to give chicken soup and an antipyretic to an ailing child or whether to take the child to the clinician for care. In addition, even if the child is seen by a healthcare provider, most medications are delivered in the home, whether by the parent or by the child, in the latter case often with parental supervision. More generally, parents are thought to be most likely to act in their child's interest and, in accordance with the classic liberal tradition (Ross 1998), are given broad deference in how they raise their children. This presumption of deference to parental decision-making in many domains, including healthcare, is deeply embedded in US law, embodied in such federal constitutional cases as *Meyer* v. *Nebraska,* 262 US 390 (1923), *Pierce* v. *Society of Sisters,* 268 US 510 (1925), *Prince* v. *Massachusetts,* 321 US 158 (1944), *Wisconsin* v. *Yoder*, 406 US 205 (1972), and *Parham* v. *J.R.*, 442 US 584 (1979). Within this domain, parents are not required to focus solely on the best interest of the child, but rather may, and often do, take into account competing needs and goals. Other countries which have ratified the CRC also acknowledge deference to parents in childrearing (UN Committee on the Rights of the Child 2001: para. 217; UN Committee on the Rights of the Child 2002: para. 58).

3 The issue of religious objection to immunization is addressed in section 5.3.4 below.

5.3.2 The role of the clinician

Parental discretion, however, is not unlimited. In responding to parental requests for medical care, the United States Supreme Court in *Parham* noted that in earlier decisions, the Court had 'asserted that parents generally have the right, coupled with the high duty, to recognize and prepare [their children] for additional obligations [cits. om.]. Surely, this includes a "high duty" to recognize symptoms of illness and to seek and *follow* medical advice' (1979: 602; emphasis added). Nor are parents able to obtain whatever medical interventions they desire. Many medical interventions, such as prescription medications and many diagnostic procedures, are available only on physician's orders. In *Parham*, for example, parental requests for commitment of their children were subject to physician approval. This type of physician control, of course, is applicable to the healthcare of both adults and children. From an ethical perspective, however, the focus on the best interest of the child provides the clinician with greater discretion than is warranted in the care of competent adults, where the guiding values of the individual patient have greater weight.

Legal issues typically arise only when parents do not agree with the clinician on a course of care. In such cases, a variety of responses may be appropriate. In cases where the course of care desired by the parents is adequate, even if not the one preferred by the clinician, the healthcare provider can simply defer to the parents' wishes. If the physician is unwilling to accede, then he or she must effectively terminate the physician–patient relationship in order to avoid liability for abandonment and, in most cases, help the family to find another healthcare provider.

5.3.3 Medical neglect and state intervention

Things become more complex when clinicians reasonably believe that the parents' failure to provide recommended care poses a threat of substantial harm to the child. All states have laws requiring that clinicians report such suspicions of 'medical neglect.'[4] If the state agency concludes that this level of harm will occur more probably than not, the state may go to court seeking an order to intervene to protect the child. If the court agrees, it has a variety of tools available, ranging from simply ordering treatment to removing the child from the home as a last resort. Issues of medical neglect most commonly arise when parents fail to deliver the ongoing care for a child with a chronic medical condition such as cancer (*Jensen* v. *Cunningham* 250 P.3d 465 (2011), diabetes (*In re Shawndel M* 824 NYS 2d. 335 (2006), or cystic fibrosis (*In Re Stephen K* 867 NE2 81 (2007). These cases are particularly challenging since ensuring treatment may require removing the child from the home, a disruption that may harm the child in other ways, as well as profoundly affecting the remaining family. Concerns about medical neglect also arise when parents fail to seek medical care for an acute illness or injury (see *Walker* v. *Superior Court* 763 P.2d 852 (1988) (failure to seek care for child with meningitis).

5.3.4 Parental religious objection

Parents often object to medical interventions on religious grounds. Examples include the Old Order Amish who refuse state-run newborn screening and immunizations, Christian Scientists who refuse all allopathic medical treatment, and Jehovah's Witnesses who refuse blood products. The Nixon administration briefly required states to enact statutes allowing people to opt out of medical care for religious reasons as a condition of receiving federal funds for Medicaid, the insurance program for the poor. As a result, most states enacted statutes allowing parents to refuse

4 Not all countries respond to medical neglect in the same way. See, for example, Ertem *et al.* (2002); Raman and Hodes (2012); Pinnock and Crosthwaite (2005).

some medical interventions for their children for religious reasons, statutes that have largely remained in place despite the fact that the federal requirement was quickly rescinded.

The state religious objection laws vary significantly in their language, with some written to apply to only one or two established religious groups (e.g. New Hampshire Statutes §169-C:3. XIX.(c) 2013; Colo. Rev. Stat. Ann. § 19-3-103(2) (2013)), while others are quite broad and extend to conscientious or philosophical objection even in the case of public health emergencies (e.g. Ore. Rev. Stat. § 431.264(2)(d) (2013); Maine Rev. Stat. 22 § 820.1.B.(3)(a) (2013)). Many statutes address specific topics, such as newborn screening and immunizations, while others apply to medical care generally.

Although an important function of these laws is to ensure that parents who follow their religious beliefs in refusing medical care for their children are not deemed neglectful, their freedom to refuse care for religious reasons, however, is not unlimited. Nor is the state powerless to intervene to protect the child from serious harm, despite the parents' religious beliefs. Alabama, in its provision dealing with parental objection, states:

> (a) … This exception [for parental religious objection] shall not preclude a court from ordering that medical services be provided to the child when the child's health requires it.
> (b) The department may, in any case, pursue any legal remedies, including the initiation of legal proceedings in a court of competent jurisdiction, as may be necessary to provide medical care or treatment for a child when the care or treatment is necessary to prevent or remedy serious harm to the child, or to prevent the withholding of medically indicated treatments from infants with disabilities and with life-threatening conditions.
>
> *(Alabama Code § 26-14-7.2 (2013))*

Colorado's statute provides that 'the religious rights of a parent, guardian, or legal custodian shall not limit the access of a child to medical care in a life-threatening situation or when the condition will result in serious disability' (Colo. Rev. Stat. Ann. § 19-3-103 2013). Provisions such as this put the parents at risk if they do not seek medical attention once the child becomes seriously ill, whether they recognize the seriousness of the situation or not. A number of cases over the years have addressed the question of whether parents can be criminally liable for failing to seek and provide medical care for their children for religious reasons, despite the presence of exemptions within the child protection laws. (See, for example, *Walker* v. *Superior Court*, 763 P.2d 852 (1988); *State of Wisconsin* v. *Neumann*, 832 NW 2d 560 (2013) (upholding convictions). But see *Hermanson* v. *State of Florida* 604 So.2d 775 (1992) (striking down conviction); *Commonwealth* v. *Twitchell* 617 NE 2d 609 (Mass. 1993) (striking down convictions but permitting prosecution of cases in the future).)

5.3.5 The ability of the minor to make their own choices about medical care

The general rule is parental permission is required for medical evaluations and treatment of minors. Failure to obtain this permission in the absence of a medical emergency can give rise to a claim for both the parent and the child for battery, that is unconsented touching of the child (*Bonner* v. *Moran*, 126 F.2d 121 (1941); *Rogers* v. *Sells*, 61 P.2d 1018 (1930); *Miller* v. *HCA, Inc.,* 118 S.W.3d 758 (2003)). Under a number of circumstances, however, the law permits minors to make their own healthcare choices.

The United States Constitution protects healthcare decision-making by minors about a narrow range of issues, providing them with rights to choose contraception (*Carey* v. *Population*

Services International, 431 US 678 (1977)) and to some extent abortion without parental permission (*Bellotti* v. *Baird,* 428 US 132 (1976); *Bellotti* v. *Baird*, 443 US 622 (1979)).[5] Statutes, therefore, are a major source of minors' rights to make other healthcare decisions. All states have laws allowing minors to obtain certain types of medical care without parental permission (English *et al.* 2010). These frequently include treatment for drug and alcohol abuse, mental health, and pregnancy, which generally accords with the UN Committee on the Rights of the Child's recommendations (2013: para. 31). States may also allow minors who have attained a certain status to make all healthcare decisions on their own, although states vary dramatically in their criteria for which minors qualify. Some of the qualifying events are marriage, emancipation, living independent and apart, enlistment in the military, pregnancy, and parenthood.

Common, or judge-made, law is the primary source of the 'mature minor' exemption to the requirement of parental permission (Slonina 2007). This doctrine allows clinicians under certain circumstances to rely on the consent of minors for clinical interventions, protecting clinicians from liability in the case of parents whose permission was not sought or of minors who subsequently want to disaffirm their prior consent to treatment. This doctrine is most often invoked in cases involving an older teen who has decision-making capacity and where the care provided was within the mainstream, met the standard of care, and was not high risk (English *et al.* 2010). Few states have specifically rejected this doctrine, but a small number of states have passed statutes essentially codifying the mature minor doctrine, allowing minors to give effective consent if they are above a certain age or have 'sufficient intelligence to understand and appreciate the consequences of the proposed surgical or medical treatment or procedures' (*Arkansas Code Ann.* § 20-9-602(7) 2010).[6]

5.3.6 Confidentiality

Confidentiality is often important to minors who are making their own healthcare decisions. The *Health Insurance Portability and Accountability Act* of 1996 (HIPAA), the primary federal law addressing confidentiality, relies primarily on state law and regulation for guidance. In this regard, some states protect the child's confidentiality more completely than others. Some states provide clinicians with discretion, for example, to notify the child's parents in certain situations. HIPAA does require that the child's confidences be honored when parents agree that their child's relationship with the clinician will be confidential (Office for Civil Rights HIPAA 2003, Personal Representatives 45 CFR 164.502(g)). Some institutions deny access to health records to both parents and minors to avoid problems.

5.3.7 *The* Gillick *case*

In a much more expansive decision than is embodied in the US mature minor doctrine, the House of Lords addressed the question of the role of minors and parents at length in the case of *Gillick* v. *West Norfolk and Wisbech Area Health Authority* 3 All ER 402 (1985), which addressed the question of whether a mother could prevent her daughter under the age of 16 from obtaining contraception.

5 States, however, may require that the child's request be reviewed by a judge.

6 See also *Alabama Code* § 22-8-4 (2013)('14 years of age or older, or has graduated from high school, or is married, or having been married is divorced or is pregnant'); *Alaska Stat.* § 25.20.025(a)(2) (2013) (if parents unavailable or unwilling to give permission); *Kansas Stat. Ann.* § 38-123b (2013) (16 years old if parent not readily available); *La. Rev. Stat. Ann.* § 40:1095 (2013) (limited to a minor 'who is or believes himself to be afflicted with an illness or disease'); *Oregon Rev. Stat.* § 109.640 (2013) (15 years old); *South Carolina Code Ann.* § 63-5-340 (2013) (16 years old but can consent to surgery 'only if such is essential to the health or life of such child in the opinion of the performing physician and a consultant physician if one is available').

At the time, applicable law encouraged physicians to urge minors to involve their parents in such decisions, but recognized that in some 'unusual' cases, it could be necessary to protect minors' confidentiality in order to encourage them to seek care. In a complex opinion, Lord Fraser held that:

> Provided the patient, whether a boy or a girl, is capable of understanding what is proposed, and of expressing his or her own wishes, I see no good reason for holding that he or she lacks the capacity to express them validly and effectively and to authorise the medical man to make the examination or give the treatment which he advises.
>
> *(pp. 6–7)*

In regard to the mother's claim that her parental rights were infringed by allowing her child to obtain medical care without her consent, Lord Fraser held that 'parental rights to control a child do not exist for the benefit of the parent. They exist for the benefit of the child and they are justified only in so far as they enable the parent to perform his duties towards the child, and towards other children in the family' (p. 8). He explicitly rejected the notion that the child's age is the only factor to be considered or that the parent has an absolute right of veto, even saying that, at times, physicians are better decision-makers.

Lord Scarman, in a separate opinion, wrote '[t]he principle of the law … is that parental rights are derived from parental duty and exist only so long as they are needed for the protection of the person and property of the child' (p. 22), citing 'the law's recognition of the parent as the natural guardian of the child [as] a warning that parental right[s] must be exercised in accordance with the welfare principle and can be challenged, even overridden, if it be not' (p. 22). Lord Scarman ultimately held that:

> as a matter of law the parental right to determine whether or not their minor child below the age of 16 will have medical treatment terminates if and when the child achieves a sufficient understanding and intelligence to enable him or her to understand fully what is proposed … Until the child achieves the capacity to consent, the parental right to make the decision continues save only in exceptional circumstances. Emergency, parental neglect, abandonment of the child or inability to find the parent are examples of exceptional situations justifying the doctor proceeding to treat the child without parental knowledge and consent but there will arise, no doubt, other exceptional situations in which it will be reasonable for the doctor to proceed without the parent's consent.
>
> *(p. 27)*

Two Lords dissented in large part on the grounds that intercourse with a female under the age of 16 was a crime at the time. Concern that females under 16 were not competent to make a decision about contraception suggested that their primary concern was about sexual activity and not decision-making *per se*. Thereby, little emphasis was placed on the impact on parents' rights in these dissenting opinions.

5.4 Emerging ethical and legal issues

New technologies affect our understanding of the best interests of children and how and by whom those are to be protected. In this section, we will discuss developments in genetics and genomics as an example of these effects. Not only is more understood about the role genetic

variation plays in health, but new technologies, such as multiplex testing and exome and genome sequencing, make it possible to assay much more of this variation at one time. In pediatrics, the question of what tests should be done typically arises in state-run newborn screening and in testing symptomatic children more generally. Until recently, there has been a general consensus that the goal of genetic testing was to provide information that would assist in the children's immediate care. In newborn screening, this has meant disorders should be screened only if near-term treatment is required, and in testing of the child after the newborn period that it is generally inappropriate to test for adult-onset disorders that do not require intervention prior to adulthood (Ross *et al.* 2013; van El *et al.* 2013).

Recently, however, the American College of Medical Genetics (ACMG) directly challenged the centrality of the child's best interests and delicate balance of decision-making when they recommended that laboratories that are performing genome or exome screening for a particular clinical condition analyze an additional 56 genes that are not implicated in the clinical question and return results to the ordering clinician who is then responsible for 'contextualizing' the results for the patient (Green *et al.* 2013). The ACMG recommended that neither patients, regardless of age, nor in the case of children, their parents be given the opportunity to reject this extra analysis, even though some of the variants sought are predictive only of adult-onset disorders.

Although the ACMG subsequently rejected mandatory testing and return, it never addressed the best interests of the child (ACMG Update Recommendation, 2014). Rather, they were concerned that patients and family members may not otherwise have the chance to learn of their own risks if children's results were not returned. In the case of children, this means that children's interests are only one factor to be considered and may be secondary to the interests of parents and other relatives. This formulation flies in the face of the definition of the child's best interests in the *Convention on the Rights of the Child* as well as general norms of decision-making for children, and is particularly surprising given the weak support of a 'duty to warn' of genetic risk in US jurisprudence. At this point, the ACMG's recommendations regarding exome and genome sequencing have no independent legal weight and raise legal issues only insofar as they influence clinicians' practice and thereby the standard of care. A potential concern, however, is the ACMG's redefinition or subordination of the child's interests to those of parents and other relatives may be expanded to state-run newborn screening programs, which are under pressure to use exome and genome analysis. The challenge, ethically and legally, will be ensuring the primacy of the child's interests in the face of these and other new technologies.

5.5 Conclusion

While promoting the best interests of the child is a governing framework in pediatric ethics, implementing this principle in practice remains a challenge. Jurisdictions vary in allocating who decides the best interest of the child. In general, parents are the default decision-makers, but both clinicians and the government can override parental choices in areas ranging from medical abuse or neglect to public health interventions such as immunizations. Jurisdictions also vary in the extent to which they honor the rights of minors to participate in or to make their own healthcare decisions as rights-bearing individuals, a discourse parallel to the debate about best interests. New technologies present challenges for the interests of children as well. Understanding these tensions may guide the evolution of laws to ensure more adequate protection of children's interests.

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6
Disability

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6.1 Introduction

Why devote a chapter to disability in a handbook on *medical* law and ethics? It is increasingly recognised that a disability, however defined, cannot automatically be equated with a medical condition, let alone a disease. Instead, a disability is an 'infinitely but various feature of the universal condition' (Bickenbach 1999: 112) that may arise from a health condition, age or an injury at a certain point in life and leads to long-term impairments. The United Nations *Convention on the Rights of Persons with Disabilities* (CRPD) 2006 embraces the latter approach and serves as a comprehensive human rights instrument that establishes a wide array of rights for persons with disabilities that also impact medical law and ethics.

Nonetheless, people with disabilities are and remain victims of human rights violations, both within and outside the healthcare sector. Various studies demonstrate that the right not to be discriminated against, as well as the right to (individual or personal) autonomy,[1] are often neglected (Sapey 2010; Bach and Kerzner 2010; Koch 2009). These and other human rights violations affect the health and access to healthcare of people with disabilities (Krahn *et al.* 2006; Department of Health and Human Services (HHS) Advisory Committee on Minority Health 2011). According to the World Health Organization (WHO) (2012), '[p]eople with disabilities have less access to healthcare services and therefore experience unmet healthcare needs' (p. 1). They experience poorer levels of health than the general population, and they may 'experience greater vulnerability to preventable secondary conditions, co-morbidities, and age-related conditions' (WHO and World Bank 2011: 10). They are also at higher risk of being victims of violence. As a result, the world is witnessing disability-related health disparities, leading to ill health, the denial of sexual and reproductive health (rights), substandard healthcare, unnecessary institutionalisation, violence and premature death (Yee 2011). Disability is thus also a medical law and ethical issue deserving attention in this book.

Before turning to the relevant legal and ethical theories, and exploring the rights, principles and issues most prominent in the interrelationship between disability on the one hand and

1 Instead of 'autonomy', the term 'self-determination' is often used. These terms are mostly used interchangeably. To stay as close as possible to the CRPD and the case law of the European Court of Human Rights (ECtHR), we use the term (personal or individual) 'autonomy' in this chapter.

medical law and ethics on the other, we will briefly discuss the various meanings of the term disability, and the way this concept was finally defined in the CRPD. In this chapter, we pay special attention to the human rights of persons with disabilities, as defined under the CRPD, within the context of healthcare, and the implications of these rights for medical professionals. Due to the fact that this book entails a separate chapter on mental health, we will not embark on the human rights of people with mental disabilities (see Chapter 7).

6.2 Definition of disability

Disabilities have traditionally been defined in terms of physical, mental, intellectual or sensory deviations from normality caused by disease, trauma or other health conditions. This reflects the deep-rooted idea that people with disabilities are unhealthy and in need of medical aid. In other words, disability is seen as a problem, one that is inherent to an individual and that needs to be addressed by medical professionals. In the past, healthcare was thus seen as a means to enable people with disabilities to live a humane and dignified life. In addition, and of particular importance from a medical law and ethical perspective, healthcare decisions were made for, but not by, people with disabilities. The concept of 'informed consent', a leading principle in medical law and ethics (Faden *et al.* 1986; Manson and O'Neill 2007), was thought not to be relevant for people deemed unable to make autonomous decisions. As a result of judgments by courts, and more often informally, people with disabilities were treated as lacking the capacity to make decisions for themselves and as not entitled to autonomy.[2]

This medical model of disability – portraying people with disabilities as persons with problems, objects of care and recipients of welfare – has been harshly criticised over the last few decades (Percy 1989; Barnes 1991; Finkelstein 1990). According to the medical model, a disability essentially denotes an inability to function in the conventional way due to a defect. It was recognised that, although such an impairment can be inherent (such as a patient suffering from a neurodegenerative disease affecting his or her cognitive competences), this is not always the case. Impairments can also be the result of an external factor that has no relationship with medicine at all, like an accident that results in a leg amputation which leads to impaired mobility. As such, not all disabilities are necessarily medical.

Proponents of the social model of disability argue that the problems of disability should not be centred on individuals, as medically inspired disability programmes are. Rather they should refer to the interaction between individuals and their environment. In fact, many obstacles faced by those with disabilities are imposed and exacerbated by the physical and social environment, often designed by able-bodied persons who fail to take into account the needs of differently abled persons. Therefore disability is not merely an individual characteristic, but a social construct that reflects the systematic denial of human rights to a group of individuals deemed less able to function in our society due to individual impairments. Disability and human rights scholars argue that healthcare is used as an instrument to negatively label people with disabilities, withholding them from participating in society as equals, and hindering efforts to bridge the gap between disabled and able-bodied persons (Krahn and Campbell 2011).

So-called social constructionists demand the breakdown of barriers inhibiting people with disabilities from participating equally in society – a demand clearly echoed in the 2001 'International Classification of Functioning, Disability and Health' [ICFDH] (Taket 2012). Despite these demands for equality, policymakers, legislators and the public at large still widely believe that preventive, curative and rehabilitative healthcare measures are the best remedies to

2 See, for example, Lewis (2012).

reduce the adverse impact of impairments on differently-abled persons (Borg, Lindström and Larsson 2009). Much to the regret of disability and human rights scholars, disability continues to be perceived as a medical and healthcare issue (Shakespeare 2012). Furthermore, medicalisation is feared to threaten the dignity of people with disabilities and justify the discrimination they experience on a daily basis, as opposed to offering a means to strengthen and ensure the equal enjoyment of human rights.

This fear is reflected in the CRPD. After long debates at the United Nations,[3] it was finally recognised that people with disabilities are entitled to full and equal human rights, despite much resistance among representatives of many states to introduce new 'disability-specific' rights. The decision to include a definition of disability in the CRPD was also a point of contention among its drafters. Opponents argued that any definition would prevent the CRPD from adequately protecting the rights of disabled groups and persons who are most at risk.[4] For this reason, in combination with the express difficulty of establishing what precisely constitutes a disability, the law of the European Union does not include a definition. Moreover, there were also fears that the absence of a definition in the CRPD would allow state parties to adopt strict definitions of disability, possibly denying many people with disabilities protection under the CRPD on a national level (Trömel 2009: 121). Others were concerned that the absence of a definition would impose costly obligations on states to accommodate differently-abled persons in education, housing, employment and healthcare, and therefore favoured its inclusion (Quinn 2009: 102). As a compromise, states agreed to an open-ended definition, stating 'persons with disabilities *include* those who have long-term physical, mental, intellectual or sensory impairments which in interaction with various barriers may hinder their full and effective participation in society on an equal basis with others' (CRPD, article 1). This refers to the group that should at least be protected under the CRPD on a national level. It is important that this definition does not build on a medical model but rather embraces the social approach to disability. Although the nature of the impairment is not emphasised, the CRPD definition draws attention to problems that may occur 'in interaction' between impairments and environmental barriers.

It should be noted that the CRPD definition purposefully states that impairments should be 'long-term'. Such delineation was included to allow states to confine entitlements, such as to social security, additional healthcare insurance, protection against dismissal and the right to personal assistance, to persons with particular impairments.

Prior to the adoption of the CRPD, the question of whether persons who were absent from work due to sickness were entitled to the same level of protection as people who were unable to work due to a disability emerged. According to the European Court of Justice (ECJ), this was not the case: '… by using the concept of "disability" in Article 1 of that directive, the legislature deliberately chose a term which differs from "sickness". The two concepts cannot therefore simply be treated as being the same' (*Chacón Navas* v. *Eurest Colectividades* [2006], ECR I-6467, para. 2). Building on the medical model of disability, the ECJ held that a disability was a medical condition more serious than a sickness. The ECJ thus did not pay attention to the fact the reactions of others to a condition, ranging from fear to hostility, can be as disabling as the condition itself. After the EU acceded to the CRPD in 2010, the ECJ adapted its case law and embraced a combination of the medical and social models. Also the long-term nature of an impairment recognised by the ECJ is now sufficient to determine whether a person is entitled to the protection

3 See, for example, Quinn (2009) and Trömel (2009).

4 On this issue see the judgment of the European Court of Justice in *Coleman* v. *Attridge Law and Steve Law* [2008] Case 303/06, ECR I-5603.

bestowed to persons with disabilities under the CRPD (joined cases C-335/11 and C-337/11 *HK Danmark (Ring and Skouboe Werge)* decided on 11 April 2013 and *European Commission* v. *Italy* (case C-312/11) decided on 4 July 2013).

To conclude, though disabilities are – at least from a human rights perspective – no longer defined in terms of mere individual or medical conditions, it is still often thought that 'the solution' to the obstacles encountered by people with disabilities in daily life lies in the medical domain, by treating the disabled individual. Like everyone else, people with disabilities have healthcare needs that may be related or unrelated to their impairments. The latter brings to the fore questions of access, how healthcare is guaranteed to persons with disabilities and how medical professionals treat people with disabilities within the healthcare sector.

6.3 Legal and ethical theory

6.3.1 From ethics to law

Medical law and ethics are both normative disciplines focused on human conduct in the field of healthcare. Different from evidence-based sciences, they do not analyse, describe, comprehend or predict human conduct, but seek to prescribe what individuals should do based on what is considered a form of morally good treatment. The focus of medical law and ethics is on the conduct of medical professionals towards patients.

Since the times of Aristotle, it has been believed that medical professionals should abide by standards of ethical behaviour. These standards, or principles, were meant to inspire and regulate professional conduct. Compliance with these standards was deemed indispensable to guarantee professional behaviour and instil public confidence in the medical profession. Members of the profession themselves defined these standards and their contents. Medical ethics is thus a form of self-regulation, for and by members of the medical profession.

The dominant standards of medical ethics were later summarised into four principles: respect for autonomy, beneficence, non-maleficence and justice (Beauchamp and Childress 2013). These principles were referenced in many professional codes of conduct, both nationally and internationally, and equally applied to medical professionals when caring for 'patients' and 'persons with disabilities', however defined (Blustein 2012).

However, these principles leave considerable room for interpretation and make it difficult to determine a universally ethical action for a medical professional in any specific case. Moreover, ethical principles cannot be enforced by (invoking the power of) the state. Rather, they are supposed to be morally binding on members of the professional group.

The atrocities committed in the Second World War, among others, against patients and research subjects with disabilities displayed the shortcomings of medical ethics (Wolfensberger 1981; Annas and Grodin 1995). In response, efforts to draft treaties and establish other legal standards for regulating the behaviour of medical professionals were introduced in the 1950s and 1960s. The focus of these laws and other legal instruments centred on protecting people with disabilities, the underlying assumption being they are unable to exercise their own autonomy.[5] The ethical principle of justice was thus equated with protection inspired by non-maleficence (from the perspective of non-disabled persons), and denied people with disabilities

5 See, for example, the *Declaration on the Rights of Mentally Retarded Persons* (UN General Assembly 1971: 93) and *Recommendation No. R(99)4 of the Committee of Ministers of the Council of Europe on Principles Concerning the Legal Protection of Incapable Adults* (Council of Europe 1999).

freedom of choice and other equal opportunities. The shift from non-enforceable medical ethics to legally binding medical law, in an effort to strengthen the ethical principles and make them enforceable, could not mask the fact that little attention was being paid to beneficence from the perspective of disabled persons, self-determination by persons with disabilities and non-discrimination.

6.3.2 From pity and charity to human rights

Medical law emerged in the 1950s and 1960s in response to the shortcomings of medical ethics and the lack of enforceable legal standards that would regulate the provision of healthcare compatible with human rights law. Like medical ethics, medical law was first primarily concerned with professional conduct and not with the rights of healthcare recipients, including persons with disabilities. This approach was akin to most of the laws applying to persons with disabilities, who were portrayed as unable to generate incomes and thus in need of welfare. The urge to assist people with disabilities often reflected pity, a self-defined form of beneficence, instead of respect for autonomy (Shapiro 1993). This was particularly true for war veterans (Anderson 2011). It was felt that these patriots, who became disabled while fighting to protect the rights and freedoms at home, were most deserving of compensation. Quota systems were introduced to ensure veterans gained access to employment and better treatment options (Waddington 1996). Introducing quota systems and other forms of segregated treatment for war veterans and other people with disabilities was not considered a breach of the right to equal treatment. It was simply argued that war veterans and other people with disabilities were not the same as others and therefore not always entitled to the same treatment. This notion of equality, where no attention is paid to the context and where in actual fact inequality is perpetuated, is known as formal equality (Ventegodt Liisberg 2011: 23; Hendriks 1995).

It was not until the late 1960s and 1970s that people with disabilities complained about these institutionalised forms of pity and charity, and asserted their human rights, notably the right to be treated as equals (Iezzoni and Long-Bellil 2012: 137). Working in sheltered workplaces, enrolling in separate schools and living in institutions became increasingly seen as methods of exclusion and discrimination. It was also acknowledged that by treating people with disabilities like others, not protecting them against discrimination and only providing them with segregated forms of different treatment, justified by the formal equality model, discouraged integration and inclusion in society. Instead of the formal equality model, a different approach to equality emerged – known as material or substantive equality – that would take into account the context of a person and historical disadvantages, and would be less concerned about the form of treatment but primarily look at its outcomes. As a result, it was acknowledged that treating disabled persons the same as others, not taking relevant factors into account, could constitute discrimination whereas forms of different treatment were not necessarily regarded as incompatible with the prohibition of discrimination (McLean and Williamson 2007). To the contrary, certain forms of different treatment were regarded as indispensable in efforts to contribute to more equality (Hendriks 1995: 40–62).

It took many decades before the call for equal rights for people with disabilities was echoed at the international level, ultimately leading to the adoption of the CRPD in 2006 (Quinn 2009: 93–9). This Convention is based on a number of general principles, including the principles of autonomy and free choice, equality, respect for difference and non-discrimination, participation, inclusion and accessibility (CRPD, article 3). Different from the four ethical principles mentioned above, the human rights principles underlying the CRPD stress the need to also take difference into account, as well as the need to break down barriers that prevent people from participating as equals in society.

As previously mentioned, the drafters of the CRPD did not intend to introduce 'disability-specific' rights. At the same time, it becomes clear from reading the CRPD that its drafters were well-aware that free choice, participation, inclusion and accessibility remained unachievable for many persons with disabilities as long as their human rights were interpreted from the perspective of formal equality. A material equality approach to the rights of people with disabilities is reflected in the general obligation to provide 'accessible information' (CRPD, article 3), to ensure the provision of 'reasonable accommodation' (CRPD, article 5), to raise awareness and combat stereotypes (CRPD, article 8) and to ensure access to the physical environment (including to 'medical facilities'), to transportation and to information and communications (CRPD, article 9). It can therefore be argued that the main goals of the CRPD are to promote the autonomy and equal rights of people with disabilities, instead of confining the goal to protecting people with disabilities against themselves, and in this way preventing these persons from participating in the life-world. Before examining the CRPD's provisions with respect to medical law and ethics, we set out some of the CRPD's foundational concepts, namely disability-based discrimination and autonomy.

6.4 Discrimination

6.4.1 Definition

According to the CRPD, state parties are obliged to prohibit all forms of discrimination on the basis of disability and guarantee to persons with disabilities equal and effective legal protection against discrimination on all grounds (CRPD, article 5(2)). This material provision has been modelled after similarly worded provisions in other human rights treaties. It is also seen as elaborating on the general principle of non-discrimination underlying the CRPD (CRPD, article 3(b)). But what is meant by discrimination?

Article 2 of the CRPD sets out that 'discrimination on the basis of disability' is a term covering

> any distinction, exclusion or restriction on the basis of disability which has the purpose or effect of impairing or nullifying the recognition, enjoyment or exercise, on an equal basis with others, of all human rights and fundamental freedoms in the political, economic, social, cultural, civil or any other field. It includes all forms of discrimination, including denial of reasonable accommodation.

This description is almost identical to the one contained in article 1, paragraph 1 of the *International Convention on the Elimination of All Forms of Racial Discrimination* (1965). It is important to note here that discrimination neither requires the intent to discriminate nor confines itself to a specific addressee. That is, the prohibition to discriminate formulated in the CRPD equally applies to states and their agents (judges, public hospitals, public healthcare providers, etc.), as well as to private persons and organizations (private healthcare providers, churches, non-governmental organizations, etc.).

However, the CRPD extends this definition so that the denial of a reasonable accommodation is also recognised as a form of discrimination (Waddington and Hendriks 2002), a concept that we return to below.

It follows from this definition that discrimination is generally understood to mean a form of detrimental or some other form of unfavourable treatment because of certain actual or perceived human features ('characteristics') or 'disability'. This allegedly discriminatory treatment is usually worse, and therefore detrimental or unfavourable in comparison to the treatment received by people with a different type of disability or without disabilities. Discrimination on

the basis of disability is therefore the denial of equal treatment or rejection of equal worth of a person due to his or her disability. The harms that result from discrimination can manifest in the treatment itself (e.g. intimidation) or as a consequence of the way a person is treated (e.g. the denial of a job).

The prohibition of discrimination and, as a corollary, the obligation to treat people equally, are widely recognised norms under international human rights law. Non-discrimination law emerged in response to forms of detrimental treatment deemed objectionable in a society built on human rights. Treating people less favourably because of particular features was considered unacceptable, because it was argued that these features closely relate to human dignity.[6] Thus discrimination denies the principle that all human beings are equally worthy and merit equal respect and protection. Discrimination is therefore at odds with the core values and principles underlying human rights law as well as the CRPD.

Discrimination, as prohibited by the CRPD, needs to be distinguished from mere 'different' or 'arbitrary' detrimental treatment. Providing information on the effectiveness and side effects of medication in braille for someone who is blind is a form of differential treatment, but would not constitute discrimination. Likewise, providing a sign-language interpreter to a person with a hearing impairment is not a form of discrimination; rather, it can be an obligation within the context of healthcare to ensure the patient receives adequate information and can consent to treatment (*Eldridge* v. *British Columbia* [1997] 3 SCR 624). As previously stated, discrimination implies disadvantageous conduct due to characteristics intimately linked to human dignity, such as gender, race and sexual orientation and gender identity. A person cannot, at least not easily, change these characteristics without significantly changing his or her identity.

For a long time it was contested that the non-discrimination norm applied to people with disabilities. Some felt a disability reflects a human defect unrelated to someone's identity or dignity. Others were concerned that non-discrimination law would make it impossible to introduce measures and policies aimed at protecting people with disabilities, helping them to cope with their impairments and providing them with necessary care and assistance. Others feared that by adding disability as a prohibited ground, the strong protection generally offered through non-discrimination law, would water down protection for all covered groups due to this inflation of grounds. Regardless, these arguments reflect negative stereotypes of people with disabilities and were otherwise defeated (Rothstein 2000). Since the adoption of the CRPD, a human rights instrument with a very high number of ratifications,[7] it can no longer be contested that detrimental treatment or other forms of less favourable treatment due to a disability constitutes discrimination, and should, as such, be prohibited and combated around the world. This also has, as we will argue below, implications for medical professionals.

6.4.2 Discrimination and healthcare

At first glance, it is difficult to see why the prohibition of discrimination on grounds of disability should concern medical law and ethics, let alone medical professionals. These disciplines, as mentioned above, are traditionally aimed at protecting and promoting justice, autonomy, beneficence and non-maleficence. In an effort to clarify why medical law and ethics should address

6 Much has been written on the meaning of the concept human dignity. See, for example, McCrudden (2008), Thies (2009) and Aasen *et al.* (2009).

7 As of 1 July 2014, the CRPD has had 147 ratifications and accessions (and 158 signatories).

discrimination and the lack of equal opportunities for persons with disabilities, we will briefly describe the various forms discrimination can take, using the designations outlined in the CRPD.

Direct disability discrimination has – according to the CRPD – 'the purpose' to discriminate. This occurs when a law, company policy or an individual, including a medical professional, treats someone less favourably than another similarly situated person because of that person's disability. For example, denying people with intellectual disabilities the right to procreate or refusing to insure a person with a history of coronary disease are forms of direct disability discrimination (CRPD, article 25(e)). Direct discrimination is, from a legal perspective, always forbidden, unless there is an accepted justification for the differential treatment.

Indirect disability discrimination entails differential treatment on the basis of an apparently neutral criterion, with as a result ('effect') that (some) people with disabilities are disadvantaged compared to non-disabled persons. Such differentiation becomes discriminatory when no objective justification is provided. Denying dogs entrance to a hospital can lead to indirect discrimination towards people with a visual impairment with a service dog. Under non-discrimination law, not permitting access to dogs constitutes indirect discrimination towards a particular group of disabled persons, unless it can be demonstrated that the presence of dogs in hospitals poses, for example, a threat to hygiene and that this threat cannot be appropriately alleviated without prohibiting service dogs.

Disability harassment, a third form of discrimination, occurs when unwanted conduct related to a disability (actual or perceived) takes place with the purpose or effect of 'nullifying' the dignity of a person and of creating an intimidating, hostile, degrading, humiliating or offensive environment (Weber 2007). One example is refusing children with severe disabilities any form of medical treatment because they pose a burden on society and the healthcare system.

In addition, the CRPD – like the so-called *Framework Employment Directive* (Directive 2000/78/EC) adopted by the European Union in 2000 – recognises a fourth form of discrimination – or, more precisely, a form of treatment necessary to enable 'the full and equal enjoyment of all human rights and fundamental freedoms by all persons with disabilities' (CRPD, article 1). Reasonable accommodation discrimination takes place in situations where a party covered by non-discrimination law fails to take into account the impairments of a person with disabilities that – in the interrelationship with his or her environment – constitute a barrier for participation and integration on an equal basis. Such is the case where a physician refuses to consult the representative of a person with an intellectual disability, arguing that speaking to the patient's representative would lead to an unjustified breach of the physician's duty to maintain patient confidentiality. The obligation to provide reasonable accommodations (CRPD, article 2) requires the covered party to take reasonable and effective steps or adjustments to remove the barriers that hinder the equal opportunities of the disabled person, unless the covered party, in all reasonableness, cannot be expected to make the adaptations needed, given the disproportionate burden the adaptations impose on that party. It is for states parties to ensure that this norm is correctly transposed and enforced under national law (see *European Commission* v. *Italy*).

6.4.3 Multiple discrimination

Before turning to the principle of autonomy, it is important to emphasise that discrimination not only occurs because of a sole ground, for example a disability, but that there is often a combination or intersection of grounds that cause or contribute to discriminatory reactions by others. This phenomenon is known as multiple discrimination (Fredman 2005). For example, where a

person is denied health insurance due to a particular disability together with his or her weight and age is multiple discrimination.

Non-discrimination case law demonstrates that the nature, type and intensity of discrimination a person experiences is often not merely dependent on a single ground ('disability'), but on a number of overlapping 'unfavourable' grounds, such as obesity, age, ethnicity or religious or sexual minority. Such a combination of 'unfavourable' grounds makes some people with disabilities more prone to discrimination than others.

In response, it was felt that non-discrimination law should also offer protection against multiple discrimination. The CRPD is the first – and so far the only – international human rights instrument expressly recognising multiple discrimination (preamble) and also offering protection to two forms of multiple discrimination: against girls and women with disabilities (CRPD, article 6) and against children with disabilities (CRPD, article 7).

The difficulty in addressing multiple discrimination by law does not negate its significance (Hendriks 2010). We wish to shed light on this form of discrimination because of its ethical importance to medical professionals and others responsible for health and healthcare policies and legislation, and because of the unambiguous references in the CRPD.

6.4.4 Discrimination and justice

In conclusion, people with disabilities may face various forms of discrimination, both within and outside the healthcare sector. Medical law and ethics cannot abstain from this issue without undermining the principle of justice. Non-discrimination law, including the prohibition of multiple discrimination, should therefore be an important aspect of medical law and ethics with respect to persons with disabilities and the way these persons should be treated by medical professionals, including healthcare institutions (Silver *et al.* 1998: 42).

6.5 Autonomy

6.5.1 Definition

Respect for autonomy is both one of the four core bioethical principles (Beauchamp and Childress 2013), including the freedom to make one's own choices, and one of the general principles of the CRPD (article 3). According to the CRPD, the autonomy of people with disabilities should also be respected in healthcare contexts, as set out in article 25. But what precisely does autonomy mean and how does it differ from the term discrimination (see section 6.4.1 of this chapter)? Like the term disability, the CRPD neither defines nor describes autonomy.

The term autonomy is derived from 'auto' (self) and 'nomos' (government or law), thus literally meaning 'self-government'. Under international law, not only people or nations are entitled to autonomy, or self-determination, but individuals have the right to self-government, that is to say the right to determine their own course of life without external pressure. Thus autonomy is above all a *negative* or non-interference right. It is therefore often associated with, according to Berlin, 'freedom from' interference by others (1958: 7). It has increasingly been recognised that autonomy cannot be equated with negative rights, but also requires positive 'freedom': the right to free choice and the right to fulfil one's own potential. Freedom of choice and the entitlement to evolve in a self-chosen way presuppose that choices can be made and are respected. Autonomy is therefore a complex concept, particularly with respect to health and healthcare. Often, choices must be made and individuals are not always in a position to make 'good' ones, due in part to insufficient information, their dependence on others, or a lack of intellectual capacity. Moreover,

healthcare providers are bound by legal and ethical standards as well as professional norms which at times prohibit them from complying with patient's wishes. This sometimes leads to a dilemma between 'professional autonomy' (the freedom of the professional group to set its own norms) and the individual autonomy of the patient.

6.5.2 The CRPD and autonomy

As noted above, autonomy is a foundational concept of medical law and ethics and is examined in more detail in Chapter 3 on consent. For people with disabilities, autonomous decision-making often boils down to whether the medical professional is willing to respect the person's decision, including the wish not to be treated, as medical professionals tend to associate 'unwise wishes' with symptoms of incompetence. The latter is not self-evident and disrespectful to people with disabilities who may have views different from those of medical professionals. At the same time, many laws allow medical professionals to override a person's consent or rejection of treatment in case of demonstrated 'incompetence' (as decided by that medical professional). Surrogate decisions are, in these cases, traditionally seen as compatible with the principles of justice, beneficence and non-maleficence, provided that they are as much as possible in line with the previously expressed wishes of the patient and not infringing his or her best interests. Thus, these laws are seen as protecting the health and well-being of the patient and doing justice to individual autonomy. As said, however, proxy or surrogate consent (which the CRPD Committee calls 'substituted decision-making') is easily applied to patients with (mental) disabilities for whom particular forms of treatment are deemed necessary. It can be argued that this situation is discriminatory towards persons with (mental) disabilities, as their autonomous will is not respected. This also raises concerns for medical law and ethics, and for the practice and standards of medical professionals, which should conform to international human rights law.

Consent, at the heart of the principle of autonomy, in the context of healthcare is referenced twice in the CRPD. First, there is a prohibition on medical or scientific experimentation without consent (CRPD, article 15). This provision targets the horrific experiments carried out on people with disabilities during the Nazi regime (Wolfensberger 1981; Annas and Grodin 1995) or, more recently, feeding radioactive material to mentally disabled children in the late 1940s (Welsome 1999). However, the absolute prohibition on experimentation without consent raises a dilemma about research with individuals that are unable to consent, but for whom gaining scientific insights may be essential to enhance treatment options. The second place where consent is mentioned in the CRPD is article 25(d), in providing equal quality in healthcare, which we will explain in more detail below.

If autonomy is to be understood as making one's own choices and having those choices respected, how is this to be applied in the context of healthcare decisions for people with disabilities? A simple answer is that decisions should be made in exactly the same way as for people without disabilities: all persons should be properly informed about treatment options and the repercussions of refusing treatment. This solution would alleviate many of the discriminatory elements of unwanted treatments especially, but not limited to, the mental health field. This would provide formal equality, but it would leave many people with disabilities vulnerable to exploitation by others if they did not receive any decision-making assistance. Article 12 of the CRPD tackles this issue by setting out two normative premises aimed at strengthening the autonomy of persons with disabilities.

First, everyone has legal capacity, in all domains of life. Legal capacity is the law's recognition of both holding and exercising a right. For example, in certain jurisdictions the law recognises adults as having the capacity and right to get married, but denies this right to an adult with an

intellectual disability by placing him or her under guardianship with restrictions on his or her legal capacity. In the context of healthcare decisions, people with disabilities are similarly denied the right to provide consent or reject a proposed medical intervention.[8] In response, the CRPD sets out the fundamental principle in article 12(2) that people should have legal capacity.

Second, article 12(3) of the CRPD maintains that states must 'take appropriate measures to provide access by persons with disabilities to the support they may require in exercising their legal capacity'. If a dentist, for example, does not understand a person's will and preferences, then a patient is entitled to the support necessary in order to make his or her treatment decisions and preferences understood by the dentist.

In doing so, the CRPD aims to ensure that people with disabilities meaningfully participate in society and truly exercise their autonomy. The Committee on the Rights of Persons with Disabilities (CRPD Committee) states that substituted decision-making systems must be *replaced* by systems of supported decision-making, a system recognising that persons with disabilities should be involved in the decision-making process even though they may need assistance, for example to assess the consequences of various treatment options. According to the Committee, states must repeal legislation allowing for systems of guardianship that are incompatible with human rights law and introduce laws 'which recognize the rights of persons with disabilities to make their own decisions and to have their autonomy, will and preferences respected' (CRPD Committee 2012a: para. 21). Rights including 'the right to free and informed consent to medical treatment, the right of access to justice, and the rights to vote, to marry and to choose their place of residence' (CRPD Committee 2013a: para. 30) are also mentioned as being at risk under substituted decision-making regimes. In September 2013, the CRPD Committee issued a draft general comment on article 12 of the CRPD. The draft document declared 'mental health laws that permit forced treatment … need to be abolished to ensure that full legal capacity is restored to persons with disabilities on an equal basis with others' (CRPD Committee 2013b: para. 7). Healthcare is clearly a domain that needs to bring its practices in line with human rights norms.

6.6 The CRPD and healthcare

The CRPD emphasises that people with disabilities have 'the right to the enjoyment of the highest attainable standard of health without discrimination' (CRPD, article 25), reiterating the classic formulation of the right to health set out in the 1966 *International Covenant on Economic, Social and Cultural Rights* (ICESCR). The focus of the CRPD, however, is not on health and healthcare. Instead, the CRPD is based on a number of general principles – as outlined above – including the principles of autonomy and free choice, equality, respect for difference and non-discrimination, participation, inclusion and accessibility (CRPD, article 3). This is not to suggest that the CRPD is irrelevant for medical law and ethics, or that health and healthcare have no importance in achieving these general principles. On the contrary, we argue that the CRPD requires an adjustment of these principles and the approach of medical law and ethics in order to do justice to the human rights of people with disabilities in the healthcare sector.

Different from medical ethics and, to a lesser extent, medical law, the CRPD is not so much focused on regulating the performance of medical professionals but rather on guaranteeing that people with disabilities, irrespective of the cause, nature or severity of their impairments, and no

8 See, for example, Hammarberg's *Who Gets to Decide?* (2012) and Lewis's 'Advancing Legal Capacity Jurisprudence' (2011).

matter their needs for medical care, actually get the healthcare they need and want. The CRPD thus also emphasises the importance of autonomy in cases where disabilities may impair the capacity of individuals to make healthcare decisions. We will illustrate this by examining the relevant CRPD provisions.

Article 25 of the CRPD is the longest and most programmatic explanation of the right to health of any of the human rights treaties. It sets out the obligation of states to 'take all appropriate measures to ensure access for persons with disabilities to health services that are gender-sensitive, including health-related rehabilitation' (CRPD, article 25). The drafters of the CRPD (namely the UN member states) then established six priorities, ensuring that people with disabilities get 'the same range, quality and standard of free or affordable healthcare and programmes as provided to other persons' (CRPD, article 25(a)). This includes access to sexual and reproductive healthcare (this is the first time that this has been articulated in international human rights law) and public health programmes. States need to provide healthcare to alleviate, insofar as is possible, someone's disability. Early identification and intervention, and 'services designed to minimize and prevent further disabilities, including among children and older persons' are among the actions which fall under this mandate (CRPD, article 25(b)). The Convention emphasises the provision of healthcare 'as close as possible to people's own communities, including in rural areas' (CRPD, article 25(c)). Articles 25(d) to (f) of the CRPD then set out overarching principles, reiterating the principles contained in article 3. They require the state to ensure that its medical professionals provide equal quality care, which is given 'on the basis of free and informed consent', an issue to which we return below. Equal quality should be achieved, according to the Convention, by pursuing actions that may include raising awareness of human rights 'through training and the promulgation of ethical standards' for medical professionals (CRPD, article 25(c)).

Article 25(e) of the CRPD reiterates the right to non-discrimination, this time with respect to health and life insurance. Article 25(f) of the CRPD establishes non-discrimination in providing a patient with disabilities healthcare, food and fluids. This is of particular concern, for example, when a person with Down syndrome needs a kidney transplant, given the reported cases where this has been denied based on the person's disability.[9] It is also a concern for end-of-life decisions and the management of people in conditions such as persistent vegetative state.

The CRPD recognises health in parallel with the broader notion of independence, a concept that implies autonomy and the obligation to provide support to exercise autonomy. The drafters of the Convention were keenly aware that health can play an important part in reversing the invisibility of people with disabilities. Healthcare systems are unable to do this alone as many determinants of health are not within the realm of control of healthcare. It is widely known that income and other socio-economic determinants have, on a population basis, a greater effect on health than the quality of healthcare. That is not to ignore the importance of essential healthcare at times (Wilkinson 1997). One socio-economic determinant is adequate housing.[10] There is now abundant evidence that poor housing can lead to poor health and people with disabilities

9 For a review of outcomes, see Martens (2006). For a case that permeated the public consciousness and resulted in a global campaign to provide an intellectually disabled girl with a much needed kidney transplant, see Change.org (2012).

10 'The Committee encourages States parties to comprehensively apply the Health Principles of Housing prepared by WHO which view housing as the environmental factor most frequently associated with conditions for disease in epidemiological analyses; i.e. inadequate and deficient housing and living conditions are invariably associated with higher mortality and morbidity rates' (Committee on Economic, Social and Cultural Rights 1991: para. 8(d)).

are particularly vulnerable.[11] The right to adequate housing is set out in article 28 of the CRPD on social protection and appears alongside other essentials of health such as water, food, clothing, social protection, poverty alleviation and so on. Housing is a prominent issue in human rights literature. It does not mean simply having a roof over one's head but is framed in terms of access to and participation in the community. Central to this right is the obligation of states to provide a range of 'in-home, residential and other community support services, including personal assistance necessary to support living and inclusion in the community, and to prevent isolation or segregation from the community' (CRPD, article 19). This provision speaks to the right to habilitation and rehabilitation, whereby health services should be directed towards enabling people with disabilities 'to attain and maintain maximum independence, full physical, mental, social and vocational ability, and full inclusion and participation in all aspects of life' (CRPD, article 26(1)).

6.6.1 When treatment becomes ill-treatment

Despite the normative clarity of the CRPD on the right to live in the community, some people with disabilities are forced to live in institutions, often for their entire lives, without their consent and they are unable to challenge the underlying decision. These institutions are often healthcare establishments such as psychiatric hospitals or social care institutions where people are forced to take psychiatric medication[12] while being deprived of basic human needs such as food, heating, water and sanitation (*Nencheva and others* v. *Bulgaria* [2013] appl. no. 48609/06). It should be added that this also raises legal and ethical dilemmas for the responsible healthcare providers: what to do when laws prescribe forms of forced treatment ignoring the consent of the patient while the conditions under which the patient will be treated amount to inhuman and degrading treatment.

Prior to the adoption of the CRPD, international law on psychiatric treatment was mainly extrapolated from other human rights treaties, such as a 1994 General Comment by the UN Committee on Economic, Social and Cultural Rights (CESCR) on disability (General Comment No. 5). As progressive as this General Comment was in many respects, it is, in retrospect, disappointing that it did not address forced psychiatric treatment. Six years later, the same Committee published a General Comment on the right to health (General Comment No. 14 2000). This document did not examine mental health in any depth, stating that mental health treatment without consent is allowed on an 'exceptional basis', without explaining why it is allowed at all or explaining these exceptional bases (CESCR 2000: para. 34). Both of these general comments referred to a non-binding document adopted in 1991 by the UN General Assembly called the 'Principles for the Protection of Persons with Mental Illness and the Improvement of Mental Healthcare' (MI Principles). The MI Principles set 'the right to be treated in the least restrictive environment, with the least restrictive or intrusive treatment appropriate to the patient's health needs and the need to protect the physical safety of others' (principle 9(1)). Also, '[n]o treatment shall be given to a patient without his or her informed consent' (MI Principles, principle 11). The MI Principles then clearly set out five exceptions to this principle, including a scenario where a doctor thinks that that it is 'urgently necessary in order to prevent immediate or imminent harm to the patient or to other persons' (principle 11(8)). This watering down of

11 See, for example, Tually *et al.* (2011) and CRESA *et al.* (2007).

12 See many of the reports of the European Committee for the Prevention of Torture, Inhuman and Degrading Treatment and Punishment (2013).

normative standards led Paul Hunt, the then UN Special Rapporteur on the Right to Health, to observe in his 2005 report on disability and the right to health that while informed consent is necessary to provide treatment and 'is consistent with fundamental tenets of international human rights law', the combined effect of the 'extensive exceptions and qualifications' 'tends to render the right of informed consent almost meaningless' (UN Economic and Social Council 2005, para. 88).

Paul Hunt's report marked a turn for the mainstream human rights movement, because it pointed out the discriminatory element of diluted standards for treatment concerning mental health. Reiterating that the right to health is subject to progressive realisation (CRPD, article 4(2)), the Special Rapporteur highlighted that 'the international right to health also imposes some obligations of immediate effect' (UN Economic and Social Council 2005, para. 34), which includes freedom from non-consensual medical treatment or, as the CRPD puts it, the obligation of states to ensure that medical professionals provide healthcare to people with disabilities on the basis of free and informed consent (CRPD, article 25(d)).

Though clear on informed consent, the CRPD is silent on forced treatment.[13] That is to say, the Convention neither explicitly permits force when someone lacks the capacity to consent to treatment (as most mental health laws around the world currently permit force), nor does it ban forced psychiatric treatment (Dhanda 2008). The Convention does not define 'informed consent' nor does it offer guidance as to the actions medical professionals should take when, for whatever reason, it is not possible to seek patient consent.

Despite this, others have stepped up to the challenge of filling the void with human rights content. In 2008, Manfred Nowak, the (then) UN Special Rapporteur on Torture, issued a report on torture and disability in which he noted that people with disabilities are subject to treatment without their consent (UN General Assembly 2008). He highlights in particular the effects of 'electroshock treatment and mind-altering drugs including neuroleptics' (UN General Assembly 2008: para. 40). Noting that these treatments are often justified against people with disabilities when they would be unacceptable if performed on others, Nowak calls for a review of the anti-torture framework in relation to disability (UN General Assembly 2008: para. 40). In 2013, Nowak's successor as special rapporteur, Juan Méndez, presented his report to the UN Human Rights Council on torture in healthcare (UN General Assembly 2013). He goes further than Nowak in observing how ill-treatment is justified by rhetorical devices such as 'best interests' which are masked as 'good intentions' of medical professionals (UN General Assembly 2013). Méndez's argues:

> [States should] impose an absolute ban on all forced and non-consensual medical interventions against persons with disabilities, including the non-consensual administration of psychosurgery, electroshock and mind-altering drugs, for both long- and short-term application. The obligation to end forced psychiatric interventions based on grounds of disability is of immediate application and scarce financial resources cannot justify postponement of its implementation.
>
> *(UN General Assembly 2013: para. 89(b))*

Méndez notes that states should boost community-based mental health which meets the needs of people with disabilities and which respects 'autonomy, choices, dignity and privacy.' He advises states to revise laws 'that allow detention on mental health grounds or in mental health

13 See the 'Special Issue: Torture Prevention and Disability', in the *International Journal of Human Rights* (2012).

facilities and any coercive interventions or treatments in the mental health setting without the free and informed consent by the person concerned' (UN General Assembly 2013: para. 89(d)). Moreover, he cites Anand Grover's 2009 report, the 'Right of Everyone to the Enjoyment of the Highest Attainable Standard of Physical and Mental Health', which discusses various international and domestic laws that enshrine informed consent as a fundamental principle, before observing that it is 'frequently compromised in the health-care setting' (UN General Assembly 2013: para. 29).

The CRPD Committee shares this view in its 'Draft General Comment on Article 12' (2013b). The Committee reiterates the wording of article 25 on the right to health and points out that:

> [States are obliged] to require all health and medical professionals (including psychiatric professionals) to obtain free and informed consent from persons with disabilities. In conjunction with the right to legal capacity on an equal basis with others, this also obligates States to refrain from permitting substitute decision-makers to provide consent on behalf of persons with disabilities.
>
> *(2013b: para. 37)*

It makes a further point about patient–doctor communications by suggesting that 'health and medical personnel should ensure the use of appropriate consultation skills that directly engage the person with disabilities and ensure, to the best of their abilities, that assistants or support persons do not substitute or have undue influence over the decisions of persons with disabilities' (CRPD Committee 2013b: para. 37).

Thus the CRPD outlines some specific operational standards for governments which should be translated into law and standards for medical professionals as well as others assisting people with disabilities.

6.6.2 A framework for policy discussion

The CRPD offers no guidance as to the actions medical professionals must take beyond a non-discrimination approach. It does, however, make a process point about how these issues are to be discussed and decided upon. Article 4(3) of the CRPD imposes on states a general obligation when laws and policies are developed and implemented. In other decision-making processes relating to persons with disabilities, governments need to 'closely consult with and actively involve persons with disabilities, including children with disabilities through their representative organizations' (Mental Disability Advocacy Center 2011: 19).

6.7 Conclusions

Medical ethics is traditionally centred on the principles of autonomy, beneficence, non-maleficence and justice. Doctors and other medical professionals ultimately decide how these principles are to be applied in individual cases. These foundational principles are also at the heart of medical law, even though other branches of law also influence medical law, including human rights law. This has, or at least should have, an impact on the way these principles are to be applied in cases of persons with disabilities, how they regulate the behaviour of healthcare providers and how they bestow rights on healthcare recipients.

These observations do not deny the fact that many medical professionals care very deeply for their patients, have a profoundly humane approach and deliver excellent quality care and

treatment for people with disabilities. At the same time, it is uncontroversial to state that the human rights of people with disabilities have frequently been disregarded or devalued within the healthcare system. This can be explained by a lack of understanding and cooperation between the human rights and healthcare domains, by discriminatory laws which result in poor practices and by a lack of inclusion of people with disability in public health and other development programmes.

The fact that people with disabilities have been treated differently for many decades by healthcare laws and medical professionals does not necessarily constitute a form of disability discrimination. Differential treatment can be a good thing, and the CRPD encourages this by obliging states and medical professionals to adjust their practices when they are seen as 'reasonable accommodations' benefiting people with disabilities. However, differential treatment can result in negative consequences, constituting unlawful, direct or indirect discrimination. The advent of the CRPD in 2006 provides an opportunity for people occupying various domains in society, notably in the field of healthcare, to critically assess their engagement with people with disabilities. This is exactly what the current and previous UN Special Rapporteurs on Torture have tried to do by reassessing the international torture framework. They together pointed out how what the international human rights mainstream almost unanimously viewed as acting in someone's best interests can be challenged as an invasion of autonomy, trivialising the notion of informed consent and perpetuating inhumane and degrading treatment that sometimes constitutes torture.

A shift in the conceptualisation of healthcare for people with disabilities through a human rights lens should be a clarion call to medical professionals and those who teach and train medical law and ethics to alter care practices in the name of justice, beneficence and non-maleficence. Such a shift also requires the political will to address some very challenging dilemmas about how to move from a model of proxy consent to one which truly respects the will and preferences of the person with disabilities when accessing healthcare, how to ensure that support in decision-making is not usurped by substitution, how to prevent supporters exercising undue influence and how to ensure a person with disabilities does not lose out on their right to health because of the (in)actions of their support network.

Medical professionals must abide by their national laws. They are in a difficult position when their national law does not comply with international human rights standards. If this is the case, medical professionals can capitalise on the power and authority of their professional organizations and liaise with patients' rights organizations about how to instigate legal reform that better meets the healthcare needs of people with disabilities – their patients.

It is also incumbent on medical professionals to become acquainted with the current international human rights standards in more depth than is possible to include in this chapter. Training should feature in medical school curricula and continue post-qualification (Iezzoni and Long-Bellil 2012: 137). This coincides with recommendations made by the CRPD Committee that training and legislative reforms should be done 'in consultation and cooperation with persons with disabilities and their representative organizations, at the national, regional and local levels for all actors'.[14]

14 See the CRPD Committee's concluding observations with respect to Hungary (2012b: para. 26). The same recommendations were made by the CRPD Committee for Spain (2011a: para. 34), Austria (2013c: para. 28) and Tunisia, where the Committee also stated that training should be provided to 'relevant public officials and other stakeholders' (2011b: para. 23).

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7
Mental health

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7.1 Introduction

This chapter discusses the rights of psychiatric patients in the common law jurisdictions of Canada. Its main focus is the system of civil commitment, whereby individuals are certified under provincial mental health legislation and detained in a psychiatric facility without their consent, and (in some provinces) treated without their consent. These individuals are usually referred to as 'formal' or 'involuntary' patients, signaling the key issue that their stay in hospital is non-consensual (Robertson 1994). This chapter also examines the rights of patients who are detained in a psychiatric facility pursuant to the criminal justice system, having been found not criminally responsible by reason of mental disorder or unfit to stand trial.

In Canada, civil commitment is a matter exclusively within provincial jurisdiction (*Constitution Act* 1867, sections 92(7), 92(13)). This means that the specific details of the criteria and process for civil commitment, as well as the rights of involuntary patients, can vary across Canada (Ambrosini and Joncas 2013). However, although there are some differences, for the most part the concepts are similar in each province. For the purposes of this chapter, the discussion will focus mainly on the law of Alberta (Alberta *Mental Health Act* 2000), but significant differences in other provinces will be noted.

By contrast, psychiatric detention under the criminal justice system, for those who have been found not criminally responsible by reason of mental disorder or unfit to stand trial, is a matter of federal jurisdiction (*Criminal Code* 1985). Hence, its interpretation and application are ultimately (through decisions of the Supreme Court of Canada) uniform across Canada.

7.2 Civil commitment

7.2.1 The process

The right to be free from unwanted medical treatment (and by extension unwanted hospitalization) has been recognized for centuries in the common law. One hundred years ago Mr Justice Cardozo stated that 'every human being of adult years and sound mind has a right to determine what shall be done with his own body' (*Schloendorff* v. *Society of New York Hospital* [1914]

105 NE 92, p. 93). This principle has been affirmed by the Supreme Court of Canada on numerous occasions, and is codified in legislation in some provinces; it is also entrenched in, and protected by, the Constitution through the *Canadian Charter of Rights and Freedoms* (*Charter*) (Picard and Robertson 2007; Verdun-Jones and Lawrence, 2013). Its essence was captured by the Supreme Court of Canada in *Starson* v. *Swayze*, 2003 SCC 32, in the statement that '[t]he right to refuse unwanted medical treatment is fundamental to a person's dignity and autonomy' (para. 75).

Nonetheless, like most common and civil law countries, Canada recognizes that civil commitment is an exception to this fundamental right, and that in certain circumstances individuals who are suffering from a mental illness may be detained in hospital without their consent (Ambrosini and Joncas, 2013; Carver, 2011; Gray *et al*. 2008; Robertson, 1994).

The system of civil commitment in Canada is almost entirely non-judicial. In most cases, individuals are committed as involuntary psychiatric patients not by judges, not by lawyers, but by doctors. In the words of one commentator, 'civil commitment represents the most significant deprivation of liberty without judicial process that is sanctioned by our society today. We have elected to leave the issue of involuntary commitment almost entirely to the discretion of psychiatrists' (Anand 1979: 251). Of course, this is not to say that there are no legal protections or safeguards built into the system. As we shall see, involuntary patients do have a number of legal rights. Nonetheless, it is important to understand that, at least initially, the process of civil commitment is one that rests primarily in the hands of the medical profession.

In most situations, civil commitment is triggered by a physician issuing a certificate which states that, based upon an examination of the patient, the physician is of the opinion that the patient meets the criteria for formal admission to a psychiatric hospital. The physician need not be a psychiatrist (Ambrosini and Joncas 2013; Robertson 1994), and indeed in practice, this first certificate will typically be signed by a family (or emergency room) physician.

The purpose (and effect) of the first certificate is to provide legal authority for the individual to be taken to a psychiatric hospital for a period of further assessment. The authorized period of assessment varies across Canada, but usually the maximum period is between 24 and 72 hours (Ambrosini and Joncas 2013; Robertson 1994). After this period has expired, the individual must be released unless a second certificate is issued, in which case the patient is then formally admitted to the psychiatric hospital for a specific period of time. In Alberta, the period of hospitalization based on the first pair of certificates is one month, but (like all provinces) it can be extended *ad infinitum* with the issuance of new renewal certificates (Alberta *Mental Health Act*, section 8). In other words, so long as two physicians are of the opinion that the criteria are still met, the patient can be kept at the hospital indefinitely.

In order for the patient to be legally detained under the *Mental Health Act*, not only must the criteria for admission be satisfied, but also the physicians who issue the certificates must comply with the procedural requirements of the Act. Failure to do so may result in the patient's detention being illegal and a successful action for false imprisonment (*Dr. X* v. *Everson,* 2013 ONSC 6134; Robertson 1994).

7.2.2 The criteria

7.2.2.1 Mental disorder

In most provinces, three requirements must be satisfied before a patient can be civilly committed. The first is that the individual is suffering from a 'mental disorder.' In Alberta this is defined as 'a substantial disorder of thought, mood, perception, orientation or memory that grossly impairs

(i) judgment, (ii) behaviour, (iii) capacity to recognize reality, or (iv) ability to meet the ordinary demands of life' (Alberta *Mental Health Act*, section 1(1)(g)).

Most provinces and territories adopt this type of functional definition, although a few (for example, Ontario) adopt a much more open-ended definition, such as 'any disease or disability of the mind' (Carver 2011; Gray *et al.* 2008; Robertson 1994).

7.2.2.2 Dangerousness, harm, and health deterioration

This is by far the most contentious requirement, both in the sense of academic commentary and also in the context of proceedings where patients appeal their certification (which is discussed below). In these proceedings, the diagnosis of a 'mental disorder' (the first criterion for civil commitment) is seldom disputed. The same is true of the third criterion (discussed below). The real focus of contention will be whether the patient satisfies the second criterion.

Until relatively recently, many provinces articulated this criterion in the language of 'dangerousness.' Under this scheme, in order to be committed, an individual must pose a 'danger' to self or others, and the danger must be serious and imminent (Carver 2011; Robertson 1994). However, in recent years, there has been a legislative trend away from the 'dangerousness' test in favor of one which focuses on harm or health deterioration (Ambrosini and Joncas 2013; Carver 2011), a trend which is not without its critics (Kaiser 2009).

The Alberta *Mental Health Act*, which was amended in 2009 (Marshall 2010), is typical of this development. It now provides that, in order to issue a certificate of civil commitment, the physician must be of the opinion that the individual is 'likely to cause harm to the person or others or to suffer substantial mental or physical deterioration or serious physical impairment' (Alberta *Mental Health Act*, section 2).

The change in language from 'danger' to 'harm' may be of little consequence. It is likely that these terms are approximately the same (Carver 2011). What is significant, however, is the inclusion of the 'deterioration' component in the new criteria, which is essentially a return to the days where patients could be committed for the protection of their own mental health (the welfare test) (Robertson 1994). In the past, the welfare test as basis for civil commitment has been held by some courts to be contrary to the *Charter* and hence unconstitutional (Carver 2011; Robertson 1994). It is interesting, however, that the current legislation in Ontario, the *Mental Health Act* 1990, encompassing the 'deterioration' criterion, has recently been held not to contravene the *Charter* (*P.S.* v. *Ontario*, 2013 ONSC 2970). Relying on previous Ontario decisions, the Court held that the *Mental Health Act* safeguards the patient's substantive rights and complies with the procedural component of the principles of fundamental justice, as required by the *Charter*.

7.2.2.3 Not suitable as a voluntary patient

The third criterion for civil commitment in most provinces is that the individual must not be suitable for admission to a psychiatric facility other than as a voluntary patient (Ambrosini and Joncas 2013; Robertson 1994). This requirement reflects the underlying principle that civil commitment should be viewed as a last resort, and thus should not be used (absent exceptional circumstances) if the individual is willing to be admitted (or remain) as a voluntary patient (Carver 2011).

It follows from this that the most common example of this third criterion being satisfied is where the person refuses to be admitted (or continue) as a voluntary patient in a psychiatric facility (Robertson 1994, 2010). Clearly, in this situation, the person is not suitable to be a

voluntary patient if he or she is not willing to consent to being one. However, there are other situations in which this third criterion may be satisfied, even where the patient is willing to remain voluntarily in the hospital. One is where the individual lacks the necessary mental capacity to be a voluntary patient (Robertson 1994, 2010). Another is where the restrictions that are required to be placed on the patient's freedom of movement and other liberties are incompatible with the status of a voluntary patient, for example limits on how often the patient can leave the unit (Robertson 2010).

Lastly, and most controversially, in practice it is quite common for individuals to be certified, even though they are willing to remain at the hospital voluntarily, because they refuse to consent to medical treatment. The purpose of the certification in this type of case is to take advantage of the provisions (in some provinces) which allow for treatment of involuntary psychiatric patients without consent, which is discussed below. The individual's refusal of consent arguably makes them 'unsuitable' to be a voluntary patient, because otherwise they cannot be treated (Robertson 2010).

The 'need for treatment' rationale is sometimes used even in cases where the patient is already legally detained in hospital and hence does not need to be civilly committed in order to be kept there. The most common example of this involves patients who are detained pursuant to the criminal justice system, having been found not criminally responsible of a criminal charge by reason of mental disorder (which is discussed below). If these patients refuse consent to medical treatment (and hence cannot be treated if they are mentally competent), in some provinces it is the practice to certify them under the *Mental Health Act* so as to take advantage of the provisions of that Act which allow for treatment without consent (Robertson 2010).

7.2.2.4 Other criteria

While most jurisdictions within Canada only have the three criteria for civil commitment discussed above, some impose other requirements. In particular, in Newfoundland and Saskatchewan, civil committal applies only to individuals who lack the mental capacity to consent to treatment (and for whom, therefore, the consent of a substitute will be needed), thus ensuring that those who are committed can be treated (Ambrosini and Joncas 2013). The purpose of this requirement is to avoid the situation which has arisen in some provinces where mentally competent patients who refuse treatment are committed, thereby effectively 'warehousing' them in hospital indefinitely without treatment (Carter 2011).

Likewise, some provinces (in particular British Columbia and Newfoundland) make 'treatability' a requirement for civil commitment. In other words, a person cannot be made an involuntary patient unless their underlying mental condition is amenable to treatment (Ambrosini and Joncas 2013; Carver 2011).

7.2.3 Community treatment orders

Five provinces – Alberta, Newfoundland, Nova Scotia, Ontario, and Saskatchewan – have enacted legislation which enables psychiatric patients to receive treatment in the community rather than in a hospital, under the provisions of a community treatment order ('CTO') (Carver 2011; Gray et al. 2008). Often this type of legislation is introduced by the government in response to a much publicized tragic event involving violence by a person suffering from a mental illness, such as the fatal shooting of the television sports broadcaster Brian Smith in Ontario in 1995 (Carver 2002; Wandzura 2008) and the fatal shooting of an RCMP officer in Alberta in 2004 (Carver 2010; Gray *et al.* 2012).

The primary target group of the CTO is the chronically mentally ill. It seeks to address the 'revolving door' problem, whereby patients are committed to a psychiatric hospital, receive treatment and improve to the point where they are no longer certifiable and must be discharged, only to discontinue their medication, deteriorate, and once more become certifiable, and the cycle begins again (Carver 2011; Marshall 2010). The CTO aims to break the cycle by providing an 'incentive' to the patient to continue taking medication. A patient who is discharged from hospital on a CTO is required to comply with the terms of the treatment plan incorporated into the CTO, which typically requires the patient attend specified, regular appointments to receive medication. If patients fail to do so, or breach other conditions in the CTO, they can be brought back into hospital – hence the 'incentive' to continue with medication.

The term 'community treatment order' is somewhat misleading in its use of the word 'order.' There does not have to be a court order; rather, a CTO is issued by physicians, if certain criteria are satisfied, as set forth in the legislation. These criteria tend to reflect the 'revolving door' problem which the CTO seeks to address. For example, in Alberta, the criteria for a CTO are as follows (Alberta *Mental Health Act* 2000, section 9.1). First, the patient must be certifiable, that is the patient meets the criteria for civil commitment under the *Mental Health Act*. Second, within the past three years the patient must have been a formal patient in a psychiatric facility or an approved hospital on more than two occasions or for a total of more than 30 days, or have been subject to a CTO. Unlike other provinces (Carter 2011; Gray *et al.* 2012), Alberta makes an exception to this requirement and provides (in limited circumstances) for a CTO even where the patient has not been previously hospitalized. In addition, for all CTOs there is the very important requirement that the treatment which the patient requires must be available in the community.

The CTO must be accompanied by a treatment plan which, among other things, sets out the proposed treatment which the patient must follow, the dates and place where the patient must attend treatment, and also identifies the health professional who is responsible for supervising the CTO.

The issue of the patient's consent to a CTO varies significantly across Canada. Some provinces require the consent of the patient (or if incompetent, the substitute's consent) in all cases. Others provide that a CTO can only be issued if the patient is incompetent. In Alberta, consent is required but can be dispensed with by the physician who issues the CTO (Carver 2011; Gray *et al.* 2012; Marshall 2010).

The CTO regime is not without its critics. Some view it as stigmatizing persons with mental disability who are living in the community by suggesting that they must be supervised by the state (Carver 2011). Others argue that the CTO is a form of 'coercion,' whereby the patient is 'forced' to agree to accept treatment in order to avoid being readmitted to hospital (Carver 2002; Kaiser 2009). Despite these (and other) criticisms, the CTO legislation in Ontario has been held not to contravene the *Canadian Charter of Rights and Freedoms* (*Thompson* v. *Ontario (Attorney General)*, 2013 ONSC 5392).

Empirical studies show that the success of CTOs in Canada has been mixed. For example, they are rarely used in Saskatchewan and Ontario (Carver 2002; Gray *et al.* 2008; Wandzura 2008). However, by contrast, studies indicate that in Alberta (the most recent province to introduce CTOs – in 2010), their use is frequent and increasing (Orr *et al.* 2012). These studies also tend to confirm what commentators have said for many years, namely that, above all, the key to the success of CTOs is that the government must ensure that there are sufficient mental health resources in the community so that the patient can access the treatment and support which is needed. Otherwise, physicians and other healthcare professionals will see little point in issuing a CTO (Dawson 2010).

7.3 Rights of involuntary patients

7.3.1 Introduction

Because civil commitment is such a significant infringement on the patient's right to autonomy and freedom, mental health legislation attempts to balance this by conferring various rights on involuntary patients. This is especially true in light of the *Charter*, with provincial governments increasingly concerned about the prospect of a constitutional challenge to their mental health legislation, amending it to include more rights for involuntary patients (Robertson 1994).

Another theme which is evident in the legislation is an attempt to ensure that the rights which are conferred on patients are meaningful and can be exercised effectively, either by patients or by someone on their behalf. This will be discussed in relation to many of the rights set out below.

7.3.2 The right to be informed

The *Canadian Charter of Rights and Freedoms* embodies the principle that, upon detention, individuals have a right to be informed of the reasons for the detention. Likewise, the Supreme Court of Canada has recognized that a patient must be informed of all material information relating to their treatment (*Reibl* v. *Hughes* [1980] 2 SCR 880). These principles are reflected in the Alberta *Mental Health Act*, which provides that upon admission, a voluntary patient has the right to be informed of the reasons for the admission, and the right to apply for a review of the admission (Robertson 1994). Because involuntary admission constitutes 'detention' within the meaning of section 10 of the *Charter*, the patient must also be advised of the right to retain and instruct legal counsel without delay (Robertson 1994).

This is an example of legislation attempting to confer meaningful rights upon patients rather than illusory ones. It recognizes that at the time of admission, many involuntary patients will be in the acute phase of a psychotic illness and may therefore not be capable of understanding the information which they are given with respect to the reasons for the admission and their right of appeal. Some provinces have attempted to address this problem with measures such as a requirement of verbal (rather than written) information, repetition of information, and the use of specially trained 'rights advisors' (Gray *et al.* 2008).

In addition, some provinces require that the information be given to the patient's 'nearest relative' as well as to the patient, in case the patient is not able to understand it or act upon it. (Robertson 1994). While laudable in its aim, this provision fails to take into account the fact that in many cases it will be the patient's nearest relative who has initiated the process of civil commitment and thus will be unlikely to encourage or assist the patient to launch an appeal of the certification.

7.3.3 The right to apply to the Review Panel

As was discussed earlier, the process of civil commitment is largely a non-judicial one, involving a physician's certificate rather than a court order. Hence it is important that involuntary patients be given a legal avenue to appeal their certificates where they believe that the criteria for commitment are not satisfied or where there has been some defect or irregularity in the process. At the same time, however, it is essential that this appeal process ensues quickly, or it risks being meaningless. In particular, statistics show that most involuntary patients are discharged from hospital within one month of their initial admission (Robertson 1994). This means that, unless the

right of appeal can be exercised quickly, it becomes illusory, because most patients will have been discharged from hospital before their appeal can be heard.

In most Canadian provinces this need for a timely appeal process is recognized by the creation of a special mental health review panel to hear appeals from involuntary patients (Gray *et al*. 2008). Alberta's scheme is fairly typical of this model. The *Mental Health Act* establishes a Review Panel comprising a lawyer (who chairs the proceedings), a psychiatrist, a physician, and a lay member. All involuntary patients have the right to appeal their certification to the Review Panel, which must hold a hearing within 21 days of receiving the patient's application (Alberta *Mental Health Act*, section 40). Individuals who are subject to a community treatment order also have the right to appeal this to the Review Panel. Unlike most other provinces, Alberta does not restrict the number of times a patient can apply to the Review Panel for a review of the certificates. Patients can appeal as often as they want, subject only to the chair's discretion to refuse to convene a hearing if he or she reasonably believes that the application is frivolous, vexatious, or not made in good faith, or that there has been no significant change in circumstances since the last appeal (Alberta *Mental Health Act*, section 38).

The proceedings are relatively informal and the Review Panel is not bound by strict rules of evidence. Nevertheless, it has an overriding duty to act fairly, which is reflected in many of the procedural safeguards contained in the legislation, such as the patient's right to be present at the hearing, the right to adduce evidence and cross-examine witnesses, and the right to be represented by legal counsel (Robertson 1994).

The object of the proceedings is to determine whether, *at the time the appeal is heard*, the patient meets the criteria for civil commitment. This timeframe is important, because as a result of treatment received in hospital, a patient who was certifiable at the date of admission may no longer meet the criteria for certification by the time the appeal is heard. The onus of establishing that the criteria are satisfied rests with the hospital (Alberta *Mental Health* Act, section 42). If the Review Panel concludes that the criteria are no longer met, it will cancel the certificates and the patient will be free to leave the hospital.

The legislation also recognizes that the right to apply to the Review Panel may be an empty right for patients who do not understand it or are unable to assert it, and whose nearest relative is not interested in initiating an appeal (Robertson 1994). Hence the *Mental Health Act* provides for mandatory review by the Review Panel every six months, if the patient has not applied for a review during that time (Alberta *Mental Health* Act, section 39). As is discussed below, the Review Panel also has jurisdiction in certain matters relating to the psychiatric treatment of involuntary patients.

7.3.4 The right to refuse treatment

As has already been discussed, a patient's right to refuse medical treatment is well established and is protected under common law, by statute, and by the *Canadian Charter of Rights and Freedoms* (Picard and Robertson 2007; Verdun-Jones and Lawrence 2013). Despite this, when it comes to involuntary psychiatric patients, their right to refuse treatment is not uniformly recognized in Canadian mental health legislation. The position varies considerably from province to province. As Peter Carver has noted, '[t]he question of whether competent involuntary patients should have the right in law to refuse psychiatric treatment is the most disputed issue in mental health law' (Carver 2011: 356).

The meaning of 'competence' to make treatment decisions is defined in most Canadian mental health legislation and tends to be fairly uniform. For example, the Alberta legislation provides that a person is competent to make treatment decisions if he or she 'is able

to understand the subject-matter relating to the decisions and able to appreciate the consequences of making the decisions' (Alberta *Mental Health Act*, section 26). In the leading decision in *Starson* v. *Swayze*, the Supreme Court of Canada emphasized that the test for competence focuses on the patients' *ability* to understand (and not just their *actual* understanding). It also emphasized that patients should not be viewed as mentally incompetent merely because they refuse to consent to treatment which others consider to be in their best interests (Carver 2011).

In some provinces (Saskatchewan and Newfoundland), the issue of the competent involuntary patient's right to refuse treatment does not arise. This is because, as we have seen, incapacity is a precondition of civil commitment in those provinces, and hence there is no such thing as a 'competent' involuntary patient.

The approach taken in the other Canadian provinces and territories on the issue of the right to refuse psychiatric treatment can be categorized into three groups (Carver 2011). At one end of the spectrum the mental health legislation in some provinces (such as Ontario) expressly recognizes the competent patient's right to refuse psychiatric treatment. It provides no exceptions to this right, and no power to override the competent patient's decision to exercise it (Carver 2011; Robertson 1994). In the context of Ontario's mental health legislation, the right to refuse treatment has also been held by the Ontario Court of Appeal to be protected by the *Canadian Charter of Rights and Freedoms* and hence is a constitutional right (*Fleming* v. *Reid*, [1991] 4 OR (3d) 74).

The approach taken in Ontario is not without its critics, who view it as unacceptable to 'warehouse' persons with mental illness by detaining them in a psychiatric hospital without treatment (Gray *et al*. 2008; Solomon *et al*. 2009).

At the other end of the spectrum are provinces such as British Columbia, where the legislation takes away the right of involuntary patients to refuse treatment and provides that they are deemed to consent to treatment (Carver 2011; Verdun-Jones and Lawrence 2013). This approach also has many critics (Verdun-Jones and Lawrence 2013), who view it as a fundamental interference with patient autonomy and who question its constitutional validity in light of the decision in *Fleming* v. *Reid*.

In the third group of provinces (which includes Alberta), the legislation attempts to find a middle ground by recognizing the competent patient's right to refuse treatment but providing that this can be overridden if the treatment is in the patient's best interests (Carver 2011; Robertson 1994). In Alberta, this power to override the patient's refusal is conferred on the Review Panel. On the application of the attending physician, the Review Panel can grant a treatment order notwithstanding the patient's refusal of consent, if it considers that the treatment is in the patient's best interests having regard to four specific factors, namely: (1) whether or not the mental condition of the patient will be or is likely to be improved by the treatment; (2) whether the patient's condition will deteriorate or is likely to deteriorate without the treatment; (3) whether or not the anticipated benefit from the treatment outweighs the risk of harm to the patient; and (4) whether or not the treatment is the least restrictive and least intrusive that meets the requirements of the other three factors (Alberta *Mental Health Act*, section 29).

This middle ground – which one writer refers to as a 'watered-down' right to refuse treatment (Verdun-Jones 1988: 58) – may also be vulnerable to challenge under the *Charter*, particularly in light of statistics which show that most applications to the Review Panel to override the competent patient's refusal are successful (Robertson 1994). In other words, this approach does not really protect the patient's right to refuse treatment in any meaningful way if that refusal can quickly, and easily, be overturned by the Review Panel.

7.4 Patients detained in hospital under the forensic system

7.4.1 Introduction

Hospitalization in a psychiatric facility also occurs within the criminal justice system, if an individual charged with a criminal offence is found by the court to be not criminally responsible by reason of mental disorder ('NCR'), or unfit to stand trial.

7.4.1.1 Not criminally responsible

A verdict of NCR will be entered if it is established that at the time of the offence the accused was suffering from a mental disorder that rendered the person incapable of appreciating the nature and quality of the act or omission, or of knowing that it was wrong (*Criminal Code* 1985, section 16(1)). 'Wrong' means morally wrong, not necessarily legally wrong (Barrett and Shandler 2006).

Every person is presumed to be capable of criminal responsibility, and hence the burden of proof of establishing an NCR defense (the required standard of proof being a balance of probabilities) rests with the party who raises the defense (*Criminal Code* 1985, sections 16(2)–(3)). Both the accused and the prosecution (under more limited circumstances) can raise the NCR defense (Barrett and Shandler 2006; Bloom 2013b).

7.4.1.2 Unfit to stand trial

Being 'unfit to stand trial' is defined as meaning that the accused is unable, on account of mental disorder, to conduct a defense or to instruct counsel to do so, and in particular unable on account of mental disorder to: (a) understand the nature or object of the proceedings; (b) understand the possible consequences of the proceedings; or (c) communicate with counsel (*Criminal Code*, section 2).

The leading case on the meaning of fitness is the decision in *R* v. *Taylor* [1992] 11 OR (3d) 323, in which the Ontario Court of Appeal established the 'limited cognitive capacity' test. This sets a fairly low threshold. In particular, the ability to understand the nature and possible consequences of the proceedings need only be rudimentary. Moreover, with respect to the ability to communicate with counsel, it is not necessary that the accused be capable of giving instructions to counsel which are in the accused's best interests. It is sufficient that the accused is capable of relating the necessary facts to enable counsel to properly present a defense (Barrett and Shandler 2006; Bloom 2013a). Testimonial incompetence (the inability to give evidence) does not in itself render an accused unfit to stand trial, nor does amnesia of the events surrounding the offence (*R* v. *Morrissey*, 2007 ONCA 770).

7.4.2 The Review Board process

In all cases where there is a finding of unfit to stand trial, and where in all cases (unless the court grants an absolute discharge) there is a verdict of NCR, the individual then comes within the jurisdiction of the provincial or territorial Review Board, which must convene a hearing within 45 days of the verdict. The Review Board is established under the *Criminal Code* for each province and territory and its purpose is to determine the appropriate disposition for the NCR or unfit accused. It sits with a minimum quorum of three members, at least one of whom must be a

judge or lawyer (who acts as chair) and at least one of whom must be a psychiatrist (Barrett and Shandler 2006; Carver and Langlois-Klassen 2006; Lamba 2013).

Proceedings before the Review Board are conducted in as informal a manner as is appropriate in the circumstances. Nonetheless, the accused has several important legal rights in the proceedings. These include the right to be present at the hearing (subject to the Review Board's power to exclude the accused in exceptional circumstances), the right to adduce evidence, cross-examine witnesses, and make oral or written submissions, and the right to be represented by legal counsel. In addition, the Review Board must provide reasons for its decision, and any party to the hearing (including the accused) has a right of appeal to the provincial Court of Appeal (Barrett and Shandler 2006; Carver and Langlois-Klassen 2006; Lamba 2013).

7.4.2.1 The NCR accused

An NCR accused must be seen by the Review Board within 45 days of the NCR verdict, and thereafter at least once every year. This annual review will continue so long as the accused remains under the jurisdiction of the Review Board (i.e. until an absolute discharge is granted). At each review, the first issue which the Review Board must determine is whether the individual poses a significant threat to the safety of the public. In making this assessment, there is no presumption that the individual poses a threat (no matter how serious the index offence), nor is there any onus of proof in the ordinary adversarial sense. The Review Board's role is an inquisitorial one. Hence it must take reasonable steps to satisfy itself whether the individual poses a significant threat to the safety of the public. The 'significant threat' threshold requires that the individual pose a real risk of physical or psychological harm to members of the public from conduct that is criminal in nature. Neither a 'miniscule risk of grave harm' nor a 'high risk of trivial harm' will be sufficient to meet this test (*Winko* v. *British Columbia (Forensic Psychiatric Institute)* [1999] 2 SCR 625; Carver and Langlois-Klassen 2006; Lamba 2013).

If the 'significant threat' test is not satisfied, the Review Board *must* grant an absolute discharge. This means that the individual is no longer under the jurisdiction of the Review Board and has no restrictions to his or her liberty. On the other hand, if the individual is judged to be a significant threat, the Review Board's jurisdiction continues and it has the power to order either that the individual be detained in a psychiatric facility or be conditionally discharged into the community. In both cases the Review Board must decide what restrictions or extensions should be ordered with respect to the individual's liberty. For example, where the Board decides that the NCR accused should be detained in a psychiatric facility, it will then decide what privileges, if any, to grant, such as passes to the hospital grounds and the city (with or without hospital staff) and other travel privileges. Likewise, where a conditional discharge is granted, the Review Board will typically restrict the individual's freedom, such as requiring that he or she live in specified or approved accommodation, and by restricting travel. The Review Board is required to make a disposition which is the least onerous and least restrictive to the accused, consistent with public safety (Carver and Langlois-Klassen 2006; Lamba 2013).

Individuals found NCR remain under the jurisdiction of the Review Board indefinitely, potentially for life, until they are granted an absolute discharge on the grounds that they no longer pose a significant threat to the safety of the public.

The government of Canada has recently introduced significant changes to the legislation dealing with NCR accused and the Review Board process. These legislative changes have been passed by the House of Commons, and are currently before the Senate (*Not Criminally Responsible Reform Act*). If enacted, the changes will significantly affect the rights of some NCR accused.

In particular, the proposed legislation will remove the requirement that the Review Board's disposition must be the least onerous and restrictive to the accused. In addition, it will empower the courts to designate an NCR accused as 'high risk' in cases of a serious personal injury offence, if the court is satisfied that there is a substantial likelihood that the accused will use violence that could endanger the life or safety of another person, or if the court is of the opinion that the acts involved in the offense were of such a brutal nature as to indicate a risk of grave physical or psychological harm to another person. The effect of such a designation is significant. In particular, it means that a 'high-risk' accused must be detained in hospital and will not be permitted to leave, even temporarily, except in very limited circumstances and subject to very strict conditions.

These legislative changes have been criticized by many commentators, including the Canadian Bar Association (2013), the Criminal Lawyers' Association (2013), and the chairs of many of the provincial Review Boards (Guly 2013; McKnight 2013; Taddese 2013). The thrust of these criticisms is that the reforms are unfair to NCR accused; they are an unnecessary and inappropriate restriction on the discretion and powers of the Review Board; and they will lead to many mentally ill offenders ending up in jail (without access to proper mental health treatment or programs) rather than in hospital, because they will choose not to raise the NCR defense.

7.4.2.2 The unfit accused

As is the case with an NCR accused, an unfit accused must be seen by the Review Board within 45 days of the court's finding of unfitness, and then at least annually thereafter. The first issue which the Review Board must consider at each review is whether the accused remains unfit to stand trial. If the Review Board concludes that the accused has become fit, the matter is referred back to court, at which time the court will make the final determination of whether the accused is fit to stand trial. If, on the other hand, the Review Board concludes that the accused remains unfit, it then makes a disposition in the same manner as for an NCR accused, with one very important exception: it cannot grant an absolute discharge for an unfit accused, even if it considers that the accused does not pose a significant threat to public safety. The Review Board, applying the overriding principle of the least onerous and least restrictive disposition consistent with public safety, must decide whether the accused should be detained in hospital (and with what privileges, if any) or be discharged from hospital subject to conditions. In both cases the unfit accused remains under the jurisdiction of the Review Board (Barrett and Shandler 2006).

The Review Board's inability to grant an absolute discharge for an unfit accused who poses no significant threat to public safety creates considerable injustice for the 'permanently unfit' individual, that is someone who is unlikely ever to become fit to stand trial. In response to the Supreme Court of Canada's ruling in *R* v. *Demers*, 2004 SCC 46, that this infringes the *Charter* and hence is unconstitutional, the *Criminal Code* was amended to address the problem of the permanently unfit. Although the Review Board still cannot grant an absolute discharge, it can now recommend to the court that the criminal proceedings be stayed, if it considers that the accused (1) does not pose a significant threat to public safety, and (2) will likely never become fit to stand trial. The court will then hold an inquiry (which it can also do of its own motion), to determine whether these two criteria are satisfied, and also whether a stay of proceedings would be in the interests of the proper administration of justice. If the proceedings are stayed, the individual ceases to be under the jurisdiction of the Review Board (Barrett and Shandler 2006; Bloom 2013a).

7.4.2.3 Charter remedies

Review Boards have recently been held to be courts of competent jurisdiction under the *Canadian Charter of Rights and Freedoms* (*R* v. *Conway*, 2010 SCC 22). This means that they have the authority to consider constitutional challenges to the legislation and grant *Charter* remedies (such as damages or declaratory relief) where the accused's *Charter* rights have been infringed (Lamba 2013; Zuckerberg 2011). It is not entirely clear what *Charter* remedies a Review Board would be able to grant. What *is* clear, however, from *Conway* is that a Review Board can only grant *Charter* remedies which fit within the Board's statutory scheme. In particular, the Review Board could not grant an order for absolute discharge as a *Charter* remedy for an NCR accused whom it considered to be a significant threat to public safety (Barrett and Shandler 2006).

7.4.2.4 Psychiatric treatment without consent

The right to refuse medical treatment is reflected in the *Criminal Code* with respect to NCR individuals, in that neither the court nor the Review Board can include in its disposition a requirement that the patient undergo treatment, unless the patient consents (*Criminal Code* 1985, section 672.55).

The position is different, however, with respect to an accused who has been found unfit to stand trial. Recognizing the importance of ensuring that criminal charges be dealt with in a timely manner and the potential unfairness in having an unfit accused remain under the jurisdiction of the Review Board indefinitely, the *Criminal Code* permits the court (but not the Review Board) to order treatment for the individual, even in the absence of consent, for a period not exceeding 60 days, for the purpose of making the accused fit to stand trial (Barrett and Shandler 2006; Bloom 2013a). This type of order tends to be used sparingly, not only because of its intrusive nature, but also because it requires the consent of the hospital and many hospital administrators and physicians are reluctant to be involved in treating a patient without consent (Barrett and Shandler 2006).

Although Review Boards lack the authority to prescribe treatment, the Supreme Court of Canada has held that they do have the power to impose orders or attach conditions regarding the *supervision* of treatment (*Mazzei* v. *British Columbia (Director of Adult Forensic Psychiatric Services)*, 2006 SCC 7). This would include, for example, the power to direct the hospital to undertake a comprehensive review of the patient's diagnosis and treatment, obtain an independent risk assessment, and issue recommendations and suggestions with respect to treatment. This supervisory role regarding treatment represents a significant expansion of the Review Board's jurisdiction. It shows that the Review Board 'should play an active role in addressing problems arising [in] the therapeutic relationship between the forensic system and the individual patient' (Carver and Langlois-Klassen 2006: 18).

Despite the fact that the *Criminal Code* prohibits treatment without consent for NCR patients, in some provinces this can be circumvented by certifying the patient under the provincial *Mental Health Act* (even although the patient is already detained in hospital under the forensic system), thereby taking advantage of the provisions of the *Mental Health Act* which allow treatment to be authorized without consent (Robertson 2010).

7.5 Conclusion

In our examination of the rights of involuntary psychiatric patients in Canada, the theme which is most apparent is that the legislation seeks to strike an appropriate balance between

competing interests. In the context of the criminal law, where individuals are detained in hospital by reason of having been found not criminally responsible or unfit to stand trial, the balance which the legislation attempts to strike is between the safety of the public and the right of the patient to be reintegrated into society. Likewise, for patients who are certified under provincial mental health legislation, the law seeks to strike an appropriate balance between the patient's *Charter* rights and society's interest in protecting the public from harm, while ensuring that persons with mental illness receive the treatment they need. In this context, the patient's right to refuse psychiatric treatment remains the most difficult and most controversial issue.

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8

End of life

Chris Gastmans and Herman Nys

8.1 Introduction

Treatment decisions at the end of life are common in contemporary clinical practice. According to Broeckaert and the Flemish Palliative Care Federation (2009), treatment decisions at the end of life, in principle, can be grouped into three categories. The first group encompasses decisions whether to initiate or withhold, continue or withdraw curative or life-sustaining treatments (e.g. cardiopulmonary resuscitation, artificial ventilation, dialysis, artificial nutrition and hydration). In this group, non-treatment decisions refer to 'withdrawing or withholding a curative or life-sustaining treatment, because in the given situation this treatment is deemed to be no longer meaningful or effective' (Broeckaert and the Flemish Palliative Care Federation 2009: 30–2). According to the British Medical Association (2007), treatment is usually unable to produce the desired benefit either because it cannot achieve its physiological aim or because the burdens of the treatment are considered to outweigh the benefits for the particular individual. This is called 'futile' treatment. Refusal of treatment occurs when the patient requests curative or life-sustaining treatment to be withdrawn or withheld.

The second group of treatment decisions according to Broeckaert and the Flemish Palliative Care Federation's (2009) conceptual framework refers to decisions made to alleviate pain and other symptoms with, for example, opioids, benzodiazepines or barbiturates. In this group, the focus of the decisions shifts from a curative and life-sustaining approach to a palliative approach. Pain control refers to 'the intentional administration of analgesics and/or other drugs in dosages and combinations required to adequately relieve pain' (Broeckaert and the Flemish Palliative Care Federation 2009: 32–3). A specific form of pain control is palliative sedation, 'the intentional administration of sedative drugs in dosages and combinations required to reduce the consciousness of a terminal patient as much as necessary to adequately relieve one or more refractory symptoms' (Broeckaert 2002: 246).

The third group of treatment decisions at the end of life addresses the use of lethal medication. Voluntary euthanasia is defined in the Netherlands, Belgium and Luxembourg – three countries where euthanasia is legalised – as the intentional termination of a patient's life by someone other than the patient, at the patient's request. Assisted suicide is 'intentionally assisting

a person, at this person's request, to terminate his or her life' (Broeckaert and the Flemish Palliative Care Federation 2009: 34–5). Non-voluntary euthanasia involves someone intentionally terminating the life of a patient, but not at the patient's request.

Thus the complex decision-making surrounding the end of life cannot be considered purely clinical; rather it also has an ethical dimension. Treatment decisions are also influenced by the legal context of a particular country (e.g. the *Patient Self-determination Act* (1991) in the US, the legalisation of euthanasia in the Netherlands, Belgium and Luxembourg) (Lewy 2011) and by the country's cultural values (Cohen *et al.* 2013; Gysels *et al.* 2012).

In this chapter, we provide a selected overview of legal and ethical frameworks that address some of the above-mentioned treatment decisions at the end of life. First, we give an overview of legal approaches to end-of-life treatment decisions from an international perspective. Second, we illustrate two major ethical approaches – principlism and care ethics – through a case analysis of euthanasia for patients with advanced dementia. This section centres on the topic of advance euthanasia directives in order to make our ethical evaluation more concrete. We conclude this chapter with an overview of some current and emerging ethical and legal issues in end-of-life care.

8.2 Legal frameworks on treatment decisions at the end of life: an international perspective

There exist no legally binding international rules dealing specifically with treatment decisions at the end of life. This is not surprising, as the legal context of a particular country influences, more than any other medical decision, treatment decisions at the end of life (see section 8.1). Therefore we will discuss the treatment decisions at the end of life within the framework of international human rights law and – given our background – especially, but not limited to, European human rights law. The *European Convention on Human Rights* (ECHR) 1950 of the Council of Europe and the jurisprudence of the European Court of Human Rights (ECtHR) are inexhaustible sources of information and inspiration regarding health and human rights law (Hendriks 2012). Crucial human rights regarding treatment decisions at the end of life are the right to life, the right to be safeguarded from inhuman or degrading treatment and the right to protection of one's private life (Dorscheidt 2012).

8.2.1 The right to life

The *Universal Declaration of Human Rights* 1948 (UDHR) confirmed the protection of all human life as a basic rule in response to the atrocities committed before and during the Second World War. Article 3 of the UDHR stipulates that '[e]veryone has the right to life, liberty and security of persons'. The *International Covenant on Civil and Political Rights* 1966 later adopted a legally binding equivalent of this provision. Article 6(1) of this *Covenant* states that '[e]very human being has the inherent right to life. This right shall be protected by law. No one shall be arbitrarily deprived of his life.' The rhetoric used in this article expresses that the right to life is the most essential human right. Because this provision does not refer to medical decisions at the end of life, it remains unclear how such decisions relate to article 6(1) of the *Covenant*. According to Dorscheidt (2012), at issue is whether it is possible to waive the right to life. Dinstein (1981) sees possibilities for legislation on euthanasia only if it provides guarantees for an authentic request to die, as well as the specific way in which the patient can admissibly abandon his right to life.

From a European perspective, the right to life is laid down in article 2 of the ECHR:

> Everyone's right to life shall be protected by law. Nobody shall be deprived of his life intentionally save in the execution of a court's sentence following his conviction of a crime for which this penalty is provided by law.

During the drafting process, it was not foreseen that the interpretation of this article would relate to treatment decisions at the end of life. Indeed, for many years, the jurisprudence of the ECtHR offered no indication that any such interpretation would arise. However, this has changed in the last decade. In the case of *Glass* v. *The United Kingdom* (Application No. 61827/00) [2004] ECHR 102 (*Glass*), a mother filed *inter alia* a complaint under article 2 of the ECHR against the Portsmouth Hospitals National Health Service Trust and its physicians. She alleged they put her ill son's life at risk by administering to him an adult dose of a sedative and pain relief medication (diamorphine) and that they placed a DNR order in his medical file without her consent or knowledge. The ECtHR did not deny that the acts and omissions of healthcare professionals in certain circumstances may engage states parties' responsibilities under the ECHR (para. 71). However, if a state party has made adequate provisions to secure high professional standards for healthcare workers and to protect the lives of patients, matters of error of professional judgment (even if established) in treating a patient are not sufficient in themselves to call that state to account for its obligation under article 2 of the ECHR to protect life. Ultimately, the ECtHR found this complaint ill-founded, and therefore inadmissible.

The judgment in *Pretty* v. *The United Kingdom* (Application No. 2346/02) [2002] ECHR 427 (*Pretty*) was the first explicit ruling of the ECtHR on the relationship between deliberate ending of life at request and article 2 of the ECHR. Diane Pretty suffered from motor neurone disease (MND), a progressive neurodegenerative disorder of the motoric cells of the central nervous system. In time, a patient with MND will experience severe breathing difficulties, eventually resulting in death by suffocation. To prevent serious deterioration, Pretty wanted to end her life in a humane and dignified way. Due to her poor physical condition, she was unable to end her life alone and wanted to enlist her husband's help in ending her suffering. However, assisted suicide is a criminal offence in the UK. Pretty therefore requested the Director of Public Prosecutions to declare that her husband would not be prosecuted if he helped her to die. This request was denied. An appeal to the Divisional Court and later to the House of Lords did not succeed either. Finally she presented her case to the ECtHR, where she argued that the British judicial authorities' refusal to grant her husband immunity from prosecution constituted a violation of, among others, article 2 of the ECHR. According to Mrs Pretty, article 2 not only protected the right to life, but also guaranteed the right to choose whether or not to continue living. Pretty was convinced that the article included the right to die in order to prevent unbearable suffering and indignity.

From the point of view of the ECtHR, article 2 leaves no room for doubt:

> Article 2 cannot, without distortion of language, be interpreted as conferring the diametrically opposite right, namely a right to die; nor can it create a right to self-determination in the sense of conferring on an individual an entitlement to choose death rather than life. The Court accordingly finds that no right to die, whether at the hands of a third person or with the assistance of a public authority, can be derived from article 2 of the Convention.
>
> *(*Pretty, *paras 39–40)*

Although in some countries assisted suicide is not punishable in specific circumstances, article 2 of the ECHR holds no obligation for the UK to accept a similar criminal regime regarding such conduct. It is considered to fall under a state party's 'margin of appreciation' to address such an act in a way that corresponds with national criminal law, and having regard to the state's responsibilities under the ECHR. Consequently, the ECtHR concluded there was no violation of article 2.

8.2.2 Treatment decisions at the end of life and freedom from inhuman or degrading treatment

The issue at stake is whether the fundamental right to protection against inhuman or degrading treatment plays a role in establishing the legal admissibility of treatment decisions at the end of life, as stated in article 7 of the *International Covenant on Civil and Political Rights* and article 3 of the ECHR. Can the state be held responsible for an individual's suffering due to his state of health, or even a continuation of life-sustaining treatment? In *Pretty,* the applicant further argued that her suffering constituted degrading treatment within the meaning of article 3 of the ECHR. Although she admitted that the state bore no direct responsibility for this treatment, she argued the state must not only refrain from such treatment, but also has a duty to protect its civilians against it. Therefore the UK would be obliged to take measures to protect her against further suffering.

However, the ECtHR concluded that article 3 was not violated. The refusal of the UK authorities to grant Pretty's husband immunity from prosecution was not equal to inhuman or degrading treatment for which the state bears responsibility for failing to protect Pretty from the suffering she must face. The ECtHR was unwilling to force the UK to permit actions that end life. No such positive obligation for a state can be derived from article 3 of the ECHR, no more than can a duty for the UK to declare that Pretty's husband will not be prosecuted if he assisted his wife in ending her life.

8.2.3 Treatment decisions at the end of life and the right to privacy

According to article 8(1) of the ECHR, '[e]veryone has the right to respect for his private and family life, his home and his correspondence'. The right to respect for his private life is especially important with regard to treatment decisions at the end of life.

First, the right to respect for private life underpins the right to give or refuse consent for any medical treatment, including at the end of life. In *Glass,* the ECtHR held that the decision to impose medical treatment on a critically ill 12-year-old boy in defiance of his mother's objections interfered with the child's right to respect for his private life, particularly his right to physical integrity. Such interference is generally admissible only if it occurs after free, expressed and informed consent. The Court observed that the boy's mother had clearly withdrawn her consent while the physicians should have respected her change of mind and refrained from intensively attempting to overcome her opposition. As a result, the ECtHR concluded the authorities' decision to override the mother's objection to the proposed treatment, in absence of a court authorisation, resulted in a breach of article 8 of the ECHR. Moreover, in *Pretty*, the ECtHR stated that the very essence of the ECHR is respect for human dignity and human freedom. Without in any way negating the principle of sanctity of life protected under the ECHR, the ECtHR considered that it was under article 8 that notions of the quality of life took on significance.

In an era of growing medical sophistication combined with longer life expectancies, many people feel they should not be forced to linger on in old age or in states of advanced physical

or mental decrepitude, which may conflict with strongly held ideas of personal identity. The ECtHR regards the freedom to refuse medical treatment, even if it concerns potentially life-saving medical treatment, vital to the principles of self-determination and personal autonomy articulated in *Jehovah's Witnesses of Moscow and Others* v. *Russia* (Application No. 302/02) 10 June 2010 (para. 135). After *Pretty*, the ECtHR repeated this point of view in several other judgments, the most recent being in *Gross* v. *Switzerland* (Application No. 67810/10) [2013] ECHR 429 (*Gross*). In *Gross,* the ECtHR held that a competent adult patient has the right to make choices according to his own view and values, regardless of how irrational, unwise or imprudent such choices may appear to others. Therefore the state must refrain from interfering with individual freedom of choice in the sphere of healthcare, for such interference would only lessen, rather than enhance, the value of life. The ECtHR clearly sympathises with the view that a person's authentic decision to end his life is part of his private life, as observed by Dorscheidt (2012).

Second, the right to private life is relevant to assisted suicide. In the *Pretty* case, the applicant, Diane Pretty, also relied on article 8 (1) of the ECHR and her right to self-determination. Pretty argued that the Director of Public Prosecutions' refusal to grant her husband the requested immunity, as well as the British ban on assisted suicide, constituted violations of her right to privacy and freedom to prevent her life from ending in an undignified way. However, the ECtHR dismissed Pretty's application based on article 8(1) of the ECHR. The ECtHR did not want to affirm that Pretty's situation was indeed an infringement of her private life. Rather, it held that the right to privacy is not absolute. In the ECtHR's view, the UK is permitted to create criminal law regulations, regulating behaviour which endangers people's lives or safety. The greater the danger, the more the idea of personal autonomy must be considered inferior to the interest of public health or public safety. Regardless of the circumstances that befall the terminally ill, their vulnerability justifies the criminalisation of assisted suicide in the UK. Therefore the ECtHR concluded that the criminalisation of assisted suicide in the UK serves a legitimate purpose and constituted a necessary interference with Pretty's right to privacy based on article 8(2) of the ECHR.

Another case on assisted suicide decided by the ECtHR is *Koch* v. *Germany* (Application No. 497/09) 19 July 2012. Mrs Koch suffered from total sensorimotor quadriplegia after falling in front of her doorstep. She was almost completely paralysed and needed artificial ventilation, constant care and assistance from nursing staff. She further suffered from spasms. However, according to her medical assessment, she had a life expectancy of at least fifteen more years. Nonetheless, she wished to end what was, in her view, an undignified life, by committing suicide with her husband's, the applicant, help. She requested the Federal Institute for Drugs and Medical Devices authorise her to obtain 15 grams of pentobarbital of sodium, a lethal dose of medication that would enable her to commit suicide at her home. The Federal Institute refused to grant her authorisation, relying on section 5(1)(6) of the German *Narcotics Act*. Consequently, together with her husband, she travelled to Switzerland where she died after committing assisted suicide with the help of a Swiss assisted-suicide organization. Her husband applied to the ECtHR claiming the refusal to provide his late wife with a lethal dose of drugs allowing her to end her life violated both their right to respect for private and family life. Relying on its case law, the ECtHR concluded the Federal Institute's decision to reject Mrs Koch's request did interfere with the applicant's right to respect for his private life under article 8 of the ECHR (para. 54). However, the state's decision ultimately fell within its margin of appreciation. Relying on comparative research, the ECtHR found that the majority of member states do not allow any form of assistance to suicide (para. 70). Only four states have allowed medical practitioners to prescribe a lethal drug to enable a

patient to end his life. It follows that the states parties to the ECHR are far from reaching a consensus on the issue. Consequently, states enjoy a considerable margin of appreciation in this context.

Third, article 8 of the ECHR is relevant in determining the legal requirements for obtaining medication to end one's own life (suicide), as demonstrated by *Gross* and *Haas* v. *Switzerland* (Application No. 31322/07) 20 January 2011 (*Haas*). For approximately twenty years, Haas suffered from a severe bipolar affective disorder. As a result of his condition, Haas felt he could no longer live in a dignified manner and attempted suicide twice. Subsequently, he decided to obtain sodium pentobarbital (SPB), a substance that would enable him to end his life safely and with dignity. Since the substance was only available through prescription, he unsuccessfully approached several psychiatrists to obtain a prescription. Later, he approached various federal and cantonal authorities (Federal Departments of Justice and Public Health and the Department of Health of the Canton of Zurich), seeking permission to obtain SPB from a pharmacy without a prescription. The Federal Department of the Interior and the Zurich Administrative Court rejected both his application and appeal. Haas finally appealed to the Federal Court, but his action failed. Before the ECtHR, Haas complained about the conditions to obtaining SPB, specifically a medical prescription based on a psychiatric assessment. Relying on article 8 of the ECHR, he alleged that since those conditions could not be met in his case, the right to which he considered himself entitled to, namely choosing the time and manner of his death, was not respected. He submitted that, in an exceptional situation such as his, the state ought to guarantee his access to the necessary medical products for suicide. In light of its case law, the ECtHR considered that an individual's right to decide by what means and at what point his life will end – provided he is capable of freely reaching a decision on the question and acting in consequence – is one aspect of the right to respect for private life within the meaning of article 8 of the ECHR.

According to the ECtHR, the issue was whether, under article 8, the state must ensure that the applicant can obtain a lethal substance without a medical prescription in order to commit suicide painlessly, by way of derogation from the legislation (*Haas,* para. 52). Although the ECtHR was sympathetic to Haas' wish to commit suicide in a safe and dignified manner without unnecessary pain and suffering, it nevertheless believed Swiss regulations, specifically the requirement to obtain a medical prescription, pursued the legitimate aims of protecting individuals from hasty decisions and preventing abuse. In particular, the ECtHR supported regulations ensuring that a patient lacking discernment does not obtain a lethal dose of SPB.

The ECtHR went on to consider such regulations all the more necessary in a jurisdiction such as Switzerland, where legislation and practice allow for relatively easy access to assisted suicide (*Haas,* para. 57). Therefore, where a country adopts a liberal approach in this respect, implementing preventive measures to counteract abuse is necessary. The introduction of such measures is also intended to prevent organizations providing suicide assistance from acting unlawfully, in secret and with significant risks of abuse. Therefore the ECtHR concluded that even assuming states have a positive obligation to facilitate suicide with dignity, the Swiss authorities complied with their obligation in the present case (*Haas*, para. 61). Hence there was no violation of article 8 of the ECHR.

Similarly, *Gross* also dealt with article 8 of the ECHR and the accessibility of SPB as a means of putting an end to one's life in their own dignified way. For many years, Gross expressed her wish to end her life. She explained she was becoming increasingly frail as time passed and was unwilling to continue suffering the decline of her physical and mental faculties. In 2005, following a failed suicide attempt, she received inpatient treatment for six months in a psychiatric hospital. This treatment did not alter her wish to die. Therefore she contacted an assisted death

organization, EXIT, for support. However, she was informed that it would be difficult to find a medical practitioner who would be willing to provide her with a medical prescription for the lethal drug.

Upon examining Gross, one psychiatrist was convinced she was able to form her own judgment. He further noted that her wish to die was reasoned and well-considered, had persisted for several years and was not based on any psychiatric illness. From a clinical point of view, the psychiatrist did not object to prescribing Gross a lethal dose of SPB. However, he refrained from issuing the prescription himself: he did not want to confuse the roles of medical expert and treating physician. Afterwards, a physician stated that she would be ready to examine Gross and to consider her request to issue the required prescription, provided that her counsel could guarantee that she would not risk any consequences from the point of view of the code of professional medical conduct. When her counsel replied that he could not give such a guarantee, the physician declined the request, as she did not want to be drawn into lengthy legal proceedings.

Gross then submitted a request to the Health Board of the Canton of Zurich for 15 grams of SPB in order to commit suicide. She submitted that she could not reasonably be expected to continue her search for a physician who was ready to issue the required medical prescription. The Health Board refused her request and all of her subsequent appeals against this decision failed. Before the ECtHR, Gross argued that by depriving her of a lethal dose of sodium pentobarbital, the Swiss authorities violated her right to decide by what means and at what point her life would end. Once again, referring to its case law, the ECtHR considered that Gross' wish to be provided with the lethal dose indeed fell within the scope of her right to respect for her private life under article 8 of the ECHR (para. 60). However, the ECtHR identified a significant difference with the *Haas* case. In the former case, the ECtHR considered that it was appropriate to examine Haas' request to obtain access to sodium pentobarbital without a medical prescription from the perspective of a positive obligation on the state to take the necessary measures to permit a dignified suicide. Inversely, the *Gross* case raised the question of whether the state had failed to provide sufficient guidelines defining if and, in the case of the affirmative, under which circumstances medical practitioners were authorised to issue a medical prescription to a person in Mrs Gross' condition (para. 63).

The ECtHR observed that pursuant to article 115 of the Swiss *Criminal Code* 1937, inciting and assisting suicide are punishable only where the perpetrator of such acts is driven to commit them by 'selfish motives'. Under the case law of the Swiss Federal Supreme Court, a doctor is entitled to prescribe SPB in order to allow his patient to commit suicide, provided that conditions outlined in the Federal Supreme Court's case law are fulfilled. The ECtHR noted that the Federal Supreme Court referred to the medical ethics guidelines on the care of patients at the end of their life, which were issued by a non-governmental organization and did not have the formal quality of law. However, the ECtHR observed that these guidelines only apply to patients whose doctor determined that their death was imminent. Because Gross was not suffering from a terminal illness, her case did not fall within this scope. Moreover, the Swiss government did not rely on any other principles or standards in outlining under what circumstances a doctor is entitled to prescribe SPB for a patient who, like Gross, was not suffering from a terminal illness. Therefore the ECtHR considered the paucity in clear legal guidelines would likely have a chilling effect on doctors who would otherwise be inclined to provide someone like Mrs Gross with the requested medical prescription. Two doctors previously consulted by the applicant had confirmed this prediction – both declined the applicant's request on the grounds that they felt the medical

practitioners' code of conduct prevented them from prescribing the drug, fearing possible professional consequences as a result of lengthy judicial proceedings. Had there been state-approved guidelines defining when it was permissible for doctors to prescribe lethal doses for assisted suicide, Gross, and patients like her, would have been spared a state of anguish and uncertainty (para. 66).

The ECtHR sympathised with Mrs Gross, acknowledging the anguish she must have endured waiting for a decision allowing her request. At issue was under what circumstances medical practitioners were justified in issuing the requested prescription in cases where an individual has come to a serious decision, in the exercise of their free will, to end his or her life, but where death would not otherwise be imminent as a result of a specific medical condition. The ECtHR concluded that Swiss law, while providing for the possibility of obtaining a lethal dose of sodium pentobarbital with a medical prescription, did not provide sufficient and clear guidelines as to the extent of this possibility, which violated the applicant's right under article 8 of the ECHR.

The four to three decision in this case demonstrates the lack of consensus among the judges of the ECtHR on this matter.

Finally, the right to respect for family life protected by article 8 of the ECHR may also be relevant when treatment decisions at the end of life are taken, as demonstrated by *Lind* v. *Russia* (Application No. 25664/05) 6 December 2007 (*Lind*). In *Lind,* the Applicant, a Russian prisoner, complained that he was not allowed to visit or say goodbye to his dying father because the Russian authorities had denied his multiple requests and appeals to be released. The ECtHR had already affirmed that the refusal of leave to visit an ailing relative or to attend a relative's funeral constituted an interference with the right to respect for family life (*Ploski* v. *Poland* (Application No. 26761/95) 12 November 200 cited in *Lind*, para. 92). However, article 8 of the ECHR does not give a detained person an unconditional right to leave to visit a sick relative or attend a relative's funeral: domestic authorities must assess each request based on its own merits (*Lind*, para. 94).

In *Lind*, the applicant's father was dying of cancer in The Hague, and had requested euthanasia, which was scheduled for 29 September 2005. This was the distinguishing feature of this case: the date of the applicant's father's death was known in advance and he was to die within a matter of days. Therefore it was truly the applicant's last opportunity to see his father. Moreover, given the applicant's father's grave condition, it was unrealistic to expect him to visit his son in detention. Taking into account these exceptional circumstances and the humanitarian considerations involved, the ECtHR believed the domestic authorities should have examined the applicant's request for release with particular attention and scrutiny. However, the ECtHR considered the domestic authorities better placed to assess the matter. Consequently, the ECtHR was unable to find that, in refusing to release the applicant, the domestic authorities exceeded their margin of appreciation (*Lind*, para. 97). Nonetheless, respect for his family life required that, once his application for release had been rejected, the applicant be provided with an alternative opportunity to bid farewell to his dying father, opportunity he was given by being allowed to talk on the phone to his father. However, the conversation had to be in Russian, lasted a minute and was interrupted by the facility administration without any explanation from the government. The ECtHR considered that this one minute conversation in a language which the applicant's father had difficulty understanding did not provide a meaningful opportunity for the applicant to bid farewell to his dying father (*Lind*, para. 98). For these reasons, the ECtHR concluded that the domestic authorities had failed to secure respect for the applicant's family life as required by article 8 ECHR.

8.3 Ethical approaches to end-of-life care: euthanasia for patients with advanced dementia as a case study[1]

Since 2002, euthanasia within a number of patient categories has been legalised in Belgium and the Netherlands, provided that strict due care criteria are applied. Section 2 of the *Belgian Act on Euthanasia* 2002 defines euthanasia as 'intentionally terminating life by someone other than the person concerned, at the latter's request' (Nys 2002: 182). This definition is commonly known as the 'Dutch definition' of euthanasia. Ironically, the Dutch Act on euthanasia, the *Termination of Life on Request and Assisted Suicide (Review Procedures) Act* 2002, does not contain this definition and the word 'euthanasia' is not even mentioned in the text of the Act. The Act always refers to 'termination of life on request', without defining the notion. Since termination of life on request coincides with what is labelled as euthanasia in the *Belgian Act*, both Acts have the same field of application. The *Belgian Act on Euthanasia* does not allow euthanising persons with severe dementia as decreed in an advance euthanasia directive. However, bills to extend to this possibility have unsuccessfully been presented to the Belgian parliament.

By contrast, in the Netherlands, euthanasia of persons with severe dementia, as decreed in an advance euthanasia directive, is allowed by law (*Termination of Life on Request and Assistance with Suicide (Review Procedures) Act*). The implementation of euthanasia in this patient population, however, is under discussion (Sheldon 2011). To our knowledge, no official documents on the ethics of euthanasia for patients with dementia exist. Despite this, some empirical (Rurup *et al.* 2005; Rurup *et al.* 2006a; Rurup *et al.* 2006b; De Boer *et al.* 2010a; De Boer *et al.* 2010b; De Boer *et al.* 2011) and philosophical (Hertogh *et al.* 2007; Gastmans and De Lepeleire 2010; Draper *et al.* 2010; Gastmans and Denier 2010; Sharp 2012; Gastmans 2013; Den Hartogh 2013; Nys 2013) studies on the issue have been conducted. The topic of advance euthanasia directives for patients with dementia enables us to present two influential ethical approaches to end-of-life care: the principles-oriented autonomy approach that generally favours the use of advance euthanasia directives on the one hand, and the care-oriented relational approach that mostly criticises advance euthanasia directives on the other hand.

8.3.1 Principles-oriented autonomy approach

Today's elderly generation regards the prospect of progressing dementia in their own way. The elderly often associate dignity with autonomy, independence and preserving one's intellectual powers (Woolhead *et al.* 2004). Some individuals believe that the fear of losing one's intellectual capacities, and the risk of being handed over to the will of others when one becomes incompetent, are notable reasons for requesting euthanasia via an advance euthanasia directive (Hardwig 2013; Den Hartogh 2013). These advance directives rely on the authority of the competent pre-dementia person (the 'then' self) to govern the welfare of the incompetent person with dementia (the 'now' self) (Dworkin 1993, 2006; Draper *et al.* 2010). Proponents of this 'precedent autonomy or critical interest' approach underline the stewardship responsibility of the 'then' self for the journey into forgetfulness (Dworkin 1993, 2006; Post 1995). As a consequence, post-dementia decisions should be based on historical lifetime values and beliefs. De Boer *et al.* (2010a: 204) clarify:

> [T]he decisions made by a competent individual as laid down in the advance directive represent the individual's appraisal of where his/her critical interests lie, and should therefore prevail above the preferences of the person with dementia.

1 The following sections build on the already published work of the authors.

An important presupposition of this approach is that individuals are perfectly capable of determining their wishes concerning their end-of-life care individually and cognitively, and in such a way that advance directives unambiguously tell caregivers what to do. Persons are, in this approach, mainly considered as beings with thoughts, intelligence, reason, reflection and consciousness (Hughes 2001). Decision aids serve to facilitate the development of advance directives, providing neutral information about the dementia process such that an informed decision can be made (Levi and Green 2010).

Respect for autonomy – one of the four principles of biomedical ethics described by Beauchamp and Childress (2012) – largely covers moral reasoning on advance euthanasia directives. The literature describes autonomy as the right to self-determination and individual choice (Den Hartogh 2013). Respect for autonomy is founded on the ideal of the autonomous agent. As an autonomous person, one is entitled to act in accordance with a freely self-chosen and informed plan. In line with this philosophical viewpoint, advance euthanasia directives are considered instruments that enable, and indeed legitimise, autonomous wishes concerning a dignified end of life.

8.3.2 Care-oriented relational approach

While the principle of respect for autonomy generally leads to an argument in favour of advance euthanasia directives, questions arise about its applicability to cases involving dementia patients. Because dementia is marked by progressive deterioration, affecting both the memory and reasoning capabilities, dementia patients fall short of the ideal of the autonomous agent that grounds the principle of respect for autonomy. Hence, according to the proponents of the care-oriented relational approach, ethical reflection on the end-of-life of persons with dementia should not start from the ideal of the autonomous agent but from the relational context in which dementia care practices are embedded.

The caregiving relationship often involves entering into a relationship with a vulnerable human being – in this case, a person with dementia who is in need of care. However, it is not always clear what care needs a particular person with dementia might have. Finding the right answer is not the result of a general and abstract balancing of principles or of logical deduction. Rather, the right answer is reached through a shared dialogical process of interpretation and mutual understanding that takes place within the care relationship (Widdershoven and Berghmans 2001). Based on this relational approach to dementia care, some problems arise in using advance euthanasia directives (Hertogh *et al.* 2007; Hertogh 2009; Gastmans and De Lepeleire 2010; Gastmans and Denier 2010; Gastmans 2013).

The first group of problems relates to interpreting patients' wishes. As many authors have already pointed out, clearly expressing one's wishes and thoughts can be difficult. However, interpreting the meaning of a patient's wishes can be an even more difficult task for people such as family members, caregivers, etc. A patient's wishes cannot be assumed or implicitly deduced from an advance directive which attempts to clarify for all those involved what must be done for the patient throughout the consecutive stages of care. What a patient would have wanted under specific circumstances needs to be constructed through fairly elaborate interpretative processes, based on what we know of his or her life, previous pronouncements (e.g. as reported in advance directives) and the patient's actual reactions to concrete proposals (Agich 2003). Even if persons with dementia might be incompetent, they still have the capacity to experience their life and the context wherein it is embedded (De Boer *et al.* 2010a). Hence contemporary preferences, needs and desires, coupled with the present well-being of the person with dementia, should be the main foci for substituted decision-making. This perspective on the relationship between the

'then' self that existed prior to the onset of dementia and the 'now' self that lives almost entirely in the present without any connection to the past, is known as the so called 'experiential interest approach' (Dresser 1995; Draper *et al.* 2010).

Even if, as in advance euthanasia directives, the proposed medical intervention (euthanasia) is clear, communication and interpretation are still needed. Most notably, the difficulty resides in determining the moment when euthanasia should be performed. Suppose, for instance, that a person diagnosed with early dementia clearly states a wish to be euthanised the moment he can no longer recognise his child. This advance euthanasia directive is not self-executing. The physician must determine whether this person's actual situation indeed matches the circumstances specified in the advance directive. This is very difficult for even the most carefully formulated specifications about the chosen moment of death (Widdershoven and Berghmans 2001; Hertogh *et al.* 2007). For example, how should one determine the act of recognition? Surely there are many ways of recognising a person. Where should the line be drawn (Widdershoven and Berghmans 2001)? The progressive developmental stages of dementia itself can render it almost impossible to determine the moment of death in such cases: patients can still have good moments from time to time, no matter how diminished these may be (Gastmans and Denier 2010).

This brings us to the category of problems with future forecasting. They refer to the fact that a person's preferences and values can change. Individuals are able to constructively adapt to even the most severe debilities. Previously communicated wishes may not reflect a change of heart (Hertogh 2009). The issue of irreversibility is more pronounced when dementia patients are involved, as it is impossible to reconsider the decisions outlined in one's advance euthanasia directive. It may be that the aforementioned person with an advance euthanasia directive resists when the procedure is performed. How is such resistance to be handled? Thus physicians and proxies are faced with the dilemma of balancing the current preferences and experiences of the person with dementia against the patient's earlier opinions laid out in a now-forgotten advance directive (Widdershoven and Berghmans 2001; Hertogh *et al.* 2007; Gastmans and Denier 2010; De Boer *et al.* 2010a). Following the 'experiential interest approach', the well-being and interests of the 'now' self are of moral significance, and the absolute primacy of precedent autonomy seems to be wrong (Post 1995). Goering clarifies:

> This does not mean that we should never make plans for our future-selves; rather, it means that we should take care to provide for flexibility in any advance directive, with the recognition that our values or priorities may change, and due to declining decisional capacities, those judgements may need to be made by others in conjunction with our future-selves, rather than solely and individually by our presently competent selves.
>
> *(Goering 2007: 63)*

Another challenge is the difficulty in respecting patient autonomy when it conflicts with the wishes of relatives, friends and caregivers. It seems in the case of advance euthanasia directives, supporting the respect for autonomy principle is much more complicated. People's wishes and values are very often of a pre-reflexive and emotional kind. Without sufficient attention to emotional cues from patients with dementia such as feelings of grief or resistance, relevant third parties (e.g. relatives, friends, caregivers) risk facing a situation in which the patient can easily draft an advance euthanasia directive on their personal computer while in a state of panic or depression, or having little or unclear information about the course of dementia. In this case, advance euthanasia directives could even increase the vulnerability of the patient, as they do not reflect the well-informed wish of the patient (Gastmans and Denier 2010).

Finally, a patient's decision to write an advance euthanasia directive has important implications for all parties involved in the patient's care (Hertogh *et al.* 2007). Because the timing of the euthanasia procedure must be made by someone other than the patient (e.g. the physician), dissensions can arise between the parties involved. Thus to what extent can our fellow man be given the responsibility to ensure that our right of self-determination is respected? The above-mentioned scenario clearly demonstrates a contradiction in the autonomy approach when applied to advance euthanasia directives in persons with dementia.

This critical discussion culminates in the basic problem weakening the use of advance euthanasia directives: the lack of communication and shared understanding between the demented patient, on the one hand, and the caregivers, on the other hand. Margaret Battin confirms:

> To end the life of a patient, even if fully legal, is not an easy process for a physician. We can assume it would be even more difficult when it is no longer possible for the physician to discuss the issue rationally with the patient and to have the patient's wish explicitly confirmed, and especially difficult when there is no evidence of current suffering other than the fact of having dementia disease.
>
> *(2007: 59)*

This observation is confirmed by studies from the Netherlands where, despite the legal recognition of advance euthanasia directives for persons with dementia, euthanasia occurs very rarely or even not at all in this patient group (De Boer *et al.* 2010b; Rurup *et al.* 2006a; Rurup *et al.* 2006b; De Boer *et al.* 2011). Dutch researchers concluded:

> [C]ommunication and interpretation are crucial in determining the circumstances as well as the exact moment of performing euthanasia and this cannot be captured in or replaced by advance euthanasia directives. This is precisely what seems to cause the fundamental problem of complying with advance euthanasia directives in cases of severe dementia.
>
> *(De Boer et al. 2010b: 261)*

According to Hertogh (2009), euthanasia for persons with severe dementia on the basis of an advance euthanasia directive seems to be equivalent to attempting to operate in the dark. He refers to a fundamental vulnerability that confronts physicians if the dialogical and interpretative aspects of end-of-life care are no longer present, and which becomes clear when caring for severely ill demented patients who are unable to discuss their euthanasia requests as formulated in advance euthanasia directives.

Given the above-mentioned difficulties that arise from conceptualising advance euthanasia directives within a principles-oriented autonomy approach, some authors suggest a care-oriented relational approach instead (Hertogh 2009; De Boer *et al.* 2010a; Gastmans and Denier 2010). According to them, taking into account the dialogical and interpretative nature of ethical decision-making should be a standard and indispensable element of good dementia care. As Moody says, '[t]he heart of the matter is not to be found in the legal instrument as much as in the process of communication and negotiation which leads up to the result' (Moody 1992: 92).

In the care-oriented relational approach, the patient's best interest should not solely focus on the patient's wishes as an isolated individual. Rather, the patient's best interest should always start with listening to the concerns expressed by the patient, close relatives, caregivers, etc. because they reflect the rich relational context in which the person's care must take shape. Understanding persons implies an understanding of the relational stories in which these persons are embedded (Hughes 2001), and shared decision-making describes a participatory process involving all

parties. There will never be a legal instrument that supplants this demanding process of communication and interpretation inherent to shared decision-making. Therefore certain authors suggest that advance euthanasia directives have as their purpose to facilitate, but not replace, ethical dialogue and the interpretation process among all decision-makers involved (Widdershoven and Berghmans 2001; Tulsky 2005).

8.4 Current and emerging legal and ethical issues in end-of-life care

In this section, we present two controversial topics frequently discussed in current end-of-life debates: end-of-life decision-making concerning severely ill newborns and the status of conscientious objections in end-of-life care.

8.4.1 End-of-life care of severely ill newborns

Neonatology specialises in treating newborns with diverse, life-threatening conditions. This can include full-term babies with multiple congenital disorders, babies who suffer from complications during delivery or extremely pre-term newborns (<26 weeks) hovering between life and death. In such cases, the spectrum of medical possibilities applied within the field of neonatology demands that positive and negative aspects of decisions, and their subsequent effects, are constantly weighed. On the one hand, it is possible to save lives and to treat children who would certainly have died in previous times. On the other hand, it remains to be asked whether life-sustaining treatment is justifiable if it will result in poor quality of life for the child (Walther 2005). In our ethical and legal exploration of these questions, we largely rely on the reports published by the Nuffield Council on Bioethics (2006), the Health Council of the Netherlands (2007) and the Committee on Fetus and Newborn of the American Academy of Pediatrics (2007, reaffirmed 2010).

8.4.1.1 The boundaries of viability

Neonatal intensive care allows for the control and support of the baby's vital functions – blood pressure, respiration, temperature, nutrition – and can provide a substitute intrauterine environment. Many newborns benefit from interventions without which their lives would have taken a different course (Nuffield Council 2006; Sauer 2001).

The perceived benefits of these interventions are complicated when babies suffer from serious disorders. Newborns with severe chromosomal disorders such as trisomy 13 will certainly die regardless of the treatment. Others, for instance those with serious brain damage or organ failure, can stay alive only with life-prolonging treatment. In these two cases, physicians and parents often opt for pain and comfort management available through palliative care, in combination with withholding/withdrawing life-sustaining medical treatments. For most of these children, this results in a dignified end of life (Nuffield Council 2006; Verhagen and Sauer 2005a; Sauer 2001).

Sometimes, however, the true extent and impact of a disorder becomes clear only later on, when the baby's life no longer depends on the application of life-sustaining medical treatment. This category of patients includes viable newborns who are likely to suffer from severely limiting physical and cognitive disorders such as cystic leukomalacia, a serious form of epidermolysis bullosa, etc. In such situations, the question of whether active termination of life is justifiable becomes relevant (Nuffield Council 2006; Verhagen and Sauer 2005a). In this context, the Dutch

Groningen Protocol 2005 (Verhagen and Sauer 2005a; Verhagen and Sauer 2005b) provoked a worldwide ethical debate concerning the question of whether it is sometimes, in very exceptional cases, justified to terminate the life of severely ill newborns (Hanson 2009; Jotkowitz *et al.* 2008; Kodish 2008; Lindemann and Verkerk 2008; Kon 2007, 2008; Chervenak *et al.* 2006; Manninen 2006; Feudtner 2005).

8.4.1.2 Legal and self-regulating framework

No jurisdiction explicitly allows active termination of newborn babies. However, in most countries, non-initiation or withdrawal of life-sustaining medical treatments are legal under specific circumstances (Sauer *et al.* 2013). In the Netherlands, active termination is tolerated within the self-regulating framework of the Groningen Protocol (Verhagen and Sauer 2005b). In 2005, the Dutch Pediatric Association and the Public Prosecutors approved the Groningen Protocol (developed in 2002 by physicians from the University Medical Centre in Groningen) for nationwide application. Key elements from the procedure include: parental consent; clear description of diagnosis and prognosis; approval from a team of physicians, of which at least one is not directly involved in the care for the patient; and legal supervision *a posteriori* (Verhagen and Sauer 2005b). In 2007, the Minister of Justice and the Secretary of State for Health approved a regulation establishing a Central Committee of Experts on late term abortion and termination of life of newborns (*Staatscourant* 2007), requiring the notification of this Committee in either case. The Committee evaluates whether the criteria of due care contained in the Groningen Protocol is respected and informs the Public Prosecutor of the results. Uncertainty regarding which cases should be presented to the Committee has resulted in low reporting rates. Consensus among the medical professions is lacking (Verhagen 2013). Very recently, however, the Royal Dutch Medical Association (KNMG) published a document containing '[c]lear criteria for medical end-of-life decisions for newborn infants with very serious birth defects' (KNMG 2013). It is expected that this document will enhance transparency in the medical practice and provide more efficient legal control (Verhagen 2013). A brief explanation of parts of this document is provided by the KNMG:

- *Decision-making and the role of parents*. Doctors are expected to communicate with parents openly, directly and regularly. Parental input is a vital part of the decision-making process, particularly where the prognosis is uncertain. Parental permission is always required for the treatment of a newborn baby. Where treatment is medically futile, doctors may – following consultation – decide independently to suspend or to not provide such treatment. This is because the doctor's primary duty of care is towards the infant, and the treatment provided must not harm or prolong harm or suffering.
- *Suspending nutritional support*. If there is no longer any justification for providing life-prolonging treatment to a baby, it will also be unacceptable to continue administering fluids and nutrition. Doctors may allow parents time to understand and accept as best they can that treatment is to be suspended. However, there will be a time limit as to how long physicians can accommodate parents' desire to continue treatment once it has been established that such treatment is medically futile.
- *Gasping and administering of muscle relaxants*. Newborn infants may be visibly suffering if they are gasping for air. Once it has been decided to withhold further treatment, the position paper states that administering muscle relaxants is justified where:

- the baby is gasping, visibly suffering, and pain relief is not sufficiently effective. Deliberate ending of life will then be justified and must be reported to the Central Committee of Experts for assessment. The position paper provides a clear framework for subsequent assessment of the appropriateness of this action;
- if the dying process is underway but is so prolonged that it is causing serious distress to the parents. Such a situation must also be reported. Justification on these grounds needs to be added to the criteria under the Regulation for the Central Committee of Experts;
- if the baby was already receiving muscle relaxants as part of its treatment. Continuing to administer this treatment may be regarded as normal palliative care if suspending it and waiting for its effects to wear off is deemed unsuitable, for instance in the interests of preventing serious discomfort or to ensure that the infant can die in his/her parents' arms. Its purpose is not to end life and thus it need not be reported to the committee of experts. This would constitute a natural death and the municipal forensic pathologist is not required to report it to the Central Committee of Experts.

(2013: 2)

8.4.1.3 Constant and unbearable suffering, pain and palliative care

An important element in the discussion regarding end-of-life care of severely ill newborns involves the aspect of unbearable suffering that cannot be alleviated. The unbearable character of suffering has to be identified objectively. In the case of newborn babies, two problems arise.

Firstly, it is difficult to objectively identify the unbearable character of suffering. Suffering is a personal matter and whether or not it is unbearable is a matter of individual experience and expression of the person concerned. A newborn baby, however, cannot express the unbearable character of a specific condition (Verhagen *et al.* 2007).

Secondly, we run into the problem of identifying future suffering. With newborn babies, health professionals are forced to undertake the difficult task of reflecting upon the levels of unbearable suffering that is expected in the child's future (chronic pain, dependency because of a serious sensomotoric disorder, verbal or non-verbal communication inabilities, the burdens of necessary future treatments, etc.) (Kompanje *et al.* 2005). It is extremely difficult for physicians and other health professionals to assess whether and to what extent there will be unbearable suffering in the future. Research shows that when asked about their quality of life in adulthood, people born with complex or life-threatening conditions – for instance with spina bifida or with extremely low birth weight – have a higher assessment of their quality of life than initially predicted by physicians or even their parents at birth (Payot and Barrington 2011; Bellieni and Buonocore 2009; Health Council of the Netherlands 2007). It is clear that the concept of 'constant and unbearable suffering' is indeed variable, according to personal accounts of competent, terminally ill patients who are able to explain the dimensions and character of their suffering (Kluge 2009; Kompanje *et al.* 2005).

The great difficulty of *assessing* whether and to what extent newborns suffer unbearably does not imply, however, that they cannot *actually* suffer seriously from their condition (Liben *et al.* 2008; Nuffield Council on Bioethics 2006). Measuring scales exist to assess pain and discomfort in newborns. These scales are based on behavioural signs that indicate pain vis-à-vis facial expressions, vocal, non-verbal expressions of pain, bodily movements and positions, physiological changes like pulse rate or breathing frequency, and hormonal response to pain and stress (Verhagen *et al.* 2007; Hunt 2006). Despite these measuring scales, pain continues to be difficult

to assess with precision and can remain inadequately treated in some cases (Liben *et al*. 2008). Hence more needs to be done to apply current knowledge about how to assess, prevent and treat pain for babies receiving intensive care.

There is wide consensus among physicians and nurses that palliative care can contribute in an important way to a dignified end of life for newborn babies, especially through adequate pain control (including palliative sedation), non-initiation or withdrawal of life-sustaining medical treatment and maintaining a supporting and comforting parental presence (Kilby *et al*. 2011; Committee on Fetus and Newborn 2007, reaffirmed 2010; Liben *et al*. 2008; Health Council of the Netherlands 2007; Nuffield Council on Bioethics 2006; Walther 2005). In detecting an underutilisation of palliative care for newborns broadly, Liben *et al*. (2008) point out that there is still an important social responsibility left partially unfulfilled.

8.4.1.4 Non-initiation and withdrawal of life-sustaining medical treatment: respect for a dignified process of dying

Although prolonging life is usually in a patient's best interests, there is a wide consensus among ethicists that 'survival of the newborn' is not the most important goal in neonatology. Sometimes, it is the primary responsibility of parents and care providers to allow for a dignified process of dying.

According to Walter (1988), the central end of medicine is to promote and enhance the (potential) purposefulness of physical and personal life. Physicians promote health, prevent death, perform surgery, relieve pain … in order for patients to continue in some fashion to pursue values that transcend physical life. This proposal addresses the *raison d'être* of medical interventions and its limits, and provides some insight into the general meaning of the terms 'benefits', 'burdens' and 'best interests' of severely ill newborns. Thus, if neonatology can intervene to ameliorate the quality of the child's condition and the (potential) pursuit of life's goals, then such an intervention can be considered a benefit to the patient and in his/her best interests. On the other hand, when a medical intervention is burdensome to the life treated, then it is contrary to the best interests and is even harmful to the child. In such cases, medicine has reached its limits on the basis of its own purpose and thus should not intervene except to palliate and comfort the severely ill newborn (Porta and Frader 2007; Meulenbergs and Schotsmans 2001; Walter 1988). Hence, from this perspective, initiation of and continuing life-sustaining medical treatments can only be considered when a specific objective is in view, when there is a reasonable chance that this objective can be attained with the therapy (effectivity) and when the application of the therapy does not pose an excessive burden on the child (Nuffield Council on Bioethics 2006; Health Council of the Netherlands 2007; Committee on Fetus and Newborn 2007, reaffirmed 2010).

8.4.1.5 Active termination of life: quality of life and respect for autonomy

Authors who support active termination of life in newborn babies mostly rely on value arguments that prioritise quality of life and respect for autonomy. In caring for severely ill newborns, it is the parents' and care providers' responsibility to bring about the best possible quality of life for the child and ensure his/her well-being. However, other ethicists argue that applying quality-of-life arguments in the decision-making process regarding end-of-life care for these children is problematic. In this context, six reasons are identified in the literature.

First, it is only possible for the person concerned to assess quality of life. Notwithstanding that standard (health-related) quality of life measures generally include objective components, quality of life is inherently subjective (Kluge 2009). Mere knowledge of a person's physical and mental limitations does not provide insight into what quality can be attached to such a life or what this life actually means for the person concerned (Kon 2007).

Second, it is not clear which criteria should be used to assess another person's quality of life. For instance, is it reasonable to compare the quality of life for a severely ill newborn baby with that of a healthy child? Doing so would shed a negative light on the life of a handicapped or ill person from the start (Meulenbergs and Schotsmans 2001).

Third, assessing future quality of life introduces uncertainty, especially in the case of extremely premature babies. Is it reasonable, in such cases, to base one's judgment on a 'worst-case scenario' (Health Council of the Netherlands 2007; Chervenak *et al.* 2006)?

Fourth, it is possible that the interests – as well as the fears and opinions – of parents, relatives and society become key factors in assessing quality of life and treatment decisions for the child (Bellieni and Buonocore 2009; Chervenak *et al.* 2006).

Fifth, quality-of-life reasoning happens to equate 'being handicapped' or 'living with a disorder' too readily with 'being unhappy'. It is questionable at least, whether this is indeed the case. After all, it should not be forgotten that people's sense of well-being is closely correlated to feelings of acceptance, and living in a social environment that enhances people's abilities despite physical limitations. Although it can be difficult to live with a handicap or disease, it is not by definition the case that everyone with a handicap is unhappy. Rather the immediate environment and society at large play a major part in this (Shildrick 2008).

Finally, we should not forget that discussions regarding the low quality of certain lives, implying that these people would be better off if they did not exist at all, are disparaging and offensive towards people who live with such deficiencies (De Wert 1991).

Another point that complicates the proactive life-termination argument in newborns is that a newborn child cannot express autonomous will in a clear and straightforward manner. Parents and care providers must interpret the child's actual condition and what the future situation will be in light of prognostic uncertainty. As already mentioned, such an interpretation is very delicate, given the short- and long-term consequences. Hence scholars argue that parents and care providers cannot rely on the principle of respect for autonomy in order to legitimise the active termination of a severely ill, newborn life (Kon 2007; Kodish 2008; Paris 2011). Respect for autonomy cannot result in an absolute disposal of the life of another person who is unable to give informed consent, which is in this case the severely ill newborn (Callahan 1991; Nuffield Council on Bioethics 2006; Jotkowitz *et al.* 2008). The problematic use of quality-of-life and respect-for-autonomy arguments as reported in current ethics literature confirms the lack of consensus among ethicists on active life-termination in newborns.

8.4.2 End-of-life care and conscientious objections

End-of-life care is closely related to the moral attitudes of the persons involved – both patient and caregiver – and their way of experiencing meaningfulness. In fact, all caring behaviour at the end of life is interwoven with normative and existential elements. As an important aspect of a free society, moral pluralism implies that citizens have the opportunity to orient their lives – including the last stages – on the basis of specific religious and philosophical convictions. Worldviews appeal to what we value and hope for in life, not only with our knowledge and

technical expertise. Similarly, it is quite clear that end-of-life care is about more than the efficient organization of care procedures and scientific know-how. Dealing with illness and death affects people in their deepest and most intimate being; it touches the most profound part of their lives. Different worldviews – Christian, Jewish, Islamic, humanist, atheistic, etc. – provide a great deal of inspiration for dealing with these sorts of human experiences and the normative questions they raise. This multifaceted variety of worldviews attempts to formulate answers to fundamental questions and enriches pluralist societies.

8.4.2.1 Moral pluralism and conscientious objections

Current literature on end-of-life care shows an increasing interest in culturally sensitive issues, including their link with religious and philosophical foundations (Andrew *et al.* 2013; Denier and Gastmans 2013; Gysels *et al.* 2012; Evans *et al.* 2012a; Evans *et al.* 2012b). Responses to conscientious objections among end-of-life care providers offer interesting analyses of the relationships between culture, religion and end-of-life care delivery (Wernow and Gastmans 2010). Moral pluralism can complicate end-of-life care when caregivers object to providing certain legal but morally controversial services, such as euthanasia or physician-assisted suicide (White and Brody 2011). The appropriateness of conscientious objections by caregivers remains controversial. Some authors suggest that such disputes arise in a healthy pluralistic society. Others see it as an unfortunate clash of patient versus caregiver autonomy, undue patient burden or the impugning of the caregiver's moral integrity (Wicclair 2006).

To begin, we review Benjamin's three conceptions of conscience. They include '(1) moral sense – an inner sense that distinguishes right acts from wrong; (2) internalized social norms – the internalization of parental and social norms; and (3) sense of integrity – the exercise and expression of a reflective sense of integrity' (Benjamin 2004: 513). In view of the complexity and prevalence of medical end-of-life decisions, it seems important to identify the primary positions and the ethical arguments upon which conscientious objections in these discussions are based.

8.4.2.2 Three positions

A review of ethical literature addressing conscientious objections by caregivers in medical end-of-life decisions reveals common ethical characteristics that correspond to three primary positions. The first position commonly holds that socio-cultural conventions do not serve as a valid basis or warrant overriding conscientious objections to end-of-life procedures that impugn the moral integrity of care providers (Wildes 1993; Boyle 1994; Wear *et al.* 1994; Engelhardt 1997; Peppin 1997; Pellegrino 2002; Orr 2007; Elshtain 2008; Sulmasy 2008; Hardt 2008). Defenders of this first position commonly claim that the right to personal conscientious objection to end-of-life procedures is compatible with their professional obligations. Their claim is based upon the belief that those objections are informed and guided by personal normative values and principles. They assert that professional and personal obligations of care are holistic in nature and argue that any attempt at dichotomisation violates individual identity. That is, when the conscientious individual is compelled to act against the dictates of his or her conscience, their very notion of personal identity, from which professional obligation derives, is violated (Engelhardt 1997; Peppin 1997; Pellegrino 2002).

Proponents agree, however, that an obligation to continue care for the patient extends until a third party arranges for the transfer of the patient's care to another caregiver, whose objections

are disclosed to the appropriate interested parties, such as patients or employers. Some decline any cooperation in areas of objection, such as patient's referral, when matters of conscientious objection arise (Peppin 1997; Engelhardt 1997; Pellegrino 2002). Others in this cluster maintain that, under the condition of proper intent, a referral of patients to accommodating caregivers remains compatible with patients' normative values and principles (Wildes 1993; Wear *et al.* 1994; Orr 2007; Sulmasy 2008; Elshtain 2008). A proper intent of referral facilitates a release of the patient from their care, but is not intended to assist the objectionable act. Like other authors, Hardt (2008) contends that a discussion about moral commitments at the outset of the physician–patient relationship might mitigate future burdens for both.

The second position maintains that personal conscientious objection is compatible with professional obligations so long as the conventional standards of society permit such objection (Wicclair 2000, 2006, 2007, 2008; Davis 2004; Charo 2005; Dresser 2005; Lawrence and Curlin 2007; Glenn and Boyce 2007; Brock 2008). Three conditions are necessary to claim a conscientious objection under this second position: the objector must be willing to disclose their objections to interested parties in a timely manner; there must be a willingness to cooperate in the referral of the patient to a professional who will accommodate the patient's requests; and the objection must not pose undue burdens on interested parties including the patient or their family.

The third position claims that socio-cultural conventions derived from professional standards of practice serve as a valid basis to override conscientious objection to end-of-life procedures (Rhodes 2006; Savulescu 2006, 2007; Adams 2007). According to this position, conscientious objection to end-of-life procedures, such as physician aid in dying or euthanasia where legally permissible, is strictly based upon personal moral preference. It is therefore incompatible with the caregiver's professional obligation to render service to society. Advocates of the third position may temporarily tolerate the practice of conscientious objection but insist it should not be an undue burden to the parties of interest. They also demand disclosure of possible objectionable end-of-life practices to their patients prior to such circumstances and insist on the patient's referral in light of their objections. Temporary toleration should not be construed as an admission of validity or support for conscientious objection; rather, toleration should be maintained until conscientious objections are made illegal (Rhodes 2006; Savulescu 2006, 2007; Adams 2007).

8.4.2.3 Recommendations

The heart of the dispute surrounding conscientious objection appears unsolvable. It is a conflict between proponents of conscientious objection, who view moral truth as a divinely given *a priori* where conscience is part of the identity of the whole person, and those who view conscience as merely a personally acquired social construct. However, both groups share some common ground. All three positions agree that the patient should be respectfully and adequately informed about the caregiver's conscientious objection to some end-of-life procedures. Almost all authors agree that the best time to disclose conscientious objection is at the beginning of the patient–caregiver relationship or, in less optimal circumstances, when conscientious objection arises at the point of request. It appears that all groups would affirm cooperation in proper access to the patient's medical data at transfer and that care should continue during this transfer. From these observations, four recommendations follow: (1) caregivers with conscientious objection should clearly disclose procedures considered morally objectionable to all primary parties of interest; (2) caregivers should have a clearly developed rationale for their objection and inform patients and institutions; (3) caregivers should determine and disclose the extent to which they will cooperate

in facilitating transfer of care, including medical information, assurance of continuum of care during the transfer process, and development of referral mechanisms; (4) caregivers should consider avenues of practice that minimise their exercise of conscientious objection. In following these recommendations, caregivers enhance the patient care experience both professionally and legally.

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Part II
Professional relationships

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9

Regulating professional practice

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Professional regulation of medical practitioners has undergone substantial change in recent decades. While medicine has traditionally been a self-regulating profession, calls for greater oversight of professional practice have encouraged new regulatory models. Using examples from the United Kingdom, Canada and Australia, this chapter analyses recent trends in the regulation of medical practice, charting the move from professional self-regulation through to contemporary models of oversight and accountability. The introduction of more rigorous requirements for assessing professional competency – including new requirements for recertification, revalidation, performance, health and the character of practitioners in addition to traditional conduct-based assessments – has been a key feature of the move to contemporary regulatory frameworks. Further developments have also introduced measures to regulate unregistered health practitioners, and to avoid the potential adverse impacts of a 'brain drain' that recruiting international health personnel might have on health systems in poorer countries.

9.1 From self-regulation to external regulation

Medicine has traditionally been a self-governing profession. Professional standards were established and enforced through systems of peer review. Medical regulatory bodies were comprised of medical members who sought to uphold the professional standards, and to hold individual practitioners to account (Davies 2007: 11; Thomas 2004: 382). Indeed, self-regulation was seen as a hallmark of the profession. Self-regulation was premised on the idea that doctors themselves were in the best position to decide about the acceptability of particular medical practices, and that practitioners would comply more willingly with standards if decisions were made by members of the profession itself (Irvine 2006a: 203).

In the period following the Second World World War, medicine became increasingly specialised and 'high-tech'. Doctors were seen to know best, and paternalism typified their relationships with patients (Irvine 2007: 256–7). Changing social contexts, however, placed pressure on the sustainability of the self-regulation model. Patients are increasingly regarded as consumers of medical services with a growing recognition of patients' rights and autonomy, while the Internet has facilitated access to medical information (Freckelton 2006: 149). In addition, a series of high-profile cases of poor professional performance prompted calls for tighter regulation of medical

practice (Freckelton 2006: 149–50), amid concerns that peer-based self-regulation may be too soft (Freckelton 2006: 150; Irvine 2007: 257). Waring *et al.* note that '[o]ne prominent feature of these inquiries was their casting of the professional ethics of medicine as part of the problem' (2010: 547). There were two aspects to this argument: first, that the profession's claims of trustworthiness 'were seen to provide a cloak under which nefarious activities could be conducted'; and second, that the professional culture made doctors reluctant to raise concerns about their colleagues (Waring *et al.* 2010: 547–8).

Against the backdrop of challenges to self-regulation, both governments and professional bodies sought to restore the public's trust in medicine (Allsop 2006; Irvine 2006b). There has been debate over the contemporary meaning of professionalism in medicine (Godlee 2008). The *Charter on Medical Professionalism*, published in 2002, was developed by the American Board of Internal Medicine, the American College of Physicians and the European Federation of Internal Medicine (for discussion see Blank *et al.* 2003). It lists the primacy of patient welfare, patient autonomy and social justice as its fundamental principles. It also lists a set of ten responsibilities which require a commitment to:

- professional competence;
- honesty with patients;
- confidentiality of patient information;
- appropriate relationships with patients;
- improving quality of care;
- improving access to care;
- just distribution of limited resources;
- integrity and appropriate use of scientific knowledge;
- maintaining trust by managing conflicts of interest; and
- fulfilling professional responsibilities.

On the issue of trust and professionalism, Donald Irvine has argued that '[m]odern professionalism is about both the encouragement and celebration of good practice and the protection of patients and the public from suboptimal practice. They are one of a piece – indivisible. Public trust is dependent on both' (2006b: 205).

The shift away from self-regulation toward greater external regulation and professional accountability is apparent. Lay (i.e. non-medical) membership of regulatory bodies has increased in response to the perceived need for greater public involvement in regulatory decision-making (Davies 2007: 267–80). In the United Kingdom, lay membership in the General Medical Council dates back to 1926, when one lay member was included to represent the interests of consumers (Davies 2007: 271; Irvine 2006a: 204). The proportion of lay membership has increased in recent decades, such that six out of the total 12 members who currently sit on the General Medical Council are lay members (General Medical Council 2013a).

Canada regulates medical professional practice at the provincial level. Membership of the councils of provincial colleges includes lay members, although the size of the councils and the proportion of lay membership vary between provinces. For example, the College of Physicians and Surgeons of British Columbia comprises ten physicians and five lay members (College of Physicians and Surgeons of British Columbia 2013: 3), while the lay members of the College of Physicians and Surgeons of Ontario number 13–15 in a council of 32-4 members (College of Physicians and Surgeons of Ontario 2011: 2).

Until July 2010, State and Territory Medical Boards managed medical regulation in Australia using the legislative framework found in the Medical Acts of various jurisdictions

(Dix *et al.* 1996: 7–41). These bodies, the first of which was established in Tasmania in 1837, were responsible for maintaining professional standards, and had the power to discipline practitioners in response to complaints (Reid 2006: 91–2). They were comprised primarily of medical practitioners, thus reinforcing the principle of peer review (Thomas 2006: 55). New South Wales introduced a co-regulatory model in the early 1990s, whereby the Medical Board and the Health Care Complaints Commission were required to consult on any proposed action against a professional in response to a complaint (Thomas 2004). The co-regulatory model marked the end of peer review as the sole determinant of professional standards (Thomas 2004: 388).

The system of medical regulation in Australia developed at the state and territory level because the Australian *Constitution* did not grant any specific federal power relating to health (Carlton 2006: 22). However, concerns about the regulatory system provided an impetus for change. These concerns included: barriers to the movement of professionals between states and territories imposed by state-based registration and regulation; inconsistencies in legislation between states and territories; the implications of such inconsistencies for consumer protection and quality assurance; a recognition of the limits of the peer-review model of regulation; and the need for flexibility and sustainability in the health workforce (Carlton 2006: 23–31).

On 1 July 2010, Australia introduced the National Registration and Accreditation Scheme (the National Scheme) with the entry into force of the *Health Practitioner Regulation National Law Act* 2009. Since 1 July 2010, this Act regulates health practitioners for states and territories other than Western Australia, which joined the National Scheme on 18 October 2010. Ten professions were part of the National Scheme from 1 July 2010: chiropractic, dental, medicine, nursing and midwifery, optometry, osteopathy, pharmacy, physiotherapy, podiatry and psychology (Nesvadba and Forrester 2009; Freckelton 2010). On 1 July 2012, four additional professions joined the National Scheme: Aboriginal and Torres Strait Islander health practice (Freckelton 2014), Chinese medicine, occupational therapy and medical radiation practice. There is a National Board for each profession (*Health Practitioner Regulation National Law*, section 31), comprising both practitioner and community (lay) members. The Australian Health Workforce Ministerial Council (comprised of health ministers from each jurisdiction) determines the composition of the National Board with the proviso that practitioner members must account for at least half and no more than two-thirds of each Board, and each Board must have at least two community members (*Health Practitioner Regulation National Law*, section 33). New South Wales retained its co-regulatory approach under the new National Scheme (Freckelton 2010: 207) and Queensland will also become a co-regulatory jurisdiction following the introduction of new legislation in that state (Forrester 2013).

9.2 Maintaining knowledge

A requirement for continuing medical education is a common feature of regulatory systems for medicine in Australia, the United Kingdom and North America. Increasingly, regulators are moving beyond continuing professional development (CPD) towards recertification and revalidation (Shaw *et al.* 2009). Canada, for example, uses a Maintenance of Certification (MOC) approach. The program runs on a five-year cycle and requires medical practitioners to earn a specified number of CPD credits each year, which are awarded for participation in CPD activities. These activities are divided into group learning activities, self-learning activities and assessment (which includes self-assessment of knowledge and performance assessments) (Royal College of Physicians and Surgeons of Canada n.d.).

In the United Kingdom, the General Medical Council initiated a system for revalidating medical practitioners. While the debates over revalidation in the United Kingdom date back to the mid-1970s (Davies 2007: 334; Shaw *et al.* 2007: 170), it was not formally implemented for United Kingdom doctors until 2012. Changing public and professional expectations over fitness to practise are important elements of the revalidation debates. The 2007 report 'Trust, Assurance and Safety: The Regulation of Health Professionals in the 21st Century' noted:

> Public and professional opinion has moved on in the course of this debate, from a position where trust alone was sufficient guarantee of fitness to practise, to one where that trust needs to be underpinned by objective assurance. Public opinion surveys suggest that people expect health professionals to participate in the revalidation of their registration and that many believe that this already takes place every year.
>
> *(Secretary of State for Health 2007: 32)*

The revalidation process includes two arms: an annual appraisal required for all medical practitioners and revalidation on a five-year cycle (General Medical Council 2013b).

In Australia, the *Health Practitioner Regulation National Law* requires that National Boards develop registration standards on certain matters, including requirements for continuing professional development (section 38(1)(c)).

Recertification and revalidation processes are designed to ensure that medical practitioners remain competent to practise medicine. Reviewing the debates over revalidation in the United Kingdom, the Picker Institute noted that '[d]iscourses of patient and public involvement (PPI) are virtually absent from the large volume of publications devoted to the subject of medical revalidation' (Sheldon *et al.* 2011: 21). However, the Picker Institute identifies four discourses: '[t]wo relate to the conceptual rationale for revalidation (patient benefit and patient-centred professionalism) and the other two cover practical processes (lay input to the process and patient feedback)' (Sheldon *et al.* 2011: 21).

9.3 The changing regulatory environment

Registration was once the traditional means of regulating health practitioners. Upon achieving the desired competencies through examinations at accredited tertiary institutions, they were then able to renew their registration on a yearly basis thereafter, unless complaints were made to the regulatory body. While many adverse events in healthcare may never result in a complaint, research indicates that serious, permanent injuries were more likely to result in complaints (Bismark *et al.* 2006). Australian research also indicates that a small number of doctors are the subject of multiple complaints (Bismark *et al.* 2011; Bismark *et al.* 2013). There is growing consideration of how best to identify and respond to doctors who receive many complaints (Gallagher and Levinson 2013; Lloyd-Bostock 2010; Paterson 2013).

Health practitioners and regulators must also be mindful of the potential for broader social changes to impact professional regulation. The emergence of social networking, for example, poses new challenges, particularly in relation to duties of confidentiality and privacy in relation to patient information, and by posting inappropriate content (Chretien *et al.* 2009; Mansfield *et al.* 2011; Terry 2010).

The traditional annual registration review without further evaluation of competency fails to have regard to the evolution of technologies and knowledge subsequent to initial registration and to systemic and cultural issues within the workplace, and ignores the many personal factors

that can compromise safe medical practice. As Dame Janet Smith stated in her fifth Shipman report, there are multiple reasons why a conclusion might be arrived at that a doctor is unfit to practise or that his or her fitness to practise is impaired:

> … (a) that the doctor presented a risk to patients, (b) that the doctor had brought the profession into disrepute, (c) that the doctor had breached one of the fundamental tenets of the profession and (d) that the doctor's integrity could not be relied upon. Lack of integrity might or might not involve a risk to patients. It might or might not bring the profession into disrepute. It might be regarded as a fundamental tenet of the profession. I think it right to include it as a separate reason why a doctor might be regarded as unfit to practise, because it is relevant even when it arises in a way that is quite unrelated to the doctor's work as a doctor.
>
> *(2004, para. 25.50; applied in* Cheatle *v.* General Medical Council *[2009] EWHC 645 (Admin) at para. 17)*

Physical illness, psychiatric disorders, personality issues, substance abuse and cognitive decline are health indicators pertinent to practitioner health. Each can adversely affect competence in medical practice temporarily or permanently. In recognition of their influence on professional performance, regulators are considering professional performance, the health of practitioners and matters of character as relevant factors to continued registration.

9.3.1 Regulation by reference to performance

A focus on professional performance, in addition to conduct, is a comparatively new phenomenon in health practitioner regulation. In the United Kingdom, it was introduced by the *Medical (Professional Performance) Act* 1995 with a requirement to have regard to the track record of the practitioner in the work he or she had actually been doing, but not to conduct an examination equivalent to that of a student's examination board (*Krippendorf* v. *General Medical Council* [2000] UKPC 45, para. 35 (*Krippendorf*)). Deficient professional performance is to be distinguished from negligence and misconduct:

> It [deficient professional performance] connotes a standard of professional performance which is unacceptably low and which (save in exceptional circumstances) has been demonstrated by reference to a fair sample of the doctor's work. […] A single instance of negligent treatment, unless very serious indeed, would be unlikely to constitute 'deficient professional performance'.
>
> *(*R (Calhaem) *v.* General Medical Council *[2008] LS Law Med 96, para. 39)*

Under Australia's national regulatory legislation 'unsatisfactory professional performance' is defined as 'the knowledge, skill or judgment possessed, or care exercised by, the practitioner in the practice of the health profession in which the practitioner is registered is below the standard reasonably expected of a health practitioner of an equivalent level of training or experience' (*Health Practitioner Regulation National Law*, section 5). Thus evaluation of whether a practitioner's performance is unsatisfactory is broadly informed by, but by no means confined to, individual instances of substandard conduct.

Performance assessment systems exist in the United Kingdom, Canada, Australia and New Zealand. A distinction exists between competence and performance, the latter being the applied notion – a concentration upon the former in the performance assessment

process can constitute an appealable error (*Krippendorf*, para. 48). Typically, performance assessments involve assessors pertinent to the particular area of the practitioner's practice. They identify gaps or deficits in a practitioner's performance and help to develop a plan for ensuring the practitioner meets the expected standards and protecting public safety. As Reid comments:

> These programs deal with professional performance with a non-disciplinary, broad-based and remedial approach and are at all times cognisant of the regulatory authority's responsibility for public protection. They have opened up an alternative pathway for managing practitioners who are neither impaired nor guilty of professional misconduct, but whose standard of practice appears to have slipped below an acceptable level.
>
> *(2006: 97)*

There is a high degree of commonality across jurisdictions in how performance assessments are conducted. The board funds the assessment, while the assessor(s) write a report. It can be broad-ranging.

A knowledge-based competence test often forms part of a performance assessment (*General Medical Council* [2014a]). In procedural areas of practice, simulation assessments may be used and provide data about the practitioner's knowledge, techniques, judgment and responsiveness (*General Medical Council* [2014a]). As Reid comments on the New South Wales approach, '[a]s performance assessment is designed to be broad-based, the assessment exercise employs a range of tools which aim to cover the competence-performance spectrum' (2006: 104–5), and may include an interview, observed consultations or procedures, a medical record review, a facilities assessment, a clinical practice interview, interviews with colleagues, supplementary assessment for matters relating to the practitioner's health, and simulation-based assessment (Reid 2006: 105–6).

In *Roehrich* v. *NSW Medical Board* [2004] NSWSC 1264 Justice Hulme observed:

> Although an assessment may lead to the making of a complaint, or a review of a practitioner's professional performance by a Performance Review Panel, or one of the other courses referred to in … the Act, an assessment cannot of itself affect a practitioner's right to practice nor be regarded in any sense as of a disciplinary nature. True it is that the powers given to assessors are calculated to involve some imposition of the time of the practitioner or other persons and the privacy or confidentiality of his records but, considered against the totality of sanctions for which the Act provides and the importance of ensuring that medical practitioners' professional performance is adequate, this interference can only be regarded as of a minor or relatively minor nature.
>
> *(para. 51)*

If a practitioner chooses not to cooperate or submit to a performance assessment, he or she can be referred to a decision-making body (*General Medical Council* [2014b]).

The practitioner being assessed generally must be supplied with a copy of the report, unless it contains information that may prejudice their health or well-being. After receiving the report, the regulatory body in the United Kingdom and Australia nominates a consultant to discuss the report with the practitioner (see, for example, *Health Practitioner Regulation National Law*, section 176). This provides procedural fairness, especially in situations when serious consequences may ensue thereafter. If there are any recommendations in the report for upskilling, education, mentoring or supervision, or any adverse findings, this provides an opportunity

for the practitioner and the representative of the regulatory body to discuss ways of dealing with them in a collegiate and constructive manner.

After this discussion, the relevant regulatory body formally receives the assessment report and a summary of the interview. It then decides the next steps, which may include (see, for example, *Health Practitioner Regulation National Law*, section 177(1); see also Reid 2006: 106–7):

- taking no further action;
- investigating the practitioner;
- referring the matter to a performance and professional standards panel;
- imposing conditions on/accepting an undertaking from the practitioner;
- requiring the practitioner to undergo a health assessment;
- cautioning the practitioner;
- referring the matter to a tribunal; or
- referring the matter to another entity (such as a health complaints entity).

Generally, matters are resolved without referring the case to a disciplinary panel or tribunal. Outcomes may include counselling, education, and conditions on registration (Reid 2006: 106–7).

The main advantage of focusing on performance measures is that the investigation need not focus upon determining whether a particular incident or interaction between a health practitioner and patient was deficient. Rather, it enables a general evaluation of the practitioner's competence in their chosen area. Evaluative measures include analysis of documentation, treatment planning, relevant knowledge, choice of techniques, ability to concentrate and exercise judgment, capacity to function in a teamwork environment and administrative or even forensic issues. The investigation can consider patterns of substandard practice and persistent issues. The practitioner's peers undertake the assessment, as it is expected that they will be better attuned to clinical deficits but able to undertake the assessment in a way that appreciates the context of decision-making and performance in the relevant area. As such, the assessment avoids the adversarial environment of a panel or tribunal. It often resolves concerns in a (relatively) private way, and centres on professional improvement, depending on the practitioner's willingness to acknowledge and address his or her difficulties.

For regulators, the principal disadvantages of performance assessments are that they can be burdensome, expensive and difficult to structure. Furthermore, the overlap between conduct, performance, health and character can be difficult to delineate.

From a practitioner's perspective, the performance assessment can be unpredictable. It can encompass issues beyond those originally identified and expose global issues in practice which may not be easily remediable. An example of the latter is cognitive impairment. Identifying relevant issues too is not always straightforward. Guidance from the Privy Council in *Krippendorf* confirmed that theoretical questions are not relevant to the functions of a performance assessment unless they shed light on the practitioner's professional performance in his or her specific area of work (para. 35). However, assessments may become unreasonable if assessors pose questions which are too extensive and detailed (*Krippendorf*, para. 39). It may also be crucial for assessors to identify and communicate the parameters of inquiry in advance so that the practitioner is not unfairly disadvantaged by answering on matters while labouring under a misimpression (*Krippendorf,* para. 40).

For complainants/notifiers, the performance assessment process can be relatively unrewarding as it does not generally involve any formal finding regarding the professional conduct under review in respect of a particular incident or incidents which may be the content of aggrievement. The overt focus of the performance assessment on mentoring and remediation can frustrate those who seek vindication of their complaint/notification and the imposition of harsh consequences.

However, as Reid comments (2006: 108): '[a]lthough the particulars of the triggering notification or complaint are not specifically investigated and are not the subject of findings […], the program's broad-based assessment and remediation-focused outcome ensures that complainants and employers are generally satisfied with the outcome.'

Although in some situations the performance pathway can be attractive for practitioners who are open to remediation, assessments may lead to litigation, directed to calling into question the assessment process and impugning its fairness, the criteria used and the findings made. Questions have been raised by practitioners relating to the independence of assessors (see *Sadler* v. *General Medical Council* [2003] UKPC 59), the quality of testing asked of the practitioner (see *Sulaiman* v. *General Medical Council* [2011] EWHC 1903 (Admin)), whether the assessment was sufficiently thorough or sufficient time was devoted to it (*Roomi, R (on the application of)* v. *General Medical Council* [2009] EWHC 2188 (Admin)), and also whether sufficient opportunity was provided to the practitioner to address the issues raised in the performance assessment (see, for example, *Krippendorf*, at para. 49).

These matters considered, performance assessments provide a constructive opportunity to identify the reasons for patient/client concerns about health practitioners' conduct. They allow for a remedial focus (Freckelton and Flynn 2004; Reid 2006), avoid adversarial legal arguments about particular instances of conduct and inform the practitioner as to whether clinical knowledge and skills need to be improved. However, in spite of its constructive potential, the shift to performance evaluation has been slow in most countries due to the expense and difficulties inherent in performance assessments.

9.3.2 Regulation by reference to health

One of the major reasons for a decline in health practitioner performance can be ill health. This can take many forms. Arguably, it is an ethical and professional obligation to be aware of changes in one's health and its implications for discharging clinical care satisfactorily. However, this is not always possible. Regulatory bodies require information be provided (arguably by an obligation for mandatory notifications) to regulatory bodies so that they can initiate health evaluations of fitness for practice, and take necessary measures to assist the practitioner and protect the public. These measures may be negotiated, although the potential for litigious disputation over impairment and its outcomes for patient safety remain.

Many health conditions impact upon a practitioner's fitness to practise. Some are remediable while others are not. The demands of health practice are apt to manifest in stress-related health problems, such as elevated rates of suicide and substance abuse. In 2011, the Australian Medical Association observed that:

> Internal stressors may come from the personality traits of the individual that chooses to practise medicine. These qualities include dedication, commitment, and a sense of responsibility, competitiveness and altruism. These attributes underpin professional success but can become a source of pressure in a doctor's or medical student's working or study life and increase the risk of anxiety and depression. A proportion of doctors and students have obsessional traits, which can predispose them to stress.
>
> There are also a large number of external pressures including but not limited to:
>
> - innate professional responsibilities of doctors;
> - increased clinical workload due to insufficient staffing and resources in the health system;

- lack of control over work–life balance;
- professional, social and geographical isolation;
- the requirement for ongoing medical education;
- the demands of keeping pace with rapid developments in medical technology and knowledge;
- changes in the administration and regulations in the health system; and
- community expectations.

(pp. 1–2)

There is a growing body of evidence that doctors, for instance, exhibit elevated rates of psychiatric symptomatology (Baldwin *et al.* 1997; Centre *et al.* 2003). In addition, there are concerning attitudes within the health professions about how to deal with illness suffered by health professionals. A 2003 Australian survey of 358 doctors showed that 90 per cent of respondents believed it was acceptable to self-treat acute conditions, while 25 per cent believed it was appropriate even to self-treat chronic conditions (Davidson and Schattner 2003; see also Bosch 2000; Chen *et al.* 2008). Ninety per cent of the general practitioners surveyed and 83 per cent of specialists believed doctors are reluctant to see another doctor, especially if the problem is not somatic (Davidson and Schattner 2003). Another difficulty has been the propensity of many doctors to try to 'work through' illness (Thompson *et al.* 2001; Cupples *et al.* 2002; McKevitt *et al.* 1997), a trend also witnessed in other health practitioners, including psychologists (Freckelton and Molloy 2007).

In response, a number of doctors' health programs have been established to support medical practitioners when they fall ill (Freckelton and Molloy 2007). Some are wholly external to regulatory agencies, some work closely with them and others exist within regulatory bodies. For those outside, such as the Victorian Doctors' Health Program (VDHP), there are particular challenges in providing or facilitating effective health services (VDHP 2013; Warhaft 2004), including balancing the confidentiality of private health information and providing necessary information to regulatory bodies so that they can make informed decisions about matters such as restriction of entitlement to practise.

The situation is further complicated in jurisdictions such as Australia. It mandates the provision of information to regulatory bodies if, among other things, a practitioner has a reasonable belief that another practitioner has 'placed the public at risk of substantial harm in the practitioner's practice of the profession because the practitioner has an impairment' (*Health Practitioner Regulation National Law*, section 140; Parker 2011; Hewitt 2013). The purpose of such mandatory notification regimes is to enable regulators to acquire the information when collegiate discomfort and fraternalism may silence the very practitioners who are best placed to identify deterioration in others' clinical capacity.

In many jurisdictions, a regulatory body can request that a practitioner submit to a health assessment if there is a notification that a practitioner may be impaired. In British Columbia, for instance, such a process is triggered in respect of medical practitioners when:

> [The registrar or executive committee] has reasonable grounds to believe that a registrant may be suffering a physical or mental ailment, an emotional disturbance or an addiction to alcohol or drugs that impairs his or her ability to practise medicine and causes the continued practice of medicine by the registrant to constitute a danger to the public.

*(*Health Professions Act *1996, section 25.6(2))*

The procedure that ensues is comparable to a performance assessment, complete with a formal report and discussion with both the practitioner and assessor to address emergent issues in a supportive manner. The outcomes from most such interactions are the acceptance by practitioners of the need for conditions upon registration and sometimes temporary suspension of registration while the issues are addressed. The health of such practitioners is generally monitored during the periods of conditional registration with a view to determining when it is appropriate for them to resume their previous practice. Such decisions are informed by further medical assessments.

There are a number of areas in which such decision-making is difficult, such as persons with substance dependencies with which they may not have fully come to terms or about which they may be prepared to be disingenuous (Marshall 2008; Warfe 2013). Other problematic areas include practitioners whose cognitive state is deteriorating with age and the onset of degenerative conditions, but who may not be ready to retire or scale down their work (Adler and Constantinou 2008). More generally, too, practitioners with chronic psychiatric conditions, such as bipolar disorders, or with personality disorders can pose difficult challenges for regulatory bodies' health programmes.

9.3.3 Regulation by reference to character

An aspect of regulating health practitioners is the insistence in many jurisdictions that those entering the ranks of the registered practitioners and those remaining under the registration umbrella, with all the benefits that accrue from such a status, be persons worthy of such a designation – that they be 'of good character' or, put another way, be 'fit and proper persons' to be registered (Freckelton 2008a).

In British Columbia, 'professional misconduct' is prescribed to include 'conduct unbecoming a member of the health profession' (*Health Professions Act* 1996, section 26). Similarly, under Australia's national regulatory scheme, a component of 'professional misconduct' is prescribed to be 'conduct of the practitioner, whether occurring in connection with the practice of the health practitioner's profession or not, that is inconsistent with the practitioner being a fit and proper person to hold registration in the profession' (*Health Practitioner Regulation National Law*, section 5). Such a designation harkens back to the notion that professionals must 'set a good example' for others and be persons of integrity. Insofar as it is based on antiquated or contextually undifferentiated psychological notions of good traits of character, such a designation is somewhat anachronistic (Freckelton 2008a).

However, there can be discontinuity from the perspective of patients between a person who in some aspect of their life has displayed attitudes and behaviours that are *prima facie* incompatible with being a trusted health practitioner and their professional qualifications for remaining in practice. Such issues may arise from sexual predation, dishonesty, gross insensitivity, sadistic attitudes or lack of empathy for patients' well-being, to name but some 'characteristics'. However, such evaluations are not readily made because their moralistic criteria can be highly judgmental.

Registration in the health professions and misconduct in practice are continually assessed in reference to old-fashioned concepts in many countries, such as character and being a 'fit and proper person', yet there are probably few options but to preserve reference to these indicia of suitability to practise. This is not a licence for regulatory bodies to be moral policemen of the health professions, but it is reasonable to postulate that some attributes are *prima facie* incompatible with being a registered health practitioner. Generally these are manifested in the context of clinical practice, but in exceptional circumstances they may also become apparent in other aspects of professional practice or even in a practitioner's private life (Freckelton 2008a).

9.3.4 Regulation of unregistered practitioners

A growing percentage of unregistered health practitioners, variously described as 'non-mainstream', 'unorthodox', 'alternative' or 'complementary', are providing health services. These practitioners offer holistic, flexible and responsive services to patients' needs in ways beyond those provided by mainstream medicine. They afford patients an element of choice in healthcare, which is consistent with principles of patient autonomy. Disillusionment with the increasingly commercial, technical and impersonal nature of conventional healthcare has popularised alternative medicine as a result.

However, these forms of complementary practice can also be counter-therapeutic. Studies demonstrate unsafe drug toxicities for certain alternative medicine approaches and warn of the risks patients assume in undergoing (potentially fatal) treatment that lacks evidence of scientific efficacy (Freckelton 2003, 2012a, 2012b). In addition, some practitioners who have been deregistered continue to conduct themselves unethically and without the constraints that accompany registered status. This risks confusion among consumers of such services.

These realities inspired a re-evaluation of registered status in many countries. While the term 'registered' connotes respectability and legitimacy, there is another perspective that focuses overtly on risk. Registered status can oblige complementarity in practice – namely practice that genuinely provides patients with options – and requires evidence-based standards of practice. In doing so, unscientific forms of practice are much more difficult, meaning that registration requirements help to support patient safety.

Some jurisdictions have increased the number of health professions that are subject to registration requirements. As of 2013, there are 14 such professions in Australia, including Chinese medicine, Aboriginal and Torres Strait Island Health Practice, chiropractic, medical radiation therapy and osteopathy. In New Zealand there are 16 professions, including dieticians, psychotherapists and midwives. In Alberta, Canada, there are 30 registered professions, including denturists, naturopaths, respiratory therapists, social workers and speech-language pathologists.

New Zealand, New South Wales and South Australia adopted an additional approach which enacts some measure of regulation for unregistered health practitioners (for discussion see Freckelton 2008b, 2012b; Weir 2013) through a code of conduct that binds all providers of health services. It permits an entity such as a Health Services Commissioner to issue prohibition orders precluding practice or a certain form of practice by an unregistered provider who has infringed basic tenets of ethical health service provision. This is sometimes referred to as a 'negative licensing scheme'.

In June 2013, this approach was consolidated in Australia. The Standing Council on Health in Australia decided to strengthen state and territory health complaint mechanisms relating to unregistered health practitioners by introducing 'a statutory code of conduct and powers to prohibit those who breach the code from continuing to provide health services' (Australian Health Ministers Advisory Council 2013: 7).

This decision was made based on a Regulation Impact Statement (RIS) which estimated around 40 incidents of serious harm involving unregistered health practitioners occur per year across Australia (Australian Health Ministers Advisory Council 2013: 83). The options considered by the RIS were: no change, strengthening industry self-regulation, strengthening complaints mechanisms and extending registration to unregistered health professions (Australian Health Ministers' Advisory Council 2013: 6–7). The RIS concluded that 'a single National Code of Conduct with enforcement powers for breach of the Code is considered likely to deliver the greatest net public benefit to the community' (Australian Health Ministers' Advisory Council 2013: 7). Such measures can be supported by the option of consumer protection actions for

false, misleading and deceptive advertising for treatment and other spurious health services (Freckelton 2012b).

There are challenges in placing constraints upon unregistered health practitioners. These challenges have become the centre of international discussions, as jurisdictions gradually broaden their regulatory umbrellas. The Australian initiative to impose basic ethical obligations on unregistered health practitioners is an important step in rendering such practitioners more accountable for the services that they offer.

9.3.5 Migration of health practitioners

The global migration of health practitioners has become an important element in contemporary health workforces. Typically migration is from poorer to wealthier countries, leading to concerns over a 'brain drain' of skilled health professionals from poor countries (Ahmad 2005). There are both 'push' and 'pull' factors contributing to the global movement of health practitioners. Low wages, poor job opportunities, civil unrest and other factors in many developing countries contribute to the 'push effect', while the prospects of job security and enhanced economic opportunities serve as 'pull' factors (Ahmad 2005: 43).

In 2010 the World Health Organization (WHO) adopted the 'WHO Global Code of Practice on the International Recruitment of Health Personnel'. The Code is not binding (article 2.1) and is designed to provide guidance to Member States working with stakeholders (article 2.2). The Code recognises the rights of health personnel to migrate, subject to relevant laws (article 3.4), but also recognises the needs of the health systems in developing countries (for discussion see Taylor *et al.* 2011). For example, article 3.2 states:

> Addressing present and expected shortages in the health workforce is crucial to protecting global health. International migration of health personnel can make a sound contribution to the development and strengthening of health systems, if recruitment is properly managed. However, the setting of voluntary international principles and the coordination of national policies on international health personnel recruitment are desirable in order to advance frameworks to equitably strengthen health systems worldwide, to mitigate the negative effects of health personnel migration on the health systems of developing countries and to safeguard the rights of health personnel.
>
> *(WHO 2010)*

The Code recommends that developed countries assist with the capacity-building of health systems in developing countries and transitioning economies (article 3.3).

While codes such as the one discussed above focus on international migration, Connell and Buchan have argued:

> International mobility is just one of many flows of health workers. Many others move within countries, from rural to urban areas, from the public to the private sector, and from the health sector to other sectors. A focus on only international migration deals with just one symptom, and not the root causes, of skill shortages: limited funding, low pay, restricted career opportunities, inadequate facilities, poor management, and economic and political instability.
>
> *(2011: 13)*

Clearly the movement of health practitioners both within and between countries will continue to pose challenges for health workforce planning and for medical regulation.

9.4 Conclusion

Regulation of medical practitioners has undergone significant change in recent years. Increasing expectations of accountability and of commitment to ethical values in clinical practice, as well as of regular and demonstrated evidence of professional competency, characterise this change. Awareness of the multiple contributors to adverse outcomes as a result of health practitioner interactions has also grown. Such contributors include performance deficits as well as poor health. With greater external oversight of professional practices, the concept of professionalism within medicine has also evolved to recognise the greater partnership between the profession and society. As professional regulation continues to evolve, with more categories of health practitioners coming under the regulatory umbrella, there are opportunities for continued dialogue around the contemporary meaning of professionalism and of professional ethics in the context of medical practice.

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10

Health professionals and the organization of healthcare

Current trends

Nola M. Ries

10.1 Introduction

This chapter addresses contemporary challenges facing modern healthcare systems and the ways in which the regulation and practices of health professionals must adapt and change to meet such demands. In many countries around the world, health systems are facing enormous, interrelated pressures. Escalating healthcare costs are a pressing concern. The increase in healthcare expenditures exceeds GDP growth in many nations (Pammolli *et al.* 2012) and is being driven by multiple factors, including aging populations and the growing burden of chronic diseases such as cardiovascular diseases, metabolic disorders, cancers and mental health conditions (Organization for Economic Cooperation and Development (OECD) 2011; Rechel *et al.* 2013). The Lancet's 'Global Burden of Disease Study,' published in 2012, underscored the major social and personal impacts of chronic, non-communicable diseases, pointing out that people are living more years with disability and disease. According to the World Economic Forum, the global financial costs of the non-communicable disease burden will exceed US$30 trillion over the next twenty years (Bloom *et al.* 2011).

The shift in the global disease burden demands new approaches to the organization of healthcare, including shifts away from acute, episodic care delivered in hospitals, to community and home-based care (World Health Organization (WHO) 2006: xix). Hospitals themselves must be transformed to deliver care in ways that prioritize the patient, value their experience of care, overcome professional 'silos,' and involve collaboration with health and community services beyond the hospital walls (Future Hospital Commission 2013). Effective collaboration among health professional groups is also key. As will be discussed, broadening the scopes of professional practice and reforming laws to enable expanded practice roles may also be key to meeting contemporary health service needs. Yet new approaches to healthcare delivery have implications for the professional relationship, including the relationship between care providers and their patients and the relationships among different health profession disciplines.

This chapter commences with an overview of professionalism in healthcare and the core elements of the professional relationship. The obligation to meet legal and ethical duties is discussed as a feature of professional status. Current debates over challenges to the professional identity are noted, especially a perceived diminution in professional autonomy for some, as governments

demand more stringent regulatory oversight and promote more efficient models of healthcare delivery. The growing trend towards inter-professional, team-based collaboration is discussed. A short case study in Canada is presented to illustrate examples of law reform that enable broader scopes of professional practice and inter-professional collaboration. The final section of this chapter discusses three linked issues impinging on the delivery and organization of healthcare: the push to evidence-based practice; greater community-based and patient-managed models of care; and the continuing emphasis on improving the safety and quality of care. This section notes legal and ethical issues that arise in these topics, and also identifies areas for further research. Last, the conclusion briefly comments on the notion of a 'new professionalism' in healthcare.

10.2 Legal theory and ethical theory

10.2.1 Key features of professionalism

Members of professions typically enjoy a claim to specialized expertise, social status, and financial security. Members also argue that their work, including entry into the profession, qualifications, practice standards, and discipline, should be controlled by the professional body itself (Plochg *et al.* 2009). Professional bodies thus typically have self-regulatory authority to restrict membership to those with prescribed credentials and to superintend the conduct of practitioners. For example, in 2009, the World Medical Association (WMA) adopted its 'Declaration of Madrid on Professionally-led Regulation,' which emphasizes the importance of professional self-regulation and also underscores the responsibilities that accompany it, including a duty to ensure the competence of members, enforce compliance with codes of ethics, deliver high-quality care for patients, and provide transparent regulation that fosters public trust and confidence (2009).

Indeed, power and autonomy are conferred on professions in exchange for an expectation – a social contract – that members of the profession will use their expert knowledge and skills to advance the interests of their patients and the public (Sullivan 2000). Members are generally expected to adhere to an ethical code of conduct and to meet standards typically enforced internally by the profession and externally through processes such as negligence litigation or other dispute resolution mechanisms (Southon and Braithwaite 2000).

10.2.1.1 Professionalism in healthcare practice

Several key elements of professionalism in healthcare practice have been identified (Wilkinson *et al.* 2009). First and foremost, health professionals are expected to comply with core ethical principles, including a duty to safeguard an effective therapeutic relationship with patients based on trust and integrity (Stirrat *et al.* 2010). Professionals should also be reliable, capable of effective communication and working relationships with others involved in the provision of care, and dedicated to maintaining and improving their own competence and that of the healthcare system. Other professional and ethical obligations include a commitment to non-discrimination (except permissible exercises of conscientious objection), acting within their scope of practice boundaries, and identifying and avoiding conflicts of interest. Such obligations are articulated in codes of ethics at international and domestic levels, and also in jurisdiction-specific legislation and case law (see, for example, the WMA's *International Code of Medical Ethics*, updated in 2006).

10.2.1.2 Challenges to professionalism

In recent years, some health professional groups, most notably physicians, have expressed concerns about the erosion of professionalism in healthcare (Davidson 2002; Cohen 2006). Describing 'threats' to professionalism, Sullivan writes:

> The professions have never been more important to the well-being of society. Professional knowledge and expertise are at the core of contemporary society. How such professional expertise is developed, how it is deployed, by whom it is deployed and for what ends are among the most pressing issues facing all modern nations. At the same time, many of the most distinctive features of the professions, especially their privileges of self-regulation and self-policing, are being curtailed.
>
> *(2000: 674)*

The current organization of healthcare – with the rise of healthcare managerialism, increasing bureaucratization, and commercial and budgetary pressures – is alleged to diminish professionalism. Sullivan contends that healthcare systems now 'substitute questions of cost and benefit for traditional relations of care and trust' (2000: 674). Discussing the practice of medicine, Jotterand similarly argues:

> Contemporary medicine is predominantly dependent on socio-economic criteria external to the traditional set of norms and values internal to medical professionalism. The dependence of physicians on social institutions for the delivery of healthcare has created a new paradigm in which physicians have a social obligation to respect cost containment policies, which sometimes affect the welfare of patients.
>
> *(2005: 118)*

Other healthcare trends, such as the increasing use of information technology and a growing prevalence of shift and part-time work, may alter the traditional professional relationship between care provider and patient. A 2013 commentary in the *British Medical Journal* asserts that today's doctors 'are simply less available for their patients' (Roland and Paddison 2013). The authors suggest that shift work during hospital training means 'a generation of young doctors is emerging with limited experience of taking personal responsibility for a defined group of patients. The idea that problems can always be passed on to someone else at the end of a shift is difficult to reconcile with the ethos fundamental to relational continuity' (Roland and Paddison 2013: 22). A recent US study reported that interns spend only 12 per cent of their time with patients compared to 40 per cent of their time on computer use (Block *et al.* 2013).

In addition to changes to the individual relationship between care provider and patient, macro-level reforms also impact professionalism. More stringent governmental oversight of health professions arguably impinges on their independence. Governments have moved to circumscribe self-regulation where professions fail to supervise their members adequately, and where care quality and patient safety issues have come to light. For example, as of December 2012, doctors in the UK must comply with a new process to demonstrate their fitness to practice. The so-called 'revalidation' process involves an annual appraisal and submission of documentation to the General Medical Council (GMC) every five years to demonstrate continuing fitness to practice. This change, which the GMC describes as 'the biggest shake up in medical regulation for more than 150 years' (2013) was spurred by high-profile cases of physician misconduct and serious patient harm (Smith 2004; Chief Medical Officer 2006).

The growth of other health practitioner groups, including those allied to medicine and nursing, as well as alternative practitioners, and successful lobbying in some jurisdictions to expand their scopes of practice, also challenge traditional relationships and hierarchies in healthcare (Welsh *et al.* 2004; Dower *et al.* 2013). As a clear and simple statement to guide professional conduct, healthcare practitioners ought to 'behave towards colleagues as he/she would have them behave towards him/her' (WMA 2006). This dictate may be compromised, however, by inter-professional conflicts over regulatory issues, including scopes of practice and roles within healthcare delivery. The ability to exert 'autonomy and dominance over other groups' (Southon and Braithwaite, 2000) has been described as a characteristic of professions and, in healthcare, the medical profession has traditionally emphasized and protected its dominant status over other health professional groups. Indeed, in its 2008 'Consensus Statement on the Role of the Doctor,' the UK Medical Schools Council asserted that '[d]octors alone amongst healthcare professionals must be capable of regularly taking ultimate responsibility' in clinical situations (Medical Schools Council 2008).

Yet the organization of healthcare is shifting dramatically to emphasize team-based practice and inter-professional collaboration. Baxter and Brumfitt observe that '[i]nterprofessional working clearly presents considerable challenges to practices dominated by power and status considerations' (2008: 240). Others underscore the imperative of moving beyond traditional power hierarchies to establish new ways of working. Sheridan explains that '[a]lthough competition between professions … has been inherent to the professionalisation process, there are interdependent relationships that must be built and maintained if good care is to be delivered over time and in different settings' (2013: 75). Health practitioner groups cannot 'afford the impression that narrow professional interests are guiding their responses' (Blumenthal and Abrams 2013: 1933) to health system reforms that ultimately aim to improve quality of care for patients. Moreover, the contemporary focus on person-centered care and shared decision-making seeks to empower patients and, in doing so, erode the paternalistic foundation on which health professional practice was built (Hodgkin and Taylor 2013).

The next section presents a case study of trends in the regulation of health professions in Canada, focusing on legislative reforms that aim to broaden practice boundaries and foster inter-professional collaboration among a wider range of health practitioners.

10.2.2 Country case study: legal trends regarding health professions in Canada

Effective and efficient healthcare delivery requires that all professionals work to the full scope of their knowledge and skills (Fairman *et al.* 2011). It has been noted, however, that '[t]eam-based care is seen as a wave of the future, but progress has been slow because inter-professional educational opportunities are few (though increasing), training silos are many, and cultural change is difficult' (Iglehart 2013). Governments in some jurisdictions, including Canada, have embarked on legal reform to enable an expanded scope of practice of some professionals, for example broadening the scope of nurses to provide more primary care services and giving certain prescribing rights to pharmacists (Tannenbaum and Tsuyuki 2013). Reforming practice restrictions to enable a wider scope of activities increases patient access to those regulated health professions (Kuo *et al.* 2013). Differing scopes of practice across jurisdictions in one country, such as different regulations at the state or province level in the US or Canada, pose unnecessary regulatory barriers to some health professionals' practice (Fairman *et al.* 2011; Elwood 2013) and create 'mismatches between professional competence and legal scope-of-practice law' (Dower *et al.* 2013: 1971).

An important regulatory trend in Canada is the move toward a common legislative framework for health professions in each province or territory, often referred to as 'umbrella legislation'. Umbrella legislation involves enactment of an overarching statute that provides a uniform regulatory framework for all professions governed by the legislation. Profession-specific laws or regulations are then developed in accordance with the umbrella act. This is in contrast to the traditional approach where separate statutes regulate each health profession and allow certain exclusive scopes of practice that prohibit anyone other than a member of the profession from providing specific services.

These reforms in several of the more populous Canadian provinces, including British Columbia, Alberta and Ontario, have sought to lay a foundation for enhanced inter-professional collaboration, and to enable regulated professionals to practise to a full scope of practice that includes shared activities with other professions. Umbrella regulation typically provides non-exclusive and non-exhaustive descriptions of professional activities. The scopes of practice for regulated professions may have overlapping or shared activities. Restricted or controlled practices are narrowly defined and detail higher-risk activities that may only be performed by members of specific regulated health professions. The same restricted activities may be granted to more than one profession; however, not all professions will be granted restricted activities. Umbrella legislation with non-exclusive scopes of practice provides a possible foundation for inter-professional collaboration. Indeed, it is argued that the regulatory frameworks, and the practice cultures they influence, are 'determinants of the shift to a culture of inter-professional regulation' (Lahey and Currie 2005: 198).

Legislative changes in some provinces aim to facilitate inter-professional collaboration (Lahey 2012). Statutes in some provinces state explicitly that a health profession regulatory college has a duty to collaborate with other professions and to promote collaborative practice among members of the profession. For example, Ontario's *Regulated Health Professions Act* 1991 states that one of the objects of a health profession College is '[t]o develop, in collaboration and consultation with other Colleges, standards of knowledge, skill and judgment relating to the performance of controlled acts common among health professions to enhance inter-professional collaboration, while respecting the unique character of individual health professions and their members' (Schedule 2, section 3(1)(4.1)). Similarly, British Columbia's *Health Professions Act* 1996 describes the role of a College in promoting and enhancing 'inter-professional collaborative practice between its registrants and persons practising another health profession' (section 16(2)(k)(i–ii)). Taking a different approach to encouraging voluntary collaboration, in 2012, the Nova Scotia Legislature passed the *Regulated Health Professions Network Act* to establish a Regulated Health Professions Network. Its mandate is 'to foster and enable collaboration among regulated health professions in a manner that upholds and protects the public interest' (*Regulated Health Professions Network Act,* section 5).

While legislative reform enables broader or more flexible scopes of practice for many professional groups (and, indeed, gives self-regulating power to a wider range of health professions) and urges inter-professional collaboration, changes to statutory instruments alone will not transform the traditional hierarchies and silos of healthcare practice. Changes to the law are arguably a necessary, but not sufficient, condition for changes to the culture and practice of healthcare. Legislation sets out broad principles but general statutory language is interpreted 'on the ground' by health organizations and professionals who may have vested and conflicting interests. As a consequence, existing policies and practices based on traditional models of power and expertise may be slow to change. Disputes over 'professional turf' are significant barriers to change, particularly if leaders focus on '[scope of] practice disputes and turf protection rather than the exploration of collaborative and interdisciplinary approaches' (Jansen 2008: 222).

Expanding on the topic of inter-professional collaboration, the following section discusses several broad and connected trends in healthcare practice, and considers the legal/ethical issues they raise for health professionals. This section also highlights areas for further research.

10.3 Current and emerging legal/ethical issues

10.3.1 Evidence-based practice

Evidence-based practice may be considered part of the trend toward a 'new professionalism' in healthcare. Paternalistic, intuitive judgments about patient care are now replaced by evidence-based practice, patient-centered care, and regular evaluation of health professionals' performance (Roland and Paddison 2013: 22). Similarly, scopes of practice limited by traditional professional hierarchies are giving way to new patterns of collaborative practice based on evidence that team approaches improve quality of care and patient outcomes. In the United States, for instance, a 2010 report from the Institute of Medicine advocated for more training opportunities and an expanded scope of practice for nurses to enable them to work as 'full partners' with doctors and other health professionals. The report criticized unduly restrictive state regulations that limit nurses' scope, despite evidence demonstrating that nurses with expanded qualifications and experience, including nurse practitioners, advanced practice registered nurses, and certified nurse-midwives, deliver safe and quality care to patients. Evidence about the competence of health practitioners to expand their practices safely and effectively provides an impetus for law reform with legal recognition of broader domains of practice and, as a result, enhanced professional status.

More research is needed on the role of different healthcare professionals in delivering care to patients with chronic diseases. A 2013 editorial in the *New England Journal of Medicine* – aptly titled, 'Putting Aside Preconceptions' – argued there is insufficient evidence to determine if the different practice cultures and areas of competence of primary care doctors and nurse practitioners 'affect their comparative ability to manage complicated diagnostic problems or treat patients with multiple, interacting chronic illnesses' (Blumenthal and Abrams 2013: 1933). Research examining the perspectives and experiences of practitioners and patients, and the impact of legal-regulatory structures on practice, is also a key component.

The push to evidence-based practice also reveals, regrettably, that many healthcare services may not actually improve health, and some interventions may make patients worse off. A 2009 commentary in the *Journal of the American Medical Association* observed that 'the aggregate effect of [healthcare spending and services] on health may be smaller than generally assumed' (Kilo 2009: 89). Many practices adopted into routine healthcare practice may lack evidence that they are any better than past practices. In a 2013 analysis of research published in the *New England Journal of Medicine* over a decade, Prasad and colleagues found 146 practices or interventions that were 'reversed' by a study, that is found to be inferior to past practices or practices that did not include the intervention (Prasad *et al.* 2013) The lead author underscored the lack of research to substantiate many commonly used practices and interventions: '[a] large proportion of current medical practice is unproven in the sense there are no good studies that really justify the practices' (McCarthy 2013: 1). Another commentator asserted that the pace of new medical developments means 'ineffective, harmful, expensive medical practices are being introduced more frequently now than at any other time in the history of medicine' (Ioannidis 2013: 780). These findings have legal and ethical implications in that practices, which become the 'standard of care' in clinical and therefore legal terms may, in fact, have little evidence to support their use.

10.3.1.1 Campaigns against too much medicine

Related to the push to evidence-based practice is a growing criticism – from inside and outside health professions – of excessive 'medicalisation.' As more medico-technological interventions are developed and promoted, conditions previously understood as normal variation in human function or behavior shift to being characterized as diseases that must be detected and treated (Moynihan *et al.* 2008). Professional associations in various countries have recently launched initiatives to identify practices that promote 'appropriate' healthcare, meaning 'the right care, provided by the right providers, to the right patient, in the right place, at the right time, resulting in optimal quality care' (Kermode-Scott 2013). For example, the Choosing Wisely initiative involves approximately 50 medical organizations in the United States and 24 in Canada that will develop evidence-based recommendations for practices or procedures that should be reconsidered or discontinued because they fail to benefit, and may even harm, patients (American Board of Internal Medicine Foundation 2014; Levinson and Huynh 2014). In the UK, the *British Medical Journal*'s Too Much Medicine project (2014) focuses on the harms of over-diagnosis and unnecessary healthcare interventions.

Some analysts have argued that liability fears drive healthcare professionals, especially physicians, to engage in 'defensive practice' by ordering tests, prescribing drugs, making specialist referrals, and providing other interventions that do little to help diagnose or treat conditions. Research in the United States, the United Kingdom and other jurisdictions has found that defensive practice is indeed common, especially among certain medical specialists groups (Studdert *et al.* 2005; Nahed *et al.* 2012; Ortashi *et al.* 2013). And worryingly, some medical students and residents report their clinical training encourages defensive behavior (O'Leary *et al.* 2012). The current emphasis on evidence-based practice may dissuade a culture of over-servicing patients, particularly if a legal standard of care shifts to support less rather than more intervention in cases where a common practice is shown to be non-beneficial. Some commentators caution, however, that judicial reliance on evidence-based sources such as clinical practice guidelines is not a panacea. Mehlman (2012) asserts, for example, that such guidelines amount to an unwarranted expansion of the self-regulatory power of health professions that develop the guidelines. A more damning criticism is that the perceived expert impartiality of such guidelines is an illusion and that powerful interest groups, including pharmaceutical companies, unduly influence the development of such standards (Spence 2014). Moreover, some health professional groups object to governmental agencies producing practice guidelines without adequate consultation with the health practitioner groups to which the rules apply. For example, the World Medical Association adopted a resolution in 2013 criticizing non-medical agencies for producing standards to be implemented in clinical practice without 'the necessary professional ethical and technical competencies,' most notably in the European Union.

10.3.2 Shifting paradigms of healthcare delivery

The growing, global burden of chronic conditions demands changes in the delivery of healthcare, with a shift 'to community-based and patient-centered paradigms of care for the treatment of chronic diseases' (World Health Organization 2006: 19). Health systems in many countries must contend with the challenge of establishing an optimal distribution of health workers, with some regions concerned about an over-supply of hospital-based physicians and a concurrent shortage of community-based workers, mental health specialists, and skilled care assistants (Imison and Bohmer 2013). Legal issues concerning the regulation of professionals and their scopes of practice are again key considerations. The World Health Organization noted

'[t]he shift from hospital-based to community-based care, and the new emphasis on multidisciplinary and intersectoral approaches, means changing roles for staff … Scope-of-practice regulations, designed to establish minimum standards and protect patients, can become impediments to the pursuit of change' (2006: 26). Analysts studying approaches to care coordination in the UK stress that commitment and support are required 'across the political, regulatory, organizational and professional spectrum towards the goal of coordinated care' for persons with complex, long-term health conditions (Goodwin *et al.* 2013: v).

Emphasis on patient self-management is another important component in the shifting paradigm of healthcare delivery. Patient self-management is described as 'an individual's ability to detect and manage symptoms, treatment, physical and psychological consequences and lifestyle changes inherent in living with a chronic condition' (Redman 2010). From a legal and ethical perspective, the adult patient with mental capacity has long been recognized as an autonomous agent, with the right to consent to or refuse healthcare interventions. While it should stand to reason that the patient is also viewed as the manager of their own health condition, the notion of patient-centered care and patient self-management is still viewed as a revolution waiting to happen (Hodgkin and Taylor 2014).

The interest in patient self-management is spurred by several developments. Importantly, patients and their advocates seek more autonomy and control in managing their condition. This is driven, in part, by a gradual destigmatization of certain illnesses where individuals are now seen as capable of managing their conditions at home and increasingly independent from institutionalized care. Technological innovations help support self-management. Many patients have vast access to online information and peer support groups. Additionally, a range of technologies is available for patient use to monitor and treat their conditions, such as devices to measure blood pressure and blood sugar and self-administered catheters for chemotherapy patients. The advent of personally controlled health records also helps facilitate greater patient autonomy concerning their health information and conditions. From the perspective of administrators who are concerned with scarce resources and controlling healthcare budgets, patient self-management offers the potential for cost savings insofar as it appropriately keeps people away from expensive hospital stays and other healthcare interventions.

10.3.2.1 Challenges of patient self-management

As currently organized, many healthcare systems – and thus the professionals who work within them – have deficiencies in the delivery of patient-self management programs. Scholars have identified several critical ethical and policy concerns (Redman 2007, 2010). First, there are worries about shifting responsibility to individual patients who may lack personal and other necessary resources to manage their conditions adequately. Examples include health literacy, an understanding of how to navigate the healthcare system, self-advocacy skills, and education on their specific condition and strategies for self-management. At the professional and institutional health system levels, failure to ensure appropriate implementation and support for patient self-management may have the undesired effect of worsening patient outcomes. For example, Redman observes that many hospital readmissions for patients with heart failure result from inadequate discharge counseling to help patients understand how to monitor and manage their condition at home (2007). Such adverse outcomes may represent failures to meet legal and ethical obligations to patients. Likewise, a shift to patient self-management poses the risk of exacerbating inequalities between patients who have the resources to be successful self-managers and those who do not.

A lack of adequate resources and training for health professionals also compromises the potential effectiveness of patient self-management initiatives. Self-management programs must be integrated into complex healthcare systems. In this regard, funding issues are key. For example, are activities related to patient self-management insured or reimbursable through public or private health insurance funds? Longer appointment times to educate and counsel patients, as well as coverage for devices that patients may use for at-home monitoring and treatment, are among some of the pressing financial implications of investing in patient self-management tools. Returning to the issue of evidence-based practice, more research is needed on the longer-term effects of patient self-management, both in terms of biomedical and psychosocial outcomes for patients and broader health system impacts.

10.3.3 Patient safety

The issue of patient safety has attracted much attention from health and legal scholars in recent years, and the growing prevalence of chronic diseases exacerbates these concerns. The World Health Organization (WHO) explains, '[a]s health services for chronic conditions have evolved, so too has their complexity. Although much has improved, the volume of information, the number of medications, and the myriad of providers has led to a number of unintended [patient safety] consequences' (WHO 2006: 28). A push to greater patient self-management may also create new safety risks, particularly as patients take more responsibility to monitor and treat their conditions independently.

Legal systems and rules have a significant influence on how health professionals deal with patient safety issues, including principles, processes, and procedures governing disclosure of adverse events, findings of liability, and compensation for harm. It has been argued that:

> A medical-societal alliance is needed to advocate a medical liability system without perverse incentives and to protect the right of injured patients to fair compensation. At the same time, the liability system must foster frank discussion of medical errors and wide dissemination of lessons learned so that proper steps can be taken to prevent recurrences.
>
> *(Cohen* et al. *2007: 671)*

Emerging comparative research explores different countries' approaches to malpractice, legal liability, and related patient safety issues (Oliphant and Wright 2012). It provides a foundation for further scholarship and gives practitioners and policy-makers insight into the experiences of other jurisdictions.

Enabling patients to be more actively involved in their own care decisions and disease management requires 'a whole-system approach' (Coulter *et al.* 2008) and, as a 2013 editorial argues, 'the growing population of people with multiple long-term conditions, disabilities, and frailty will demand a different model of care and support – a primarily social not medical model' (Hodgkin and Taylor 2013: 7). Moreover, such system-level changes can be facilitated by legal-regulatory reforms and innovations, such as: patient charters or bills of rights; statutory requirements for healthcare organizations; and professional regulatory bodies that can engage with patients in meaningful ways to collect, report, and act on feedback about patient experiences and quality of care. Patient charters or bills of rights have been adopted in various jurisdictions, including a number of European countries, Australia, Hong Kong, Israel, New Zealand, and South Africa (Flood and May 2012). Health law scholars point out that patient charters are most effective when they articulate clear rights, can be interpreted and applied coherently with other sources of law, including professional discipline procedures, and have affordable and efficient

means of complaint resolution and enforcement (Flood and May 2012). Healthcare laws in certain jurisdictions create organizations to provide oversight, to report on quality of care issues, and to receive and investigate patient complaints, including Canada (for example, Health Quality Ontario and British Columbia's Patient Care and Quality Review Board), the United Kingdom (Care Quality Commission), and Australia (Commission on Safety and Quality in Health Care). Comparative analyses of the activities and impacts of such bodies is an important area for future health law research, including analysis of different statutory models and identification of best practices.

10.4 Conclusion

This chapter has considered a number of important trends in contemporary healthcare, relating these issues to professionalism in healthcare, the regulation of health professions, and legal and ethical implications. As the organization of healthcare is facing multiple pressures, some argue that a new model of professionalism in healthcare is required. A 'new professionalism,' which ties together many of the themes in this chapter, is described:

> It places a stronger emphasis on accountability, recognizing the benefits of creating a different dynamic between patients and professionals, and assuming a stronger sense of responsibility for the ways in which the wider health system works and for all dimensions of quality. It promotes a desire constantly to improve what clinicians do, accepting change as an asset rather than a threat. It commits to using a range of different approaches to developing and mobilizing knowledge about how to improve care and to building the formal evidence base underpinning improvement. Finally, it emphasizes the importance of clinicians working in multidisciplinary teams across organizational boundaries. Most fundamentally, no longer is a commitment to improving the quality of patient care an 'add-on.' It is a central part of the role of a clinician and a core value of the new model of professionalism.
>
> *(Stanton* et al. *2011: 48)*

We are thus in an era of changing approaches to healthcare organization and in the regulation of healthcare practitioners. Fortunately, common interests and shared goals exist among all stakeholders in health systems, including patients, practitioners, policy-makers and regulatory authorities. A fundamental aim of healthcare is to produce safe and beneficial outcomes for patients in a cost-effective manner. Patients ought also to be recognized and supported as meaningful managers of their care, both at the personal level in their interactions with health professionals, and at the socio-political level in how health systems are structured and practitioners regulated.

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11
Healthcare-associated infections

Lara Khoury

11.1 Introduction

Healthcare-associated infections (HAIs) – also called 'nosocomial infections' – are recognized as a serious public health problem affecting both patients and healthcare workers (Lange *et al.* 2012: 79–80). The term 'nosocomial' is derived from the Greek words *nosos* (sickness) and *komien* (treat), or *nosokomeion* (one who tends to the disease), and the Latin *nosocomium*, meaning hospital (Ellenberg 2004; Duneton *et al.* 1995). Because these narrow meanings do not acknowledge the variety of ways, settings, and environments in which modern healthcare is delivered (Lange *et al.* 2012: 77–9), the expression now preferred is 'healthcare-associated (or related) infections'.[1]

Increased HAI rates near the end of the twentieth century[2] make these infections a growing concern for health organizations, public health authorities, the medical profession, and the broader community. Modern factors explaining the increased prevalence of HAIs include the overpopulation of hospitals, antibiotic prescription patterns, and an aging population. In addition, medical progress has introduced more invasive procedures that give access to infection, and has increased the survival rates of patients susceptible to a higher risk of infection, such as patients with major burns, organ or bone marrow transplant recipients, premature babies, and the elderly. Finally, new sources of HAIs include the effect of building construction on immunodepressed patients – a factor in the development of Legionnaires' disease or *aspergillosis* – and the emergence of new bacteria with multiple antimicrobial resistance, such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE) (Comité sur les infections nosocomiales du Québec (CINQ) 2004: 7).

At any given time, there are 1.4 million people worldwide suffering from HAIs (World Health Organization (WHO) 2006: para. 2). Between 5 and 10 per cent of patients admitted to modern hospitals around the world contract one or several infections (WHO 2005). The European Centre for Disease Prevention and Control (ECDC) estimates that HAIs occur in an average of one in 20 hospitalized patients in the European Union, causing 4.1 million patients

1 In French, the expression *infection associée aux soins* (IAS) is also preferred (e.g. Ministère de la santé, de la jeunesse et des sports, direction génerale de la santé, direction de l'hospitalisation et de l'organization des soins & Comité technique des infections nosocomiales et des infections liées aux soins [CTINILS] 2007: 3).

2 Some refer to an epidemic (Charney 2012).

to suffer from HAIs and 37,000 deaths each year (Council recommendation 2009, recital (3); Commission of the European Communities 2008: 4).

On any given day, one in twelve adults and one in ten children admitted to a Canadian hospital acquires an HAI (AMMI/CHICA 2012). In 2003, Zoutman *et al.* reported that 220,000 infections are acquired every year in Canadian healthcare institutions, resulting in over 8,000 annual deaths (Zoutman *et al.* 2003: 271). In contrast, Gingin and Hurley calculated that by 2002, HAIs had affected over 320,000 patients, had resulted in costs of close to $1.5 billion CAD, and had killed between 12,000 and 18,000 people annually (Gingin and Hurley 2012: 107). These infections are the second most frequent adverse event affecting hospitalized patients after medication errors (Zoutman *et al.* 2003: 266). Some consider them the fourth leading cause of death in Canada (Charney 2012: 6), while others believe they are third, behind only heart disease and cancer (Gingin and Hurley 2012: 107).

The Centers for Disease Control and Prevention (CDC) estimates that one in 20 hospitalized patients in the United States contracts an HAI (CDC website; CDC and Association of State and Territorial Health Officials (ASTHO) 2011: 3) and that in 2002 there were approximately 1.7 million patients with HAIs in American hospitals (Klevens *et al.* 2007: 160). Approximately 50 per cent of major hospital health complications are associated with these infections (Lange *et al.* 2012: 82). HAIs are one of the ten leading causes of death in the United States, resulting in approximately 99,000 deaths annually (Klevens *et al.* 2007: 160; Charney 2012: 1–2). In 2009, the CDC estimated that the overall annual direct medical costs of HAIs in US hospitals ranges from $28.4 to $33.8 billion or $35.7 to $45 billion USD, depending on the adjustment method used (Scott *et al.* 2009: 7).

In 2012, the French Ministry of Health's nationwide *Enquête nationale de prévalence des infections nosocomiales* showed that on any given day, 5 per cent of patients in participating healthcare establishments – representing 90.6 per cent of hospital beds in France – developed an HAI (Ministère des Affaires sociales et de la santé 2012: 1). In 2012, Decoster *et al.* estimated that 3,500 deaths occur annually in France as a result of HAIs, 800 of which they considered preventable (2012: 310).[3]

Finally, 6.4 per cent of patients in England contracted an HAI in 2011 (Health Protection Agency 2012: 4). It was estimated in 2007 that over 300,000 patients contract an HAI every year and that 9,000 deaths were caused by healthcare-related MRSA or *C. difficile* that year alone (House of Commons 2009: 3). HAIs cost England £1 billion every year (House of Commons 2009: 3).

Several organizations and entities have formally defined nosocomial infections and HAIs. Generally, the patient must contract the infection after being admitted for treatment. In other words, the infection must have been absent at admission. For instance, the European Union Council defines HAIs as 'diseases or pathologies related to the presence of an infectious agent or its products in association with exposure to healthcare facilities or healthcare procedures or treatments' (EU Recommendation 2009).

Other organizations prefer to leave HAIs undefined. During parliamentary debates in February 2002, just weeks before the *Loi du 4 mars 2002* changed the way HAI victims would be compensated in France, Senator Jean-Louis Lorrain proposed to define a nosocomial infection as 'any infection that occurs during or after hospitalization but was absent at admission' (Sargos 2002: para. 276 (our translation)). Then Minister of Health Bernard Kouchner objected

3 Based on a prospective study carried out in 2007 and 2008 in 14 French hospitals.

to this definition, raising potential difficulties in interpretation, and consequently no definition was adopted in the *Loi du 4 mars 2002* (Sargos 2002: para. 276).

Some definitions use timeline indicators to help demonstrate the link between the provision of healthcare and the development of the infection. Most notably, the World Health Organization (WHO) wrote in 2002 that '(n)osocomial infections … are infections acquired during hospital care which are not present or incubating at admission. Infections occurring more than 48 hours after admission are usually considered nosocomial' (WHO 2002b: 4). The EU Commission Decision of 8 August 2012 similarly states that the onset of infection symptoms must be on day three or later of the current hospital stay (admission being day one) (European Commission 2012/506/EC, page 40).[4] Such timelines are meant to facilitate identifying the exact moment of onset as many infections are asymptomatic for some time after they are contracted. However, some authors believe that with the increased spread of HAIs and the rise in antimicrobial resistance, the use of time periods may no longer be applicable (Lange *et al.* 2012: 79).

HAIs can be of endogenous or exogenous origin. Endogenous HAIs are caused by a patient's own flora and may develop at the occasion of an invasive act, for instance. Exogenous infections may be acquired from another person (patient or staff member) or from microorganisms contained in the medical environment or on instruments (WHO 2002b: 2). Invasive treatments are more likely to transmit infections (Groutel 1999). Indeed, the most common types acquired in healthcare settings are surgical wound infections, urinary tract infections, and respiratory tract infections. These can arise from the most common agents of infection, namely bacteria (e.g. *Staphylococcus aureus* and *Clostridium difficile*), viruses (e.g. HIV and hepatitis C), parasites, and fungi (e.g. *Aspergillus*) (WHO 2002b: 6–7).

One of the main challenges both medical and legal professions face is the assessment of the causal origin of an HAI. Often, HAIs are the result of a complex interaction between multiple possible causes (Santé et Services sociaux Québec 2005: 8) that may or may not relate to the healthcare provided by healthcare institutions and actors. Factors related to healthcare may include lack of asepsis of the premises, medical devices and instruments; substandard hygiene of the staff; increased invasiveness of medical procedures; physical proximity of hospitalized patients; use of antibiotics that kill the patient's protective flora or drugs that weaken the patient's immune system; and lack of compliance with prevention and control practices. Factors external to healthcare and, as such, outside the control of healthcare institutions and their staff may also complicate the causal analysis. For instance, infection may result from a hospital visitor's infectiousness, a patient's compromised immunity due to his or her state of health, or the microorganism's intrinsic virulence or resistance to antimicrobial agents.

Added challenges exist when wider systemic factors play a role in the occurrence of HAIs. These may include the absence or inefficiency of hospitals' control and prevention teams, overcrowding of hospitals, or acquired antibiotic resistance. They can also pertain to the scarcity of available resources and the decisions regarding their allocation; deficient management and priority setting at the institutional, local, regional, and national levels; the lack of authority held by prevention and control teams, and confusion in the respective responsibilities of relevant actors; aging buildings and infrastructure; lack of specialised human resources; and deficient or non-existent surveillance (e.g. in Santé et Services sociaux Québec 2005; CINQ 2004).

The next section examines the role of legal normativity in the prevention, control and elimination of HAIs, as well as in providing support to their victims. Through examples, it studies

4 In the case of surgery or the placing of an invasive device, the onset must be before day three if the surgery or the placing of the device occurred on day one or two of the current hospital admission.

how legislation, public inquiries, class action lawsuits, amicable resolution of conflicts, and state compensation funds reinforce this role in numerous jurisdictions.

11.2 Legal theory

It is widely acknowledged that a large proportion of HAIs are preventable (CDC and ASTHO 2011: 6; Harbarth *et al*. 2003: 260 and 264; Hughes 1988) and the cost of adopting adequate precautions is lower than the cost brought on by the infections they could avoid (Hughes 1988; CINQ 2004: 2).[5] Consequently, many jurisdictions center their efforts on ensuring adequate prevention measures are implemented. Such initiatives often take place at the level of public policy. Nevertheless, this section focuses on the role formal legal norms – legislative or regulatory texts – play in the prevention and control of infectious risks in the healthcare sector, as well as in responding to injuries that occur when these risks materialize.

Legislative approaches to regulating risks associated with HAIs have taken place predominantly at the national level, although the European Union has been active at the regional level. In this section, we first consider the legislative and regulatory oversight international and regional communities provide for the prevention and control of HAIs (section 11.2.1). Next, we examine the role certain legislatures – in Canada, the United States, England and France – play in imposing, or proposing, norms for the prevention and control of HAIs (section 11.2.2). We then turn our attention to two typical reactions to the occurrence of infectious outbreaks in healthcare establishments: the holding of public inquiries and the undertaking of class action law suits (section 11.2.3). This section closes with the review of a modern technique for compensating victims of HAIs, namely the management of litigation through conciliation, and the establishment of compensation funds for victims (section 11.2.4).

11.2.1 The oversight of the international and regional communities

The WHO has taken on a leadership role in raising awareness of HAIs. It has educated professionals and the public about the nature of HAIs, their causes, and means of prevention, and taken regulatory initiatives to curtail their spread. Most notably, in May 2002, the 55th World Health Assembly (WHA) – the decision-making body of the WHO – adopted a resolution urging member states to pay 'the closest possible attention' to the issue of patient safety and to establish and strengthen science-based systems necessary for improving patient safety and the quality of healthcare (WHA Resolution 55.18 2002, section 1; see also WHO 2002c). This Resolution expresses concern over the incidence of adverse events that challenges quality of care and causes human suffering as well as financial loss and opportunity costs to health services (WHA Resolution 55.18 2002, recital). In response to this concern, the WHO launched in October 2004 the WHO Patient Safety program, and chose HAIs as the first 'Global Patient Safety Challenge' for 2005–2006 (WHO 2006: para. 5). This challenge, called 'Clean Care is Safer Care,' produced guidelines on hand hygiene in healthcare settings[6] (WHO 2009: 12–23), with the goal of ensuring that 'infection control is acknowledged universally as a solid and essential

5 The American SENIC study (see Hughes 1988), which assessed surveillance and control activities in American hospitals in 1970 and 1976, estimates that 32 per cent of HAIs are avoidable if certain conditions are respected. More recently, Harbarth *et al*. noted, based on their 2003 review of published reports, that between 10 and 70 per cent of HAIs are preventable depending on the setting, study design, baseline infection rates, and type of infection.

6 Revised in 2009.

basis towards patient safety' (WHO, n.d.). Since its launch, 129 member states have taken up the challenge, and approximately 15,000 hospitals now implement its guidelines (WHO 2012).

The WHO additionally launched a 'WHO Infection Prevention and Control in Health Care' initiative to help member states reduce HAIs 'by assisting with the assessment, planning, implementation, and evaluation of national infection control policies' (WHO 2002a). In 2002, it published a detailed practical guide to HAI control in healthcare facilities (WHO 2002b). The guide makes recommendations regarding control programs, surveillance, outbreaks, prevention methods, the design of the healthcare environment, antimicrobial use and resistance, and the prevention of infections among healthcare workers (WHO 2002b).

The *Treaty on the Functioning of the European Union* (Consolidated version 2012) serves as the legal basis for many initiatives undertaken in Europe to tackle HAIs. Article 168 of the Treaty states that '[a] high level of human health protection shall be ensured in the definition and implementation of all Community policies and objectives,' adding that Community action shall be directed towards improving public health, preventing physical and mental illness and diseases, and obviating sources of danger to health. It also requires that member states coordinate among themselves their policies and programs in this respect and allows the Commission to promote this coordination (*European Community Treaty*, article 168(2)).

In 1994, the Council of Europe decided to prioritize the issue of communicable diseases (Decision 2119/98/EC of the European Parliament and of the Council 1998, recital (3)). Thereafter, European legislative approaches centered on the creation of a regional program of surveillance and control, recognizing the need for coordinated efforts among the member states.[7] By decisions of the European Parliament and of the Council, programs of Community action in the field of public health have also been created. The objectives of the latest program, covering the 2008–2013 period,[8] include actions to 'improve patient safety through high-quality and safe healthcare, including in relation to antibiotic resistance and nosocomial infections,' which it describes as threats to health in Europe (Decision 1350/2007/EC of the European Parliament and Council 2007, recital (8), article 2(2) and action 1.2.3). The program also aims to strengthen cooperation between the member states in improving citizens' health security (Decision 1350/2007/EC of the European Parliament and Council 2007, recital (5)). One of the actions provided for by this program seeks to '[e]ncourage action aimed at increasing awareness of the problems and including comparable and reliable data on nosocomial infections,' as well as 'promoting knowledge and exchanges of experience on the way in which surveillance results concerning infections caused by germs resistant to normal treatment (antibiotics) are analysed, processed, and used by the actors in the field' (Decision 647/96/EC of the European Parliament and Council 1996, Annex I, action 5).

In 2006, the Council of Europe also adopted a recommendation on the management of patient safety and prevention of adverse events in healthcare. It followed with the decision to make patient safety, including the prevention and control of HAIs, a strategic item under the Commission's legislative and work program in 2008 (Commission of the European Communities 2008: 2). This led to the 2009 Council Recommendations on patient safety, which address HAI prevention and control through, *inter alia*, reporting and learning systems, as well as education and training (Council Recommendation 2009, recital (10); European Parliament Resolution 2009). Stating the importance of HAI prevention and control as a long-term strategy for healthcare

7 See section 11.4.1 of this chapter.

8 This program, which came into force in January 2008, was preceded by a program covering the 2003–8 period. The period 1996–2002 was covered by a program of Community action on the prevention of AIDS and certain other communicable diseases (Decision 647/96/EC of the European Parliament and Council 1996).

institutions, it recommended the adoption and implementation of such strategy and detailed its objectives (Council Recommendation 2009, recommendation 8 and recital (14)). By June 2011, 18 member states had a national and/or regional strategy in place to implement the recommendations (European Commission 2012: 7).

Most of the above initiatives are non-binding. Formal legal norms are mostly produced at the national level.

11.2.2 Legislative and regulatory approaches: prevention and control obligations for healthcare institutions

Statutory intervention with regard to HAIs may take many forms, ranging from general legislation pertaining to patient safety to legislation specifically tackling HAIs. Moreover, the absence of specific legislation dealing with HAIs does not mean there are no prevention and control programs in place; they may be provided for through policy. This section nevertheless centres on examples of formal legislative initiatives imposing obligations on healthcare institutions and actors for the prevention and control of HAIs. It goes beyond the scope of this chapter to address broader normative documents pertaining to patient safety, adverse events in healthcare, medical accidents, and reportable communicable diseases, which are nevertheless relevant to fully understanding the law's treatment of HAIs.

After a brief overview of Canadian, French and American laws on the prevention and control of HAIs, we examine indirect legal incentives used to address this issue.

11.2.2.1 Legislation as a vector for organizational change – Canada, France, and the United States

The establishment of infection control committees and procedures may be the result of voluntary action on the part of institutions or encouraged through policy. In some jurisdictions, however, HAI prevention and control is mandated formally through legislation. This has been the case in Canada, although not uniformly across all provinces. Some Canadian hospitals have a legal obligation to establish infection control committees (Ontario), risk management committees (Quebec) or Health Services Committees (Northwest Territories) in charge of such prevention and control, as well as procedures to handle infections in hospitals (*Hospital Management Regulations* 1990 (Ontario), subsection 4(b)(vi); *Hospital Standards (Yukon Hospital Corporation) Regulation* 1994 (Yukon), subsection 6(1)(b)(vi); *Act Respecting Health Services and Social Services* (Quebec), sections 183.1 and 182.2; *Hospital and Health Care Facility Standards Regulations* 2005 (Northwest Territories), sections 14(6)(b), 59 and 61(5); *Operation of Approved Hospitals Regulation* 1990 (Alberta), section 16(i)). In Manitoba, legislation gives the relevant medical officers specific authority to make orders to hospitals in relation to infected patients and infection control procedures if they find them lacking (*Public Health Act* (Manitoba), section 45). Canadian legislation also imposes obligations on other types of healthcare institutions, such as personal and long-term care homes (*Personal Care Homes Standards Regulations* (Manitoba), section 36; *Long-Term Care Homes Act* 2007 (Ontario), section 86; *Ontario Regulation 79/10* 2010, section 229) and land and air emergency medical response services (*Land Emergency Medical Response System Regulation* 2006 (Manitoba), section 18; *Air Emergency Medical Response System Regulation* 2006 (Manitoba), section 10; *Stretcher Transportation Services Regulation* 2006 (Manitoba), section 13) to implement infection control programs and, in the case of care and nursing homes, to provide staff with education programs in the prevention and control of infections (*Personal Care Homes Standards Regulations* 2005 (Manitoba), section 36; *Long-Term Care Homes Act* 2007 (Ontario), section

76(1); *Ontario Regulation* 79/10 2010, section 219(4); *Nursing Homes Operation Regulations* 1985 (Alberta), subsection 17(1)(d)).

France has tackled the issue of HAIs through legislative action since as early as 1988. Obligations were imposed to organize surveillance of HAIs, as well as to create a 'CLIN' (*Comité de lutte contre les infections nosocomiales*) in all public healthcare establishments and private clinics participating in public healthcare delivery (Décret 88-657 du 6 mai 1988; Stingre and Verdeil 2004: 111 and 112–21). CLINs are committees in charge of organizing and coordinating surveillance, prevention, and continuing education for the fight against HAIs (Ministère des Affaires sociales et de la santé (MASS) 2009; Stingre and Verdeil 2004: 126–8). This initiative was extended to private healthcare establishments in 1998, the year a national program was implemented with the objective of reducing the frequency of infections in French healthcare establishments (Loi 98-535 du 1 juillet 1998, article 4, now *Code de la santé publique* (CSP), article L. 6111-1; Stingre and Verdeil 2004: 111). Since 1992, an additional five coordination centres called CCLIN (*Centre de coordination de lutte contre les infections nosocomiales*) have been entrusted to provide support to health establishments (Arrêté du 3 août 1992, articles 6–7; Stingre and Verdeil 2004: 111). A national structure, the CTINILS (*Comité technique des infections nosocomiales et des infections liées aux soins*)[9] proposes orientations for national policies, provides expertise in the assessment and management of infectious risks, and examines all scientific and technical questions in this area (Arrêté du 23 septembre 2004, articles 1–2; Arrêté du 3 août 1992; Stingre and Verdeil 2004: 111, 124–6). Numerous other French legal texts impose obligations regarding asepsis and HAI prevention measures, and create bodies to address HAIs (see Sargos 2002: 1117; Khoury 2004: 650 and note 136; Stingre and Verdeil 2004).[10]

The United States also shows 'a significant trend of increasing state action to address the burden of HAIs on the U.S. healthcare system' (Reagan and Hacker 2012: 77). Numerous laws promote HAI prevention. As it is impossible to paint a complete picture of American normativity related to HAIs in only a few lines only brief highlights are mentioned. In 2009, the United States Department of Health and Human Services developed the 'National Action Plan to Prevent Healthcare-Associated Infections,' in order to assess national progress in reducing HAI rates and to provide a road map for preventing HAIs in healthcare facilities (US Department of Health and Human Services). The priorities outlined in the action plan formed the basis of prevention efforts at the federal, state and local levels thereafter (CDC and ASTHO 2011: 7–8). In 2011, the CDC called upon all states, especially on state health agencies, to initiate or enhance their HAI programs in light of several federal initiatives underway (CDC and ASTHO 2011: 3 and 6).

Acute care hospitals that participate in Medicare or Medicaid, or those that are accredited through the Joint Commission, must have an infection control program (US Government Accountability Office 2008). In addition, many state laws require the establishment of infection control and prevention measures or programs (e.g. *California Health and Safety Code* 2013, § 1288.8; *Georgia Rules and Regulations for Hospitals* 2012, r. 290-9-7-.13 and 290-9-7.16; *Indiana Administrative Code* 2013 Title 410, regulation 5-1.5-2, regulation 16.2-3.1-18, regulation 1.5-3-5; *General Laws of Massachusetts* 2013 Chapter 111, § 51I; *Nebraska Administrative Code* 2013, § 9-006-08; *Nevada Administrative Code* 2012, § 449.3152; *New Jersey Administrative Code* 2013, § 8:43G-14.1; *Illinois Compiled Statutes* 1997 20 ILCS 1705, § 10.5; *Illinois Compiled Statutes* 1996 210 ILCS 85, § 6.23; *Illinois Compiled Statutes* 2007 210 ILCS 83, § 5). Many state laws also require the use of hospital infection control committees or other types of institutional bodies

9 Called the CTIN (*Comité technique des infections nosocomiales*) prior to 2004.

10 They are too numerous to be described fully here: see Khoury (2004: note 136).

entrusted with the prevention and control of infections (e.g. *Georgia Rules and Regulations for Hospitals,* r. 290-9-7.16; *Indiana Administrative Code* 2013 Title 410, regulation 15-1.5-2; *Nevada Administrative Code* 2012, § 449.3152; *New Jersey Administrative Code* 2013, § 8:43G-14.1; *New Mexico Annotated Statutes* 2009, § 24-29-3), sometimes referring specifically to the necessity to follow CDC guidelines (*New Jersey Administrative Code* 2013, § 8:43G-14.1; *California Health and Safety Code* 2013, § 1288.8; *Prevention and Control of Multi-Drug Resistant Organisms* 2007, § 20 (Illinois)). Some provisions deal precisely with hygiene and asepsis requirements (e.g. *California Health and Safety Code* 2013, § 1279.7; *Georgia Rules and Regulations for Hospitals*, r. 290-9-7.16). In many states, such as New York, South Carolina, and New Hampshire, the hospital prevention program is statutorily required to provide education on HAI prevention to hospital staff (CDC and ASTHO 2011: 25). Some state laws provide for healthcare establishments to evaluate the judicious use of antibiotics (*California Health and Safety Code* 2013, § 1288.8 for acute care). In addition, the *Patient Protection and Affordable Care Act* of 2010 (PPACA) (US) mandates the Secretary of State to establish a national strategy for quality improvement in healthcare. One of the priorities of this strategy is to 'improve research and dissemination of strategies and best practices to improve patient safety and reduce medical errors, preventable admissions and readmissions, and health care-associated infections' (PPACA, § 3011). The *Act* also establishes a Center for Quality Improvement and Patient Safety as part of the Agency for Healthcare Research and Quality, whose responsibilities include researching practical methods to address HAIs, including MRSA, VRE, and other emerging infections (PPACA, § 3501).

11.2.2.2 Indirect legal normativity: codes of practice, registration requirements and financial incentives

In addition to directly requiring infection prevention and control, legal normativity is also expressed more flexibly through mechanisms aimed at encouraging or indirectly compelling such measures. England provides an interesting example as it addresses the prevention and control of HAIs through binding regulation, its registration process, and a non-binding code of practice. Financial incentives, such as those used in Canada and the United States, demonstrate other techniques for placing indirect pressure on healthcare institutions.

Following an earlier reform in 2006,[11] the *Health and Social Care Act* 2008 (*H&SC Act*) (England) created the Care Quality Commission (CQC).[12] Established in 2009, the CQC is a single inspection agency responsible for the registration, review, and inspection of England's health and social care services. The 2008 *Health and Social Care Act* also grants the Secretary of State the power to adopt regulations for safeguarding individuals from the risk or increased risk of exposure to HAIs[13] or of rendering patients susceptible or more susceptible to them (section 20(5)). It also allows the Secretary of State to issue a Code of Practice with any requirements related to the prevention or control of HAIs (*H&SC Act*, section 21). In accordance with the *Act*, the *Health and Social Care Act 2008 (Regulated Activities) Regulations* (England) (the *Regulations*) came into force in April 2010. These regulations prescribe the kinds of activities that are

11 Originally, the *Health Act* 2006 added a series of new provisions to the *Health and Social Care Act* 2003 dealing with, among other matters, the possibility for the Secretary of State to issue a code of practice for the prevention and control of HAIs (*Health Act* 2006 (England), section 47A).

12 Replacing the Commission for Healthcare Audit and Inspection created under the 2003 *Health and Social Care Act* (England), as well as the Mental Health Act Commission and the Commission for Social Care Inspection. A further reform took place under the *Health and Social Care Act* 2012 (England).

13 Defined at section 20(6) of the *H&SC Act*.

regulated, outline the requirements for carrying out these activities, and provide for the registration of persons performing them.[14] In December 2010, the Department of Health also adopted the *Health and Social Care Act 2008 Code of Practice on the Prevention and Control of Infections and Related Guidance* (*Code of Practice*), applicable to registered providers of all healthcare and adult social care in England.

The *Regulations* state[15] that a registered person *must, so far as reasonably practicable*, ensure that service users – persons employed to perform a regulated activity and others who may be at risk of exposure to an HAI arising from a regulated activity – are protected against *identifiable risks* of acquiring an HAI (section 12). To do so, it must rely on the means specified in detail in the Regulations, as well as in the *Code of Practice* (*Regulations*, section 12; *Code of Practice*, part 2). These include the effective operation of systems designed to assess the risk of an HAI and to prevent, detect, and control its spread; the provision of appropriate treatment; and the maintenance of appropriate standards of cleanliness and hygiene in relation to premises, equipment, reusable medical devices, and materials at risk of being contaminated with an HAI (*Code of Practice*, p. 13). Nuances are inserted in the text to acknowledge that such prevention can never be perfectly achieved: obligations are imposed 'so far as reasonably practicable' and apply only against 'identifiable risks' of acquiring an HAI. The *Code* also sets out ten criteria against which the Care Quality Commission judges whether a provider complies with the cleanliness and infection control requirement imposed by the *Regulations*. Despite its textured language, the *Regulations* do provide for sanctions. Failure to comply with sections 9 to 24, which include obligations regarding cleanliness and infection control, is an offence that may lead, on summary conviction, to a fine not exceeding £50,000. However, a registered person may present a defence based on the fact that they took all reasonable steps or exercised all due diligence to ensure that the provision in question was complied with (*Regulations*, section 27).

The English legal approach also uses the registration process to ensure compliance with the *Code of Practice*. The Care Quality Commission must take the *Code* into account when it makes decisions about providers' registration[16] (*Regulations*, section 26), an evaluation which must be proportionate to the risk of infection (*Code of Practice*, pp. 10–11 and part 3). Providers must therefore take the *Code* into consideration when deciding how they will comply with registration requirements: 'by following the Code, registered providers will be able to show that they meet the requirement set out in the regulations' (*Code of Practice*). Where a provider does not comply with its legal obligations as set out in the *Regulations* and the *Code of Practice*, the Commission may use its enforcement powers or take any other action. However, it may do so only after verifying whether the breach occurred because the *Code*'s norms were not appropriate to the type of service provided. As the *Code* is not mandatory[17] (*H&SC Act*, section 25), registered providers may demonstrate that they meet 'the regulations in a different way (equivalent or better) from that described' in the *Code* (*Code of Practice*, pp. 6 and 10–11).

Another indirect means of improving prevention and control of infection in healthcare establishments is through financial penalties or advantages. In Canada, the *Excellent Care for All Act* 2012 (ECFAA) of Ontario has mandated since 2012 that compensation given to healthcare executives be linked to achieving quality improvement targets (sections 1, 8 and 9). In 2008,

14 A first set of regulations was adopted in 2009 but was replaced very shortly after by the 2010 Regulations.

15 Reproducing in great part section 5 of the 2009 Regulations, with some modifications.

16 Regulations made under the *H&SC Act* describe the care activities that may only be carried out by providers registered with the Commission (*Code of Practice*, p. 9).

17 Failure to observe the *Code of Practice* does not make a person liable to any criminal or civil proceedings, although the *Code* is admissible as evidence in such proceedings.

the United States' Centers for Medicare and Medicaid Services (CMS) ceased giving additional payments for hospitalizations resulting in complications deemed preventable, including some HAIs (see also *Public Health* 2013, Chapter 11, section 51H (Massachusetts)). This policy drew increased attention to the targeted HAIs, although its effect on health outcomes remains unclear (Lee *et al.* 2012: 314–15). Moreover, the PPACA penalizes hospitals if they do not perform well with regard to hospital-acquired conditions (section 3008).

In addition to statutory governance, HAIs are also subject to public inquiries and class action lawsuits when they lead to outbreaks.

11.2.3 Public inquiries, audits and class action lawsuits

The spread of HAIs and the occurrence of outbreaks have led to public inquiries and audits to identify their causes and future solutions for prevention. Public inquiries and audits are therefore also a source of normativity in this sector.

11.2.3.1 Public inquiries and audits: Canada

Canada provides an example of how public inquiries can serve as non-legislative vectors of change. For instance, a 2004 Ontario Ministry of Health and Long-Term Care Report (MHLTCR) enumerated 103 recommendations after an audit of all hospital infection-control practices in the province ordered by the government following the spread of SARS in this province. One of the Report's recommendations was for the creation of a Health Protection and Promotion Agency (HPPA) whose core functions would include the establishment of standards and guidelines for infection control.[18] This Agency has existed since 2007 and now operates as Public Health Ontario. The Report also proposed the establishment of a standing Provincial Infection Control Committee responsible for supervising existing audits of hospital infection control policies, programs, and resources and undertaking additional ones. Informed by these audits, the Committee would also be entrusted with developing provincial infection control standards for all healthcare facilities in Ontario, as well as mechanisms to ensure compliance with existing and new infection control standards (MHLTCR, pp. 20–1 and 29). This Committee, known as the Provincial Infectious Diseases Advisory Committee (PIDAC), was created in 2004.

Additionally, the Alberta Minister of Health and Wellness requested in 2007 that the Health Quality Council of Alberta conduct a review of the underlying causes and contributing factors that led Alberta's Medical Health Officer to close St Joseph Hospital to new admissions and to shut its Central Sterilization Room in March 2007 after several patients contracted MRSA. (This event also led to a class action lawsuit.[19]) The Minister also asked for an assessment of other sites in the health region with respect to infection prevention and control policies and procedures, as well as risk management and sterilization practices. Interestingly, the investigating team concluded that one of the root causes of the problem was found in the legislation governing the health region and the healthcare establishment (Health Quality Council of Alberta 2007: 1).

A final example, from the province of Quebec, is Coroner Rudel-Tessier's 2007 report inquiring into the origin of *Clostridium difficile* (*C. difficile*) infections that killed 16 patients at Hôpital Honoré-Mercier in St-Hyacinthe. Coroner Rudel-Tessier blamed the hospital

18 The recommendations also deal with training, the availability of specialized staff, the funding of control programs, emergency preparedness, the communication infrastructure, and surveillance.

19 See section 11.2.3.2 of this chapter.

management for giving insufficient authority to the infection prevention and control team. Among other factors, she found that patients' state of health, their physical proximity to each other, poor hygiene, the absence of surveillance, and the excessive workload of the staff had contributed to the outbreak (Rapport Rudel-Tessier 2007). The initiation of a class action lawsuit followed the publication of her report in 2008 and was settled for $1 million CAD in 2011 (*Dorion* v. *CSSS Richelieu-Yamaska* 2012 QCCS 727).[20] Indeed, infectious outbreaks in healthcare facilities in Canada and the United States have sparked numerous class actions over the past ten years.

11.2.3.2 Class action lawsuits in Canada and the United States

In Canada, the spread of SARS in Toronto-area hospitals in 2003 led to several class action lawsuits (*Williams* v. *Canada (Attorney General)* (2005) 76 OR (3d) 763; *Williams* v. *Canada (Attorney General)* (2009) 95 OR (3d) 401; *Abarquez* v. *Ontario* (2005), 257 DLR (4th) 745; *Laroza* v. *Ontario* (2005) 257 DLR (4th) 761). Other lawsuits were launched by patients who were exposed to or contracted tuberculosis through contact with an infected patient (*Healey* v. *Lakeridge Health Corp* (2006) CarswellOnt 6574; *Healey* v. *Lakeridge Health Corp* (2010) CarswellOnt 556), and by persons affected in an outbreak of Legionnaire's Disease and Pontiac Fever at a home for the elderly in Ontario which infected 135 persons and killed 23 (*Glover* v. *Toronto (City of)* (2009) 70 CPC (6th) 303; *Glover* v. *Toronto (City of)* (2010) 95 CPC (6th) 206). In 2008, an outbreak of the multidrug-resistant bacteria *Pseudomonas aeruginosa* at the Toronto General Hospital led to a class action after the death of 17 patients (*Sherman* v. *University Health Network* (2011) CarswellOnt 13165). A last notable Canadian example is the class action against an Alberta hospital and regional authority on the ground that failure to implement infection control practices led to patients contracting MRSA (*Bruce Estate* v. *Toderovich* (2010) AJ No. 1324[21]).

Most Canadian class action cases have not made it to final judgment, and several have been settled out of court. In addition to the aforementioned settlement by Hôpital Honoré-Mercier, a class action against the Scarborough Hospital by dialysis patients who contracted or were at risk of contracting hepatitis B or C was settled in 2010 (*Notice of the Settlement of the Dialysis Class Action against the Scarborough Hospital* 2010). A 2008 class action against the Joseph Brant Memorial Hospital, alleging negligence in cleaning, maintenance, and disinfection during a one-year *C. difficile* outbreak that killed 91 patients was also settled for $9 million CAD (*Elliot Estate* v. *Joseph Brant Memorial Hospital* 2013 ONSC 124; see also *Rose* v. *Pettle* (2004) 23 CCLT (3d) 21 Ontario). Two claims grounded on the improper sterilization of ultrasound equipment and gynecological instruments (*Farkas* v. *Sunnybrook and Women's College Health Sciences Centre* (2004) OJ No. 5134 (SCJ); *Farkas* v. *Sunnybrook and Women's College Health Sciences Centre* (2009) 179 ACWS (3d) 764 (SCJ)) were settled for $1.2 million CAD and $179,850 CAD respectively (in the second, no patients had been infected). Interestingly, this last settlement required the defendant to publish a notice outlining the changes in policy and procedure implemented in response to the sterilization breach, and to have its Chief Executive Officer apologize and offer a public statement discussing these changes. It also provided for the defendant's insurer to conduct an education seminar on the topic of infection control (*Rideout* v. *Health Labrador Corp* (2007) NLTD 150).

20 For an English example, see Mid Staffordshire NHS Foundation Trust Public Inquiry (2013, recommendations 106 and 107).

21 See below.

However, claims against the province of Ontario by patients and nurses – and their families – who contracted SARS during the 2003 outbreak were struck out for, *inter alia*, absence of a duty of care on the part of the province. Plaintiffs argued that the province was negligent in managing the risks associated with SARS and the protection of their safety.[22] The Court of Appeal of Ontario ultimately dismissed the actions. It believed, among other conclusions, that imposing a duty of care in this respect would create a conflict with the overarching duties the province owes to the public at large in protecting their health (*Laroza* v. *Ontario*; *Williams* v. *Canada (Attorney General)*; *Abarquez* v. *Ontario*). The demonstration of a duty of care is also jeopardized where claimants only invoke exposure to the risk of contracting an infection, rather than actual infection (e.g. *Bruce Estate* v. *Toderovich*).

The United States has also had its share of HAI-related class action lawsuits. Patients exposed to infection risk have waged class actions for the re-use of single-use material (e.g. *Kinney* v. *Siouxland Urology Associates* (2011) WL 796237 (DSD) where certification was denied; *Calvillo* v. *Siouxland Urology Associates* (2011) WL 5196542 South Dakota);[23] or improper sterilization of equipment (e.g. *Creech* v. *Foote Memorial Hospital* (2004) WL 1258011 (Mich. App.); *Creech* v. *Foote Memorial Hospital* (2006) WL 2380825 (Mich. App.), certified in part; *Doctors Hospital Surgery Centre, LP* v. *Webb* (2010) 704 SE 2d 185 Georgia, certification reversed on appeal). Other examples include a case alleging the omission to disclose the infectious tuberculosis status of a physician and to take precautions to protect patients from exposure (*Hannis* v. *Sacred Heart Hospital* (2000) 49 Pa. D. and C.4th 13 (Pa.Com.Pl.), certified). Certification of such class actions is not necessarily obtained straightforwardly. For instance, in a claim against a surgical centre for non-compliance with sterilization protocols of endoscopes, the certification obtained in the first instance was reversed partly because individual factual questions pertaining to causation predominated over common questions within negligence claims for damages related to anxiety, emotional distress, and loss of consortium (*Doctors Hospital Surgery Centre, LP* v. *Webb*; *Kinney* v. *Siouxland Urology Associates*; *Rader* v. *Teva Parenteral Medicines Inc.* (2011) 276 FRD 524).

Finally, legislation also plays a role in the response to injuries suffered by victims of HAIs, sometimes through innovative techniques, as is the case in France.

11.2.4 Conciliation and state compensation – the French model[24]

In addition to the possibility of litigation by victims of HAIs under civil and administrative liability rules, France has had a mechanism for amicably resolving litigation and a state compensation fund for HAI victims since 2002 (*Loi n° 2002-303 du 4 mars 2002 relative aux droits des malades et à la qualité du système de santé* 2002; *Loi n° 2002-1577 du 30 décembre 2002 relative à la responsabilité civile médicale* 2002). The *Loi du 4 mars 2002*, modifying the *Code de la santé publique*, is a major legislative initiative dealing in part with HAIs, transfusional HIV,[25] and medical accidents in general. Specific provisions pertaining to HAIs create a special regime dealing with the liability of physicians and hospitals and create a compensation fund to benefit the most injured victims of these infections.

22 Precise allegations are found at paragraph 7 of the 2009 decision.

23 Case stayed until a decision in *Kinney* v. *Siouxland Urology Associates* was issued.

24 Compensation schemes were also set up by the Government of Ontario following the SARS crisis in this province (Jacobs 2007: 535–6).

25 CSP, article L 3122-1-L 3122-5. These are not discussed here although they qualify as HAIs.

HAI victims can seek liability under the relevant provisions of the *Code de la santé publique*. These affirm the principle of liability based on fault, but create an exception for HAIs, holding public and private healthcare establishments, services, and organizations liable without negligence unless they present evidence of absence of causation (*cause étrangère*) (CSP, article L 1142-1(I)). Physicians escape the application of this rule: victims must demonstrate their fault (CSP, article L 1142-1(I)).

The 2002 provisions also introduced a special conciliation mechanism for claims made under these provisions.[26] Conciliation is administered by the CRCIs (*Commissions régionales de conciliation et d'indemnisation*), the CNAM (*Commission nationale des accidents médicaux*), and the ONIAM (*Office national d'indemnisation des accidents médicaux, des affections iatrogènes et des infections nosocomiales*). A CRCI is a multidisciplinary body,[27] presided over by a judge, in charge of facilitating the amicable settlement of litigation concerning HAIs (CSP, articles L 1142-5–L 1142-6). It is charged with inquiring into and formulating an opinion on the circumstances, causes, nature, and extent of the damages, as well as on the applicable compensation regime within six months after a claim is instituted (CSP, article L 1142-8). Its conclusion rests on the opinion of experts chosen from a national list managed by the CNAM (CSP, article L 1142-10, article L 1142-12). If the CRCI believes that a claim falls under 'national solidarity,' the ONIAM must make a compensation offer to the victim within four months of receiving the CRCI's opinion. Compensation must be provided within one month after the claimant accepts the offer (CSP, article L 1142-17, article L 1142-22). If the CRCI believes that the liability of a healthcare actor is involved, the actor's insurer must provide the victim with a compensation offer, and with compensation should the victim accept, within the same time frame (CSP, article L 1142-1, article L 1142-14). In cases where the insurer remains silent, refuses to make an offer, or the person liable for the injury is not insured, the ONIAM takes the place of the insurer, but is subrogated to the victim's rights against the person responsible for the injury or their insurer up to the amount it has paid in compensation (CSP, article L 1142-15). Hence, the process instituted by the *Loi du 4 mars 2002* prioritizes the interest of HAI victims in receiving fast compensation.

The 2002 provisions also establish the principle of 'national solidarity' for HAI victims through a no-fault, no-responsibility compensation fund. Two types of access to the fund exist. The first, referred to as the 'subsidiary regime,' is available for HAI victims who have not been successful in seeking the liability of relevant healthcare actors, either because they could not prove the physician's fault or because the healthcare establishment was able to point to another cause for the injury (CSP, article L 1142-1(II)). However, the patient's injury must have caused partial permanent incapacity of 24 per cent or more (CSP, article D 1142-1) and the infection must be directly imputable to an act of 'prevention, diagnosis or treatment.'

After insurers reacted against the subsidiarity of this regime by withdrawing from the healthcare insurance market, the legislator introduced a second regime (Pansier 2003: 26). Since December 2012, HAI victims who are deceased or who suffer from partial permanent incapacity

26 Judicial claims are still possible (CSP, article L 1142-19). However, if the tribunal believes that the case is admissible to direct or subsidiary compensation by the ONIAM, the latter becomes a defendant in the proceedings (CSP, article L 1142-21). In cases where the tribunal concludes that the ONIAM must compensate the patient through the mechanisms of direct access to the compensation fund by virtue of article L. 1142-1-1, the ONIAM has no recourse against the concerned healthcare professional, establishment, service, or body or their insurers unless fault has been committed, such as through 'characterized failure' (*manquement caractérisé*) to comply with the obligations imposed by regulation for the fight against HAIs (CSP, article L 1142-21).

27 Aside from the presiding judge, members include representatives of patients, healthcare professionals, persons responsible for healthcare establishments, and representatives from ONIAM and the insurers (CSP, article L 1142-6).

of over 25 per cent are offered direct access to the fund (CSP, article L 1142-1-1). In cases where compensation has been paid by virtue of the above two regimes, the ONIAM is subrogated to the rights of the victims and can sue the professional, establishment, service, or organizations concerned (CSP, articles L 1142-1 II, 1142-17, and L 1142-17-1). This system has been criticized, particularly on the grounds that the minimum partial incapacity condition is too stringent (Pansier 2003: 5). Authors also contend that members of the medical profession are held less accountable for their actions (Bertella-Geffroy *et al.* 2002).

Individual litigation has also been undertaken by victims of HAIs, despite serious challenges, as the state of Canadian litigation demonstrates.

11.3 Illustration at the national level: individual litigation in Canada

Individual litigation by HAI victims is revealing of the role that private law plays in responding to medical accidents, as well as in regulating the behaviors that may lead to them. This section briefly addresses the Canadian common law and civil law litigation pertaining to liability for HAI occurrences. It then contrasts this body of case law with French litigation prior to the adoption of the *Loi du 4 mars 2002* to demonstrate the ways in which France has become one of the more progressive jurisdictions in securing judicial compensation for victims of HAIs.

Beyond the liability of physicians who carried out the medical act allegedly at the origin of an infection, the liability of healthcare institutions is often sought. In addition to their potential vicarious liability for the negligence of healthcare staff, healthcare institutions could be held personally negligent for failing to adopt reasonable infection prevention and control protocols, or for their negligent implementation (McQuoid-Mason 2012: 353). In practice, however, both Canadian physicians and healthcare institutions have rarely been held negligent for the occurrence of an HAI.[28] In individual lawsuits claiming compensation for injury caused by alleged HAIs, plaintiffs face major hurdles when attempting to prove negligence, causation, or failure to provide information regarding the risks of infection (Khoury and Iokheles 2009: 227).

11.3.1 Demonstration of negligence

Most Canadian cases assessing negligence in relation to an HAI tackle the issue from a diagnostic or post-occurrence treatment angle (e.g. *Rietze* v. *Bruser (No. 2)* (1978) CarswellMan 99); *Hajgato* v. *London Health Association* (1982) 36 OR (2d) 669; *Hajgato* v. *London Health Association* (1983) 44 OR (2d) 264; *Thorne* v. *Murphy* (1985) CanLII 873 (British Columbia); *Andree* v. *Pierce* (1986) MJ No. 121 (Manitoba); *Smith* v. *Miller* (1988) OJ No. 2365; *Painchaud-Cleary* v. *Pap* (2002) JQ no 1026 (Quebec); *Aldcroft* v. *Cameron* 2004 BCSC 1624; *Mangelana* v. *McFadzen* (2006) 275 DLR (4th) 178 (Northwest Territories); *Hasmani (Litigation Guardian of)* v. *Nagai* (2007) CarswellOnt 2198; *Lévesque* v. *Hudon* 2013 QCCA 920). They more rarely inquire whether negligence may be at the *source* of the infection. It is surely because of difficulties in proving that their infection originated from a negligent act that plaintiffs rather allege negligent diagnosis and treatment of the infection once it is contracted.

Courts in Canada have generally been reluctant to hold physicians and institutions negligent for the occurrence of an infection for two reasons. First, the risk of infection is inherent to many medical acts and therefore may occur regardless of whether reasonable precautions were taken

28 The issue of negligence in the treatment of an HAI is not discussed here as it raises questions that are no different from those that arise in all cases of alleged negligent medical treatment.

or how carefully the act in question was performed (e.g. *White* v. *Turner* (1981) 120 DLR (3d) 269 (Ontario), para 77; *Andree* v. *Pierce* (1986) MJ No. 121 (Manitoba); *Normand* v. *Stranc* (1994) 10 WWR 175 (Manitoba), para 62; not at issue on appeal in *Normand* v. *Stranc* (1995) 9 WWR 446). This is particularly true if the infection was post-operative, or of endogenous origin (e.g. *Arlinski* v. *Donis* (1986) BCJ No. 2253; *McArdle Estate* v. *Cox* (2003)13 Alta LR (4th) 19, paras 35 and 48; *Best* v. *Hoskins* (2006) AWLD 1300 (Alberta), paras 88 and 104; *Baert* v. *Graham* (2011) 371 Sask. R. 1, 518 WAC 1). Because infections are known complications of many medical procedures, relying on inferences to demonstrate negligence is also a challenge (e.g. *Hajgato* v. *London Health Association* (1982); *Wintle* v. *Piper* (1994) 93 BCLR (2d) 387; *Parragh* v. *Eagle Ridge Hospital and Healthcare Centre* (2008) BCJ No. 1836, paras 63–4). When the risk of infection is inherent to the procedure undertaken, some plaintiffs have opted to challenge the appropriateness of the choice of the procedure itself (e.g. *Tremblay* v. *Maalouf* (2000) RRA 772 (Quebec), pp. 775 and 779; *Lévesque* v. *Baribeau* (2001) RRA 639 Québec; *Baert* v. *Graham* (2011) 371 Sask. R. 1).

Second, considering the impossibility of completely eradicating infection risks in healthcare settings, courts believe there is no negligence as long as reasonable precautions were taken to reduce or control the risk of infection before, during, and after the medical act (e.g. *A.G.* v. *Hôpital Fleury* (2008) RRA 459 (Quebec), paras 94–5; *J.G.* v. *Taguchi* (2008) RRA 206 (Quebec), paras 32–3, 41 and 43; Khoury 2012: 784). The success of an allegation that physicians and healthcare institutions omitted to take precautions against a known risk of infection often depends on accepted professional standards of practice (e.g. argument rejected: *Garceau* v. *Lalande* (1998) RJQ 1279 (Quebec), p. 1288; *Doucet* v. *Bourque* (1999) NBJ No. 168; *Rossman* v. *Sas* (1999) OJ No. 3028; *Marchand* v. *Jackiewicz* (2010) CarswellOnt 1723 (*obiter dictum*); argument accepted: *Semeniuk* v. *Cox* 2000 ABQB 18; *Tremblay* v. *Maalouf* (2000) RRA 772 (Quebec), pp. 776 and 778). Still, Canadian courts rarely assess the reasonableness of general preventive measures adopted by healthcare institutions (e.g. *Jablonski* v. *Marosi* (1985) EYB 1985-145409 (Quebec); *Tonizzo* v. *Moysa* (2007) AJ No. 430 (*obiter dictum*)). There is a tendency to deny the occurrence of institutional negligence as long as precautions and control standards existed and were generally respected at the relevant time (Khoury 2012: 788–9; Khoury 2004: 634). Claims against hospitals have also been dismissed by courts invoking the general impossibility of preventing a particular infection from occurring (*Bissell (Next friend of)* v. *Vancouver General Hospital* (1979) BCJ No. 481) or the fact that the precautions necessary to prevent such an infection would have been unworkable (*Dineen* v. *Queen Elizabeth Hospital* (1988) RRA 658 (Quebec); Khoury 2004).

Given the importance of professional standards of practice when assessing the occurrence of negligence, the detailed and sophisticated prevention and control standards developed over the past few decades are likely to play a central role in HAI-based litigation. While failure to comply with these standards is not evidence of negligence *per se*, at least in Canadian law, they provide good indicators of the prevention and control norms considered to be reasonable by experts in the field (e.g. *Kovacich* v. *St Joseph's Hospital* (2004) OJ No. 4471).[29]

11.3.2 Causal analysis

Before Canadian courts, causation is a particularly burdensome requirement to prove for patients who allege that the defendant – healthcare institution, physician or healthcare staff –

29 Data compiled by the Infection Control Committee of the defendant hospital was one of the elements used to evaluate the general situation regarding the occurrence of necrotizing fasciitis resulting from a Group A *Streptococcus* infection, as well as its nosocomial nature and the risk of its occurrence.

is at the source of an infection.[30] Patients must of course establish that the infection was contracted in the healthcare setting. The timing of onset of an infection can be extremely difficult to determine, as many infections are asymptomatic for some time after contraction (e.g. *Hajgato* v. *London Health Association* (1982); *Havens* v. *Hotel-Dieu of St Joseph Hospital* (1989) OJ No. 1095). However, the typical incubation period may assist experts in this regard. Even if it is possible to link an infection to the provision of healthcare, establishing the exact origin of the infection may be difficult, if not impossible, in light of the many factors that may be at play (Khoury and Iokheles 2009: 206 and cases cited). Claims are typically rejected when there is an alternative explanation for the infection unrelated to any act of negligence. This is often the case for post-operative infections and infections of endogenous origin known to arise in the absence of negligence on the part of healthcare professionals and providers (Khoury and Iokheles 2009: 207 and cases cited). Canadian courts rarely rely on factual inferences to prove causation in this context (Khoury and Iokheles 2009: 214–24 and cases discussed), although they have done so in a few cases (*Aristorenas* v. *Comcare Health Services* (2004) CarswellOnt 3599, reversed on this point on appeal in *Aristorenas* v. *Comcare Health Services* (2006) 42 CCLT (3d) 220; *Parragh* v. *Eagle Ridge Hospital and Healthcare Centre* 2008 BCSC 1299). Finally, some judges dispense with attempting to identify the cause of an infection when they believe that none of the possible causes could result from negligence (Khoury and Iokheles 2009: 224–6 and cases analyzed).

Most of the case law in Canada concerns individual occurrences of infections. Causal inquiries might certainly be easier in outbreak situations where several infections occur in the same environment, at the same time, in patients treated by the same medical team, or in patients receiving similar treatment (Khoury and Iokheles 2009: 219–20). These circumstances, coupled with an identified culpable microorganism, could provide a court with sufficient indicators to infer the link between an infection and the healthcare provided, although this would not necessarily denote negligence (e.g. *Parragh* v. *Eagle Ridge Hospital and Healthcare Centre*, pp. 37–8 and 63–4; Khoury and Iokheles 2009: 220–1). However, even in outbreaks the evidence can conflict on the issue of causation due to the multiplicity of possible infection sources within the healthcare setting (e.g. Rapport Rudel-Tessier's 2007). Although they have rarely been part of Canadian courts' analyses, the findings of infection prevention and control teams could help determine the sources of outbreaks if admissible in evidence before the court (Khoury and Iokheles 2009: 219–20).

11.3.3 Informed consent

Finally, plaintiffs suffering from HAIs often plead that the risk of infection inherent in their procedure was not disclosed and that if it had been, they (in civil law) or the reasonable patient (in common law) would not have consented to the medical act. As is the case for any medical risk, the obligation to disclose infection risks associated with healthcare depends on the probability they will occur and the seriousness of their consequences (e.g. disclosure not required: *Chouinard* v. *Landry* (1987) RJQ 1954 (Quebec); *Jablonski* v. *Marosi*; *Williamson* v. *Kozak* (2003) ABQB 953; *Hajgato* v. *London Health Association* (1982), affirmed on appeal in *Hajgato* v. *London Health Association* (1983) 44 OR (2d) 264; disclosure required: *Cantin-Cloutier* v. *Gagnon* (2001) RRA 75 (Quebec)). However, Canadian courts have stated that patients are presumed to have basic knowledge of the risks inherent in any operation, including scarring, bleeding, and infection (*Hajgato* v. *London Health Association*; *Videto* v. *Kennedy* (1981) 33 OR (2d) 497; *White* v. *Turner*, para. 54; *Drolet* v.

30 Cases in which the causal analysis focuses on whether negligence in *treating* an infection has caused the plaintiff's injury are not discussed here since the causal assessment they necessitate is typical of that undertaken in any case alleging failure to properly diagnose and treat a medical condition.

Parenteau (1994) RJQ 689 (Quebec); Baudouin and Deslauriers 2007: 2–53; Picard and Robertson 2007: 143–4), although some authors doubt whether one can presume that a reasonable patient knows the risks of infection associated with surgical procedures (Kouri and Nootens 2012, para. 314). A risk of infection that goes beyond the general risks of surgery, and is specific to a surgery or procedure, must be disclosed (e.g. *Thorne* v. *Murphy*, para. 13; *Wintle* v. *Piper* (1992) BCJ No. 1414). Disclosure is also required if the patient asks questions, voices particular concerns (*Aldcroft* v. *Cameron*; *Hopp* v. *Lepp* (1980) 112 DLR (3d) 67 SCC) or is at a particular risk of developing an infection. Finally, extremely rare infection risks do not need to be disclosed, as determined in two cases involving necrotizing fasciitis (*Kovacich* v. *St Joseph's Hospital*; *Best* v. *Hoskins*). On the basis of the above, it is likely that disclosure would be required in the presence of an unusually high or severe infection rate, or in the presence of a potential or confirmed outbreak, as such risks obviously do not constitute general and common infection risks related to all medical procedures.

The difficulties faced by Canadian plaintiffs are in sharp contrast with the activism of French courts.

11.3.4 Some comparisons with France

Prior to France's legislative scheme of 2002,[31] French courts were particularly concerned with the situation of HAI victims. Both the Cour de cassation (with jurisdiction over private clinics and healthcare actors within such clinics) and the Conseil d'État (public hospitals and their healthcare staff and physicians) imposed an obligation of result on clinics, public hospitals, and physicians.[32] This meant that these actors could be liable for the sole occurrence of an HAI, even absent negligence on their part (Daël 1993: 575; *Civ.1re 29 juin 1999*, *Bull. Civ.* 1999.I.22; Hocquet-Berg 2000: 625). Victims, however, had to prove that the infection resulted from a medical act that had taken place in the doctor's office or healthcare establishment or, in other words, that it was not present or incubating at the moment of admission (Khoury 2004: 640–1). The *Loi du 4 mars 2002* partially reversed this case law, by reinstating the principle of fault-based liability for physicians (CSP, article L 1142-1).

Contemporary legal trends with regard to the prevention of HAIs also center on the reinforcement of surveillance programs and the exchange of information. Moreover, a contentious issue has emerged: the public disclosure of infection rates by individual healthcare establishments.

11.4 Current and emerging legal issues: surveillance, reporting, and disclosure to the public

11.4.1 Surveillance and reporting

The reinforcement of global surveillance and information exchange systems has become a central aspect of international reforms on HAIs. In many jurisdictions, the law participates in this reinforcement.

In the European community, coordinated surveillance has been the focus of several recent initiatives. A 1998 decision of the European Parliament and Council set up a network for epidemiological surveillance and control of a number of communicable diseases, including HAIs (Decision 2119/98/EC of the European Parliament and Council 1998, recital (1) and article 1). It requires that member states provide the community network with information, notably on

31 Section 11.1.4 of this chapter.

32 However, between 1996 and 1999 they imposed a presumption of fault on physicians in cases where patients developed an HAI (*Cass civ 1re 21 May 1996*, JCP éd. G. 1996.I.3985; Khoury 2006).

cases of HAIs (Decision 2119/98/EC of the European Parliament and Council 1998, article 4) and on the urgent control measures they adopt in response to communicable diseases. Member states must coordinate among themselves, in liaison with the Commission, the national measures they adopt or intend to adopt (Decision 2119/98/EC of the European Parliament and Council 1998, article 6). Relevant information on HAIs detected in their national surveillance systems must also be disseminated within the network (European Commission Decision 2000/96/EC 2000, article 6, annex I). The 1998 decision was implemented through the HELICS projects (*Hospitals in Europe Link for Infection Control through Surveillance*), which in 2005 became part of the IPSE project (*Improving Patient Safety in Europe*). In 2008, the IPSE was transferred to the ECDC, an independent agency which has assisted the European Union since 2005 by 'identifying and assessing the risk of current and emerging threats to human health by infectious diseases' (European Commission, *Public Health*). It gathers surveillance data from European Union members, analyzes and interprets this data, and disseminates information through surveillance reports and standardized tables and charts. One of its main programs addresses antimicrobial resistance and HAIs. Since 2008, the ECDC coordinates a European disease-specific network (HAI-Net) to manage HAI surveillance.[33] In addition, the European *Clostridium difficile* surveillance network (ECDIS-Net), funded by the ECDC, focuses specifically on surveillance of *C. difficile* infections.

In 2007, the European Parliament and the Council reiterated the need to monitor the state of public health across the European Union. It advocated for the exchange of information facilitated by a program of community action, while insisting on the need to improve dissemination of information to the public (Decision 1350/2007/EC of the European Parliament and Council 2007, recital (17)). In a 2009 recommendation, the Council also stressed the importance of establishing and strengthening surveillance systems at the regional, national, and healthcare institution levels, and of maintaining and improving comprehensive reporting and learning systems on the causes and extent of adverse events (Council Recommendation 2009, recital (15) and recommendation 8(c)). Furthermore, it emphasized the need to collect comparable and aggregate data at the community level in order to establish efficient and transparent patient safety programs, structures, and policies (Council Recommendation 2009, recitals (10)–(11)).

Legislation strengthens surveillance and reporting at the national and institutional levels in Europe and beyond. The situation in the United States is particularly interesting in this regard, as the growing concern for patient safety motivated several states and territories to adopt legislation pertaining to the reporting – sometimes publicly – of infection rates in healthcare facilities. The wide range of legislative options adopted by the different American states, described as 'highly variable' (Reagan and Hacker 2012: 75; Haustein *et al.* 2011: 472), exemplifies the variety of possible reporting approaches. They include obligatory data reporting to the state agency responsible for the oversight of the state's HAI program, voluntary reporting, and reporting to the public with or without the identity of the facilities revealed (Reagan and Hacker 2012: 75). According to the CDC, 29 states and Washington, DC required HAI reporting to the state health agency or another state-level entity such as a hospital association or a quality improvement organization as of 2011 (CDC and ASTHO 2011: 15). The vast majority of states with mandatory reporting also have a mandate to publicly report data pertaining to HAIs (CDC and ASTHO 2011: 16).[34] In 2012, 22 states adopted a comprehensive reporting strategy, namely requiring the submission of data to relevant state agencies as well as public reporting with facility

33 The HELICS project laid the foundations for a European Network and created a surveillance system (WHO 2010: 9). Two HALT projects (*Healthcare-Associated Infections and Antimicrobial Use in European Long-Term Care Facilities*) funded by the ECDC have also taken place, one from 2009 to 2011 and another starting in 2013.

34 See section 11.4.2 of this chapter.

identifiers (Reagan and Hacker 2012: 77). Only a small number of states required confidential reporting to a state agency or only had voluntary public reporting policies (Reagan and Hacker 2012: 76–7).

Since 1994, the Canadian Nosocomial Infection Surveillance Program (CNISP) has the mandate to provide information on HAI rates and trends at Canadian healthcare facilities (AMMI/CHICA 2012). Its objective is to enable the comparison of rates and 'to provide data that can be used in the development of national guidelines on clinical issues related to healthcare-associated infections' (Public Health Agency of Canada (PHAC) 2013).[35]

In France, the creation of a coordination body, the RAISIN (*Réseau d'Alerte, d'Investigation et de Surveillance des Infections Nosocomiales*) sought to reinforce surveillance in 2001 (Stingre and Verdeil 2004: 111). An *Observatoire des risques médicaux*, attached to the ONIAM, has existed since 2004. One of its responsibilities is to analyze all data pertaining to HAIs, including information about their compensation and consequences (*Loi du 13 août 2004*, article 15; CSP, article L 1142-29). The *Institut de veille sanitaire* has also participated in infection surveillance since 1998, but its mission is much broader, as it is charged with surveying all sanitary risks. In addition, France's *Code de la santé publique* requires that all healthcare professionals or establishments that observe or suspect the occurrence of an HAI declare it to the director of the *Agence régionale de santé* (CSP, article L 1413-14). Moreover, when a CRCI concludes that a patient's injury is due to an HAI and causes a partial permanent incapacity of more than 25 per cent, it must inform the aforementioned director as well as the ONIAM (CSP, article L 1142-8).

Voluntary surveillance has been in effect for many years in England (Public Health England n.d.). In the 1990s, the Health Protection Agency commissioned and ran a Nosocomial Infection National Surveillance Scheme (NINSS) based on voluntary and confidential reporting (Haustein *et al.* 2011: 472). After MRSA became a major issue in England, the NINSS was not developed further. In 2001, focus shifted to mandatory reporting of *Staphylococcus* bloodstream infections by all acute hospital trusts (Haustein *et al.* 2011: 472). Mandatory surveillance was later extended to glycopeptide-resistant *Enterococcal* bacteraemia in 2003, *C. difficile* in 2004, methicillin-sensitive *Staphylococcus aureus* and *Escherichia coli* (*E. coli*), both in 2011 (Haustein *et al.* 2011: 472; Public Health England n.d.).

HAI-specific reporting can also be required by legislation devoted to public health or communicable diseases. For instance, in Canada, the Manitoban *Public Health Act* requires the reporting of *C. difficile*, MRSA, and VRE infections (*Reporting of Diseases and Conditions Regulation* 2009); *C. difficile* is reportable under the New Brunswick *Public Health Act* (*Reporting and Diseases Regulation* 2009); and MRSA and VRE must be reported under Nova Scotia's *Health Protection Act* (*Reporting of Notifiable Diseases and Conditions Regulations* 2005). Finally, Alberta's *Communicable Disease Regulation* 1985 requires the reporting of HAIs whenever there is an outbreak.

The law frequently mandates surveillance at the institutional level as well. Ontario law requires hospital boards to establish and operate a communicable disease surveillance program (*Hospital Management Regulations*, section 4(1)(e)). It obliges physicians and registered nurses to report suspected infections with an agent of a communicable disease to the medical officer of the health unit in which their services are provided (*Health Protection and Promotion Act* 1990, section 26; *Hospital Management Regulations*, section 14(2)). The same obligation applies to hospital administrators and superintendents of institutions if an entry in the records states that a patient is infected or may be infected with an agent of a communicable disease (*Health Protection and Promotion Act* 1990, section 27). In the Northwest Territories, statutory provisions also oblige medical or professional staff members of healthcare establishments to report to the hospital

35 The CNISP faced significant budget cuts in 2013 (AMMI/CHICA 2012).

management boards and to the Chief Public Health Officer the existence or suspected existence of any condition indicating an HAI (*Hospital Insurance and Health and Social Services Administration Act* 1988, section 61(1)(2)(3)). Finally, risk management committees within Quebec healthcare institutions are in charge of establishing monitoring systems that include local registers of medical incidents and accidents. The purpose of these registers is to analyse the causes of incidents and accidents, including HAIs, and recommend prevention and control measures to the institution's board of directors (*An Act Respecting Health Services and Social Services* (ARHSSS), section 183.2(3)).[36] Drawing on these local registers, the Minister of Health must maintain a national register of healthcare-related incidents and accidents (ARHSSS, section 431).

Greater transparency and communication with patients are notable trends in recent patient safety initiatives, including those aimed at preventing HAIs. The demand for transparency has come mainly from the media, patient advocacy groups, legislative bodies and accreditation organizations (Haustein *et al*. 2011: 471). Legal requirements exist in some jurisdictions for the disclosure of adverse events to patients (for instance, ARHSSS, sections 8 and 235.1; CSP, article L 1142-4), but the final section focuses on the more controversial topic of mandatory public reporting of HAI rates in hospitals. The examples below demonstrate the diversity in approaches to reporting, disclosure, and benchmarking around the world.

11.4.2 Public disclosure of hospital infection rates

The United States provides one of the best examples of the use of legal normativity to impose public reporting of information regarding HAIs. A major Consumers Union campaign launched in 2003 encouraged legislative developments in HAI reporting by urging states to adopt laws requiring public disclosure of hospital-specific infection rates (Stricof *et al*. 2013: 294). Indeed, legislative provisions on HAI reporting have been largely driven by consumer demand for transparency and accountability, as well as by public outrage over the spread of HAIs in the United States (CDC and ASTHO 2011: 4, 7 and 14). The majority of states with HAI reporting statutes require that this reporting be public (Reagan and Hacker 2012: 75).[37] Moreover, the majority of these laws require that facilities be identified in public reports (Reagan and Hacker 2012: 75 and 77).

Most states with public reporting legislation use the CDC's National Healthcare Safety Network (NHSN), a web-based data collection and surveillance system (CDC and ASTHO 2011: 15–16; e.g. *Health and Safety Code* (California), § 1288.55). From data reported by participating healthcare facilities, the NHSN produces 'Healthcare-associated Infections Summary Data Reports' to provide the public with national and state-specific information on efforts to prevent HAIs (CDC 2013).[38] Healthcare facilities use NHSN in all 50 states, as well as Washington, DC and Puerto Rico. As of December 2012, 30 states and Washington, DC required or planned to require the use of NHSN for state-specific reporting (Malpiedi *et al*. 2013: 3).

36 Definitions of incident and accident can be found at sections 8 and 183.2. Healthcare institutions in Quebec must also report to the Minister of Health and Social Services on MRSA and VRE when there are indications that they have infected a serious burn victim (*Regulation respecting the information that institutions must provide to the Minister of Health and Social Services*, schedule V).

37 Thirty-three states have such provisions (Reagan and Hacker 2012: 77). Of the states with HAI legislation, only Utah has not included public reporting provisions in its legislation.

38 Prior to 2004, HAI rates were recorded through the National Nosocomial Infection Surveillance System established in 1970. It was combined with other national surveillance systems into the Internet-based NHSN in 2004 (Tokars *et al*. 2004: 1347)

Mandatory public reporting is sometimes limited to specific infections or procedures (CDC and ASTHO 2011: 16). For instance, the HAIs that must be reported to California's department of health are central-line-associated bloodstream infections, MRSA, VRE, *C. difficile*, and surgical site infections (Health and Safety Code, § 1288.55). In Missouri, disclosure concerns incidence rates for certain types of surgical site infections, ventilator-associated pneumonia, central-line-related bloodstream infections and other infections that may be established by the state's department of health (*Missouri Nosocomial Infection Contract Act of 2004* (NICA), § 192.667(12)). In Utah, reporting to the state health agency is mandated for certain HAI outcomes and only reporting process measures, such as compliance with infection control procedures, are the object of a public report (CDC and ASTHO 2011: 16). The format of the reports varies, with some states requiring that the healthcare facility provide summary reports, while others entrust this task to the state itself (CDC and ASTHO 2011: 20). Some reports are provided to the state legislature while others are placed online for direct public access (CDC and ASTHO 2011: 20). Likewise, the frequency of reporting is highly variable (CDC and ASTHO 2011: 20). Finally, some legislation requires that public reporting compare infection rates for each healthcare facility in the state (Reagan and Hacker 2012: 79), while others demand that the HAI rates be risk-adjusted (e.g. NICA, § 192.665(7)).

The legislation of the state of New York is often cited as an example. Its *Public Health Law* 2013 has required mandatory reporting of HAIs since 2005, and specifically demands that each general hospital maintain a program capable of identifying and tracking HAIs for the purpose of public reporting and quality improvement (*Public Health Law*, § 2819). The data must be reported to the New York State Department of Health, which makes this information available on its website (*Public Health Law*, § 2819(3)). After a one-year pilot project in 2007, reports were made available on a yearly basis including HAI rates at each hospital (New York State Department of Health 2013).

After receiving authorization to pay hospitals a higher annual update to their payment rates upon successfully reporting designated quality measures, the Centers for Medicare and Medicaid Services instated the 'Hospital Inpatient Quality Reporting Program.'[39] Reported information from over 4,000 Medicare-certified hospitals is collected using NHSN and made publicly available on the Medicare Hospital Compare website, including a specific section concerning HAIs (CDC and ASTHO 2011: 8; Hospital Compare). Financial incentives are in place to encourage hospitals to participate in this reporting program (CMS 2013a, 2013b).

Finally, in addition to state legislation, the *Patient Protection and Affordable Care Act* 2010 requires that the Center for Quality Improvement and Patient Safety make its research findings available to the public (PPACA, section 3501) and that websites be set up to share 'performance information summarizing data on quality measures' (PPACA, section 3015). The PPACA also mandates public reporting of the measures for hospital-acquired conditions that are currently used by the CMS when adjusting the amounts of payment to hospitals based on HAI rates (PPACA, section 10303).

At the European level, recommendations issued by the European Union in 2009 insist on empowering and informing citizens. They recommend the establishment or strengthening of blame-free reporting and learning systems on adverse events in general (Council Recommendation 2009: 2–3). One of its specific recommendations was that institutions should be 'making available objective and understandable information about the risk of healthcare associated infections, the measure implemented by the healthcare institution to prevent them and on how patients can help to prevent those infections' (Council Recommendation 2009, section 8(e)(i)).

39 This program was originally created in 2003 by s. 501(b) of the *Medicare Prescription Drug, Improvement, and Modernization Act* (CMS 2013b).

Canada's Association of Medical Microbiology and Infectious Disease (AMMI) and Community and Hospital Infection Control Association (CHICA) jointly produced a 2006 position paper in which they advised against using individual hospital-generated reporting of infection rates as a way of comparing or ranking hospitals (AMMI/CHICA 2006). Despite this opposition, some Canadian provinces have also moved in the direction of transparency, although not always in response to statutory interventions. When requested by the Ontario Minister of Health, public hospitals are mandated by statute to disclose information concerning indicators of the quality of healthcare they provide. This information includes diagnoses of HAIs, activities to reduce them, and mortality rates. Moreover, this information must be disclosed through the hospital's website and 'through such other means and to such other persons as the Minister may direct' (*Hospital Management Regulations*, section 22.2). In May 2008, the Ministry of Health and Long-Term Care announced the public reporting of patient safety indicators including rates for *C. difficile,* MRSA, VRE, and central-line-associated primary bloodstream infections (Ontario Ministry of Health and Long-Term Care 2013). Since December 2012, Ontario hospitals have provided reports on a number of HAIs through Health Quality Ontario's patient safety public reporting website (Health Quality Ontario 2013).

In British Columbia, health authorities collect and report information on *C. difficile* and MRSA rates using the Provincial Infection Control Network (PICNet) website. In March 2013, media pressure in New Brunswick led its largest health authority to release the number of *C. difficile* and MRSA infections reported in its ten hospitals during the 21 preceding months (McHardie 2013). Since April 2013, monthly reports for *C. difficile* and MRSA infections have been available on the website for the province's Chief Medical Officer (Office of the Chief Medical Officer of Health (Public Health) – New Brunswick 2014).

Lastly, the Quebec Ministère de la Santé et des Services sociaux produces a quarterly bulletin informing the public about the surveillance of *C. difficile* infections, providing provincial, regional, and hospital incidence rates. Healthcare institutions in Canada are also asked to report their rates of either *C. difficile* or *Staphylococcus aureus* when obtaining accreditation by Accreditation Canada,[40] an 'evaluation process used to assess and improve the quality, efficiency, and effectiveness of health care organizations' (Nicklin 2013: 1) which is mandatory in only a few provinces, such as Quebec and Alberta (Eggertson 2007: 1403; Nicklin 2013: 5). Whether or not these reports are made public is left to the discretion of the participating institutions.

England also has a system for public reporting of HAIs (Haustein *et al.* 2011: 471). Reporting of MRSA bloodstream infection rates has been mandatory since 2001, and publicly available on the Public Health England (formerly the Health Protection Agency) and the Department of Health websites since 2002 (Haustein *et al.* 2011: 472). Public reporting of other types of infections developed thereafter (Haustein *et al.* 2011: 472), and tables for all mandatory reporting infections are available on the Public Health England website.

While the above jurisdictions mostly choose to publicly report rates of infection – and have therefore been preoccupied with the *results* of infectious outbreaks – the French approach has been to focus on process disclosure (Haustein *et al.* 2011: 471 and 473). In 2005, the French Ministry of Health set up the publicly available ICALIN (*Indicateur composite des activités de lutte contre les infections nosocomiales*), with the goal of encouraging healthcare establishments to measure their initiatives and results in the fight against HAIs. This indicator discloses the actions undertaken in the healthcare facility, using a notation system that reveals its performance in preventing HAIs (Ministère des Affaires sociales et de la santé, 2013).

40 Formerly the Canadian Council on Health Services Accreditation.

Some argue, especially in jurisdictions with a private healthcare system, that the ability to compare infection rates across institutions allows informed patient choice (Reagan and Hacker 2012: 79) and that payers want performance data in order to become better purchasers of healthcare services (Wong *et al.* 2005: 210). However, there are worries that data communicated to the public might be flawed, misleading, misinterpreted, or misunderstood (Wong *et al.* 2005: 210; Haustein *et al.* 2011: 475). Methodological issues are particularly troubling and authors emphasize the need to standardize and risk-adjust the data for differences in population or range and type of medical procedure (Haustein *et al.* 2011: 471). For instance, in 1991 the CDC worried that inter-hospital comparisons might be invalid or misleading because rates were not adjusted for patients' intrinsic risk for infection; surveillance techniques were not uniform among hospitals or were used inconsistently; and inaccurate recording and insufficient sample size might affect the validity of the rates (CDC 1991: 610). Even where there is risk-adjustment, the scientific validity of the adjustment method may be questioned. The need for uniform definitions and surveillance methods has also been raised (Haustein *et al.* 2011: 471), as well as worries about the effect of the complex and contentious nature of some HAI diagnostics (Haustein *et al.* 2011: 471).

Other objections to public reporting include cost, variations in surveillance practices among reporting hospitals, under-reporting, the comparability of data from each reporting hospital, and patients' confidentiality (Stricof *et al.* 2013: 294; Wong *et al.* 2005: 210). Some commentators have also noted the paucity of evidence that reporting improves the quality of patient care or their safety or decreases HAI incidence (AMMI/CHICA 2006; Haustein *et al.* 2011: 471 and 475) or that patient decision-making is improved by public reporting of HAI rates at individual institutions (AMMI/CHICA 2006; Haustein *et al.* 2011: 475; Daneman *et al.* 2012). However, Haustein *et al.* observed an impressive and unexpected decrease in the reported incidence of MRSA bloodstream infections in England after public reporting became compulsory there (2011: 477). Moreover, Daneman *et al.* found that public reporting of *C. difficile* rates in Ontario hospitals, which began in 2008, was associated with a substantial reduction in these infections (2012). Haustein *et al.* remark that reporting acts as an 'external reinforcement' and is indeed associated with changes in organizational culture and increase in prevention activities (Haustein *et al.* 2011: 471 and 476). Similarly, Daneman *et al.* hypothesize that public reporting in Ontario 'elevated *C. difficile* to greater prominence on hospital quality improvement agendas, and motivated hospitals to adhere more closely to best practices in *C. difficile* prevention' (2012).

11.5 Conclusion

The law has been called to play an active role in the fight against HAIs, particularly in the last two decades. It has done so through a multiplicity of statutory interventions that tackle issues such as prevention, control, management, surveillance, and reporting. Publicly mandated inquiries and audits have also played a part in bringing about change. Moreover, class action lawsuits have risen in response to infectious outbreaks and consequent deaths. Yet individual litigation in Canada, the jurisdiction studied in this respect, presents serious challenges to patients due largely to the difficulties in identifying precise sources of infections and connecting them to acts of negligence. Because of the limited success of individual litigation, and the fact that most class action lawsuits do not make it to final judgment, it is doubtful whether the power of judicially created legal normativity can assist in HAI prevention and response. Nevertheless, France offers an interesting example of a jurisdiction where legislators, courts, and administrative agencies have collaborated to achieve these goals, partly through non-traditional means such as legislatively mandated conciliation systems and a state compensation fund. Finally, the public reporting of infection

rates among healthcare institutions is an ongoing contemporary issue which, while growing in importance in the United States and elsewhere, is still controversial in some countries.

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12

Liability and the legal duty to inform in research

Ma'n H. Zawati

12.1 Introduction

Early medicine was characterized by paternalistic medical practices. The Ancient Greek physician Hippocrates, for example, opined that '[physicians] will apply dietetic measures for the benefit of the sick according to [their] ability and judgment. [They] will keep them from harm and justice' (*Hippocratic Oath* 1943). In the modern era, medical paternalism continued to be legitimized through a combination of medical beneficence and a 'pledge [from physicians] to do their best to protect patients from harm' (Chin 2002: 152; Gillon 1985: 1971; Weiss 1985: 184–5; Husak 1981: 27). Contemporary authors have defined paternalism as an 'interference with a person's freedom of action or freedom of information, or the deliberate dissemination of misinformation, where the alleged justification of interfering or misinforming is that it is for the good of the person who is interfered with or misinformed' (Buchanan 1978: 372; McCoy 2008; Rich 2006). Consider, for example, the 1847 Code of Ethics of the American Medical Association (AMA), which reads:

> The *obedience of a patient* to the prescriptions of his physician should be prompt and implicit. He should *never permit his own crude opinions* as to their fitness, to influence his attention to them. A failure in one particular may render an otherwise judicious treatment dangerous, and even fatal.
>
> *(Chin 2002: 152, our emphasis)*

Similarly, in 1903, the AMA's Principles of Medical Ethics explained that '[o]rdinarily, the physician should not be forward to make gloomy prognostications, but should not fail, on proper occasions to give timely notice of dangerous manifestations to the friends of the patient; and even to the patient, *if absolutely necessary* …' (section 5, our emphasis).

In the second half of the twentieth century, the rise of Western individualism (Childress 1982: 66) coupled with the mounting influence of the civil rights movement (Philips-Nootens *et al.* 2007: 139) led to a decline in paternalistic medical practices. Today, the principle of autonomy has become the main ethos of healthcare provision. In medicine, the right (of a patient) to make an informed choice about his or her medical care, without undue interference from others, characterizes this principle (Laurie 2002: 186–7). Physicians are encouraged to consider whether 'withholding … information [would] result in less harm on balance than divulging it' (Buchanan 1978: 377–8).

Patients have thus become central contributors to the therapeutic decision-making process. Respect for patient autonomy has generated a new duty for physicians – that of adequately informing their patients prior to and during the delivery of medical care (Dworkin 2002, 2003: 235; McCullough and Wear 1985: 285).

In the research setting, this duty to inform takes a different shape. The lower the therapeutic benefit of a medical intervention, the greater the duty to inform; this is true for cosmetic surgery, organ donation, and non-therapeutic research (Philips-Nootens *et al.* 2007: 204–15; Picard and Robertson 2007: 176–8). In other words, compared to a clinician, a researcher will be held to a higher duty of care when informing a participant. A breach of this duty could potentially give rise to legal liability if it causes bodily, material, or psychological injury.

Legal liability offers claimants compensation for (1) actual losses incurred and (2) loss of potential gain. This principle is true for medical malpractice claims, which have come a long way since the days of Hammurabi and his Code of Laws (circa 1780 BCE), which states: '[i]f a physician make[s] a large incision with the operating knife, and kill[s] [the patient], or open[s] a tumor with the operating knife, and cut[s] out the eye, his hands shall be cut off' (article 218). Indeed, the aim of liability suits is not to punish defendants (although punitive damages are sometimes accorded by the courts), but rather to promote a culture of prevention (Baudouin and Deslauriers 2007a: 7).

But why is the issue of liability pertinent to the duty to inform in the context of medical research? The answer relates to a critical but largely neglected outcome of liability: education. Although much ink has been spilled in the past on the physician's duty to inform in the clinical setting (McGivern and Ivolgina 2013), much less time has been devoted to the ever-changing field of medical research. Consider, for example, the issue of population biobanks, which study data and samples collected on a large population scale over long periods of time (Knoppers *et al.* 2012). Due to the very nature of these biobanks, participants are informed that the aim of the research study is to establish a resource for future research in health and genomics (following ethics approval) (CARTaGENE 2012). Given that such biorepositories are built for future, unspecified research by as-yet unnamed researchers, full disclosure in such cases can be difficult to achieve. What is the scope of the duty to inform and what are the consequences of its breach? Is the duty to inform monolithic, or can it change in conformity with different jurisdictions? These are just a few examples of the panoply of questions surrounding medical research, made even more complicated by their increasingly longitudinal and international nature (Knoppers and Zawati 2011: 1181), in which researchers rely less on constant intervention and more on cutting-edge technologies that generate vast amounts of often uninterpretable data (Levy *et al.* 2007: 254). Whole-genome sequencing is but one example of such new technologies, where the information produced could reveal serious health risks for the research participant requiring clinical care. This puts researchers in a difficult position: that of having to make decisions in situations where their obligations are not necessarily well defined.

This chapter will focus on the duty to inform in the context of medical research, and will highlight the risks of liability that researchers face as a consequence of the increasingly blurred lines between research and clinical care. Section 12.2 of this chapter will discuss the duty to inform as enunciated in international normative documents that frame medical research. Although the duty to inform is often linked with the notion of consent (see Chapter 3), it should be noted that these two concepts are not synonymous, and should be considered as interrelated but ultimately separate. While consent is seen to crystallize the duty to inform, the latter encompasses a number of additional elements. These elements will be presented through a review of regional and national laws and regulations.

In order to provide a concrete illustration of the principles examined in section 12.2, section 12.3 will examine how Canadian case law has dealt with the duty to inform in the context of research. Finally, section 12.4 will address the increasingly blurred lines between the clinical and research settings through a succinct overview of recent developments in genomic research. More precisely, this section will discuss emerging issues of liability that researchers face in the fulfillment of their duty to inform.

12.2 The duty to inform in normative documents

12.2.1 International instruments: the consent process and beyond

A comparative review of international norms reveals that the duty to inform has been consistently referenced in the context of research (see Table 12.1). For example, the *Nuremberg Code* of 1949 asserts in its first article that 'the duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment' (*Trials of War Criminals before the Nuremberg Military Tribunals under Control Council Law No. 10* 1949, article 1 (*Nuremberg*)). The article also affirms that the duty to inform is a 'personal duty and responsibility, which may not be delegated to another with impunity' (*Nuremberg*, article 1). In this example, a link is forged between the duty to inform and its most common crystallization, participant consent. Similarly, the 2013 version of the *Declaration of Helsinki* stipulates that:

> Each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, post-study provisions and any other relevant aspects of the study.
>
> *(article 26)*

However, in this case, consent does not entirely confine the duty to inform, but rather also applies to later phases of research projects. Indeed, article 26 of the *Declaration of Helsinki* requires that research participants 'be given the option of being informed about the general outcome and results of the study.' The use of the keywords 'general' and 'outcome' foresees the application of the duty to inform even at the very end of the research project.

Likewise, the Council for International Organizations of Medical Sciences' (CIOMS) *International Ethical Guidelines for Biomedical Research Involving Human Subjects* adopts a similar stance with regard to general results, but adds an additional duty to inform participants 'of any finding that relates to their particular health status' that could manifest at any time during the research project (2002: guideline 5(7)). The United Nations Educational, Scientific and Cultural Organization's (UNESCO) *International Declaration on Human Genetic Data* also encapsulates this duty to inform, and provides for the right of a participant to decide whether or not he or she is informed of research results (2003: article 10); this stance has been held by UNESCO since the publication of its 1997 *Universal Declaration on the Human Genome and Human Rights* (article 5(c)).

12.2.2 Regional normative instruments: from the duty to inform to a duty of care

In the context of research, regional normative instruments are relatively similar to international documents in their treatment of the duty to inform (see Table 12.2). The seminal *Convention on Human Rights and Biomedicine* (*Oviedo Convention*) of the Council of Europe states

Table 12.1 Selected international norms

Nuremberg Code *Trials of War Criminals before the Nuremberg Military Tribunals under Control Council Law No. 10* (1949).	**Article 1** The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved, as to enable him to make an understanding and enlightened decision. This latter element requires that, before the acceptance of an affirmative decision by the experimental subject, there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards reasonably to be expected; and the effects upon his health or person, which may possibly come from his participation in the experiment. The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.
Declaration of Helsinki World Medical Association (WMA) (2013) *Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects.*	**Article 26** In medical research involving human subjects capable of giving informed consent, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, post-study provisions and any other relevant aspects of the study. The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate at any time without reprisal. Special attention should be given to the specific information needs of individual potential subjects as well as to the methods used to deliver the information. After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject's freely-given informed consent, preferably in writing. If the consent cannot be expressed in writing, the non-written consent must be formally documented and witnessed. All medical research subjects should be given the option of being informed about the general outcome and results of the study.
Declaration on Human Genetic Data United Nations Educational, Scientific and Cultural Organization (UNESCO) (2003) *International Declaration on Human Genetic Data*.	**Article 8** (a) Prior, free, informed and express consent, without inducement by financial or other personal gain, should be obtained for the collection of human genetic data, human proteomic data or biological samples, whether through invasive or non-invasive procedures, and for their subsequent processing, use and storage, whether carried out by public or private institutions. Limitations on this principle of consent should only be prescribed for compelling reasons by domestic law consistent with the international law of human rights. […] **Article 10** When human genetic data, human proteomic data or biological samples are collected for medical and scientific research purposes, the information provided at the time of consent should indicate that the person concerned has the right to decide whether or not to be informed of the results. This does not apply to research on data irretrievably unlinked to identifiable persons or to data that do not lead to individual findings concerning the persons who have participated in such a research. Where appropriate, the right not to be informed should be extended to identified relatives who may be affected by the results. […]

	Article 13 No one should be denied access to his or her own genetic data or proteomic data unless such data are irretrievably unlinked to that person as the identifiable source or unless domestic law limits such access in the interest of public health, public order or national security.[…]
Ethical Guidelines for Biomedical Research Involving Human Subjects Council for International Organizations of Medical Sciences (CIOMS) (2002) *International Ethical Guidelines for Biomedical Research Involving Human Subjects*.	**Guideline 5** Before requesting an individual's consent to participate in research, the investigator must provide the following information, in language or another form of communication that the individual can understand; […] 3. the purpose of the research, the procedures to be carried out by the investigator and the subject, and an explanation of how the research differs from routine medical care; […] 7. that, after the completion of the study, subjects will be informed of the findings of the research in general, and individual subjects will be informed of any finding that relates to their particular health status; 8. that subjects have the right of access to their data on demand, even if these data lack immediate clinical utility (unless the ethical review committee has approved temporary or permanent non-disclosure of data, in which case the subject should be informed of, and given, the reasons for such non-disclosure); 9. any foreseeable risks, pain or discomfort, or inconvenience to the individual (or others) associated with participation in the research, including risks to the health or well-being of a subject's spouse or partner; 10. the direct benefits, if any, expected to result to subjects from participating in the research; 11. the expected benefits of the research to the community or to society at large, or contributions to scientific knowledge; […] 13. any currently available alternative interventions or courses of treatment; […] 16. policy with regard to the use of results of genetic tests and familial genetic information, and the precautions in place to prevent disclosure of the results of a subject's genetic tests to immediate family relatives or to others (e.g. insurance companies or employers) without the consent of the subject; […] 19. whether it is planned that biological specimens collected in the research will be destroyed at its conclusion, and, if not, details about their storage (where, how, for how long, and final disposition) and possible future use, and that subjects have the right to decide about such future use, to refuse storage, and to have the material destroyed (see Guideline 4 Commentary); […] 22. the extent of the investigator's responsibility to provide medical services to the participant; […]
Declaration on the Human Genome United Nations Educational, Scientific and Cultural Organization (UNESCO) (1997), *Universal Declaration on the Human Genome and Human Rights*.	**Article 5** (a) Research, treatment or diagnosis affecting an individual's genome shall be undertaken only after rigorous and prior assessment of the potential risks and benefits pertaining thereto and in accordance with any other requirement of national law. (b) In all cases, the prior, free and informed consent of the person concerned shall be obtained. If the latter is not in a position to consent, consent or authorization shall be obtained in the manner prescribed by law, guided by the person's best interest. (c) The right of each individual to decide whether or not to be informed of the results of genetic examination and the resulting consequences should be respected.

Table 12.2 Selected regional norms

Recommendation on Research on Biological Materials of Human Origin Council of Europe (2006) *Recommendation Rec(2006)4 of the Committee of Ministers to Member States on Research on Biological Materials of Human Origin* (EU).	**Article 14** […] 2. The purpose(s) of a collection should be specified. The principles of transparency and accountability should govern its management, including access to and use and transfer of its biological materials and disclosure of information. 3. Each sample of biological material in the collection should be appropriately documented, including information on any relevant consent or authorization. […]
Convention on Human Rights and Biomedicine Council of Europe (1997) *Convention on Human Rights and Biomedicine* (EU).	**Article 5** An intervention in the health field may only be carried out after the person concerned has given free and informed consent to it. This person shall beforehand be given appropriate information as to the purposes and nature of the intervention as well as on its consequences and risks. The person concerned may freely withdraw consent at any time. **Article 10** […] 2. Everyone is entitled to know any information collected about his or her health. However, the wishes of individuals not to be so informed shall be observed. 3. In exceptional cases, restrictions may be placed by law on the exercise of the rights contained in paragraph 2 in the interests of the patient.
Clinical Trials Directive Council of Europe (2001) Directive 2001/20/EC, *of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use* (EU).	**Article 3** 2. A clinical trial may be undertaken only if, in particular: […] (b) the trial subject or, when the person is not able to give informed consent, his legal representative has had the opportunity, in a prior interview with the investigator or a member of the investigating team, to understand the objectives, risks and inconveniences of the trial, and the conditions under which it is to be conducted and has also been informed of his right to withdraw from the trial at any time; […] (d) the trial subject or, when the person is not able to give informed consent, his legal representative has given his written consent after being informed of the nature, significance, implications and risks of the clinical trial; if the individual is unable to write, oral consent in the presence of at least one witness may be given in exceptional cases, as provided for in national legislation; (e) the subject may without any resulting detriment withdraw from the clinical trial at any time by revoking his informed consent; […]

Additional Protocol Council of Europe (2005) *Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research* (EU).	**Article 13** 1. The persons being asked to participate in a research project shall be given adequate information in a comprehensible form. This information shall be documented. 2. The information shall cover the purpose, the overall plan and the possible risks and benefits of the research project, and include the opinion of the ethics committee. Before being asked to consent to participate in a research project, the persons concerned shall be specifically informed, according to the nature and purpose of the research: (i) of the nature, extent and duration of the procedures involved, in particular, details of any burden imposed by the research project; (ii) of available preventive, diagnostic and therapeutic procedures; (iii) of the arrangements for responding to adverse events or the concerns of research participants; (iv) of arrangements to ensure respect for private life and ensure the confidentiality of personal data; (v) of arrangements for access to information relevant to the participant arising from the research and to its overall results; (vi) of the arrangements for fair compensation in the case of damage; (vii) of any foreseen potential further uses, including commercial uses, of the research results, data or biological materials; (viii) of the source of funding of the research project. 3. In addition, the persons being asked to participate in a research project shall be informed of the rights and safeguards prescribed by law for their protection, and specifically of their right to refuse consent or to withdraw consent at any time without being subject to any form of discrimination, in particular regarding the right to medical care. **Article 26** 1. Research participants shall be entitled to know any information collected on their health in conformity with the provisions of Article 10 of the Convention. 2. Other personal information collected for a research project will be accessible to them in conformity with the law on the protection of individuals with regard to processing of personal data. **Article 27** If research gives rise to information of relevance to the current or future health or quality of life of research participants, this information must be offered to them. That shall be done within a framework of health care or counseling. In communication of such information, due care must be taken in order to protect confidentiality and to respect any wish of a participant not to receive such information. […]

that participants in a research project 'shall beforehand be given appropriate information as to the purposes and nature of the intervention as well as on its consequences and risks' (1997: article 5). This principle is reiterated in other European norms, such as *Directive 2001/20/EC* (2001: article 3) and the *Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin* (2006: article 14).

Article 10 of the *Oviedo Convention* recognizes a 'right to information,' such that participants '[are] entitled to know information collected about [their] health' unless they exercise their right not to know. However, this right is not absolute, and may be restricted in the interests of the patient (*Oviedo Convention*, article 10(3)). These restrictions may be invoked, for example, where clinically significant information is discovered about a child participant that could be actionable during childhood (Hens *et al.* 2013: 6).

The *Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research* (*Additional Protocol*) emphasizes the importance of providing participants with 'adequate information in a comprehensible form' (2005: article 13(1)), and confirms that patients are entitled to know 'any information collected on their health in conformity with the provisions of Article 10 of the Convention' (article 26(1)). Furthermore, the *Additional Protocol* creates a 'duty of care,' such that '[i]f research gives rise to information of relevance to the current or future health or quality of life of research participants, this information must be offered to them' (article 27). The *Additional Protocol* specifies that this information must be disseminated through a framework of healthcare or counseling, and a researcher is obliged to protect both the confidentiality of the information and the participants' wishes (article 27).

Thus, according to the regional documents, as reviewed above, the duty to inform not only includes the provision of adequate information to participants during the consent process, but also enshrines a 'right to information' that requires researchers to disclose specific findings to participants throughout a research project.

12.2.3 National perspectives: liability and the duty to inform

Legal liability is a jurisdiction-specific branch of law, whose more comprehensive parameters can only be gleaned from a review of national legal instruments. While it is possible to undertake the daunting task of reviewing and analyzing hundreds of laws and regulations from numerous countries around the world, this section will only highlight the legal duty to inform and legal liability in a few civil and common law countries. The common law review will focus on the United Kingdom and Australia, while the civil law review will include France and the province of Quebec in Canada.

12.2.3.1 Common law jurisdictions: the tort of negligence

In the United Kingdom, the duty to inform/duty to disclose is primarily discussed in the context of clinical care, and is usually subsumed within the broader duty of care. In order to determine the type of information that should be disclosed in this context, English courts follow the 'professional standard' test as articulated in the seminal *Bolam* v. *Friern Hospital Management Committee* [1957] 2 All ER (*Bolam*) case. In *Bolam*, the court established:

> A doctor is not guilty of negligence if he has acted in accordance with a practice accepted as proper by a responsible body of medical men skilled in that particular art … Putting it

> the other way round, a doctor is not negligent, if he is acting in accordance with such a practice, merely because there is a body of opinion that takes a contrary view.
>
> *(p. 122)*

This standard refers to 'what professionals would generally view as appropriate disclosure, as opposed to a patient-oriented standard based upon either what the particular patient (a subjective standard) would wish to know or what patients in general wish to be made aware of (an objective standard)' (Price 2002: 150). The English courts reaffirmed the *Bolam* principle in *Sidaway* v. *Bethlem Royal Hospital Governors* [1985] 1 All ER 643 (*Sidaway*). However, in that case, a justice for the majority noted an exception to this test where there is a 'substantial risk of grave adverse consequences' (*Sidaway*, p. 663). In such cases, a physician could be found negligent if he or she fails to disclose patient information even if the professional standard is non-disclosure. Disclosure requirements in the context of research are considered greater than those required during treatment 'by virtue of the additional contribution to the public interest in particular' (Price 2002: 261) – and thus create an even higher duty of 'subjective' disclosure. This is the case for both therapeutic and non-therapeutic research (Price 2002: 261, 263–4).

In Australia, a clear distinction is made between the duty to inform and the duty to obtain consent for a given medical procedure (Chalmers 1998: 69). Despite the existence of legislation to this effect, 'the law has developed judicially' on this topic (Chalmers 1998: 69). In contrast with the United Kingdom, Australian courts have not always applied the *Bolam* principle:

> In Australia, it has been accepted that the standard of care to be observed by a person with some special skill or competence is that of the ordinary skilled person exercising and professing to have that special skill. But, that standard is not determined solely or even primarily by reference to the practice followed or supported by a reasonable body of opinion in the relevant profession or trade. Even in the sphere of diagnosis and treatment, the heartland of the skilled medical practitioner, the *Bolam* principle has not always been applied.
>
> *(*Rogers v. Whitaker *[1992] 109 ALR 625 (*Rogers *1992), 631)*

Instead, the standard of reasonable care is not 'owned' by professional bodies:

> Further, and more importantly, particularly in the field of non-disclosure of risk and the provision of advice and information, the Bolam principle has been discarded and, instead, the courts have adopted the principle that, while evidence of acceptable medical practice is a useful guide for the courts, it is for the courts to adjudicate on what is the appropriate standard of care after giving weight to 'the paramount consideration that a person is entitled to make his own decisions about his life'.
>
> *(*Rogers *1992: 631)*

According to Australia's *National Health Medical Research Council Act*, the National Health and Medical Research Council (NHMRC) regulates research studies (1992: article 7; Chalmers 1998: 111). Section 2.2.4 of the NHMRC's *National Statement on Ethical Conduct in Human Research* (*National Statement*) states, in reference to the duty to inform:

> The process of communicating information to participants … should not be merely a matter of satisfying a formal requirement. The aim is mutual understanding between

> researchers and participants. This aim requires an opportunity for participants to ask questions and to discuss the information and their decision with others if they wish.
>
> *(2007)*

Article 2.2.6 of the *National Statement* enumerates those elements that should be disclosed to research participants, including (but not limited to) alternatives to participation and the likelihood or form of the dissemination of research results (NHMRC 2007).

In view of the foregoing, how can a researcher be sued for failing to meet the duty to inform? In such cases, negligence is the most probable cause of action in both the Australian and English contexts. In order to recover under the tort of negligence, a claimant must satisfy the four following elements: (1) the existence of a duty of care; (2) a breach of that duty; (3) harm; and (4) causation. This text will focus on the first two elements. In both Australia and the United Kingdom, the 1932 case of *Donoghue (or McAlister)* v. *Stevenson* [1932] All ER Rep 1 provides guidance on determining whether an individual owes a duty of care:

> Who, then, in law is my neighbour? The answer seems to be – persons who are so closely and directly affected by my act that I ought reasonably to have them in contemplation as being so affected when I am directing my mind to the acts or omissions which are called in question.
>
> *(p. 11)*

Plaintiffs must therefore demonstrate that the researcher owed a duty of care, and that he or she breached this duty by failing to adequately satisfy his or her duty to inform. As previously mentioned, the English standard of care is that of the 'medical [professional] skilled in the art' (*Bolam*, p. 122). In Australia, the *Civil Liability Act* 2002 specifies that:

> A person practising a profession ('a professional') does not incur a liability in negligence arising from the provision of a professional service if it is established that the professional acted in a manner that (at the time the service was provided) was widely accepted in Australia by peer professional opinion as competent professional practice.
>
> *(section 50(1))*

That being said, the court in *Rogers* v. *Whitaker* held that professional opinion is not the determining factor in the establishment of civil liability (p. 631). In point of fact, the *Civil Liability Act* states: '[h]owever, peer professional opinion cannot be relied on for the purposes of this section if the court considers that the opinion is irrational' (section 50(2)).

12.2.3.2 Civil law jurisdictions: *la responsabilité civile*

In civil law jurisdictions, the duty to inform has been advanced through civil codes. For example, in the Canadian province of Québec, the duty to inform has been incorporated in both the *Civil Code of Québec* 1991 (CCQ) and under professional norms, such as the *Code of Ethics of Physicians* 2008. The latter enshrines the legal duty to provide the patient/participant with explanations that are pertinent to their 'understanding of the nature, purpose and possible consequences of the examination, investigation, treatment or research which [the physician] plans to carry out' (*Code of Ethics of Physicians*, article 29). The physician–patient relationship, which is classified as a contractual relationship, is bound by the *Civil Code of Québec*'s chapter on contract for services, which specifies that a contractor '… is bound to provide the client, as far as circumstances

permit, with any useful information concerning the nature of the task which he undertakes to perform' (article 2102). Similar to the UK, the duty to inform in research is as great as, if not greater than, in the clinical setting (*Weiss* v. *Solomon* [1989] RJQ 731 (*Weiss*)). In Quebec, a physician is expected to disclose the patient's diagnosis (*Laferrière* v. *Lawson* [1991] 1 SCR 541); the nature and objectives of the intervention or treatment (Baudouin and Deslauriers 2007b: 49); risks (*Chouinard* v. *Landry* [1987] RJQ 1954); and the existence of any other possible therapeutic options (*Reibl* v. *Hughes* [1980] 2 SCR 880 [*Reibl*]; *Schierz* v. *Dodds* [1986] RJQ 2623, in Philips-Nootens *et al*. 2007: 145). Additionally, health professionals must be able and available to answer patient questions (Philips-Nootens *et al*. 2007: 145; *Hopp* v. *Lepp* [1980] 2 SCR 192 (*Hopp*)). These duties to inform are amplified in the context of research, and will be discussed in detail in section 12.3 of this chapter.

In France, the duty to inform is enshrined in the *Code de la santé publique* (CSP) 2013. This law states that every person has the right to be informed about his or her state of health (article L1111-2), which would also include information pertaining to the proposed treatment, investigation, the potential benefits and the foreseeable risks.

The *Code de la santé publique* also discusses the duty to inform in the context of research. Similar to the requirements in the clinical setting, 'investigators' are asked to inform their participants about the objectives, methodology, and length of the research project as well as medical alternatives, the expected benefits, and the foreseeable risks (CSP, article L1122-1). Additionally, the same article provides that participants have the right to be informed of general research results at the end of research projects, according to the modalities outlined during the informed consent process. The new *Loi Jardé* 2012 (which has been adopted but is not yet in force) specifically addresses the return of research results. These new provisions mandate that researchers provide participants with feedback during baseline assessments (CSP, article L1121-1), as well as feedback concerning general research results (CSP, article L1121-1). Moreover, participants have a right to information concerning their health during and at the conclusion of the research project; this information must be presented as a written document, and must be given to the individual who has consented to receive the information (e.g. guardians/parents) (CSP, article L-1122-1).

Similar to common law jurisdictions, a breach of the duty to inform in civil law could result in the liability of researchers for damages. Actions in such cases will not necessarily be those of 'negligence,' but of medical malpractice under the general rules of civil liability or *responsabilité civile*. These actions will require the presence of: (1) fault; (2) injury; and (3) a causal link. Plaintiffs must prove the existence of each of these components: '[e]very person has a duty to honour his contractual undertakings. Where he fails in this duty, he is liable for any bodily, moral or material injury he causes to the other contracting party and is liable to reparation for the injury' (CCQ, article 1458). This same standard applies in France, where article 1382 of the French *Code civil* states that '[a]ny act whatever of man [*sic*], which causes damage to another, obliges the one by whose fault it occurred, to compensate it.' Article 1383 further explains that a person is 'liable for the damage he causes not only by his intentional act, but also by his negligent conduct or by his imprudence' (*Code civil*).

The duty to inform in France also finds a jurisprudential basis in the *Arrêt Teyssier* 1942 DC 63, Gaz. Pal. 1 decision, in which the Cour de Cassation held that the duty to inform is a necessary corollary of the right to respect for persons, and violating this duty would amount to a serious violation of patient rights (p. 63).

It should also be noted that 'fault' is differentiated from 'error' in the context of the duty to inform. An error becomes a fault where a reasonable person in the same circumstances would have acted or omitted to act in a different manner (Philips-Nootens *et al*. 2007: 47–9).

For example, a researcher who fails to adequately inform his research participant about the risks of a particular project could be found liable if: (1) this omission has caused damage; and (2) if a reasonable researcher in the same circumstances would have disclosed these risks. The reasonable researcher should be vested with comparable experience and, more importantly, comparable expertise. Professional guidelines as well as ethical normative documents play a role in determining the standard of care. Expert witnesses may also refer to these documents in support of their testimony.

12.3 Legal duty to inform in research: a Canadian common law and civil law perspective

In the Canadian common law context, the therapeutic duty to inform is the provision of sufficient information (i.e. material risks, as well as special or unusual risks) (*Reibl*, para. 4; Picard and Robertson 2007: 134–49) to enable patients to make the best decision possible. In *Reibl* v. *Hughes*, a landmark common law decision, Judge Laskin of the Supreme Court of Canada wrote: '[w]hat the doctor knows or should know that the particular patient deems relevant to a decision whether to undergo prescribed treatment goes equally to his duty of disclosure as do the material risks recognized as a matter of required medical knowledge' (para. 16). In *Hopp* v. *Lepp*, the Supreme Court specified that the scope of the duty to inform includes answering 'any specific questions posed by the patient as to the risks involved … [and] … without being questioned, [disclosing] to [their patients] the nature of the proposed operation, its gravity, any material risks and any special or unusual risks attendant upon the performance of the operation' (para. 29). This articulation has since become the minimum standard with which physicians are expected to comply in the common law provinces. However, in Quebec, civil law courts have tended to reject the 'reasonable patient' threshold as proposed in *Reibl* v. *Hughes* and have instead upheld a test that focuses on what a reasonable physician would disclose in the circumstances (*Pelletier* v. *Roberge* [1991] 41 QAC 161, para. 51; *Chouinard* v. *Landry* 1987; Philips-Nootens *et al*. 2007: 149–55).

As previously mentioned, the amount of information needed to satisfy the requirements of the duty to inform in the clinical setting is quite minimal compared to the requirements in cases of non-therapeutic research. This differential duty stems from two Canadian decisions: *Halushka* v. *University of Saskatchewan* [1965] 53 DLR (2d) 436 (*Halushka*) and, from Quebec civil law, the case of *Weiss* v. *Solomon*.

In the 1965 case of *Halushka*, a student was paid fifty dollars to be part of an experiment at the University Hospital, which involved the administration of a new anesthetic and the insertion of a catheter. The participant was informed that the procedure would last a couple of hours, and that this was a 'perfectly safe test … conducted many times before' (*Halushka*, para. 3) and that 'there was nothing to worry about' (para. 2). During the procedure, the participant suffered a complete cardiac arrest and remained unconscious for four days. As a result, the new anesthetic was withdrawn from clinical use. The participant subsequently sued for damages. The Saskatchewan Court of Appeal held that the disclosure of information in this case was inappropriate, incorrect, and ultimately constituted non-disclosure. The court contrasted the duty to inform in research with the duty to inform in clinical care by stating that 'the duty imposed upon those engaged in medical research … to those who offer themselves as subjects for experimentation, as the respondent did here, is at least as great as, if not greater than, the duty owed by the ordinary physician or surgeon to his patient' (*Halushka*, para. 29).

The Court then justified its elevation of the duty to inform by explaining that:

> There can be no exceptions to the ordinary requirements of disclosure in the case of research as there may well be in ordinary medical practice. *The researcher does not have to balance the probable effect of lack of treatment against the risk involved in the treatment itself.* The example of risks being properly hidden from a patient when it is important that he should not worry can have no application in the field of research. *The subject of medical experimentation is entitled to a full and frank disclosure of all the facts, probabilities and opinions* which a reasonable man might be expected to consider before giving his consent.
>
> *(*Halushka*, para. 29, our emphasis)*

Taking these arguments together, the Court articulated a standard whereby the fewer the therapeutic benefits derived from a medical procedure, the greater the duty to inform.

In the 1988 case of *Weiss* v. *Solomon*, the Superior Court of Quebec restated the elevation of the duty to disclose in research. In this case, a patient who underwent cataract surgery was invited to participate in a research project (distinct from his surgery) involving the administration of ophthalmological drops and a fluorescein angiography. Following the injection of the fluorescein, the patient suffered a ventricular fibrillation and died (*Weiss*, para. 4). It was determined, among other things, that the patient's risk of collapse or death due to his pre-existing heart problem was not sufficiently disclosed. The Court referred to both the *Halushka* case and the *Civil Code of Lower Canada* (CCLC) 1866, the precursor to the *Civil Code of Québec* (which is currently in force). The Court relied upon articles 19 and 20 of the CCLC, which enshrined the inviolability of the person and the issue of majority consent to medical experimentation, respectively. The Court then reiterated the importance of full disclosure in the context of non-therapeutic research (*Weiss*, para. 89). It also characterized full disclosure as going beyond the disclosure requirements of clinical settings.

Together, *Halushka* and *Weiss* represent the state of Canadian common and civil law in matters relating to the disclosure of information in research; however, their respective standards are subject to challenge in an era when non-therapeutic research is becoming increasingly international, collaborative, longitudinal, and less individually-oriented. Can we hold a researcher undertaking observational studies to the same duty to inform? For now, the answer is yes. In fact, the standard required by these two decisions contains two important limitations: (1) research typology; and (2) the scope of the duty to inform. First, at a time when research methodologies are becoming increasingly diversified and research is producing more and more uninterpretable data, a one-size-fits-all legal approach to research typology becomes problematic. For example, the research featured in *Halushka* and *Weiss* is very different from research concerning population biobanks, where no drugs are administered, no devices are inserted, and no toxicity is assessed. Second, although *Halushka* and *Weiss* provide guidance on the duty to inform in the context of consent, they fail to address the issue of return of results in the context of research. Does the return of findings fall within the scope of the duty to inform? Given the increasingly blurred lines between research and clinical care, this issue has become all the more important.

12.4 Blurring the lines between research and clinical care: genomic research as a case study

With its sequencing of the human genome over a decade ago (International Human Genome Consortium 2001; Collins *et al.* 2003), the Human Genome Project (HGP) influenced the practice of medicine (Collins and McKusick 2001) by opening 'huge potential for research into the ways in which genes relate to human conditions, diseases, capacities, impairments

and susceptibilities' (Australian Law Reform Commission 2003: 379). Although the Project's outcomes have yet to directly affect the healthcare of most people (Collins 2010: 674), it is fair to say the human genome has catalyzed, albeit humbly, the translation of knowledge from the bench (research) to the bedside (clinic), such that 'powerful drugs have been developed for some cancers; genetic tests can predict whether people with breast cancer need chemotherapy … and drug response can be predicted accurately for more than a dozen drugs' (Collins 2010: 674).

Mere decades ago, the practice of medical genetics was limited to the study of Mendelian disorders and to chromosomal anomalies (Collins and McCusick 2001: 540). Even though practitioners knew most common diseases had both hereditary and environmental factors, they were often limited to the analysis of family history (Collins and McCusick 2001: 540), which was 'largely unsuccessful in uncovering the basis of common diseases that afflicted most of the population' (Lander 2011: 191). Today, 'more than 1,100 loci [locations of genes on a chromosome] affecting more than 165 diseases and traits have been associated with common traits and diseases' (Lander 2011: 191) thanks to genome-wide association studies (GWAS) (Collins 2010: 674). Despite this, many challenges in the field of human genetics persist (Green et al. 2011), not the least of which include legal challenges facing genomic researchers.

Often, there is a fine line between what constitutes research and clinical care. Conflation of the two can create problems in fact and in law, especially if the researcher happens to be a clinician. An example of this conflict is apparent where a researcher is faced with validated research findings that have potential clinical value. This section will not delve into the larger discussion around the return of research results and incidental findings (see such analysis in Chapter 18 of this Handbook), but rather will use this topic to further the analysis in section 12.3 on the clinician-researcher's duty to inform, using Quebec civil law as a case study. Could a researcher holding a PhD in genetics be held to the same duty to inform standard as a clinician-researcher? Is a clinician-researcher first and foremost a researcher, or a clinician held to a clinical duty to inform or to an elevated standard? In order to answer these questions, it is necessary to review the dual roles and responsibilities of the clinician-researcher.

12.4.1 The curious case of the clinician-researcher

There is no consensus in the literature as to the extent of the dual role of the clinician-researcher. Some authors stress that the research setting is a natural extension of medical care and similar obligations are generated as a result (Czoli et al. 2011, p. 2). Under this interpretation, medical research is considered to be a subset of medical practice; if a conflict arises, the 'obligations of clinical care trump research obligations' (Czoli *et al.* 2011: 3). Proponents of this position find support in the Preamble of the *Declaration of Helsinki*, which states:

> The Declaration of Geneva of the WMA binds the physician with the words, 'The health of my patient will be my first consideration,' and the International Code of Medical Ethics declares that, 'A physician shall act in the patient's best interest when providing medical care.'
>
> It is the duty of the physician to promote and safeguard the health, well-being and rights of patients, including those who are involved in medical research. The physician's knowledge and conscience are dedicated to the fulfillment of this duty.
>
> *(2013, articles 3–4)*

A second group of authors adopt a contrary stance, and maintain that the duties of physicians and researchers are distinct (Henderson *et al.* 2007: 1736). This distinction arises from the differences

between the aims of research and clinical care. While the former seeks to produce generalizable results, the latter seeks to benefit individual patients (Miller and Brody 2003: 21). Obligations in medical research must reflect these differences, and must thereby dispel the therapeutic misconception (de Melo-Martín and Ho: 2008: 202–3), where a 'research subject … inaccurately attributes therapeutic intent to research procedures' (Lidz and Appelbaum 2002: V55).

Although the literature surrounding this topic articulates a number of 'middle-ground' positions (Czoli *et al.* 2011: 5–7), a recent study surveying physicians concluded:

> Although several physician-researchers referred to a fundamental difference between the practices of medical care and research, and even devised strategies to help keep the two roles separate, we heard little that directly aligns with a strict difference position, perhaps indicating that a complete divorce between the two practices is uncomfortable for or undesired by physician researchers.
>
> *(Czoli* et al. *2011: 5)*

In brief, while there exists a difference between the research and clinical settings, this distinction does not generate differing obligations.

12.4.2 Return of research results and incidental findings in Quebec: a case study

In genomic research, the potential for discovering health-related findings of clinical significance to research participants is becoming ever more prevalent (Cho 2008). Large-scale human genomic research has been made possible by powerful technologies (such as genomic microarrays, scanning technologies, and other research instruments) that can generate massive amounts of information (Wolf *et al.* 2008). The issue of how to handle these findings is not only topical, but also increasingly challenging for researchers.

In contrast with the international and regional documents reviewed here, as well as France's *Loi Jardé*, the province of Quebec does not outline any legislative norms surrounding the return of research results and incidental findings. This legislative lacuna begs the question of whether clinician-researchers are under any legal obligation to return results derived from research projects. If so, does this obligation form part of the duty to inform under Quebec law? At present, the duty to inform in Quebec pertains to patient consent and does not adequately contemplate the issue of return of results (*Weiss*).

The case of a clinician-researcher involved in a rare diseases study can be used to illustrate the issue at hand. In such research projects, whole-genome and whole-exome sequencing may be used to determine the causative gene for a given disorder (Choi *et al.* 2009). While some individual findings may be pertinent to the research study, others may be completely incidental to the study's original purpose. Is there a legal obligation to return these incidental results to participants, especially if they prove to be analytically valid, clinically significant, and potentially actionable (Wolf *et al.* 2012)? In such cases, 'analytical validity' refers to the ability to precisely and reliably identify a particular genetic characteristic (Knoppers *et al.* 2013), while 'clinically significant' and 'actionable' findings have a 'well-recognized and significant risk' for which an accepted therapeutic or preventive intervention is available (Knoppers *et al.* 2013, p. 246).

It should be noted that, in all likelihood, the return of results does not fall under the civil law's duty to rescue. The duty to rescue is enshrined in Quebec's *Charter of Human Rights and Freedoms* 1975, which states:

> Every person must come to the aid of anyone whose life is in peril, either personally or calling for aid, by giving him the necessary and immediate physical assistance, unless it involves danger to himself or a third person, or he has another valid reason.
>
> *(article 2)*

The relevant keywords in article 2 are 'life is in peril' and 'immediate.' Given these stringent requirements, it is very unlikely that the type of findings derived from whole-genome or whole-exome sequencing would fall under Quebec's duty to rescue. At most, a genetic condition could be said to have imminent health consequences – 'imminent' but not 'immediate.' This same principle is applicable to article 38 of Quebec's *Code of Ethics of Physicians*, which provides:

> A physician must come to the assistance of a patient and provide the best possible care when he has reason to believe that the patient presents with a condition that could entail serious consequences if *immediate* medical attention is not given.
>
> *(our emphasis)*

In the absence of any clear legislative norms surrounding the issue of return of results, a duty to inform may be inferred from two sources: (1) research protocols; and (2) 'the standard of care,' or more precisely, 'les règles de l'art' (the rules of the art). Research protocols play an important role in determining the procedures for a given research project. That research protocols are reviewed by Research Ethics Boards is evidence of their importance to research and its processes (Canadian Institutes of Health Research *et al*. 2010 (TCPS): Chapter 6). As ruled in *Weiss* v. *Solomon* (para. 115), it is important to abide by research protocols. If protocols foresee the return of certain results under certain conditions, then this obligation should be respected, particularly if the participant previously consented to this obligation. In this case, failure to return participant results and incidental findings may constitute fault under the principles of civil liability.

In cases where the research protocol is silent on the issue of return of results, the researcher can always defer to the Research Ethics Board (REB) for advice on how to manage his or her findings. That said, the implication of REBs in such cases could result in the liability of the host institution. According to *Weiss* v. *Solomon* (para. 116) and the *Civil Code of Québec* (article 1463), the principal (in this case the hospital or the institution) is liable for damages stemming from injuries that are caused by its agents (in this case, the REB).

Regardless of whether research protocols consider the return of research results and incidental findings, much of the proof still depends upon expert court testimony, which is typically based on general practice, professional guidelines, and ethical norms. Professional guidelines and ethical norms are particularly important where there is an absence of applicable legislation. For example, the *Tri-Council Policy Statement* (TCPS), a pan-Canadian guideline governing human research, creates an onerous obligation for researchers to return material incidental findings discovered in the course of research. Although 'incidental findings' are those findings that are beyond the scope of any given research study, the term 'material' has been broadly defined as having significant welfare implications for the participant, whether 'health-related, psychological or social' (TCPS, article 3.4). Unless the research community collectively distances itself from the above approach, courts may choose to consider such an obligation in the context of civil liability for negligence in research. Recently, the Panel on Research Ethics (a group of experts tasked with developing the TCPS) has proposed that article 3.4 be amended to permit the REB to decide whether an obligation to return incidental findings exists (Interagency Advisory Panel on Research Ethics 2013). Here again, however, if the REB is negligent in the course of its

review, the host institution may be liable for damages (provided that all the elements of article 1463 of the *Civil Code of Québec* are satisfied).

Researchers are not a homogenous community. Could a researcher with a PhD in genetics be held to the same standard as a clinician-researcher in the context of return of results? While some authors believe researchers should be held to the same standards as physicians on grounds of public order (Kouri 1991: 94), the equation of expectations with standards is unreasonable given the circumstances. A physician will interpret clinical findings very differently from a researcher. Consequently, the standard of liability in such cases should be a researcher with similar expertise and experience – and not a clinician.

12.5 Conclusion

Winston Churchill once said, '… this is not the end. It is not even the beginning of the end. But it is, perhaps, the end of the beginning' (1942). In response to the questions raised in the introduction, this text has demonstrated that the duty to inform can adapt to different jurisdictions. However, the *scope* of this duty is far more nebulous. A review of international and regional normative documents in section 12.2 indicates that the duty to inform has been consistently referenced in the context of research. The scope of this duty not only includes the provision of adequate information during the process of consent, but also involves the disclosure of research results and incidental findings to participants. A few regional norms have gone so far as to create a 'right to information' and a 'duty of care,' which require a researcher to disclose information that may be of relevance to the participant's current or future health or quality of life (*Additional Protocol*, article 27). A review of national norms indicates that disclosure requirements in research are considered greater than those required during treatment.

What are the consequences of breaching the duty to inform? Depending on the jurisdiction, an action in negligence (common law) or in 'fault' (civil law) can be the result. Both legal traditions require the presence of a duty and necessitate a breach (common law) or fault (civil law). Also in both legal traditions, the standard of care will be determined by expert testimony that relies on common practice, professional guidance, and/or ethical norms.

Section 12.3 of this text analyzed the duty to inform in Canada through a review of two seminal cases from 1965 and 1989, respectively. These decisions were, however, limited in two ways: first, they did not consider whether the duty to inform should be applied beyond the purview of initial consent; and second, they envisaged a 'one-size-fits-all' approach to research typology.

Section 12.4 discussed these limitations in light of the emerging issues concerning the return of research results and incidental findings. Although no clear legislative obligation exists, the return of results could be subsumed under a broader duty to inform if: (1) the return of results is mentioned in the research protocol; and/or (2) the return of results forms part of the standard of care as determined by reasonable experts in the same circumstances. Section 12.4 also highlighted the potential role of ethical norms in the absence of a clear legislative text. On that note, in his list of five lessons learned from the first decade of the genome era, Francis Collins called for 'good policy decisions … crucial to reaping the benefits that should flow from the coming revelations about the genome' (Collins 2010: 675). It seems fitting to conclude with a similar call for policymakers to develop both prospective and participatory guidance that is not unduly onerous for researchers (Knoppers and Zawati 2011). Investigators who are asked to abide by reasonable obligations will be able to bring their research projects to completion in an ethical and efficient manner. Given the high level of trust the public places in research endeavors, responding to these obligations can only sustain research for the future.

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Part III

Medical interventions and emerging technologies

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13

Emerging legal and ethical issues in reproductive technologies

Vardit Ravitsky and Raphaëlle Dupras-Leduc

13. 1 Introduction

Reproductive technology is one of the greatest medical success stories of our time. Since the advent of *in vitro* fertilization (IVF) in 1978, an estimated 5 million babies have been born worldwide as an outcome of this revolutionary technology (Chambers *et al.* 2014), alleviating the burden of infertility and bringing joy to millions of parents and families. The broad social acceptability of reproductive technology has been marked by the 2010 Noble prize in medicine being awarded to Dr Robert Edwards (Nobel prize 2010), developer of IVF and the metaphorical 'father' of Louise Brown, the world's first IVF baby. IVF and some of its associated techniques such as intracytoplasmic sperm injection (ICSI) and preimplantation genetic diagnosis (PGD), have now become commonplace. In the United States, over 1 per cent of all births are of babies conceived through reproductive technology (Centers for Disease Control and Prevention *et al.* 2010). This number is even higher in most European countries, where it is estimated that as many as 6 per cent of births are achieved using assisted reproductive technologies (Nyboe Andersen and Erb 2006). In addition, prenatal screening and testing have now become an integral part of prenatal care in all developed countries (Rapp 2000).

At the same time, reproductive technology has contributed to 'more radical changes to the understandings of parenthood, kinship, fertility and technology' (Franklin 2013: 1), bringing about an avalanche of legal and ethical challenges. IVF has changed the way infertility is socially framed and defined, shifting it from a psycho-social condition of 'involuntary childlessness' to a medical condition that can be resolved through high-tech interventions (Becker and Nachtigall 1992). These interventions, however, are very costly, raising issues of justice and equal access, and catalyzing debates regarding the appropriateness of public funding.

The emergence of IVF also opened a host of new possibilities for creating families, expanding individuals' reproductive autonomy while raising novel challenges. For example, gestational surrogacy allows gay couples to have genetically related children. This allows for further emancipation of gay families, but challenges jurisdictions to determine legal mechanisms that recognize new types of kinship, such as the legal parental status of a non-genetic parent in a gay couple (Margalit 2013; Storrow 2012). Moreover, gestational surrogacy created for the first time in human history a distinction between a genetic and a birth mother, opening up a Pandora's Box

of ethical uncertainties in defining motherhood. It also provoked a diversity of responses regarding the legality of surrogacy agreements, the legal status of the parties involved and the monetary compensation of the surrogate.

Another assisted reproductive option is gamete donation, which allows couples to have a child that is genetically related to the fertile partner, and single and lesbian women to reproduce using donor sperm. Due to the prevalence of anonymous donation, however, it created a 'donated generation' (Miller 2008) of individuals deprived of access to the identity of one of their progenitors. These various reproductive avenues have also opened up national and international markets of reproductive labor, producing fertile ground for the possible exploitation of vulnerable surrogates and egg donors.

Prenatal testing empowers parents with an unprecedented degree of control over the health (and even the identity) of their future children, but this new found control is intertwined with the heartache and moral distress surrounding the decision to terminate a pregnancy (Katz Rothman 1993; Rapp 2000). PGD provides a solution by allowing access to genetic information before pregnancy has been initiated (American Society for Reproductive Medicine (ASRM) 2008; Harton *et al.* 2011), but raises social and legal challenges regarding the appropriate threshold of testing (Ravistky 2009).

Now, a new technology – non-invasive prenatal testing (NIPT) – that allows the testing of fetal DNA found in maternal blood expands old debates regarding appropriate testing and the protection of women's reproductive autonomy. Innovation has been persistently pushing the technological envelope further in other areas as well. For example, elective egg freezing allows women to possibly expand their reproductive capacity into their 40s and 50s (Brezina *et al.* 2013; European Society of Human Reproduction and Embryology (ESHRE) 2012). Furthermore, mitochondrial transfer might soon allow them to become genetic mothers to healthy babies that would not inherit their mitochondrial disease, creating what is technically a baby with three genetic parents (Human Fertilisation and Embryology Authority (HFEA) 2013).

On the backdrop of this rich and complex terrain, two prevalent elements emerge. First, technological innovation regularly outpaces the ability of legal systems to respond to new challenges, often leaving controversial uses of new technologies unregulated and leading to their resolution by the courts on an *ad hoc* basis. Second, the regulatory responses to these challenges vary greatly between jurisdictions, reflecting the unique sets of cultural values and political contexts of different societies (Donchin 2011; Ouellette *et al.* 2005). For example, different countries offer various mechanisms for publicly funding IVF, ranging from none to full funding with a variety of associated provisos and limitations. Other examples include different prohibitions and limitations on uses of reproductive technologies such as gamete donation, surrogacy, PGD, and now elective egg freezing and mitochondrial transfer.

These legal limitations set the stage for flourishing and lucrative cross-border international markets for reproductive services (Shenfield *et al.* 2010), a phenomenon dubbed 'reproductive tourism' (Bassan and Michaelsen 2013). Individuals in need of certain services travel from countries with strict regulation to those jurisdictions with relatively lax or no regulation, creating ethical and legal complexities that are even harder to address considering the international context in which they arise.

This chapter will present some emerging areas of debate, addressing ethical, social, and legal issues that arise within each and offering some insight into possible future approaches.

13.2 Public funding of IVF

For those who are unable to conceive a child, infertility – commonly defined as failure to conceive after 12 months of unprotected sexual intercourse – may be the most painful and

protracted problem they experience in life (Gurunath *et al.* 2011; World Health Organization (WHO) 2013b). For many, IVF may be the only solution to potentially alleviate this devastating condition that affects approximately 8–10 per cent of the population (Hughes and Giacomini 2001). The financial cost of IVF, however, is considerable. On average, IVF can cost $10,000 US per cycle (or $34,000 per live birth for women over 38) (Suchartwatnachai *et al.* 2000). As such, the costs can easily become prohibitive, leading to disparities in an area that is fundamental to human well-being (Katz *et al.* 2002).

This leads to the question of whether 'a responsible and caring society should seek ways to recognize and support the desire of individuals to have children' (Royal Commission on New Reproductive Technologies 1994). Public funding of IVF has therefore emerged as a highly controversial issue, involving heated public and policy debates (Hughes and Giacomini 2001; Tännsjö 2007). The challenge facing policymakers in this area is to develop policies that are appropriately justified and that reflect the unique cultural and social values of the society in which they are made.

Various Western countries have adopted a spectrum of approaches towards public funding of IVF using various ethical justifications (Agence d'évaluation des technologies et des modes d'intervention en santé (AETMIS) 2009; Mladovsky and Sorenson 2010; Comité directeur de bioéthique 2012). For example, Israel covers 100 per cent of the cost with an age limit of 45 for women using their own eggs, for as many cycles as required to allow for two live births per couple, including single and lesbian women. The UK also fully covers the cost of IVF and priority is given to women between the ages of 23 and 39 who have an identified cause of infertility or who have not been able to conceive for three years, including single and lesbian women. France offers full IVF coverage for women under 43 years of age, but only for heterosexual couples who are married or have lived together for a minimum of two years. In the Netherlands, the first cycle of IVF is not covered, but two subsequent cycles are fully covered with no age limit for women, both single and lesbian, using their own eggs. Germany covers 50 per cent of the cost, and women must be between the ages of 25 and 40. While the law itself does not exclude single and lesbian women, the German Medical Association's guidelines indicate that only married couples, and in some specific cases unmarried heterosexual couples, should have access to publicly funded IVF (AETMIS 2009). In North America, Quebec is currently the only jurisdiction that fully funds IVF (since 2010) and coverage includes single and lesbian women (*Health Insurance Act* 1970; *Regulation respecting the application of the Health Insurance Act* 1981; Quebec 2013). Funding approaches thus vary greatly in terms of level of coverage and eligibility criteria.

13.2.1 The status of infertility

The literature exploring the conceptual and ethical implications of public IVF funding raises numerous considerations such as justice, equitable access, cost-effectiveness, public health, cultural values and norms, and feminist perspectives. In this chapter, we focus on two ways in which the status of (in)fertility is conceptualized: from a medical or *physical* perspective (e.g. is infertility a disease, a condition, a medical need, a handicap?) and from a *conceptual* perspective (e.g. is fertility a human right, a basic human need, an interest, a privilege?).

13.2.1.1 The physical/medical status of infertility

Is infertility a disease? A study that surveyed over 8,000 people in six European countries found that only 38 per cent of them agreed with the statement 'infertility is a disease' (Adashi *et al.* 2000), demonstrating the complexity of this issue. The implications of the question are clear: if

perceived as a disease, public funding for its treatment is construed as justified and what remains to be determined is its prioritization in relation to other required treatments competing for limited resources (Hughes and Giacomini 2001; Mladovsky and Sorenson 2010; Tännsjö 2007); if not, its funding may be unjustified from the outset.

The World Health Organization (WHO) suggests that infertility is 'a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse' (WHO 2013a). Moreover, the WHO's definition of health as 'a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity' (2013b) was applied in the following way in the context of reproductive health:

> Reproductive health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity, in all matters relating to the reproductive system and to its functions and processes. Reproductive health therefore implies that people are able to have … the capacity to reproduce and the freedom to decide if, when and how often to do so. Implicit in this last condition are the rights of men and women to be informed and to have the right of access to appropriate healthcare services that will … provide couples with the best chance of having a healthy infant.
>
> *(Glasier* et al. *2006: 1596)*

These definitions, however, are broad and expansive, and they are often seen as portraying an ideal rather than a realistic basis for policy decisions regarding public funding.

Several arguments have been proposed against considering infertility as a disease. First, infertility does not lead to mortality or morbidity, does not entail any physical pain, and does not directly affect the functioning of other physical systems in the body. It has thus been argued that it is not medically necessary to treat it. Similar arguments were used in 1994 by an Ontario judge to justify de-insuring IVF (Hughes and Giacomini 2001) and by the Supreme Court of Nova Scotia in 1999 to argue against public funding (*Cameron* v. *Nova Scotia (Attorney General)* [1999] NSJ No. 297; Hughes 2008). Second, the diagnosis of infertility is uncertain and variable between countries. In most countries, a couple can be diagnosed as infertile after one year of unprotected sexual intercourse without conception, despite the fact that in many of the cases pregnancy can be achieved given more time. Moreover, a diagnosis of infertility is often given when the medical cause of the inability to conceive is unknown.

On the other hand, several arguments have been proposed in support of the notion that infertility is a disease or a medical condition. First, infertility is a dysfunction of a bodily system that cannot fulfill its natural function. This idea closely aligns with Daniels' (2008) definition of diseases as deviations from the natural functional organization of a typical member of a species, when those deviations may lead to a negative impact on the individual's access to equal opportunities. Second, infertility can be treated – or alleviated – through medical intervention. It thus follows a classical medical model that sees a progression from pathology, to symptoms, to medical consultation, to diagnosis and finally to treatment. At the same time, some have noted that IVF does not actually *cure* infertility. It leaves individuals clinically infertile, while alleviating or bypassing infertility to allow conception. However, if an infertility treatment is determined by achieving a live birth, then IVF can indeed successfully treat infertility in many cases.

The debate regarding whether or not infertility qualifies as a disease is thus complex and its resolution does not seem to be in sight. As Shanner noted almost 20 years ago:

> Any progress on such a discussion requires a lengthy exploration of the purposes and goals of medicine, the basic concepts of health and disease, the limits of therapeutic as opposed

> to cosmetic or elective treatments, and the prioritization among many qualities of life and other values that involve our bodies.
>
> *(1995: 856)*

Despite these conflicting factors, there is broad agreement regarding the devastating implications of infertility for those who suffer from it. As described by Lord, '[m]any clinicians involved in infertility find that the level of distress and suffering that they see in their patients is far greater than that seen in patients with other benign disorders that are treated free of charge' (Lord *et al.* 2001: 256).

13.2.1.2 The conceptual status of infertility

Is reproduction a human right, a basic human need, an interest, a privilege, or a luxury? While this question remains controversial (Warnock 2002), there is broad agreement that reproduction is a basic human drive or interest shared by a vast majority of human beings. Which elements of it are biologically/evolutionarily imprinted and which are culturally or socially constructed remains debatable. However, the human interest in being free and able to found a family and become a parent is widely acknowledged. Certain international documents reflect this view, such as the 1948 *Universal Declaration of Human Rights*: 'Men and women of full age, without any limitation due to race, nationality or religion, have the right to marry and to found a family' (article 16).

The debate surrounding reproduction as a human right touches on the basic distinction between the negative and the positive aspects of such a right (Quigley 2010). The 'right to found a family' has been traditionally interpreted as expressing a negative right – for example, the right not to be forcibly sterilized or perhaps pay out of pocket for assisted reproduction without state interference or limitations (Robertson 1994). However, public funding of IVF opens up an interpretation of this right to reproduce as a positive right – a right to access services and resources required in order to procreate. Like other positive rights, such as health and education, the implementation of such a right is context-specific – what resources are available and how a given society chooses to prioritize the needs of its citizens based on its shared social values.

The public funding of IVF thus remains a highly controversial area. Much of the difficulty in justifying such funding stems from disagreements on how to frame infertility from a physical or conceptual perspective and whether there is a right to assistance in overcoming it. Moreover, even in societies that acknowledge the interests in reproduction as strong enough to warrant public funding, this decision remains dependent on the availability and prioritization of resources in the face of competing demands on the health budget.

13.3 The future of frozen human embryos

The use of *in vitro* fertilization to overcome infertility is increasing. Around 1.5 million IVF cycles are performed each year worldwide, with an estimated 350,000 babies born annually (ESHRE 2013). Many cycles of IVF involve the creation of more embryos than can be implanted in the uterus and therefore 'leftover' embryos remain. The current practice is to freeze – or cryopreserve – these embryos for possible future use. On average, 3.4 embryos are cryopreserved following each cycle of IVF (Gunby *et al.* 2011). The number of leftover frozen embryos is thus increasing constantly.

Many countries put a legal time limit on embryo cryopreservation (for example, two years in Denmark, five years in Belgium and Australia, ten years in the UK) (National Health and

Medical Research Council 2007; Bangsbøll *et al.* 2004; HFEA 2009; Provoost *et al.* 2011; Takahashi *et al.* 2012). However, there is no legal time limit in the USA and Canada (ASRM 2013c; *Assisted Human Reproduction Act* 2004 (Canada)). From a clinical perspective, the time-limit for conceiving a healthy baby from a frozen embryo is not known. The 'oldest' frozen embryo to produce a healthy baby was cryopreserved for almost 20 years (Dowling-Lacey *et al.* 2011). The notion that women or couples may reappear after years of not being in touch and demand to use their leftover embryos for reproduction is thus a threatening prospect that underlies clinics' reluctance to dispose of embryos, even when then are legally entitled to do so.

Recently, researchers have become interested in the ethical, social, legal, psychological, and symbolic aspects of the decision process surrounding cryopreservation of embryos. Studies have explored the factors influencing decision-making regarding the disposition of embryos, such as the conceptualization of the embryo, its perceived moral status, trust in the medical establishment, and absence of appropriate options (Bangsbøll *et al.* 2004; de Lacey 2007; Fuscaldo *et al.* 2007; Hammarberg and Tinney 2006; Lyerly *et al.* 2011). However, most of these studies are based either on speculations regarding the reasons underlying decision-making, or on empirical studies that ask couples hypothetical questions regarding their decision-making. Few studies examine the real-life experiences, emotions, moral reasoning, and general thought process of couples who have lived through decision-making regarding their embryos.

13.3.1 What are the options?

Currently, embryos may be frozen (which involves an annual fee to cover the cost of cryopreservation which, in North America, can be approximately $500 (Rudick *et al.* 2010)); disposed of; donated to other couples; donated for research purposes; used for training embryologists; or used to improve assisted reproduction techniques. While these options are already complex, additional issues should be addressed. For example, what should be the fate of frozen embryos in the event of one partner's death? Should the surviving partner be allowed to use them for reproduction? What should happen in the event that one partner becomes incompetent to make a decision, or in the event of separation, divorce, or disagreement regarding the future of the embryos? Similar cases have appeared before courts in various countries and have been resolved in very different ways. For example, a US court decided that without the consent of both parties, embryos may not be used (*Davis* v. *Davis* [1992] 842 SW2d 588, 597 (Tennessee)). However, an Israeli court allowed a woman to use the frozen embryos in recogniton of her 'right to motherhood,' despite her husband's objection (*Nakhmani* v. *Nakhmani* [1995] FH 2401/95 50(4) PD661; Halperin-Kaddari 1999).

13.3.2 Consent and abandonment

The complexity of these decisions therefore requires appropriate consent mechanisms. Currently, most clinics do not dedicate enough time to a face-to-face discussion in making this decision. Women and couples are often sent home with a consent form to reflect on their decision alone, with few resources for information or support. The scant literature on counseling and consent regarding cryopreservation demonstrates that patients' counseling needs are unmet and their consent is not fully informed (Bankowski *et al.* 2005; Machin 2011). To date, many clinics do not include circumstances of death or disagreement in their consent process prior to cryopreservation, and therefore do not have a mechanism in place for addressing such eventualities (ASRM 2013a; Hoffman *et al.* 2003).

In 2013, the ASRM acknowledged that 'programs should require each individual or couple contemplating embryo storage to give written instructions concerning disposition of embryos

in the case of death, divorce, separation, failure to pay storage charges, inability to agree on disposition in the future, or prolonged lack of contact with the program' (ASRM 2013a: 1). To achieve this laudable goal, novel ways to inform patients should be developed to try and overcome barriers such as time constraints and others.

'Embryo abandonment' (ASRM 2013a; Asemota *et al.* 2013; Walsh *et al.* 2010) creates further challenges for clinics. In such cases, couples do not renew their contact with the clinic and stop paying their annual fees after a few years of cryopreservation. The recent ASRM committee opinion states:

> [A]s an ethical matter, a program should be free to dispose of embryos after a passage of time and unavailability of a responsible individual or couple that reasonably indicates that the couple has abandoned the embryos. A program's willingness to store embryos does not imply an ethical obligation to store them indefinitely.
>
> *(ASRM 2013a: 2)*

However, many clinics are reluctant to dispose of abandoned embryos and continue to keep the frozen embryos indefinitely, incurring the cost of cryopreservation themselves. This creates a financial and logistical burden on clinics, as well as a heavy moral burden on clinic directors and staff.

The complexity of embryo abandonment lies partly in determining the conditions of abandonment. For example, what would be considered diligent effort on the part of the clinic to contact the progenitors of the embryo, and how many years should pass without any contact to consider an embryo 'abandoned'? The ASRM suggests five years as the cutoff, but any proposed number would be arbitrary from an ethical perspective. The future of abandoned embryos thus continues to pose great ethical, legal, and social challenges that policymakers will have to address in the near future.

13.4 Elective egg freezing

Elective egg freezing, or 'social' egg freezing, is a relatively new option available to younger women who are not yet ready to conceive, but wish to increase their chances of conceiving at a later time. In 2012, two important professional societies published their clinical recommendations regarding this emerging practice. The American Society for Reproductive Medicine stated that the technique should no longer be considered experimental, although it did not endorse its routine elective use (ASRM 2013b; European Society for Human Reproduction and Embryology (ESHRE) 2012). The ESHRE asserted that it did not find convincing arguments against the elective use of the technique (ESHRE 2012). These recommendations received considerable media attention (Gootman 2012; Inhorn 2013; Knight 2013; Maranto 2013; Mason 2013; Morgan and Taylor 2013; Richards 2013; Rosen 2013), making elective egg freezing a hotly debated social issue. Indeed, this technique raises ethical and regulatory challenges which have been explored in the academic literature in recent years (Donnez 2013; Goold and Savulescu 2009; Lockwood 2011; Petropanagos 2010).

13.4.1 Clinical dimensions

Egg freezing is a technique that allows the long-term storage of eggs. Although no reliable data are available, it is believed that to date thousands of babies have been born worldwide from previously frozen eggs. This technique can be used in IVF when more eggs are retrieved than

needed for reproduction, or as a means of fertility preservation in the case of patients suffering from a condition or undergoing a treatment that might compromise their fertility, such as chemotherapy. *Elective* egg freezing, however, is a novel use of the same technique by healthy younger women who freeze their eggs to increase their chance of conceiving a child later in life. Considering that for many women in their forties, an egg donation from a younger donor is required for a successful use of IVF, elective egg freezing may be described as 'self-donation' where the young donor and the older recipient are in fact the same woman.

Elective egg freezing is controversial because it involves an invasive risky procedure performed on a healthy woman who is not undergoing IVF for fertility treatment nor facing medical risks to her future fertility, except the typical reduced quality of older eggs. Egg retrieval itself carries risks such as ovarian hyperstimulation syndrome, bleeding and infection (ESHRE 2012; Goold and Savulescu 2009) and little is known about its long-term implications for the woman's health (Carbone and Cahn 2013). These risks must be understood in the context of limited data on how the use of previously frozen eggs impacts conception, perinatal outcomes, and the long-term health of offspring. Some have expressed concerns that the procedure may represent a 'false promise' of preserving fertility in the light of current low success rates of IVF in general (ASRM 2013b; Brezina *et al.* 2013; Goold and Savulescu 2009; Lockwood 2011; Shkedi-Rafid and Hashiloni-Dolev 2011; Wyndham *et al.* 2012).

These elements highlight the importance of developing appropriate counseling and consent procedures for elective egg freezing. Since the balance of risks and benefits is distinct from fertility treatment or preservation, the counseling of healthy women considering egg freezing should be tailored to their unique context and provide the most updated evidence regarding the medical risks of the procedure and the actual chances of conception in the future.

13.4.2 Social dimensions

In Western societies, delayed motherhood has become prevalent due to women's greater prominence in the workforce. Current social trends put women's 'reproductive age' out of sync with their 'developmental age'. While women are in their (physiological) reproductive peak in their early and mid-20s, this is a time during which they can be socially expected to invest in education and career building to secure future financial stability. The biologically ideal window for reproduction has thus become, for many women, a logistically impossible time to start a family. Indeed, the proportion of women giving birth in their early forties in Canada, for example, has doubled between 1988 and 2008 (Daniluk and Koert 2012).

In light of these social forces and trends, elective egg freezing is often perceived as a means of promoting women's autonomy, allowing them to expand the natural reproductive cycle and to choose motherhood at a time that is appropriate for them (Capps *et al.* 2013; Rybak and Lieman 2009; Shkedi-Rafid and Hashiloni-Dolev 2011; Wyndham *et al.* 2012). It is also perceived as promoting gender equality by 'leveling the playing field,' allowing women to have children later in life, a choice that previously belonged only to men (Goold and Savulescu 2009; Rybak and Lieman 2009; Wyndham *et al.* 2012).

Reproductive autonomy is affirmed by international organizations and conventions such as the World Health Organization (2013) and the *Convention on the Elimination of All Forms of Discrimination against Women* 1979. In light of these documents, one can argue that elective egg freezing is a powerful technological tool to promote autonomy and equality and to fight discrimination.

However, this portrayal of the technique overlooks two important elements. First, elective egg freezing is an expensive option, costing approximately $4,000 to $15,000 (USD) plus the additional costs of medication ranging between $2,000 and $4,000 (USD), and annual storage

fees of around $440 (Goold and Savulescu 2009; Harwood 2009; Martin 2010). As such, this is an option only available to a rich minority, unless covered by health insurance. The elevated cost of this option therefore means that while it may level the playing field between men and women, it may create a new type of reproductive inequality between rich and poor women and/or couples.

Second, the emphasis on elective egg freezing as promoting reproductive autonomy and individual choice fails to acknowledge the social context of delayed motherhood. Some speak about 'women who have just waited too long to have their children' (Lahl 2012), as if the decision is purely an individual one, which implies lack of appropriate planning or self-centered preferences. If delaying motherhood is simply a 'lifestyle choice' (Sandelowski 1990), then elective egg freezing may be an appropriate solution, perceived as a 'price' women must pay for their life choices despite being medically risky and financially demanding.

However, this portrayal of elective egg freezing 'obscures the social and economic circumstances as to why childbearing may be deferred by many women' (Capps *et al.* 2013: 18), failing to address the tremendous social pressures experienced by younger women to establish themselves before becoming mothers. The strong social message is that to be a responsible mother, a woman should first get an education, establish a career, and attain financial and relationship stability (Cooke *et al.* 2012; Lockwood 2011; Wyndham *et al.* 2012). In light of these pressures, the choice to delay motherhood must be understood not solely in individualistic terms, but rather in the context of the social reality of today's Western societies (Cooke *et al.* 2012). From this perspective, elective egg freezing can be portrayed as an individual solution to a social problem, one that puts 'the onus of the problem' on the woman as an individual (Farrell 2012). This fails, however, to address the social dimensions of the problem in terms of policies that would allow women to choose motherhood earlier in life, such as paid maternity leave, subsidized childcare, and family-friendly work environments.

13.5 Donor conception

The use of donor sperm and egg to conceive a child, also known as 'third-party assisted conception,' has become a well-established practice since the advent of IVF. No confirmed data exist, but it is estimated that hundreds of thousands of children have been born to date worldwide using donor conception. This practice raises numerous ethical, psychosocial, and legal issues, such as telling donor offspring the truth about the circumstances of their conception (McGee *et al.* 2001; Patrizio *et al.* 2001), the impact of donor conception on identity formation and family dynamics (Ravitsky 2010, 2012), the legal establishment of parental status of the non-genetic parent, and guaranteeing that donors do not have any legal or financial liability or obligation towards offspring (Blyth and Frith 2009). Donor conception also raises many challenges from a clinical perspective, such as screening procedures for donors and medical follow-up with donors to update medical history that may affect offspring (ASRM 2013c; Ravitsky 2012). This section focuses on an issue that emerged in recent years as extremely contentious and has received ample academic, legal, and media attention: donor anonymity and the access of donor-conceived individuals to information about their origins.

13.5.1 Donor anonymity and the right to know one's genetic origins

Donor conception was traditionally based on the assumption that donors should remain anonymous. This was meant to protect donors from liability in a period when legal mechanisms were not yet developed to address the challenges of donor conception (Blyth and Frith 2009). It was also meant to protect the status of non-genetic parents, from a legal as well as from a

psychosocial perspective. Protection of donor anonymity was also based on the notion that donor offspring are better off shielded from the truth about the circumstances of their conception, and that access to donor identity would therefore be irrelevant. The perspectives of donor-conceived individuals themselves have initially been a neglected element in the growing practice of donor conception.

Over the years, however, the interests of donor-conceived individuals in having access to the identity of their donors have come to the forefront. As the first generation of donor-conceived offspring came of age, these young adults started sharing their perspectives. Many tell stories of psychological distress, describing a strong need to know their genetic origins as an essential part of constructing their identities. Their perspectives and interests have now become the center of a lively academic debate (McGee *et al.* 2001; Patrizio *et al.* 2001) as well as a driver for support networks, educational campaigns, and legislative changes (Blyth and Frith 2009).

While most countries still protect donor anonymity, a trend towards openness is gathering momentum and a growing number of countries are adopting laws and regulations banning anonymous donation. To date, these jurisdictions include Sweden (1985), Austria (1992), Victoria (Australia) (1998), Switzerland (2001), The Netherlands (2004), Norway (2005), the UK (2005), Finland (2007), Western Australia (2004), New Zealand (2005), and New South Wales (Australia) (2010) (Blyth and Frith 2009; Thorpe *et al.* 2012).

In North America, donor anonymity is still well established. In the US, legislators have only recently taken a first step in the direction of allowing offspring access to information about donors. Effective 22 July 2011, a new law in the state of Washington requires sperm and egg donors to provide a medical history and identifying information to fertility clinics, allowing donor-conceived individuals to request this information once they reach the age of 18 (*Uniform Parentage Act* 2011). This is a significant legislative milestone in a country that has consistently shied away from any type of regulation of the infertility industry. Although donors may still veto disclosure of their identifying information, offspring in Washington have guaranteed access to at least non-identifying medical history, a tremendous improvement over the current reality in all other US states where fertility clinics can destroy donor medical records on a whim before the child turns 18.

Although the Canadian *Assisted Human Reproduction Act* of 2004 mandated the registration of donors and donor-offspring, this measure was never implemented and clinics could elect to destroy donor records. This was an all-too familiar experience for Olivia Pratten, a journalist conceived through anonymous sperm donation who has been unsuccessfully attempting for years to access medical and identifying information about her donor. Pratten decided to take her case to court in an effort to change this legal reality for future generations (*Pratten* v. *British Columbia (Attorney General)*, 2012 BCCA 480; Motluk 2011). Interestingly, the High Court in the United Kingdom heard a similar case in 2002 *(Rose* v. *Secretary of State for Health* [2002] EWHC 1593), which was partially responsible for consequent legislation banning anonymous gamete donation.

Pratten argued that donor-conceived individuals are systematically discriminated against in comparison to adoptees that have legal rights to information about their genetic origins. In May 2011, the Supreme Court of British Columbia rendered a decision in her favour (*Pratten* v. *British Columbia (Attorney General)*, 2011 BCSC 656), but the Attorney General of British Columbia appealed the decision shortly after and won (*Pratten* v. *British Columbia (Attorney General)*, 2012 BCCA 480). Pratten's subsequent appeal to the Supreme Court of Canada was ultimately unsuccessful (*Olivia Pratten* v. *Attorney General of British Columbia et al.* [2013] CanLII 30404). Canada thus missed a unique opportunity to address the issue at the federal level, and in coming years Canadian provinces will have to make legislative decisions on this topic.

The legal and ethical debate surrounding this issue is far from over. In the meantime, jurisdictions that allow donor conception can enhance educational efforts, endorse a culture of

openness and acceptance, fight the stigma of infertility and promote a more nuanced understanding of family relationships, including genetic relatedness and non-relatedness.

13.6 Non-invasive prenatal testing

From its early days, prenatal genetic testing (PGT) has been raising sensitive ethical, legal, and social issues. While it allows the detection of numerous hereditary conditions – a valuable source of information for individuals – pregnancy termination remains the only course of action following an undesired genetic diagnosis. At a social level, PGT raises a host of difficult policy choices for medical institutions, healthcare insurers, and society: which tests should be allowed, offered, or funded, based on what criteria, and for whom. These choices reflect a social assessment of when it is justified to 'screen out' certain conditions or disabilities. Despite these challenging and sensitive issues, PGT enjoys a high level of social acceptability and has become an integral part of prenatal care in Western countries. This is due in large part to its impact on the promotion of reproductive autonomy and the reduction of the incidence of certain hereditary conditions, an important public health benefit.

Now, non-invasive prenatal testing (NIPT) is being gradually introduced (Agarwal *et al.* 2013; Hill *et al.* 2012b; Hui and Hyett 2013; Yotsumoto *et al.* 2012). It allows genetic testing of cell-free fetal DNA using a maternal blood test (Hill *et al.* 2013; Lewis *et al.* 2013). It thus eliminates the risk of miscarriage associated with current invasive procedures, namely amniocentesis and chorionic villus sampling. It is performed earlier in the pregnancy than either of these current tests, as early as 8–9 weeks gestation. Although NIPT offers early and safe access to predictive genetic information, and thus has the potential to revolutionize prenatal care, it also raises a host of novel concerns.

13.6.1 Counseling and consent

To date, professional societies recommend limiting the use of NIPT to women who are considered to be at a high risk for Down syndrome and some other genetic conditions, based on traditional screening tests (American College of Obstetricians and Gynecologists Committee on Genetics 2012; Devers *et al.* 2013; Gregg *et al.* 2013). However, NIPT has the potential to replace current screening and diagnostic tests in the near future (Benn and Chapman 2009; Henry and Greely 2010) and may eventually be offered to all pregnant women as a routine one-step diagnostic test, without prior screening (Schmitz *et al.* 2009b).

This future scenario may compromise informed decision-making. Currently, prenatal testing requires that women are properly counseled on the risk of miscarriage and give written consent prior to invasive testing. A safe diagnostic test runs the risk of being performed without counseling or consent (Deans and Newson 2011; Hill *et al.* 2012a; King 2011). A pilot study of 231 clinicians shows that this may indeed be the case – in the absence of risk of miscarriage, many perceived consent for NIPT as less important than for invasive testing (van den Heuvel *et al.* 2010). There are thus concerns that rather than enhance the reproductive autonomy of women and couples, NIPT may in fact threaten it (Benn and Chapman 2010; Hall *et al.* 2009; Henry and Greely 2010; Schmitz *et al.* 2009a; Skirton and Patch 2013; van den Heuvel *et al.* 2010).

Since NIPT will be offered to an increasing number of women, it may also significantly increase the need for counseling (Kooij *et al.* 2009; van den Heuvel *et al.* 2010), a need that cannot be met even with regard to current screening tests (Greely 2011; Seavilleklein 2009). NIPT therefore requires the development of appropriate tools for patient and provider

education, counseling, informed decision-making, and consent to protect and promote reproductive autonomy (Bianchi *et al.* 2014; de Jong *et al.* 2010; Lench *et al.* 2013; Ravitsky 2009, 2011). These tools should be creative and innovative, and emphasize the role of obstetricians and primary care physicians rather than rely necessarily on traditional models developed for genetic counselors. They should address the actual concerns of patients and clinicians, as well as concerns related to the social acceptance and impact of NIPT. Furthermore, these tools should also address practical implementation concerns, such as whether the test should be offered and performed on two different days in order to create a 'space' for reflection and consideration (Deans and Newson 2011; King 2011).

In the more distant future NIPT may detect a broad range of genetic conditions, since technological advances such as next-generation sequencing will allow detection of multiple conditions. In this context, counseling patients will become even more challenging (Allyse *et al.* 2012; Chachkin 2007) and additional ethical and legal issues will arise, such as the complexity of counseling regarding multiple conditions at once, each with its own characteristics and prognosis, or regarding genetic results of unclear clinical significance.

13.6.2 Social concerns

The expected 'routinization' of NIPT also raises concerns regarding increased social pressure to test and terminate affected pregnancies as an expression of 'responsible motherhood.' Since it is done early in the pregnancy, the results can be available before significant maternal-fetal bonding has occurred. Moreover, early termination is medically safer, emotionally less traumatic and more easily available than second trimester termination (Ravitsky 2009). These elements and the future availability of NIPT may lead to an implicit ethical, and perhaps even legal, obligation to test and consequently to the notion that women are 'responsible for bearing a child with a disability' because they had information about the genetic status of their fetus and still chose to carry their pregnancy to term (Deans and Newson 2011; Newson 2008). Genetic counseling is traditionally non-directive, but pre-test counseling for NIPT will be provided by health professionals without specific training in genetics. One of the challenges will be to ensure that the discussion of Down syndrome and other conditions remains balanced (Hippman *et al.* 2012).

Since NIPT is expected to lead to an increase in diagnoses and in pregnancy terminations, the probable result will be a decreased prevalence of individuals with Down syndrome and other conditions in the population. This raises concerns regarding stigmatization, discrimination, and decrease in support systems and research for individuals and their families with certain genetic conditions (Chachkin 2007; de Jong *et al.* 2010; Greely 2011; Hall *et al.* 2009; Haymon 2011; Schmitz *et al.* 2009b). These concerns may adversely affect the social acceptability of NIPT and will have to be addressed as the technology is introduced and implemented, possibly by proposing appropriate policy and regulatory mechanisms.

13.6.3 Legal and policy perspectives

From a legal perspective, NIPT raises challenges related to the obligations of healthcare providers to offer the test (Motluk 2012). It may add further uncertainty to already complex questions such as wrongful life and wrongful birth lawsuits, which have emerged as a morally problematic and legally unsettled area. Wrongful life and wrongful birth claims are claims of negligence brought against healthcare providers for acts or omissions occurring prior to or during pregnancy that result in the birth of a child with a disability or a medical condition. They are based

on the assertion that the mother would have terminated her pregnancy had she been adequately informed or counseled by her healthcare provider regarding the risk or presence of the condition, or regarding available tests that can detect it. In wrongful birth cases the claim is brought by the parents against the provider, while in wrongful life cases the claim is brought by, or on behalf of, the child. Wrongful life cases are therefore more controversial, as the plaintiff child essentially asserts that not having been born would be preferable to living with the effects of the ensuing condition. Both types of claims might potentially be made in the future, in cases where providers fail to offer NIPT once it becomes commonplace. The birth of a child with a condition that could have been detected through NIPT may cause parents to seek compensation for not being offered the test or informed of its existence.

Questions remain about the ethical acceptability of such lawsuits (Hogg 2010; Muriithi 2011; Stein 2009), how courts should respond to such cases (Nelson 2011), whether or how to best compensate parent(s), and the nature and scope of duties owed by doctors to future children (*Paxton* v. *Ramji* 2008 ONCA 697). Wrongful life claims have not been recognized in Canada, or most other jurisdictions, with the exception of three American states (California, New Jersey, and Washington), Israel (*Zeitzov* v. *Katz* [1986] 40(2) PD 85), and the Netherlands (*X* v. *Y (Molenaar)* [2003] 234–5, 236–7, 238, 240 (The Hague Court of Appeals). In France, the French Court of Cassation found that a healthcare provider's negligence in failing to diagnose a pregnant woman with rubella gave rise to claims on behalf of both the mother and the child, who was born with a disability (*X* v. *Mutuelle d'Assurance du Corps Sanitaire Français et al. (Perruche)* [2000] JCP 2293). This case raised great controversy, and resulted in the enactment of a law preventing children born with disabilities from bringing claims of this nature to court, and barring parents with wrongful birth claims from collecting damages for the increased cost or 'special burdens' associated with raising a child with a disability (*Loi no. 2002-303 relative aux droits des maladies et à la qualité du système de santé* 2002 (France)). Moreover, when this law came into effect, its application extended to wrongful birth and wrongful life cases. At the time many of these cases were pending before French courts, therefore depriving parents from claiming the 'special burden' damages they otherwise would have been entitled to. As a result, the French government was successfully challenged before the European Court of Human Rights, which found these parents had property interests in their anticipated damages awards for 'special burdens,' and the law therefore violated their right to peaceful enjoyment of property (*Draon* v. *France* [2005] Application No. 1513/03; *Maurice* v. *France* [2005] Application No. 11810/03).

In contrast to wrongful life claims, wrongful birth claims are more widely accepted in Canada and abroad, although the method of assessing damages in such claims remains unsettled. While some courts award damages for the full cost of child rearing (e.g. *Cattanach* v. *Melchior* [2003] HCA 38), others opt not to award any damages on the grounds that the birth of a child should be seen as a blessing regardless of whether it is the result of a provider's negligence. More moderate approaches include awarding damages for the increased cost of raising a child with a disability, costs of raising the child offset against the value that the child's life has brought to the parents and, more commonly, awards for damages incurred in relation to pregnancy, child birth, and the initial cost involved in having a newborn baby (see Nelson 2013; *Roe* v. *Dabbs*, 2004 BCSC 957, paras 189–94, for a detailed discussion of case law illustrating the different approaches to damages).

Furthermore, NIPT raises intellectual property (IP) challenges related to the use of various testing technologies developed by private companies, as well as the impact of patents on specific genetic tests (Agarwal *et al.* 2013). Substantial debate and calls for effective policy have centered on the potential impact of patents on access to useful genetic technologies (Caulfield 2011;

Hopkins and Hogarth 2012; Huys *et al.* 2012; Van Overwalle *et al.* 2006; Verbeure *et al.* 2006), including relevant case law on the patentability of human genetic material (*Association for Molecular Pathology* v. *U.S. Patent and Trademark Office* [2011] 653 F.3 d I329; Pollack 2012). The advent of inexpensive whole genome sequencing will shift the nature of the patent debate and introduce new social and clinical issues (Dobson and Evans 2012), for example, the degree to which whole genome sequencing will infringe existing patents (Borrell 2010; Holman 2012). This patent debate is highly relevant to NIPT technologies, which will likely involve testing for a range of conditions that may be associated with one or more patents.

While in some countries NIPT is available on the private market (Morain *et al.* 2013) and individuals can choose whether to pay for it out-of-pocket (Agarwal *et al.* 2013; Allyse *et al.* 2012), it is expected that in some countries, including Canada, NIPT will be integrated into universal healthcare coverage. Policymakers and the public therefore need to address questions regarding what tests to offer, to what populations and for which conditions (Hill *et al.* 2013).

Moreover, the social and ethical implications of public funding may be more far reaching than simply allowing individuals to purchase the test, because public funding sends a stronger message of endorsement for the technology. While this message can validate the safety and utility of the test, it can also be seen as an extension of current social trends that pressure women to test and terminate affected pregnancies. It might also be seen as raising risks of stigmatization and marginalization of individuals who live with those conditions or disabilities that society chooses to 'screen out' (Hill *et al.* 2013; Lewis *et al.* 2013).

13.7 Conclusion

The 80th anniversary of Huxley's *Brave New World* gives us pause to consider current advances in the area of reproductive technology and fears of a dystopia. Overall, most of the ominous scenarios described in so lively a manner in this futuristic account have not materialized. Rather, reproductive technologies have brought medical solutions to infertility and allowed a growing degree of control over pregnancy outcomes. Broadly speaking, they have enhanced the reproductive autonomy of women and families, equipping them with better tools to decide when and how to have children. The tremendous benefits introduced by reproductive technologies and prenatal testing are thus widely acknowledged and their social acceptability is high.

At the same time, the ongoing emergence of new technologies constantly raises novel ethical, social, and legal challenges. This chapter has described many of these challenges and attempted to outline possible approaches for optimally addressing them. As we look forward, nuanced ethical analysis, refined legal tools, and an informed public debate remain crucial in developing justified and well-balanced approaches that enhance and protect individual autonomy while promoting public health goals.

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14

Regenerative medicine

Socio-ethical challenges and regulatory approaches

Carla Beak and Rosario Isasi

14.1 Introduction

The advancement of regenerative medicine (RM) has become a popular goal. It is promoted and supported by patients, healthcare providers and governments in an effort to reduce the growing medical and financial challenges in healthcare. This chapter aims to provide a general overview of the ethical, legal and social issues (ELSI) associated with regenerative medicine, beginning by defining the term and briefly summarizing the state of the industry. It discusses issues arising from the use of human cells, challenges of clinical translation, and questions of social justice that emerge from innovations in the field. Lastly, the chapter will turn its focus to the role of the regulatory system in managing the progress and development of regenerative therapies. It will review the ways in which select jurisdictions have adapted existing frameworks to incorporate product development in regenerative medicine, specifically cell-based and combination products, into their regulatory regimes. The chapter then considers elements important to creating a regulatory environment conducive to responsible innovation and international harmonization in RM.

14.1.1 Definition of regenerative medicine

The term regenerative medicine was coined in 1999 to bring the areas of cell transplantation, tissue engineering, stem cells, and nuclear transfer under one umbrella with 'one unifying concept: the regeneration of living tissues and organs' (Atala 2009: 575–6). While the field itself is not new, deriving its formal roots early in the twentieth century with studies of regeneration and transplantation (Maienschein 2011), it has experienced resurgence since the derivation of human embryonic stem (ES) cells in 1998 (Shamblott *et al*. 1998; Thomson *et al*. 1998) and the creation of induced pluripotent stem (iPS) cells in 2006 (Takahashi and Yamanaka 2006) (see Box 14.1). As such, innovation in RM is an area of interest for scientists, companies and nations aiming to solve healthcare challenges.

Box 14.1 *Stem cells in RM*

Stem cells (SCs) have an important role in RM research because of their unique therapeutic potential. Stem cells have two key characteristics: (1) they have the capacity to self-renew (make exact copies of themselves) for long periods of time; and (2) they have the ability to differentiate (mature) into other more functional cell types (Ilic and Polak 2011: 118). Stem cells can be classified by their differentiation potential – the degree to which they are able to form different mature cell types. ES and iPS cells are pluripotent (they retain the ability to differentiate into cells of the three germ layers: ectoderm, mesoderm, and endoderm). Fetal and perinatal cells are, in general, multipotent (can differentiate into cells of more than one type but not necessarily into all the cells of a given germ layer), whereas adult stem cells are usually oligo- or unipotent (can differentiate into one type of cell only, e.g. muscle or neuron) (Abdulrazzak *et al.* 2010: S689; Ilic and Polak 2011: 118–19). Few adult tissues have been found to have true stem cells. Most can be more appropriately described as progenitor cells, which like stem cells can be multipotent (give rise to several different mature cell lineages) but are not capable of long-term self-renewal (contribute to the maintenance of a tissue for life) (Grompe 2012: 685; Riazi *et al.* 2009: 59–60). Research in SC biology has grown considerably across the globe in the past decade (Ben-David *et al.* 2012: 666). Because of their ability to proliferate and form numerous cell types, there is hope ES and iPS cells can be used in cell-based therapies to cure various diseases. iPS cells in particular are of great interest as they are often considered as a biologically equivalent yet more ethical alternative to ES, although this is a contested assertion (Brown 2009; Hyun 2010: 72–3; Zacharias *et al.* 2011: 637–8; Kiskinis and Eggan 2010: 52–3; Panopoulos *et al.* 2011; Puri and Nagy 2012; Robinton and Daley 2012; Yamanaka 2012: 680–1). Unfortunately, the characteristics that make these cells useful also make them technologically difficult to work with and potentially unsafe (Kato *et al.* 2012: 766; Parker and Perlingeiro 2013: 389). There is still a need for basic research, standardization and validation of the technology before most stem cells can be used therapeutically in RM (Brunt *et al.* 2012: 330–1; Helmy *et al.* 2010; Pedersen *et al.* 2012; Riazi *et al.* 2009; Sun *et al.* 2010). As such, many of the SC products and therapies currently making their way through clinical trials use adult stem cells from blood and bone marrow where safety has been better established (Bubela *et al.* 2012; Daley 2012: 741; Trounson 2009).

There is currently no 'universally agreed' upon definition of RM (REMEDiE 2011: 4), due in part to the diverse and interdisciplinary nature of the field. In fact, interdisciplinarity is a key feature of RM, as it integrates expertise from disciplines such as stem cell biology, transplantation, genetics, molecular biology, and tissue engineering (Greenwood *et al.* 2006: 63). Nonetheless, one commonly used definition proposed by Daar and Greenwood submits that:

> Regenerative medicine is an emerging interdisciplinary field of research and clinical applications focused on the repair, replacement or regeneration of cells, tissues or organs to restore impaired function resulting from any cause, including congenital defects, disease, trauma and aging. It uses a combination of several technological approaches that moves it

> beyond traditional transplantation and replacement therapies. These approaches may include, but are not limited to, the use of soluble molecules, gene therapy, stem cell transplantation, tissue engineering and the reprogramming of cell and tissue types.
>
> *(Daar and Greenwood 2007: 181)*

While a good starting point, there have been questions regarding the scientific accuracy of this broad definition, particularly the inclusion of 'repair' as a regenerative process. Thus a more simplified version of the definition was proposed: 'regenerative medicine replaces or regenerates human cells, tissues or organs, to restore or establish normal function' (Mason and Dunnill 2008: 3–4). The field is also challenged with questions regarding whether the use of certain technologies and methods should be considered within the scope of RM. While it is common to develop project-specific definitions and boundaries to clearly frame research and analysis, this chapter takes a broad view of the technologies and therapeutic modalities falling within the realm of RM. As summarized previously:

> Regenerative medicine deploys small molecule drugs, biologics, medical devices and cell-based therapies.[1] However, the term is more colloquially used to mean advanced therapies based on cells, tissue engineering,[2] developmental and stem cell biology, gene therapy, cellular therapeutics and new biomaterials (scaffolds and matrices).
>
> *(Department for Business Innovation and Skills (BIS) 2011: 6)*

14.1.2 RM industry

Several efforts have been made to gauge how the field of RM is progressing as an industry (Ginty *et al.* 2011; Jaklenec *et al.* 2012; Lewis 2013; Mason *et al.* 2011) and what this means for health care (Kessler 2007; Parenteau *et al.* 2012; Prescott 2011). As would be expected due to the diverse nature of RM, these studies find that the field is developing on different fronts and over a range of activities. Markers such as revenue, clinical trials in progress, and patent activity demonstrate the industry's positive trajectory. Currently, however, a scarcity of market products indicates that product development driven by medical need, technological feasibility, and affordability should be a priority. Additionally, scientific progress in the field has been promising (Atala 2012; Fisher and Mauck 2013; Horch *et al.* 2012), which has generated both hope and hype for the industry (Brunt *et al.* 2012: 328). Yet, it has been noted:

> A brief review in the recent bibliography concerning advances in TE and [RM] would raise the impression that 'we are almost there' … Interestingly enough, that was exactly the spirit

1 A central focus of RM research and translation efforts are in the cell therapy, using a variety of cell types and approaches (Culme-Seymour *et al.* 2012). While cell therapy with stem cells from bone marrow for the treatment of hematopoietic diseases has been in use clinically for more than 50 years, it is probably the only safe and controlled stem cell-based therapy routinely used today (Ilic and Polak 2011: 124). Essentially all other stem cell treatments remain experimental (Daley 2012: 740).

2 Tissue engineering (TE) is defined as the use of a combination of cells, engineering, materials, and methods to manufacture ex vivo living tissues and organs that can be implanted to improve or replace biological functions, usually through the use of scaffolds for restoration or regeneration of tissues or organs (British Standards Institution (BSI) 2012b: S83). While some reports use the terms TE and RM interchangeably (Jaklenec *et al.* 2012: 155), others consider RM a superordinate concept (Horch *et al.* 2012: 1158), and others bring the concepts together – TERM – capturing the broad nature of the field (Fisher and Mauck, 2013: 1).

> some 10 years ago … An ever perpetuating evolution is yet to bring the long awaited revolution in the health sector.
>
> *(Polykandriotis* et al. *2010: 2351)*

So while there are great hopes for RM, only time will tell which products and strategies will be clinically useful and translate into healthcare practice. This progress may take decades if the field follows the historical pattern of gradual technological change, and will require the development of complementary technologies, organizational innovation, and new forms of governance (Hopkins *et al.* 2007: 585). Moreover, the policies that accompany this process will require thoughtful consideration of ELSI.

14.2 Legal and ethical issues

14.2.1 ELSI in RM

Before detailing some of the principal socio-ethical concerns relevant to RM, it is important to highlight two general issues that permeate ELSI considerations. First, from a technological standpoint, RM does not present new ethical issues to those seen in other research areas (such as cell biology, genetics and genomics, transplantation and reproductive research). Rather, the complexity and variability of products and processes used in RM enhances the level of risk to patients, which increases the breadth and degree of ethical issues and raises the level of concern compared to other products (Lowenthal *et al.* 2012: 409; Trommelmans *et al.* 2009: 464). There are three main features of RM products that lead to this higher level of risk: (1) they show a certain amount of variability because they contain metabolically active cells in a dynamic extracellular environment; (2) they are intended to integrate, interact, and evolve with the body to achieve regeneration of the tissue; and (3) because of this interaction, the process of regeneration is impossible to fully reverse once started – the product itself can be removed, but the influence of cells or biomolecules on surrounding tissues cannot be undone (Oerlemans *et al.* 2013: 43–4).

Second, from a social standpoint, it may be difficult to ensure stakeholders are aligned in the development and application of socio-ethical, legal, and regulatory requirements for RM product research and development. Researchers (primarily biologists and biomaterial specialists) may have limited familiarity with ethical issues, and ethicists may be unfamiliar with the complexity of RM science and its ethical considerations (Trommelmans 2010: 24). Product developers are predominantly academics and small to medium-sized enterprises (SMEs) who may lack the development resources and experience of Big Pharma (Ginty *et al.* 2011: 242; Lewis 2013: 19, 23–9). Regulators have limited experience with RM technologies and products, so they may be conservative in their regulatory approach (McAllister *et al.* 2012: 94; Messenger and Tomlins 2011: H11). Insurers are tasked with ensuring social interests (value for money and meaningful health outcomes) are considered before incorporating RM products into public health systems (Jensen and Jacques 2011; Warren 2013). The public has been a powerful lobbying force for technological development, but is quite uninformed regarding nuanced ELSI considerations (Bubela *et al.* 2012). Furthermore, all of this is taking place globally in contexts 'where Western ethical sensitivities are not always the prime concern' (Trommelmans 2010: 24), and where legal and regulatory frameworks may not exist or be enforced. Thus within this context, three main areas of ELSI consideration are presented: the use of human cells; clinical translation; and social justice in innovation.

14.2.1.1 Use of human cells and tissues

The public is familiar with the unresolved socio-ethical, legal, and political debates around the use of stem cells (International Stem Cell Forum Ethics Working Party (ISCF-EWP) 2006), particularly with regard to the derivation of stem cells from embryonic sources (Isasi and Knoppers 2009a), but which now have expanded to include other cells like iPS (Hyun 2010; Zarzeczny *et al.* 2009). While the socio-ethical arguments remain unsettled in some jurisdictions (Isasi 2009a; Isasi and Knoppers 2006), the science continues to progress, and legislation and professional guidelines have been developed to steer the field. Some guidelines address areas like banking and databases, covering issues of governance (ethics and scientific review, oversight, etc.), protection of and access to samples and data, and benefit sharing and disposal policies (International Stem Cell Banking Initiative (ISCBI) 2009; ISCF-EWP 2012; The Organization for Economic Cooperation and Development (OECD) 2009). Other guidelines address human stem cell research and speak to areas like ethical research practices, obtaining informed consent from donors/subjects, and mechanisms for the oversight of research (International Society for Stem Cell Research (ISSCR) 2006).

In application, however, there is still a host of issues that need to be considered. There are issues that need to be addressed when considering public versus private banking systems (such as exploitation and equity) (European Science Foundation (ESF) 2010: 8), clinical versus research banks (such as access, standardization, and public investment) (Ilic and Stephenson 2013; Isasi and Knoppers 2009b) and data transfer and sharing systems (incentives, privacy, ownership) (Kato *et al.* 2012: 765–6; Trommelmans 2010: 25). Of particular concern are inconsistencies and challenges in the area of informed consent. For example, in ES cell research, issues regarding gamete and embryo donor rights and conflict of interests at recruitment warrant examination (Cohen and Majumder 2009: 83–90; Lo *et al.* 2010). Regardless of sample source, obligations regarding confidentiality, traceability, return of results and benefits, withdrawal of samples, sample storage and exchange are salient ethical issues for policymaking – to name a few (ISCF-EWP 2012; Isasi *et al.* 2011; Knoppers and Isasi 2010; Lowenthal *et al.* 2012).

14.2.1.2 Clinical translation

There are many international and national codes and guidelines that address the ethics of research involving human subjects (Office for Human Research Protections 2013). They cover issues ranging from ethics review, oversight, informed consent (at the community, family, and individual levels), subject rights, and scientific standards. In 2008, the ISSCR adopted a best practice guideline entitled *Guidelines for the Clinical Translation of Stem Cells* (*Guidelines*). The *Guidelines* address cell processing and manufacture, preclinical studies, and clinical research with the aim to ensure 'that basic stem cell research is responsibly translated into appropriate clinical applications for treating patients' (ISSCR 2008: 2). But perhaps before considering effective strategies for translation, the first question should be whether RM technology is ready for clinical translation at all. Many commentators fear experimental RM therapies are entering the clinic without the basic scientific information needed to assess mechanism of action, determine risk of side effects (safety), or establish standard processes for assessing quality and functionality (efficacy). This 'hyperacceleration' of translation is not unfamiliar to biotechnology; it is often associated with conflicts of interest, and as such can have a significant impact on human subjects as well as public trust (Wilson 2009).

The presence of strong preclinical research is a necessity for clinical translation. Currently in RM, there are limits to the utility of preclinical data, in part due to the relevance of animal

models (Henderson *et al.* 2013; Kato *et al.* 2012: 765; Trommelmans *et al.* 2009: 463). This has led to an increase in the use of first-in-human (FIH) experiments in early clinical research to determine safety and efficacy, which raises a number of ethical issues (Chapman and Scala 2012). In these early stage trials, important questions arise regarding patient recruitment (disease stage, pay-to-participate) and the use of appropriate outcome measures and controls (standard of care, sham surgeries) (Ginty *et al.* 2011: 247; Kato *et al.* 2012: 766; Niemansburg *et al.* 2013: 68–70; Sipp 2012). These aforementioned issues feed broader ones regarding the evaluation of risks and benefits, and how this impacts the informed consent process.

A favourable risk : benefit ratio is an important ethical requirement in clinical research (Niemansburg *et al.* 2013: 65–7). For many RM products, performing a definitive risk-benefit analysis is difficult since the products are novel and complex. It is challenging to compare these interventions to existing standards of care, and patient responses will vary depending on factors such as disease stage. Combine this with the prevalence of therapeutic misconception – the false belief in the clinical benefit of an experimental procedure – and obtaining genuine informed consent from participants becomes a significant challenge (Trommelmans 2010: 25). Considerations must also be made for vulnerable populations, as discussed in Chapters 5–7. Because of their long lifespan post treatment and the use of proxy consent, there are different ethical implications for research on children, which changes the risks tolerated and the procedures considered suitable for child participation (Oerlemans *et al.* 2013: 44). Even more concerning is consent for the use of experimental cell therapies in clinical situations where basic scientific evidence has not been obtained, where standard research protocols are not followed, and where regulatory and safety guidelines are not met (Bianco *et al.* 2013). This is a trend seen in the growing medical tourism industry, a topic discussed in Chapter 24.

14.2.1.3 Social justice in innovation

RM is a global industry, and many governments are investing in RM innovations. Therefore, it would be ill advised to ignore the broader social issues and implications of investment in this area. RM technologies raise a number of social justice-related questions. Who will benefit from the therapies that are developed? Will the therapies be suitable for use in the entire population (Giacomini *et al.* 2007)? As these new therapies are expected to be expensive, who should get access to them (Trommelmans 2010: 25)? Will the nations that dedicated time and resources in research be the ones to access and benefit from therapies once commercialized (ESF 2010: 10)? Is it appropriate to use RM technologies in the prevention of aging or in cosmetic enhancement (Trommelmans 2010: 25)? The ISSCR *Guidelines for Clinical Translation of Stem Cells* highlight the importance of public engagement in its discussion of social justice considerations, which includes recommendations on the reporting of results, genetic diversity in cells used, and fair access to therapies developed in both resource rich and poor countries (ISSCR 2008: 16–17). The issue of access is discussed in Chapter 22.

These discussions relate to those regarding the social objective of innovation and the repercussions of private commercialization of publicly funded national research (Caulfield *et al.* 2012; Regenberg and Mathews 2011). Considering that public support, financially and politically, continues to drive RM innovation, it is especially important that the public be aware of the implications of the research. It has also been noted that fiscal, regulatory, and scientific issues are absent from media reports and hidden from public discourse (Bubela *et al.* 2012). The cost of RM therapies is expected to be high, requiring a significant health payoff to justify its use (Giacomini *et al.* 2007: 1499). While RM will no doubt provide new and superior therapies for any number of indications, many commentators are doubtful of the anticipated savings the

healthcare system will witness given the costs and high bar for therapeutic value of RM research. In addition, governments need to assess the value of investment in RM innovation in relation to other health care approaches (Trommelmans 2010: 25). It should be considered that the economic benefit of RM may not materialize, and that using it as a justification for public funding may have unintended consequences (Caulfield 2010; Hopkins *et al.* 2007: 585–6).

14.2.2 Regulation of RM

While RM innovations promise improvements in individual and population health, there is a need to balance enthusiasm and investment with attention to resource distribution and safety. It is in determining this balance that regulations play a role, helping to direct product development and ensure safety and efficacy. Alongside governmental hopes that RM will reduce healthcare costs and stimulate economies (Alberro 2012: 605; BIS 2011: 3), there is a concern that RM products pose challenges to existing regulatory systems (Bravery 2010: S789). As we have discussed, RM can incorporate a combination of drugs, medical devices, and/or cell therapies. The complexity and novelty of these products make them difficult to classify for regulatory purposes and stretch the limits of our existing knowledge about how to assess their safety and efficacy (von Tigerstrom 2011: 84). The regulatory process is only one element in a complex network of biomedical research governance that includes institutions, systems, collaborations, and economical and reputational pressures (BIONET 2010a: 42). As we learned from the attempted translation of gene therapy technologies, however, preclinical and clinical regulation of novel therapies is a key lever in steering the new industry (Wilson 2009: 324). Moving forward without effective regulation not only puts patient safety at risk, but also undermines the social trust and support in RM that has been pivotal to its development.

14.2.2.1 Role of regulations

The primary role of regulation is to ensure new products and therapies are safe and effective. In the research setting, scientists and clinicians regard laws and regulations as an essential part of any ethical framework in biomedical research (BIONET 2010a: 13). Consequently, since RM is a global endeavour, regulatory coherence, regulatory gaps, and implementation of ethical standards on the ground are important considerations for multinational research collaborations (BIONET 2010b: 41–3). In the context of commercialization, experience in medical innovation has shown that clear and effective regulations are an essential facilitator of progress in this process (Messenger and Tomlins 2011: H11). Regulatory agencies play a central role in controlling the structure, cost, and approach of the regulatory system, which in turn influence the companies and products entering the market (Tait *et al.* 2007: 7–8). Regulations will change and adapt as the science advances, and as researchers and regulators learn more about the properties of novel therapies. However, it is the regulatory system and clinical trial process that ensure public safety during this time of scientific advancement (Werner *et al.* 2012: 103).

14.2.2.2 Challenges with regulations

Despite its vital role, the regulatory system has faced its share of challenges in the RM field. The diversity of stakeholders (each with their own interests) makes it difficult to cultivate an ongoing dialogue with regulators, which makes policy development challenging (Whittlesey and Witten 2012: 595). A legitimate lack of knowledge and experience with RM products hinders the

establishment of standard regulatory requirements, and regulators are required to review applications on a case-by-case basis (BIS 2011: 47). In turn, product developers, at times under direction from inexperienced regulators, can waste time collecting the wrong data for regulatory submissions (Plagnol *et al.* 2009: 554). In addition, there are concerns that regulatory systems give multinational companies a dominant role over innovation in healthcare through lengthy, expensive, and complex regulatory requirements that stifle new entrants and innovations (Tait *et al.* 2007: 29–30). Even countries with mature regulatory regimes struggle to maintain an efficient regulatory system for RM-related products. A recent report by the UK House of Lords Science and Technology Committee, which focused on the translation and commercialization of RM research, found '[t]he twin challenges of improving perceptions of the regulatory system and streamlining it are so great that both immediate and long-term action are needed' (House of Lords 2013: 42).

14.2.2.3 Importance of product classification

Classification is an essential consideration in regulating new products. The type of product or therapeutic approach selected during product development impacts what regulatory category applies and, in turn, the regulatory requirements that must be adhered to. Because classification dictates the scientific evidence required, it is important for researchers to be able to predict classification decisions with some certainty (von Tigerstrom *et al.* 2012: 626). In fact, it has been recommended that RM product developers allow regulations to drive the innovation process in an effort to avoid regulatory burdens down the road (Ginty *et al.* 2011: 245). Unfortunately, many RM products at this stage are unique and definitions and product classifications are 'not yet settled' (Harmon *et al.* 2011: 2). Product classification has a significant effect on the degree of efficacy and safety that must be demonstrated before the product can be approved for patient use, and hence impacts development time and costs (Messenger and Tomlins 2011: H12). As such, it is on the product classification front that many of the regulatory and legal battles over RM technologies and their uses are occurring (see Boxes 14.2 and 14.3).

14.2.2.4 Importance of standards and harmonization

While product classification is important for the regulatory path, the technical standards used to evaluate RM products will dictate the difficulty in navigating this path. If clear standards (addressing specifications, methods, practices and/or definitions) are in place, a product's variability will be minimized and its safety will improve. Standard setting regulations and guidelines require that scientifically established norms and requirements (i.e. standards) be followed. Examples include Current Good Manufacturing Practice (CGMP) and Current Good Tissue Practice (CGTP). An Ernst & Young review concluded there was a significant, yet often unrecognized, role for standards in creating and developing emerging technologies (BIS 2011: 35).

Unfortunately, RM will prove a difficult field in which to establish standards. A therapy that uses living cells cannot be standardized in the same way as a conventional pill: different quality and safety requirements are needed (Duffy 2011). Although standardization is generally useful in alleviating uncertainty, there is also a risk that efforts to adopt uniform standards will raise the regulatory bar 'too high' (von Tigerstrom *et al.* 2012: 627). Research also indicates that it is difficult to establish the proper infrastructure to meet regulatory requirements, especially for investigators from educational institutions. Compliance with quality standards such as CGMP is onerous and costly, and thus necessitates sufficient funding to meet these standards (von Tigerstrom *et al.* 2012: 627).

Box 14.2 *National challenges to EU regulation: the Stamina Foundation*

As described by Bianco *et al.*, the Stamina Foundation in Italy performs what it calls a novel proprietary method of mesenchymal SC (MSC) in vitro isolation and differentiation into neurons, for which there is no retrievable scientifically published account (patent applications have been submitted in the US and European patent offices under the names of Foundation members). The cell preparation is then injected into patients to treat a range of neurological diseases including lysosomal storage diseases, Parkinson's disease and other kinds of irreversible brain or spinal damage. Treatments were taking place in collaboration with a public hospital. From a regulatory perspective, the treatment was intended for 'compassionate use,' defined as a treatment unapproved, but tested as safe, and with preliminary evidence of potential efficacy in the absence of a sound therapeutic alternative to treat a single case outside of a formal clinical trial. The EMA has deferred to member countries for specific regulations regarding its use (*Regulation (EC) No. 1394/2007*, article 28). In 2006, the Italian government issued rules intended to provide guidance in these cases. However, the rules were insufficient, creating room for unauthorized and unproven treatments. Multiple violations were detected by the Italian regulatory body, the Italian Medicines Agency (AIFA), which ordered the practice to be stopped in 2012. In addition, testing of a vial of cells (that were to be infused into patients) following an inspection of the Stamina laboratory in Brescia found that the claims for the cell identity, purity, and properties could not be supported (Bianco *et al.* 2013: 2–3).

The shut-down of the Foundation's activities led to mass public outcry and lawsuits by patients and families. Multiple courts ruled in favor of the patients and ordered the hospital to resume treatments in spite of the AIFA ban. The Italian government was then forced to issue *ad hoc* regulatory measures. Under Senate debate, regulations and good manufacturing practice (GMP) requirements intended to apply were cancelled, and instead they proposed equating stem cell therapies with direct transplantation of tissues and cells. This would cancel their definition as 'medicines' and thus exempt them from AIFA and EMA regulation and oversight (Bianco *et al.* 2013: 2). This signalled a striking departure in policy which stunned the scientific community, who considered the Stamina Foundation's therapy highly questionable and feared the lack of regulatory oversight would hurt patient safety and undermine the credibility of the cell therapy field (Margottini 2013a). In the end, cooler heads prevailed and stem cell therapies will remain regulated as advanced therapies. While Stamina continued to treat patients already undergoing the therapy, it could not accept new patients. However, the new bill also set aside €3 million for a clinical trial of the Stamina treatment, a large sum considering stem cell research last received national support in 2009 – to the amount of €8 million (Margottini 2013a). The clinical trial was to be led by AIFA, the Italian National Health Institute, and the National Italian Transplant Centre, be designed by a scientific board, and follow rules set out by the EMA and AIFA under *Regulation (EC) No. 1394/2007*. These requirements included using cells manufactured according to GMP, which Stamina's director claimed would hamper the efficacy of the treatment (EuroStemCell 2013; Margottini 2013a). Additional issues quickly emerged as evidence surfaced that the method's patent application contained falsified data and the Foundation postponed commitments to reveal the methodology to the trial design committee (Abbott 2013). Ultimately the committee rejected the method for use in a clinical trial. With the Ministry of Health announcing that a clinical trial will not take place, the fate of patients currently undergoing treatment is uncertain (Margottini 2013b).

Box 14.3 *Challenge to FDA authority: Regenerative Sciences*

The most notable legal challenge to the regulatory power of the FDA in RM, specifically cell therapy, is that of Regenerative Sciences Inc. of Colorado. This ongoing legal battle began in 2008 when the FDA sent the Medical Director of Regenerative Sciences a letter stating that, based on information obtained on the company website, the FDA had determined the company was promoting the use of MSCs as biological drugs (under section 201(g) of the *Federal Food, Drug and Cosmetic Act* 1938 (*FD&C Act*) and section 351(i) of the *Public Health Service Act* 1944 (*PHS Act*)), and, as such, it falls under FDA regulation. The procedure (Regenexx™) involves removing the patient's bone marrow, which is then sent to a lab, isolated and then grown and expanded using growth factors drawn from the patient's blood. The cells are then injected into the patient to regenerate bone and cartilage for the repair of orthopedic conditions. The FDA claimed that as the cells are intended for the cure and treatment of disease in man, they can be considered a biological drug. Therefore an Investigational New Drug Application is required for clinical use in humans, and a Biological Licence Application, which reveals the safety and efficacy for the intended use, is required for interstate commerce. The human cells, tissues, and cellular- and tissue-based products (HCT/Ps) in question did not meet the requirements for exclusion from the licensure requirements (21 CFR 1271.10). Therefore, the firm was found in violation of the Acts (Malarkey 2008).

This letter was followed up by multiple inspections in 2009 and 2010 which found that the laboratory in question did not operate in conformity with CGMP. Regenerative Sciences then filed a complaint against the FDA claiming it did not have jurisdiction to regulate the homologous use of stem cells. After a series of decisions and motions in 2010 and 2011, the most recent ruling came on 23 July 2012 in *US* v. *Regenerative Sciences, LLC et al.* (2012) 878 F. Supp. 2d 248. The question presented was whether the Regenexx™ procedure constituted a biological drug subject to FDA regulation or whether it is merely an intrastate method of medical practice subject only to the laws of the State of Colorado. The FDA asserted that the Regenexx™ procedure constituted the manufacturing, holding for sale, and distribution of an unapproved biological drug product, and that Regenerative Sciences had also violated the *FD&C Act*'s prohibition on adulteration and misbranding a drug. Regenerative Sciences argued that the Regenexx™ procedure constitutes the practice of medicine as defined by Colorado law and that the FDA lacks jurisdiction to regulate it. In addition, it claimed that the procedures occur entirely intrastate and is not covered by the Commerce Clause or the *FD&C Act*, which limit federal power to interstate commerce. The court found in favor of the FDA on all counts, and dismissed Regenerative Sciences' eight counterclaims. While Regenerative Sciences agreed to stop using the Regenexx™ procedure pending the lawsuit, the court believed there to be a 'cognizable danger of recurrent violation' and granted the FDA's request for a permanent injunction (*US* v. *Regenerative Sciences, LLC et al.*). Officials from Regenerative Sciences have said they plan to appeal the ruling (Swinderman 2012). However, commentators have noted that 'the rules of statutory interpretation and administrative procedure will weigh in the agency's favor in this case, especially with this particular set of facts' (Chirba and Noble 2013: 4). They also noted that suing an agency is often a losing battle, and question whether such cases will do much to lower regulatory hurdles (Chirba and Noble 2013).

During the past decade, regulatory frameworks and the development of standards have improved, and this will facilitate commercialization (Messenger and Tomlins 2011: H16). It is important to note that national standards are of limited value in a global enterprise such as RM: standards must be agreed upon at the international level in order to maximize their utility. Harmonizing international policy, therefore, is especially important in RM where standardization of processes and products is not always attainable. Harmonization – the adjustment of inconsistencies among different procedures or systems to make them uniform or mutually compatible – can range from informal cooperation to the development of common technical requirements (von Tigerstrom 2008: 657).

14.3 Regulatory approaches

14.3.1 Regulatory frameworks

Several jurisdictions have begun the process of updating their regulatory systems to integrate increasingly novel and complex technologies like RM, which do not fit into existing frameworks designed for pharmaceuticals and medical devices. In particular, the European Union (EU) and the United States (US) developed new governing bodies with the relevant expertise, and regulations to establish new product categories, which are a starting place for the regulation of RM products. Other jurisdictions, such as Canada, to date have relied on a more informal approach (via policies) to manage RM products through existing regulations. Tables 14.1 to 14.3 (pages 256–261) offer a brief overview of the regulatory systems in the EU, the US, and Canada, focusing primarily on the regulatory approach required for cell-based RM therapies that may consist of other components (i.e. are combination products). In particular, the regulations highlight product classification, standards for the use of cells and tissues, requirements for clinical testing, manufacturing practices, authorization for sale, and product surveillance.

14.3.2 Summary: potential for harmonization

This tabular description of each country's regulatory system is by no means exhaustive. It omits many details, such as labeling, and areas that are relevant to a variety of RM products, such as the use of medical devices. However, it does illustrate how different jurisdictions have adapted their regulatory systems to the new, complex products emerging in RM. In particular, it allows us to identify the similarities and differences in regulatory approaches, as well as their weaknesses and strengths. Fortunately, there is general agreement among the three jurisdictions with regard to the regulatory approaches used. In fact, an analytical report issued by the Tissue Engineering and Regenerative Medicine International Society (TERMIS) identified six similarities between the US Food and Drug Administration (FDA) and European Medicines Agency (EMA) approaches (which also apply to the Canadian context). They:

1. Adopt a risk based/tiered approach to evaluate specific risks unique to each submission.
2. Identify specific pathways for therapies to reach market quickly if they are safe and effective.
3. Promote long-term follow up on safety, efficacy, and durability of products and outcomes.
4. Enter into agreements for parallel advice and collaborations with industrial organizations on the regulation of product development and conduct joint reviews.
5. Encourage sponsors to meet so agencies can offer specific guidance to sponsors in key technological areas of concern.

6. Accept international studies for marketing applications if they meet specific requirements for data validity, GCP, and appropriate supporting information.

(Bertram et al. *2013: 192)*

While most commentators have been in favor of the EMA's approach to the regulation of these complex products, implementation will dictate whether the regulations are effective in protecting the public while encouraging innovation. Indeed, differences in implementation at the national level could undermine the establishment of safety and effectiveness standards. For example, each member state will have different ethics committees, ethical viewpoints, and oversight mechanisms, which may impact how clinical trials are performed (Ginty *et al.* 2011: 247). In addition, the potential for legal maneuvering at the national level could compromise regional regulatory efforts (see Box 14.2). However, the EU regulatory approach offers great potential in setting an example for harmonization – creating overarching standards while respecting national interests. By having a centralized regulatory approach, the US has the potential to offer a more consistent regulatory regime, although concerns have arisen regarding the effectiveness of the Primary Mode of Action approach to regulating combination products.

As a dominant force in both RM research and commercialization, the US has the privilege of being able to set its own regulatory path, independent of other jurisdictions. Nonetheless, perhaps more than any other jurisdiction, the FDA faces legal challenges to its authority (see Box 14.3). Considering the global nature of RM, the impact of its regulatory approach in and outside of US borders should be considered. This could influence countries like Canada, which to date has had limited regulatory guidance for RM products. Instead, regulators are guided by policy addressing areas such as combination products, which is interpreted and implemented on a case-by-case basis. While individual case analysis provides regulators with the flexibility required to manage the unique needs of each product, it also allows for potential arbitrary applications or inconsistencies, and leaves researchers and product developers with little guidance or certainty. Lastly, it is especially important for smaller jurisdictions like Canada to ensure its regulatory system is harmonized with those of larger entities like the EU and the US to fully participate in the RM field. Harmonization is thus a stated goal in the Canadian regulatory modernization efforts, and an important area of discussion in developing countries as well (Viswanathan *et al.* 2013).

14.4 Emerging issues

14.4.1 Moving forward on the regulatory front

Balancing clarity and consistency with flexibility is a particular challenge for regulators, as this balance is essential to facilitate the emergence of a new and evolving field. Communication is often cited as the key to addressing the challenges regulatory bodies face in establishing clear, harmonized regulatory frameworks with standards that are responsive to the changing needs of the industry. To ensure quality, safety and efficacy of novel products and therapies, regulators must develop an understanding of the scientific issues at hand, and rely on early contact with industry to address matters of product classification, scientific uncertainty, and product certification (Harmon *et al.* 2011: 3). They must work with scientists to frame safety guidelines based on acceptable risk, and promote involvement and communication from standard-setting organizations, health authorities, production, and preclinical testing specialists (Goldring *et al.* 2011: 626). For these collaborations to occur, a regulatory agency must have adequate resources and

Table 14.1 Regulation of RM products in the EU: Advanced Therapy Medicinal Products

Introduction

The European Medicines Agency (EMA) is responsible for the scientific evaluation of applications for market authorization of new products via the EU's centralized procedure. The EU has created a new product category, Advanced Therapy Medicinal Products (ATMPs), and an expert committee, the Committee for Advanced Therapies (CAT), specifically to manage the complex products entering the regulatory system from the RM field. The associated regulations (*Regulation (EC) No. 1394/2007*) outline market authorization procedures and requirements specific to ATMPs, referencing additional regulations as they apply.

***Regulation* (EC) No. 1394/2007 on Advanced Therapy Medicinal Products and amending *Directive 2001/83/EC* and *Regulation* (EC) No. 726/2004**

Regulation (EC) No. 1394/2007 lays down the specific rules concerning the authorization, supervision and pharmaco-vigilance of ATMPs. ATMPs (defined as a gene therapy medicinal product, somatic cell therapy medicinal product, or tissue engineered product) are biological medicinal products (any substance presenting as having properties for treating or preventing disease, produced or extracted from a biological source) as defined under Directive 2001/83/EC (Annex I). However, because of the novelty, complexity and technical specificity of ATMPs, specially tailored and harmonised rules were needed.

Regulation (EC) No. 1394/2007 states that, due to the complexity of combined ATMPs containing viable cells or tissues, whatever the role of the medical device, the pharmacological, immunological, or metabolic action of these cells or tissues should be considered to be the principal mode of action of the combination product. Such combination products should always be regulated under this Regulation.

Article 3 states where an ATMP contains human cells or tissues, the donation, procurement, and testing of those cells or tissues shall be in accordance with Directive 2004/23/EC. It requires member states to put in place a quality system based on the principles of good practice.

Clinical trials on ATMPs should be conducted in accordance with principles and ethical requirements laid down by Directive 2001/20/EC and Commission Directive 2005/28/EC, which, for example, require member states to establish Ethics Committees and observe good clinical practice. Article 4 of *Regulation (EC) No. 1394/2007* states the Commission shall draw up guidelines on good clinical practice specific to ATMPs.

Supplemental Regulations:

2001/83/EC: community code relating to medicinal products for human use. It requires an application for a market authorization, which is to be issued before a medicinal product may be placed on the market.

Annex I: analytical, pharmaco-toxicological, and clinical standards and protocols in respect of the testing of medicinal products (replaced by *2003/63/EC*). It details the requirements for the Marketing Authorization application dossier.

2004/23/EC: on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage, and distribution of human cells.

2001/20/EC: on the approximation of the laws, regulations, and administrative provisions of the member states relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use.

Manufacturers of ATMPs should be in compliance with the principles of good manufacturing practice as set out in the Commission Directive 2003/94/EC, and adapted where necessary to reflect the specific nature of those products. Article 5 of *Regulation (EC) No. 1394/2007* states the Commission shall draw up guidelines in line with the principles of good manufacturing practice and specific to ATMPs. The centralized authorization procedure, as laid down in *Regulation (EC) No. 726/2004*, is compulsory for ATMPs. It outlines the application procedures and requirements (such as the submission of preclinical and clinical data) to obtain market authorization from the European Commission. The opinion is drawn up by the Committee for Medical Products for Human Use under guidance from CAT. The application shall be refused if the quality, safety or efficacy of the product has not been demonstrated. Marketing authority cannot be granted by individual member states. Article 9 of *Regulation (EC) No. 1394/2007* states where a combined ATMP is concerned, the whole product shall be subject to final evaluation by the EMA. Article 14 states that in addition to requirements for pharmacovigilance described in *Regulation (EC) No. 726/2004*, the applicant shall detail the measures envisaged to ensure the follow-up of efficacy of ATMPs and adverse reactions. Where there is particular cause for concern, a risk management system must be set up or specific post-marketing studies be carried out. Article 15 states that the holder of a marketing authorization shall establish a system of ensuring that the individual product and its starting and raw materials can be traced. The hospital, institution or private practice where the ATMP is used shall establish a system for patient and product traceability.	*2005/28/EC*: laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products. *2003/94/EC*: laying down the principles and guidelines of good manufacturing practice in respect of medicinal products for human use and investigational medicinal products for human use. *EC No. 726/2004*: laying down community procedures for the authorization and supervision of medical products for human and veterinary use. It created a centralized authorization process within the EMA and established the Committee for Medical Products for Human Use. It is distinguished from *2001/83/EC* which recognizes authorizations given by the competent authority of one member state and requires they be recognized by all member states.

EU Directives and Regulations can be found at EUR-Lex: http://eur-lex.europa.eu/en/index.htm. Additional information can be found on the EMA website: http://www.ema.europa.eu/ema/. For an analysis see Ginty *et al.* (2011: 246–7); Messenger and Tomlins (2011: H13); BSI (2012a).

Table 14.2 Regulation of RM products in the US: human cells, tissues, and cellular and tissue-based products

Introduction	
The Food and Drug Administration (FDA) is the centralized department mandated with regulating therapeutic products in the US, including licensing for clinical trials and market authorization. It executes its mandate via three departments of relevance to RM products: the Center for Drug Evaluation and Research (CDER), the Center for Biologics Evaluation and Research (CBER), and the Center for Devices and Radiological Health (CDRH). To manage issues that have arisen in the development of new RM technologies, the regulatory category of human cells, tissues, and cellular and tissue-based products (HCT/Ps) was created (21 CFR 1271). In addition, regulation was implemented to guide management of combination products (21 CFR 3). The Office of Combination Products (OCP) was created to develop guidance and help determine which center should lead the regulation, based on the products' primary mode of action (PMOA).	
***Title 21 Code of Federal Regulations Part 1271* Human Cells, Tissues, and Cellular and Tissue-Based Products (21 CFR 1271)**	
21 CFR 1271 determines the applicable regulatory regime for cell therapy products and requires the registration of HCT/Ps (articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient). It distinguishes between HCT/Ps regulated under section 351 of the *Public Health Service Act* 1944 (*PHS Act*) and section 361 of the *PHS Act*. To be regulated solely under section 361, a product must (1) be minimally manipulated, (2) be intended for homologous use, (3) not combine cells with another non-exempted article, and (4) not have a systemic effect or be dependent on the metabolic activity of living cells for its primary function (excluding exemptions). As cell-based RM products would typically not meet these criteria, they are generally regulated under section 351 of the *PHS Act*. In addition to all other applicable regulations, section 351 *PHS Act* products must register with the FDA, submit a list of HCT/Ps manufactured, and comply with subparts B (procedures for registration and listing), C (donor eligibility: screening and testing), and D (Current Good Tissue Practice: to prevent introduction, transmission or spread of communicable diseases) of 21 CFR 1271.	**Supplemental Regulations:** 42 USC 262 (351 *PHS Act*): Regulation of Biological Products. Defines biological product and requires a licence for their sale. It also outlines labeling, inspection, and recall rights and penalties for non-conformity. 42 USC 264 (361 *PHS Act*): Regulations to Control Communicable Diseases. Authorizes the Surgeon General to make and enforce regulations to prevent the introduction, transmission, or spread of communicable disease. For a *351 PHS Act* product, 21 CFR 58 applies: Good Laboratory Practice for Nonclinical Laboratory Studies.
***Title 21 Code of Federal Regulations Part 3* Product Jurisdiction (21 CFR 3)**	
For combination products, 21 CFR 3 also applies. This implements section 503(g) of the *Food, Drug, and Cosmetic Act* (*FD&C Act*) 1938. Because of the complexity of the products, there is no single development paradigm for combination products. Three potential product categories are recognized: • Drugs: Regulated by 21 CFR parts 200–299, 300–369 under CDER, requires a new drug application (NDA) for market authorization.	21 USC 353(g) (503(g) *FD&C Act*): Exemptions and consideration for certain drugs, devices, and biological products. It states in the case of combination products that the PMOA dictates lead agency and regulatory regime.

• Devices: Regulated by 21 CFR parts 800–898 under CDRH, requires a premarket approval application (PMA) for market authorization. • Biological products: Regulated by 21 CFR parts 600–680 under CBER, requires a Biologics Licence Application (BLA) for market authorization. The centre which receives the premarket application will determine the PMOA (most important therapeutic action) of the product and assign the lead center accordingly. The OCP consults, resolves disputes, and ensures timely review. No specific GMP guidelines exist for combination products so each set apply: 21 CFR parts 210 and 211 for finished pharmaceutical and drug products, and/or 21 CFR part 820 for devices. Parts of biological product regulations may apply (21 CFR 600–680), but there are no GMP requirements specifically referenced for HCT/Ps. For clinical investigations of combination products, typically only one investigational application is required. This is either an IND application (21 CFR 312 – applies to biological drugs) or Investigational Device Exemption (IDE) (21 CFR 812). The objectives of the IND review are to assure the rights of subjects and the quality of scientific evaluation of the product. This includes study approval by an Institutional Review Board and following the principles of good clinical practice.	21 CFR 210: current good manufacturing practice in manufacturing, processing, packing, or holding of drugs; general. 21 CFR 211: Current good manufacturing practice for finished pharmaceuticals. 21 CFR 820: Quality system regulation. 21 CFR 312: Investigational New Drug Application. It exempts drugs from premarketing approval requirements for shipping a drug in the context of a clinical trial. Describes IND application requirements as they apply to section 351 *PHS Act* products.
***Title 21 Code of Federal Regulations Parts 600–680* Biological Products (21 CFR 600–680)**	
21 CFR 600–680 outlines requirements for biological product licensing. 21 CFR 600 outlines standards for establishments, including personnel and records. 21 CFR 601 outlines biologics licensing filing procedures, including the demonstration of preclinical and clinical data. Approval of a BLA constitutes a determination that the establishment(s) and the product meet applicable requirements to ensure the safety, purity, and potency of the product. As a 351 product, parts of section 505(o) and 505-1 of the *FD&C Act* (21 USC 355) also apply. This includes post-marketing studies and/or clinical trials, and the development of risk evaluation and mitigation strategies (REMS) if deemed necessary.	21 USC 355(o) (*505(o) FD&C Act*): New Drugs – Post-market studies and clinical trials; labeling. 21 USC 355-1 (*505-1 FD&C Act*): Risk evaluation and mitigation strategies.

US Acts, Regulations and additional information can be found at http://www.fda.gov/. For an analysis see Ginty *et al.* (2011: 245–6); Lee *et al.* (2010) Messenger and Tomlins (2011: H12–13); BSI (2012a).

Table 14.3 Regulation of RM products in Canada: biologic drugs

Introduction	
Health Canada's (HC's) Health Products and Food Branch (HPFB) is responsible for the oversight of therapeutic products. It executes its regulatory responsibilities through the Therapeutic Products Directorate (TPD) for drugs and devices, and the Biologics and Genetic Therapies Directorate (BGTD) for biologics, cell, and genetic therapies. It also maintains the Therapeutics Products Classification Committee (TPCC), which can be consulted to make recommendations on the classification of products and the development of related policies. There are two main categories of products in the Canadian system: drugs and devices. A subset of the drug category is the biologic drug, which has been interpreted to include cell-based products. There are currently no specific regulations that deal with combination products or cell therapy products. HC relies on policy which utilizes the product's principal mechanism of action (PMOA) for classification.	
Food and Drugs Act	
The *Food and Drugs Act* 1985 is the enabling legislation for the regulation of health products. Part I of the *Act* outlines restrictions for the sale of food, drugs, cosmetics, and devices. Part II deals with administration and enforcement, such as inspections and marketing authorizations. Schedule D identifies drugs categorized as biologics. While not specifically listed, cell-based products are considered by HC to be Schedule D biologic drugs. The *Act* is implemented via Regulations: *Food and Drug Regulations*; *Medical Devices Regulations 1998*; *Safety of Cells, Tissues and Organs [CTO] for Transplantation Regulations* 2007; *Natural Health Products Regulations* 2003; and *Processing and Distribution of Semen for Assisted Contraception Regulations* 1996. The *Food and Drugs Act* does not specifically mention combination products. The policy adopted states that where the PMOA by which the claimed effect or purpose is achieved by pharmacological, immunological, or metabolic means (*in vivo*), the combination product will be subject to the *Food and Drug Regulations*; otherwise it will be regulated under the *Medical Device Regulations*. As such, cell-based products will primarily fall under *Food and Drug Regulations*, specifically Part C – Drugs. The sponsor would either apply to the TPD or the BGTD for classification. The Directorates will consult, and if they cannot agree, it is referred to the TPCC.	**Supplemental information:** Modernization of Canada's regulatory regime is currently underway, involving a comprehensive review of the regulatory framework in order to create a more flexible system with common principles that apply across product lines. *Safety of Cells, Tissues and Organs for Transplantation Regulations* apply only to minimally manipulated cells and tissues. It does not apply, for example, to non-homologous use, autologous use, medical devices with cells (Part 3 *Medical Devices Regulations*), or cells and tissues used in a clinical trial (Part 5 *Food and Drug Regulations*). Policy: Drug/Medical Device Combination Products, Effective Date: 2006/03/01

***Food and Drug Regulations* Part C**	
Food and Drug Regulations state no person shall sell a drug that is not labeled as required by these *Regulations*, which includes the need to apply for and receive a Drug Identification Number (DIN). The introduction also outlines adverse reaction reporting requirements. Part C Division 1A describes the process for applying for an establishment licence. It defines activities for which GMP compliance is to be demonstrated before the issuance of a drug establishment licence. Part C Division 2 details the GMP required for the sale of a drug. GMP guidance was written with the view to harmonize GMP standards with those from other countries and international organizations. Mutual Recognition Agreements (MRAs) establish recognition of GMP compliance certification between regulatory authorities that are designated as equivalent. Part C Division 5 details the requirements for the clinical trial application (CTA) that requests permission to distribute the drug to investigators for use in clinical trials involving human subjects. The CTA contains information regarding the objectives of the proposed trial and data to support product quality. If benefits outweigh the risks, a No Objection Letter is issued. Trials require informed consent and good clinical practice. Research Ethics Board approval must be obtained at each institution and sponsors should register their clinical trials. Part C Division 8 describes the requirements for new drug submissions. A new drug submission shall contain sufficient information and material to assess the safety and effectiveness of the new drug (including ingredients, locations, clinical effectiveness, labels, etc.). A Notice of Compliance (NOC) is issued after satisfactory review of a submission, finding the benefits outweigh the risks of the product. If a NOC has been issued the manufacturer must maintain records for the potential audit of any information. Upon receipt of a NOC, a DIN will be assigned.	DIN is a unique eight-digit number that permits the manufacturer to market the drug in Canada. Lets users know the product has passed review and serves as a tool to track the product. For Biologics, Radiopharmaceuticals and Genetic Therapies: in addition to the standard drug requirements, sponsors must include more detailed chemistry and manufacturing information. In addition, the new drug submission process requires Product Specific Facility Information (manufacturing methods) and an On-site-Evaluation Inspection. If a NOC and DIN are obtained, products are monitored through a lot release schedule where for higher-risk products each lot is tested and additional surveillance is performed. A Notice of Compliance with conditions (NOC/c) may also be issued under the NOC/c Policy. It requires the sponsor to undertake additional studies to confirm the clinical benefit of the product. It is restricted to promising new drug therapies for serious conditions with no alternative therapy or that will offer a significant improvement on risk-benefit.

Canadian Acts and Regulations can be found at Justice Laws Website: http://laws-lois.justice.gc.ca/eng/. Additional information can be found on the HC website: http://www.hc-sc.gc.ca/index-eng.php. For an analysis see von Tigerstrom (2011).

expertise (Bravery 2010: S792). Unfortunately, regulatory bodies are often 'chronically underfunded' and their capacity – including expertise, personnel, and financial resources – cannot keep pace with the demands made of them (von Tigerstrom 2011: 117–20). This may present a significant barrier to progress.

Ultimately, the ability of a regulatory system to recognize and manage the potential hazards of RM products is central to its success. With new technologies come new and unknown risks, and regulators are tasked with balancing these risks with benefits to patient health (Messenger and Tomlins 2011: H11; Bravery 2010: S793–S794). When assessing risk-benefit, all the complex steps moving from bench to bedside are relevant and consequently inform ethical decision-making (Hyun 2010: 74). The establishment of sufficient trial end points, post-trial follow-up, and trial registries will be essential to determining long-term patient outcomes and for future evaluations of risk and benefit (Trommelmans *et al.* 2009: 464). Clinical trial registries add to the information base, and are increasingly encouraged or required by regulatory bodies (Health Canada 2013; Isasi 2009b; US National Institutes of Health 2013). Similarly, post-market surveillance is important because RM products are less predictable in the long term (Oerlemans *et al.* 2013: 46). The collection and utilization of this type of data to inform safety evaluations should be an industry priority.

While regulatory frameworks must be 'alive' to innovation, they must also be 'conservative' in order to ensure patient safety in a potentially high-risk area like RM (Harmon *et al.* 2011: 4). Regulatory reforms are needed to make existing systems more efficient and effective, but it is important to remember most therapies are found wanting during clinical trials (Werner *et al.* 2012: 100). This is an issue of science rather than of regulation. Uncertainty regarding data requirements comes from an incomplete understanding of the science underlying a product, and for any new technology the challenge is to determine what data is required to show safety, efficacy, and quality (von Tigerstrom 2011: 120). This is a natural part of the industry applying scientific developments in emerging technologies, and it is expected that many of these issues will be resolved through technological improvements and more research into the science (BIS 2011: 33).

When discussing what the emerging field of RM needs from its regulatory system, many would agree that a clear regulatory framework, even if strict, is paramount (Plagnol *et al.* 2009: 554). However, it is also important to keep in mind that technocratic reactions to new science are cumulative, and increased regulatory demands do not necessarily result in better decisions (Harmon *et al.* 2011: 4). This would imply that being too aggressive in the application of complex legal and regulatory measures at the early stages is ill advised. Finding the appropriate balance is the task at hand.

14.5 Conclusion

The advancement of RM science offers the potential for cutting-edge solutions to healthcare challenges, but will require concerted efforts in policy and regulations to ensure these solutions are safe and socially beneficial. Ethical, legal, and social justice issues arise from various aspects of the technology, such as from the use of human cells (which are variable and risky), from the clinical translation of novel and complex products, and from the commercialization of publicly funded research. These areas have been explored and guidelines have been developed to aid the innovation process. However, gaps exist and questions regarding the validity of the informed consent of participants and of public awareness at all stages of research and development pervade assessments of the industry. Clear and effective regulatory regimes provide a mechanism to mitigate some of the potential negative consequences of RM innovation. Regulations ensure that

products entering the market are of high quality and are safe and effective. Unfortunately, the long, complicated and expensive regulatory pathways currently in place for existing therapies are often unsuitable for the complex cell-based products in development, and unbearable to the SMEs developing them.

Crafting regulatory systems appropriate for RM products is now the challenge. Governments recognize this task, and are beginning to create new regulatory bodies and regulatory categories able to address the unique nature of RM innovations. These efforts have been mindful of the importance of standards in manufacturing and clinical testing. As the science and regulations co-evolve, industry and regulators will need to be cognizant that international harmonization is equally important in this global, interdisciplinary, and fast-paced field.

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15
E-health

Stefaan Callens and Laura Boddez

15.1 Introduction

The international healthcare market is developing rapidly and different healthcare systems are converging. Privately financed healthcare systems pay more attention to justice and equal access. Publicly financed healthcare systems are introducing cost-efficiency techniques privately financed healthcare systems used in the past. At the same time, healthcare actors are increasingly leaving their own national borders to participate in cross-border care. With cross-border activities in healthcare growing more frequent, *patients* tend to be treated in other countries to avoid long waiting lists. Alongside this, *consumers/patients* use the Internet to search for medical information or to order medicinal products from pharmacies located in other countries. Moreover, *doctors* demand more and varied telematic information from their colleagues than previously. *Healthcare professionals*, *hospitals* and *laboratories* increasingly rely on information and communication technology (ICT) applications to disseminate health data for treatment and other purposes throughout several countries. Many healthcare institutions (like national health insurers, hospitals, laboratories, etc.) are becoming more involved on the international healthcare stage and communicate health data between member states for treatment and other purposes. Against the backdrop of these developments, e-health plays an important role in both developed and developing countries (World Health Organization (WHO) 2012a: 7).[1] It is clear that e-health in itself has an impact on healthcare systems and healthcare actors. Given the supportive role of ICT-development in wider systems, such as social welfare systems, it is reasonable to believe it will also influence healthcare systems.

E-health is popularly defined as 'health services and information delivered through the Internet and related technologies' (European Group on Ethics in Science and New Technologies to the European Commission 2012: 33; Kelly 2011: 27). E-health describes the application of information and communication technologies across the whole range of functions that affect the healthcare sector. According to the European Commission, e-health comprises the following

1 However, the implementation of e-health services proves to be more difficult in low-income countries than in higher-income countries and emerging economies (WHO 2012b: 53).

four interrelated categories of applications: (a) clinical information systems; (b) telemedicine[2] and home care, personalised health systems and services for remote patient monitoring, teleconsultation, telecare, telemedicine and teleradiology; (c) integrated regional/national health information networks, distributed electronic health record systems and associated services such as e-prescriptions or e-referrals; and (d) secondary usage of non-clinical systems (such as specialised systems for researchers or support systems such as billing systems) (eHealth Taskforce 2007: 10). E-health is continuously changing as the emergence of mobile health – defined as 'the use of mobile communication and devices for providing healthcare services or achieving health outcomes' (PricewaterhouseCoopers (PwC) and Groupe Speciale Mobile Association (GSMA) 2012: 14) – demonstrates. Therefore an ethical and legal framework for e-health must also be broad enough to encompass current as well as future solutions (PwC and GSMA 2012: 14).

E-health can be used in a beneficial way when addressing key challenges our health systems face (e.g. demographic change, reduced human resources) (Stroetmann *et al.* 2012: 3). According to the European Group on Ethics in Science and New Technologies to the European Commission:

> reductions in health budgets and competition for limited resources require enhanced efficacy and efficiency of health services. For meeting all of these challenges, adequate information and knowledge are required and e-Health applications offer the prospect of acquiring information which is accurate, reliable and timely.
>
> *(2012: 33)*

Thus e-health is considered an important tool in establishing efficient healthcare delivery around the world (WHO 2012a: 12). In addition, the development, adoption and implementation of a broad range of e-health applications – such as electronic health records, health information websites, e-prescribing, home health monitoring and tele-health – has the potential to enhance quality of care. It also promises improved access to health treatment and advice, empowering patients to make informed healthcare decisions (European Group on Ethics in Science and New Technologies to the European Commission 2012: 33).

In this chapter, we provide an overview of international documents related to e-health. It will become obvious that it takes time to provide a framework that encompasses all of the issues related to e-health. Moreover, we are of the opinion that there are still several issues related to e-health that need specific attention when creating rules regarding its use. These issues are described in section 15.3.

15.2 The impact of international documents for e-health

15.2.1 World Health Organization

At the international level, e-health is receiving a great deal of attention from the WHO. In 2005, the WHO launched the Global Observatory for eHealth (GOe), an initiative dedicated to the study of e-health, its evolution and its impact on health in countries. So far, the WHO has adopted three e-health resolutions. In the most recent, the WHO requests the Director-General,

2 Telemedicine is defined by the European Commission in its *Communication on Telemedicine for the Benefit of Patients, Healthcare Systems and Society* as '(t)he provision of health care services, through the use of ICT, in situations where the health professional and the patient (or two health professionals) are not in the same location. It involves secure transmission of medical data and information, through text, sound, images or other forms needed for the prevention, diagnosis, treatment and follow-up of patients' (2008: 3).

within existing resources 'to provide support to Member States, as appropriate, in their promotion of the full implementation of e-health and health data standard in all e-health initiatives' (World Health Assembly 2013:), among other things. In addition to these specific resolutions, the WHO also enacted a declaration on the promotion of patients' rights in Europe in 1994. Particularly, the principles regarding the right to access, correction, completion, deletion, clarification and/or updating of medical data and the right to informed consent are important (WHO 1994: 11–12). When processing health data using ICT, one should take into account patient privacy protections outlined in article 12 of the *Universal Declaration of Human Rights* 1948. This article states that 'no one shall be subjected to arbitrary interference with his privacy, family, home or correspondence, nor to attacks upon his honour and reputation. Everyone has the right to the protection of the law against such interference or attacks' (*Universal Declaration of Human Rights*, article 12).

In support of e-health policy and strategic development, the WHO and the International Telecommunication Union (ITU) will soon launch a National e-health Roadmap Development Toolkit to support member states with the development of their own comprehensive e-health strategies (WHO 2011: 77). The WHO also announced that it will support the use of mobile health in member states to maximise its impact (WHO 2011: 3).

15.2.2 Council of Europe

Article 8 of the *European Convention on Human Rights* 1950 is important to developing an e-health infrastructure since it provides a general right to privacy protection.[3] Relatedly, the *Convention on Human Rights and Biomedicine* 1997 contains specific rights that are significant in an e-health environment, such as the right to informed consent, the right to private life in relation to information about his or her health, and the right to any information collected about his or her health. For the protection of medical data in particular, the Council of Europe issued *Recommendation No. R(97)5 on the Protection of Medical Data* (1997).

15.2.3 European Union[4]

E-health has likewise received recognition at the EU level. Despite excluding health services from *Directive 2006/123/EC on Services in the Internal Market* 2006, it is clear the Commission has enacted effective rules governing healthcare. In turn, these rules have an important impact on healthcare systems, including the creation of an EU legal framework for e-health. The subsequent section first describes European policy initiatives on e-health, and gives an overview of legal documents related to its nature and implementation.

15.2.3.1 Policy of the Commission Regarding E-Health

The Commission is aware that e-health and/or telemedicine may contribute to delivering better quality of care and to better patient involvement in the management and follow-up of their health

3 Article 8 states: '1. Everyone has the right to respect for his private and family life, his home and his correspondence; 2. There shall be no interference by a public authority with the exercise of this right except such as is in accordance with the law and is necessary in a democratic society in the interests of national security, public safety or the economic well-being of the country, for the prevention of disorder or crime, for the protection of health or morals, or for the protection of the rights and freedoms of others' (*European Convention on Human Rights*).

4 This part is based on 'The EU legal framework on e-health', by S. Callens (2010).

condition(s) (European Commission 2007: 5). Within two decades, the Commission has invested 1 billion Euros in funding over 450 projects (European Group on Ethics in Science and New Technologies to the European Commission 2012: 33)[5] and several research programmes related to e-health.[6] Moreover, the Commission established an *Action Plan* for a European E-health Area in 2004 (European Commission 2004). In the *Action Plan*, health and healthcare formed a key part of the Commission's vision for an information society. It imagined a new generation of computerised clinical systems, advanced telemedicine services and health network applications to improve health, to provide continuity of care and to allow citizens to be more involved in and assume greater responsibility for their own health. The Commission believed that e-health would be an instrument for restructured, citizen-centred healthcare systems, while respecting the diversity of Europe's multicultural, multilingual healthcare traditions in the process (European Commission 2004: 4).

The 2004–2012 e-health action plan increased awareness among member states regarding the importance of making e-health an integral part of their health systems. Today, every EU member state has an e-health strategy in place and is working towards fully achieving it. Nevertheless, the European Commission found it necessary to enact a new *E-Health Action Plan* in recognition of evolving market and behavioural trends since 2004. Now, more than ever, people are monitoring their health and well-being online or through devices such as smartphones. The new *Action Plan* 2012–2020 reflects this shift and aims to enhance user confidence in digital tools and apps while ensuring that the market conditions encourage continued innovation (European Commission 2012a: 2).

The Commission issued in 2012 the *Commission Staff Working Paper* on the applicability of the existing EU legal framework to telemedicine services (European Commission 2012b). Due to its diverse nature and unique characteristics, cross-border telemedicine falls within the scope of EU legal instruments. In the past, there was no specific EU legislation governing cross-border telemedicine. The objective of the *Staff Working Paper*, therefore, was to enhance legal clarity for all actors involved in the provision of telemedicine services (European Commission 2012b: 4). The document clarifies the EU legislation's applicability to issues such as reimbursement, liability, licensing of healthcare professionals, and data protection when providing telemedicine across borders.

Since 2013, the Commission has engaged in 'discussions on legal issues affecting eHealth, within the eHealth Network and other fora, such as the European Innovation Partnership on Active and Healthy Ageing (EIP AHA), as well as cross-sectoral legal work linking eHealth to other ICT-led innovation, with the first conclusions foreseen in 2013–2014' (European Commission 2012c: 8). In order to bring legal clarity for health and well-being apps, a European Commission green paper on mobile health and well-being apps is scheduled to come into effect in 2014. The Commission will also initiate discussions among Member States on reimbursement schemes for e-health services based on effectiveness and efficiency criteria. The Commission will also launch a study under the upcoming Health Program 2014–2020 to examine member states laws' on electronic health records and make recommendations to the eHealth Network on legal aspects of interoperability.

15.3 Treaty on the Functioning of the European Union

Besides the policy documents of the Commission, it is important to mention the legal documents that apply to e-health. The *Treaty on the Functioning of the European Union* 2010 (TFEU) contains a number of important principles in addressing e-health, namely the right to the protection of

5 E-health also represented an important aspect of the Digital Agenda for Europe (European Commission 2010).
6 An overview of e-health projects 2007–2013 is available online (eHealthNews 2006).

personal data (article 16), the free movement of goods (articles 34–36), the freedom to provide services within the EU (article 56),[7] the competition rules (articles 101, 102 and 106) and the subsidiary competence of the EU in the health field (article 168).

The European Union seeks to create a single internal market characterised by open competition. Therefore a system of competition law was developed to prevent the disruption of free competition or to neutralise any such disruption (Prosser 2010; Lear *et al.* 2010). Community competition rules prohibit undertakings in anti-competitive activities, such as agreements to set prices or abuse of a dominant position (TFEU, articles 101–102). Article 101 of the TFEU prohibits all agreements between undertakings, decisions by associations of undertakings and concerted practices that may affect trade between member states, and that have as their object or effect the prevention, restriction or distortion of competition within the common market. Article 102 of the TFEU prohibits abuse of a dominant position by one or more undertakings. Article 106 of the TFEU is also important to healthcare, as it permits partial exemption from the competition rules for some undertakings. This article states that undertakings entrusted with the operation of services of general economic interest shall be subject to the rules contained in the TFEU. In particular, the article outlines rules on competition, insofar as the application of such rules does not obstruct the performance, in law or in fact, of the particular tasks assigned to them. The development of trade must not be affected to such an extent as would be contrary to the interests of the Community.

The rules of European competition law, for example, can apply to electronic networks. Independent healthcare practitioners may have a common computer server to exchange patient information. Such collaboration does not come under the prohibition of cartels if some conditions are fulfilled. Firstly, the electronic system in principle may not be used for the exchange of competitively sensitive information about patients, prices, turnover, etc. (Beurden 2003: 106–8), as the exchange of such information can eliminate competitive undertakings. Secondly, an information network must be open. If the participants of a network benefit from this network, and others who do not participate cannot achieve these economic benefits, it will be difficult for healthcare practitioners to establish themselves in the market (Dutch National Competition Authority 2010: 98).

Moreover, article 168 of the TFEU defines the role of the European Union as complementing national policies, setting out procedures by which the European Union institutions act in the health field and delineating the types of measures that may be enacted. This article ensures a high level of human health protection in the definition and implementation of all EU policies and activities (WHO 2012a: 25). However, the TFEU also requires that healthcare service decisions be made at the national or local level (the legal principle of subsidiarity). The EU thus has only a limited legal competency on health matters. It can adopt measures that complement national initiatives or incentive measures designed to protect and improve human health, in particular to combat the major cross-border health scourges (WHO 2012a: 25).

15.4 Directives and regulations applicable to e-health

There is a wide range of directives and regulations applicable to healthcare actors who use e-health strategies. This section lists pertinent documents and discusses issues in e-health implementation.

7 'Telemedicine is a service and as such falls under the provisions of the TFEU (i.e. its Article 56). The European Court of Justice has, on several occasions, stated that health services fall within the scope of the freedom to provide services (Article 56 TFEU) and neither the special nature of health services nor the way in which they are organized or financed removes them from the ambit of this fundamental freedom' (European Commission 2012b: 7).

15.4.1 Data Protection Directive

Directive 95/46/EC on the protection of individuals with regard to the processing of personal data and on the free movement of such data 1995 (*Data Protection Directive*) is the EU-level legislation on privacy, to which all member states in the EU must comply, and guides the processing and free movement of personal data. It outlines several mandatory compliance principles for e-health actors that process personal data concerning health. These principles apply to national healthcare systems or other e-health actors that create health grids, electronic national records or information systems that may be used for treatment, quality review or research purposes. In order to help member states interpret their duties under the *Directive*, representatives of the national data protection authorities established a Working Party, formally known as the Article 29 Data Protection Working Party (WHO 2012a: 25). Its function is to advise the European Commission on the implementation of the *Data Protection Directive* in the member states and to report on the processing of personal data relating to health in electronic health records (EHR) (Article 29 Data Protection Working Party 2007).

The *Data Protection Directive* applies to the processing of personal data wholly or partly by automatic means, and to the processing of personal data by other means, which form part of a filing system or are intended to form part of a filing system[8] (*Data Protection Directive*, article 3). Generally, article 8 of the *Data Protection Directive* prohibits the processing of personal data concerning health. However, this prohibition does not apply where the processing of health data is required.[9] For example, the processing of health data for the purposes of preventive medicine, diagnosis, the provision of care or treatment or the management of healthcare services is permitted where such data are processed by a health professional subject to national law or rules established by national competent bodies obliging professional confidentiality, or by another person also subject to an equivalent confidentiality obligation.

According to the *Data Protection Directive*, personal data used in e-health projects, for example, must be processed fairly and lawfully. Furthermore, data must only be collected and processed for specified, explicit and legitimate purposes. The data must be adequate, relevant and not excessive in relation to the purposes for which they are collected. Furthermore, the data must reveal the identity of subjects for no longer than is necessary, and only for the purposes for which the data was collected or is required for further processing. Data subjects must also be informed about the processing of their personal data (*Data Protection Directive*, article 6).

Data transfer between member states for e-health projects ensures adequate protection of the data during transfer to the second member state, since it is responsible for providing a similar level of protection. The *Data Protection Directive* stipulates that the transfer of data undergoing processing or intended for processing after transfer to a third country may take place only if the third country ensures an adequate level of protection (*Data Protection Directive*, article 25.1; Rowe 2003). Adequacy is assessed in light of all the circumstances surrounding a data transfer operation or set of data transfer operations. Particular consideration is given to the nature of the data, the

8 A filing system is 'any structured set of personal data which are accessible according to specific criteria, whether centralized, decentralized or dispersed on a functional or geographical basis' (*Data Protection Directive*, article 2(c)).

9 The European Court of Justice stated in *Lindqvist* (2003), Case C-101/01 ECR I-12971, that the act of referring, on an Internet page, to various persons and identifying them by name or by other means constitutes 'the processing of personal data wholly or partly by automatic means' within the meaning of article 3(1) of the *Data Protection Directive*. Such processing of personal data in the exercise of charitable or religious activity is not covered by any of the exceptions in article 6(2). In this case, the fact that it was mentioned on the Internet that an individual had injured his/her foot and was on half-time leave on medical grounds constitutes personal data concerning health within the meaning of article 8(1) of the *Data Protection Directive*.

purpose and duration of the proposed processing operation(s), the country of origin and country of final destination, the rules of law (both general and sectoral) in force in the third country, and the professional rules and security measures in place (*Data Protection Directive*, article 25.2).[10]

The frequency of data transfers between the EU and the United States, and uncertainty surrounding the 'adequacy' standard, prompted the United States Department of Commerce to issue the 'Safe Harbor Principles' under its statutory authority to foster, promote and develop international commerce. The European Commission has recognised these Safe Harbor Principles in *Decision 2000/520/EC* of 26 July 2000 (European Commission 2000).

A replacement of the *Data Protection Directive* is envisioned. The Proposal of the European Commission for a *General Data Protection Regulation* was submitted on 25 January 2012 (European Commission 2012g).

15.4.2 E-commerce Directive

Directive 2000/31/EC on certain legal aspects of information society services, in particular electronic commerce, in the Internal Market 2000, the so-called *E-commerce Directive*, discusses certain legal aspects of information society services in the internal market. These services are defined as any service normally provided for remuneration, at a distance and by electronic means,[11] for the processing (including digital compression) and storage of data, and at the request of a service recipient (*Directive 98/34/EC laying down a procedure for the provision of information in the field of technical standards and regulations and of rules on Information Society services* 1998, article 1.2).[12] 'At a distance' denotes service provision without the simultaneous presence of both parties (Van Eecke 2001: 369). Since the economic activities of an information society service can consist of services giving rise to online contracting, several e-health applications can be the subject of an information society service. The *E-commerce Directive* may apply to online medicine purchases, as well as to services that transmit or provide access to information via a communication network. The *E-commerce Directive* may also apply to physicians who pay a fee to access a file using electronic research registers, who use a website to promote their activities or for sending medical information among physicians against remuneration (Van Eecke 2001: 375).

The *E-commerce Directive* obliges e-health actors who act as an information society service to provide the recipients of the service and competent authorities with direct and easy access to at least the following information: their name; the geographic address at which they are established; their details, including an electronic mail address; where their activity is subject to an authorisation scheme; the particulars of the relevant supervisory authority; as concerns the regulated professions, any professional body or similar institution with which they are registered; professional title and member state where it has been granted; a reference to the applicable professional rules in the member state of establishment and the means to access them (*E-commerce Directive*, article 5). According to the *E-commerce Directive*, member states must ensure that e-health actors

10 For exceptions to article 25 of the *Data Protection Directive*, see articles 26.1 and 26.2 of the *Directive*; see also Andoulsi *et al.*'s 'Bottlenecks and challenges and RTD responses for legal, ethical, social and economic aspects of healthgrids' (2008: 21). The *Data Protection Directive* also states that member states may authorise a transfer or a set of transfers of personal data to a third country that does not ensure an adequate level of protection of personal data, where the controller adduces adequate safeguards through appropriate contractual clauses between the sender and the recipient of the personal data (Data Protection Directive, article 26.2). In this context, the European Commission has proposed standard contractual clauses that ensure an adequate level of protection of transferred personal data (for example, the storage of pharmacogenetic data or research data concerning health).

11 Communication by phone, fax or global system for mobile communications does not fall under the *Directive*.

12 The recipient can be a patient or a physician asking for an opinion.

indicate any relevant codes of conduct to which they subscribe and indicate how those codes can be consulted electronically (*E-commerce Directive*, article 10.2).[13]

Member states must guarantee that the take-up and pursuit of the activity of an information society service provider may not be made subject to prior authorisation or any other requirement having equivalent effect (*E-commerce Directive*, article 4.1). Article 4.1 of the *Directive* shall be without prejudice to authorisation schemes that are not specifically and exclusively targeted at information society services, or that are covered by *Directive 97/13/EC on a common framework for general authorizations and individual licences in the field of telecommunications services* 1997. This important principle articulated in article 4 of the *E-commerce Directive* is a major challenge for national e-health networks or telemedicine projects for which the competent public authorities want to provide reimbursement under certain conditions.

15.4.3 Medical Device Directives

E-health often requires medical software and/or implanted devices used to diagnose or treat patients. Therefore *Directive 90/385/EEC regarding active implantable medical devices* 1990, *Directive 93/42/EEC regarding medical devices* 1993 and *Directive 98/79/EEC regarding in vitro diagnostic medical devices* 1998 (*Medical Device Directives*) are also important for e-health projects. The *Medical Device Directives* harmonise the rules pertaining to the free circulation of medical devices in the EU. Products that fall within their scope must meet all essential safety and administrative requirements, and must bear an EC-conformity mark to show that they comply with the *Medical Device Directives*. Such products may then be sold throughout the European Economic Area without, in principle, being the subject of additional national legislation. The *Medical Device Directives* define a medical device as:

> any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, together with any accessories, including the software intended by its manufacturer to be used specially for diagnostic and/or therapeutic purposes and necessary for its proper application intended by the manufacturer to be used for human beings for, among other things, the purpose of diagnosis, prevention, monitoring, treatment or alleviation of disease, injury or handicap and the control of conception and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means.
>
> (Medical Device Directives, *article 1.2(a)*)

Software used in an e-health project for general purposes is not a medical device. However, software intended by the manufacturer to be used for one or more of the medical purposes established in the definition of a medical device is a medical device.

The manufacturer must design and manufacture medical devices in such a way that some essential requirements are met, such as taking into account the generally acknowledged state of the art and to eliminate or reduce risks as much as possible. Devices that are in accordance with national provisions that have transposed the existing European harmonised standards will be presumed by EU member states to be compliant with the essential requirements laid down by the Directive.

13 In order to facilitate the free provision of services in general, there are specific rules aimed at the abolition of obstacles to the free movement of persons and services, which extend the possibility of pursuing professional activities under the original professional title (European Union 2005; Peeters 2010).

In the context of the *Medical Device Directives*, manufacturers are obliged to place on the market or to put into service only medical devices that do not compromise the safety and health of patients, users and other persons, when properly installed, maintained and used in accordance with their intended purpose. In designing and producing state-of-the-art medical devices, the manufacturer must meet essential requirements that ensure patient safety and reduce risks. Devices that are in accordance with national provisions that have transposed the existing European harmonised standards will be presumed by EU member states to be compliant with the essential requirements laid down by the Directive (*Medical Device Directives*, article 5). Devices other than those custom-made or intended for clinical investigation must bear an EC-conformity mark when placed on the market. Clinical evaluation is also required and it remains to be seen how medical software vendors will fulfil this obligation.

Clinical evaluation is needed for every medical device. This clinical evaluation can be done in different ways. For instance, it may be based on the relevant scientific literature, by conducting a clinical investigation, or by combining both methods (*Directive 2007/47/EC*, Annex II, 10(a)). For active implantable devices and Class III devices,[14] there must always be a clinical investigation (*Directive 2007/47/EC*, Annex II, 10(b)). Therefore clinical investigation will be necessary for medical implantable software or software listed under Class III.

The European Commission has since enacted two proposals to revise the *Medical Device Directives* (European Commission 2012d; European Commission 2012e). These proposed 'new rules aim to ensure that patients, consumers and healthcare professionals can reap the benefits of safe, effective and innovative medical devices' (European Commission 2012f: 1).

15.4.4 Directive on the Recognition of Professional Qualifications

Directive 2005/36/EC on the recognition of professional qualifications 2005 (including for medical doctors and a number of medical specialties) is recognised universally among EU member states. The aims of this *Directive* are to ensure that the European Union member states enact uniform, transparent and non-discriminatory rules recognising professional qualifications and experience, so as to allow professionals to work temporarily or permanently throughout the Union. However, this Directive will not apply in the case of (cross-border) telemedicine since the health professional and the patient are not simultaneously present. Article 5.2 of this Directive states that Title II (dedicated to the free provision of services) shall only apply where the service provider moves to the territory of the host member state to pursue his or her profession on a temporary and occasional basis. In the case of telemedicine, the health professional is not physically moving to the territory of another member state, only the 'service' itself moves. This *Directive* intends to recognise healthcare qualifications across EU borders. It is only applicable where the service provider actually moves to the territory of a host member state and thus does not apply to all e-health services.

15.4.5 Patients' Rights Directive

E-health is covered in the scope of *Directive 2011/24/EU on the application of patients' rights in cross border healthcare* 2011 (*Patients' Rights Directive*).[15] Cross-border healthcare services, including

14 Medical devices are divided into classes. For the classification rules, see *Directive 93/42/EC regarding medical devices* 1993 (European Union 1993).

15 This Directive contains two express references to telemedicine (European Commission 2012b: 7); see articles 3(d) and 7(7)) and its scope covers 'the provision of health care to patients, regardless of how it is organized, *delivered* or financed' (article 1(2)).

e-health, must be provided in line with the standards and guidelines on quality and safety in the member state of treatment (for e-health: the one of the service provider). According to article 3(d), 'Member State of treatment' refers to the member state on whose territory healthcare is actually provided to the patient. In the case of telemedicine, healthcare is provided where the healthcare practitioner is established.

Article 14 of the *Patients' Rights Directive* establishes a voluntary network of national authorities knowledgeable in the area of e-health. The eHealth network is charged with drafting guidelines that enhance interoperability between electronic health systems, facilitate continuity of care and safeguard access to safe and quality healthcare.

15.4.6 Other directives and regulations

Directive 2002/58/EC concerning the processing of personal data and the protection of privacy in the electronic communications sector 2002 (*Directive on privacy and electronic communications*) is also relevant. It contains specific requirements for providing publicly available communications services electronically, through secure and confidential networks (European Commission 2012b: 16).

Also pertinent is *Directive 98/34/EC laying down a procedure for the provision of information in the field of technical standards and regulations and rules on Information Society services* 1998 (*Transparency Directive*). Member states wishing to adopt regulation on telemedicine as an information society service must notify the Commission and other member states before adoption (European Commission 2012b: 11).

E-health business may also involve contractual agreements. These contracts describe various obligations and, often, special clauses concerning relevant parties. A contract related to e-health between professionals and consumers (for example, a contract between a patient and a teleexpert, or a contract between a patient and a pharmacist regarding the delivery of medicinal products) may be classified as a contract at a distance. *Directive 97/7/EC on the protection of consumers in respect of distance contracts* 1997 (*Directive on Distance Contracting*) will apply to any contract concerning goods or services concluded between a supplier and a consumer under an organised distance sales or service-provision scheme run by the supplier, who, for the purpose of the contract, makes exclusive use of one or more means of distance communication up to and including the moment at which the contract is concluded (*Directive on Distance Contracting*, article 2.1). Prior to the conclusion of any distance contract, the consumer shall be provided with sufficient information regarding the supplier's identity, the nature and cost of the services, arrangements for payment, delivery or performance, and the right to withdraw. Consumers must receive verifiable confirmation of the information stipulated in the contract in a timely fashion, unless the information has already been given, with the same provisos, prior to conclusion of the contract. For any distance contract, consumers will have a period of at least seven working days in which to withdraw without providing reason and without penalty.

E-health projects also often require electronic signatures. Electronic signatures are to be treated equal to handwritten signatures in the EU. An electronic signature means data in electronic form which are attached to or logically associated with other electronic data and which serve as a method of authentication (article 2.1 *Directive 1993/93/EC on a Community framework for electronic signatures*). Article 3.7 of *Directive 1999/93/EC* states that member states may use electronic signatures in the public sector upon meeting additional requirements. However, such requirements shall be objective, transparent, proportionate and non-discriminatory, and relate only to the application at hand. Such requirements may not constitute an obstacle to cross-border services for citizens (*Directive 1999/93/EC*, article 3.7).

A number of pieces of EU legislation regarding e-health projects should be considered, namely rules concerning the competent judge and the applicable law, i.e. *Regulation 44/2001 on jurisdiction and the recognition and enforcement of judgments in civil and commercial matters*, *Regulation 593/2008 on the law applicable to non-contractual obligations* (*Rome I*) and *Regulation 864/2007 applicable to non-contractual obligations in tort law* (*Rome II*).

15.5 Current and emerging issues pertinent to e-health[16]

Despite legal and regulatory issues related to e-health at the international and/or EU level, it is our opinion that a more detailed legal framework is needed to allow the use of this activity in healthcare systems. This framework should consider all interests at stake, such as data protection, public health, quality of care, cost-effectiveness, etc. It requires more legal provisions (for example, rules are needed on liability and reimbursement matters) and greater attention to new technical developments (for example, the lack of clarity for health and well-being mobile applications, the role of data centres) (European Commission 2012c; Stroetmann 2012).

15.5.1 Towards more similar liability rules

Certain e-health domains, like telemonitoring, raise several and often complex liability issues. For example, who will be liable for errors during a monitoring session (the physician or healthcare professional, the healthcare institution, the manufacturer of the device (liability for defective products), the telephone/Internet company, the call centre)? Which member state supervises physicians in cross-border healthcare? Which legislation is applicable in case of cross-border healthcare? Liability can stem from professional conduct or a defective product. Moreover, depending on whether a contractual relationship exists between the damaged person and the person responsible for the damage, a case of contractual liability or tort liability could arise (European Commission 2012b: 19).

To date, there is no international consensus document regulating liability in cases of telemonitoring. Nevertheless, the EU general liability rules (*Rome I* and *Rome I* – see above) are also applicable in healthcare. *Directive 85/373/EEC on the approximation of the laws, regulations and administrative provisions of the Member States concerning liability for defective products* 1985 (*Product Liability Directive*) and the *Patients' Rights Directive* may be applicable in case of damage caused by telemonitoring.

It is, however, obvious that different medical liability legislation in the EU member states (including legislation concerning compensation for damages caused by medical acts) may hinder the application of telemonitoring. Patients seeking cross-border healthcare services may not necessarily always remain under the scope of legal protection offered by their own legal system. Therefore the EU and other international organizations should take heed in liability issues.

Countries that enact legislation concerning compensation for damages caused by medical acts should ideally not exclude damage that is caused by medical acts carried out in another member state. The *Patients' Rights Directive* declares EU member states must ensure there are mechanisms for patients to seek redress and compensation if they suffer harm. If in a telemonitoring project the physician does not reside in the member state where treatment is taking place and the patient suffers harm due to treatment/monitoring at a distance (from another member state), the local no-fault legislation of the member state of residence of the patient should ideally apply to the patient. It would be good for promoting (internationally) e-health projects if

16 This section is based on 'Legal aspects of personal health monitoring' (Callens 2013: 57–62).

no-fault legislation of a member state (or specific legislation with a compensation system for damage caused by medical activities) should not be limited to harm caused in the patient's state of residence. In that case only the local e-health projects that cause damage could be covered by specific compensation rules.

15.5.2 Transparency

If the telemonitoring device is to function as an alert device, this should be clearly communicated to patients. Patients should be informed what actions they must take and what actions to expect from the treating physician. The patient must also be informed about the information flows and the categories of persons who might have access to their data. Patients should be allowed access to login files. Authorised healthcare professionals with access to electronic patient files should be informed of the possibility that patients or competent persons of the health institute may verify access. Patients must also be informed about the device and the treatment plan. Patients (or their representative) must consent to the treatment and the (further) processing of health data for purposes other than treatment.

The globalisation of healthcare actors requires greater harmonisation in health data processing, particularly as data exchange between international or European e-health actors will not be limited to the treatment of patients during monitoring sessions and may also be processed for evaluation, research or statistical purposes. Currently, harmonised rules on further processing are lacking. Several member states of the EU have formulated strict rules for the processing of medical data for research purposes while others are more flexible. Article 8 of the *Data Protection Directive* leaves too much room for different legislation among member states. Legislative differences are detrimental to the establishment of an internal market, where international quality review projects, epidemiological studies, clinical trials, etc. are emerging, and especially in the context of globalised healthcare.

In other words, remedying the current weakness of the *Data Protection Directive* requires more European action. Adopting a proposal for the new *General Data Protection Regulation* (see above) is one example of this action. The proposal contains innovative ideas, such as the 'the right to be forgotten' in the online environment or the right to delete all personal data that are publicly available. One other key feature includes mandating *explicit* patient consent for data processing rather than assumed consent.

15.5.3 Challenges for healthcare practitioners and hospitals

The role of different health professionals may change in view of developing telemonitoring. We believe that nurses and medical assistants may play a growing role. Surveillance of monitoring systems also implies that there will be a shift from inpatient to outpatient treatment. The role of the hospital will change, eventually monitoring outpatients not physically present or admitted to the hospital. Because of the cross-border effect of telemonitoring, some hospitals may also become international, or at least for the moment European-wide, referral centres. The use of monitoring devices will also lead to changes in the way physicians and hospitals function. Physicians, other healthcare professionals and hospitals will need to be on standby for their patients in case of an emergency. This requires organising a guard duty, probably with many other healthcare professionals in light of the increasing physician shortage in several member states. In implementing telemonitoring services, the guard duty will need to consider the influx of patients to follow patients who are not physically present in the hospital. Many of these patients may reside in regions other than where the treating hospital is located. E-health, and

in particular telemonitoring, will simplify cross-border healthcare and reference centres will treat more patients (from several countries). Thus telemonitoring urges healthcare personnel and hospitals to work collaboratively beyond their national boundaries.

15.5.4 Towards the reimbursement of e-health services

In the EU member states, it is often still required that the patient and health professional are both present in order for a medical act to be legally recognised and reimbursed. This condition is not fulfilled in many telemonitoring projects whose value lies in the free movement of services without an in-person consultation. The question then becomes whether or not the condition still legitimises withholding reimbursements for telemonitoring projects. Not surprisingly, new monitoring projects often end due to a lack of financing structure. Although reimbursement is an issue to be treated by the individual member states, clear EU-level criteria for reimbursement, much like *Directive 89/105/EC relating to the transparency of measures regulating the pricing of medicinal products for human use and their inclusion in the scope of national health insurance systems* 1988 outlined for medicinal products, might be useful.

The rules of reimbursement for cross-border care as provided in the *Patients' Rights Directive* (2011) are of import to telemedicine. The member state of affiliation must guarantee reimbursement of the costs an insured person incurs upon receiving cross-border healthcare if it is among the benefits the insured person is entitled to in the member state of affiliation.

15.5.5 Relationship between patient and industry: challenges concerning publicity, promotion and competition

The role of the medical devices and the pharmaceutical industry will change if healthcare settings increasingly apply telemonitoring projects, web portals designed to share information between patient and healthcare professional, mobile health apps, etc. Delegates and employees from the medical device industry may be in direct contact with the patients when, for example, implanting a monitoring device, to give information about its function or about the health status of the patient. The data may be gathered in a data centre that will send the necessary information a treating physician needs. In the past, the industry's only contacts were with health professionals and distributors; there was, in principle, no direct contact between the industry and patients. Telemonitoring projects are changing this dynamic, especially if the device manufacturer owns the data centres or if the industry installs and/or follows up with the device.

Specific rules at the European level will be needed to regulate the relation between the healthcare industry and the patient in the monitoring sector, in order to avoid illegal promotion and/or advertising, illegal overconsumption or unfair competition. If devices, or even data centres, are made available to hospitals or health professionals free of charge, this may be considered an illegal advantage for the healthcare professional/facility. Administering free products and/or services may also violate competition rules. In rethinking the role/function of the industry, it is clear that it will become more involved in the treatment and follow-up of patients with a device or web portal. More and more custom-made devices adapted to the specific needs of the patients will be developed and used. Patients will need to become more familiar with how the device works and what to do when it malfunctions. However, healthcare professionals will no longer be the only providers of this information, nor will they deliver the devices. Patients will obtain devices from the manufacturer/supplier and not necessarily from the (hospital) pharmacist. If retailers, consumer product companies and others can deliver the devices to patients, these companies may want to inform patients directly and assist them in using the device. It will be a

challenge for these companies to ensure there is a clear distinction in practice between providing information and advertising at the time of initial contact between the company and the patient.

Telemonitoring also allows data processing for several purposes. The data centre may gather information related to the implanted/used device in monitoring projects and/or the patient which may be processed by the industry prior to reaching the health professional. The question is whether the companies who deliver implants can own the data centre, perhaps making it more difficult for hospitals to work with several types of implants due to competition law, or whether new independent healthcare players should run them.

Until now, there was no extensive European legislation concerning the advertising and distribution of medical devices used in telemonitoring projects. If the industry begins to play a more active role in direct patient use of monitoring devices, clearer rules are needed at the EU-level. Namely, legislation will serve to distinguish between information provided by the industry and advertising, to address issues of promotion and cost of data centres or health personnel involved in telemonitoring projects, to allow patients to choose who assists them in using the device and to monitor the use of data processing at data centres.

15.6 Conclusion

Many healthcare players (such as national health insurers, hospitals, laboratories, etc.) are now international healthcare actors and may feel the need to communicate health data between member states for treatment and other purposes. Patients communicate with healthcare professionals from other countries through telemonitoring projects without having to go abroad. Thus a clear legal framework for e-health is needed. Until now, data processing, distance contracting and medical device marketing have dominated discussions surrounding e-health strategies. However, despite rules and policy attention, several e-health issues require a more critical legal gaze. Clear criteria on the reimbursement of e-health activities, similar rules concerning (no-fault) liability and greater care in ensuring transparency in relationships between patients and the industry are needed.

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16

Promotion and sales of self-tests on the Internet

Elke Sleurs, Louiza Kalokairinou, Heidi Carmen Howard, and Pascal Borry

16.1 Introduction

Currently, the field of medicine is confronted with new developments that allow individuals to access health information outside of a context where healthcare professionals are involved. In a recent report, the Nuffield Council on Bioethics identified this phenomenon as 'online medicine':

> developments in digital technology, largely involving the internet, that offer new ways for individuals to obtain and share health advice, diagnosis and medication, and that provide new possibilities for storing, accessing and sharing health records, monitoring individuals' health status and communicating with health professionals and other patients.
>
> *(2010: 22)*

This definition covers developments such as online health information, online personal health records, the online sales of pharmaceuticals, telemedicine, direct-to-consumer body imaging and personal genetic profiling (Nuffield Council on Bioethics 2010).

In this chapter, we focus on one specific type of development that was grouped under this umbrella of 'online medicine'. In particular, we discuss the increasing offer of tests that are available and that allow consumers to measure or identify a particular disorder, risk factor or trait based on body material such as blood, saliva, urine or faeces (Grispen *et al.* 2011). As such, this chapter will focus on direct-to-consumer (DTC) testing that is initiated, and often interpreted, without the involvement of a healthcare professional.

As described in a Dutch report, various types of test offers are currently being sold (Weijden *et al.* 2007). The first type involves tests for home use, in which the consumer uses and interprets the test at home. The second type includes situations where bodily materials are sent to a laboratory which returns the results by post or online (i.e. home-collected tests). In a third type of test, the consumer has his or her sample taken at a laboratory and the results are also returned by post or made accessible online. The fourth kind comprises self-tests offered to consumers through an organization stationed in public areas, such as supermarkets (i.e., street-corner tests). In this case, the results are immediately made available and communicated to the individual, as

for example the national cholesterol test offered by the Dutch Heart Association (Deutekom *et al.* 2008). These different situations in DTC testing are often described under the same denominator as self-tests because they allow individuals to obtain health information about themselves without the involvement of any healthcare professional (Grispen *et al.* 2011; Weijden *et al.* 2007; Ronda *et al.* 2009; Ryan *et al.* 2006; Wilson *et al.* 2006; Ryan, Greenfield and Wilson 2006). Self-tests are described as tests on bodily material that are not undertaken on the advice of physicians; that are purchased and performed by the consumer; and are aimed at tracing a particular condition or predisposition that can lead to the development of a particular condition (Weijden *et al.* 2007).

The availability of self-tests is widespread and increasingly growing. Kearns *et al.* described this expanding market: 'Currently numerous biotechnological institutes are targeting new frontiers in self-testing diagnostic devices that aim to be client-centered, technically robust and financially affordable' (2010: 200). Already in 2006, Ryan *et al.* identified more than 100 unique tests in the United Kingdom for over 24 diseases sold by 19 retailers. Based on a questionnaire study among Internet users in the Netherlands, Ronda *et al.* (2009) reported the use of self-tests for 25 conditions. Recent research by Lovett *et al.* (2012) identified 127 different DTC medical tests advertised online. Among these are tests that measure markers related to cardiovascular conditions and diabetes; sexually transmitted diseases (such as chlamydia, gonorrhea and HIV); nicotine, alcohol and drug use; or cancers (such as prostate, breast or colon cancer). There are also tests available to check for male or female infertility. Since 2008, various companies have also offered genetic tests online, providing information about different types of traits or phenotypes (Borry *et al.* 2010). Some offer information about susceptibility to common complex disorders, whereas others provide information about non-disease-related phenotypes like eye colour. Additional tests address the metabolisation of certain drugs or provide information about carrier status for autosomal recessive conditions. Furthermore, some companies provide information about genealogy or ancestry. Finally, while some companies analyse specific variants related to one or a few phenotypes, other companies analyse thousands to millions of genetic variants for a large number of different traits or disorders.

In this chapter we will first discuss the advantages and challenges posed by DTC testing, as reported in the literature and in various policy documents and recommendations worldwide. Secondly, we will discuss regulations relevant to DTC testing in Europe, notably the *in vitro* diagnostic medical devices legislation. We address certain drawbacks to the current regulatory framework and discuss the newly proposed Regulation on *in vitro* diagnostic medical devices (2012). We also refer to the *Additional Protocol to the Convention on Human Rights and Biomedicine Concerning Genetic Testing for Health Purposes* 2008 and national legislation enacted by different European countries that addresses genetic testing.

16.2 Policy reports: advantages and challenges of DTC tests

Direct-to-consumer testing has been the topic of various reports, guidelines, recommendations and statements. However, the number of documents addressing the specific subtype of DTC genetic testing clearly outnumbers the documents related to DTC testing in general (i.e. other types of tests offered DTC that are not genetic). The American Society of Clinical Pathology (2005) and the Dutch Society of Clinical Chemistry (2006) both addressed the latter. A national bioethics commission, the National Consultative Ethics Committee for Health and Life Sciences (2004), also discussed the challenges related to self-tests, specifically in the context of HIV.

In contrast to the few documents addressing the offer of different types of non-genetic DTC tests, numerous position statements, policies and recommendations have discussed specifically genetic testing offered direct-to-consumer (Skirton *et al.* 2012). Various professional societies and colleges have produced such documents, notably the American Society of Human Genetics (ASHG) (Hudson *et al.* 2007), the American College of Medical Genetics (ACMG) (2004), the European Society of Human Genetics (ESHG) (2010), the American College of Obstetricians and Gynecologists (2008), the American College of Clinical Pharmacology (Ameer and Krivoy 2009), the American Society of Clinical Oncology (Robson *et al.* 2010), the Human Genetics Society of Australasia (2012), the National Society of Genetic Counselors (2011), the Swiss Society of Medical Genetics (2009), the German Society of Human Genetics (2011) and the International Society of Nurses in Genetics (2009).

In addition, public bodies have also commented on DTC genetic testing, including the Nuffield Council on Bioethics (2010), the Belgian Advisory Committee on Bioethics (2004), the Austrian Bioethics Commission (2010), the National Council of Ethics for the Life Sciences in Portugal (2008), the French National Consultative Ethics Committee for Health and Life Sciences (2004), the Secretary's Advisory Committee on Genetics, Health, and Society (2010) and the Human Genetics Commission (2003, 2007, 2010). A report was also prepared by the Science and Technology Options Assessment for the European Parliament (2008). Furthermore, the European Academies Science Advisory Council and the Federation of European Academies of Medicine have recently published a report (2012). In Germany, DTC genetic testing has also been discussed in a report by the German National Academy of Sciences (2010).

The existence of more policy documents addressing DTC genetic testing compared to non-genetic tests may reflect a certain type of genetic exceptionalism. Genetic tests are often treated differently than other medical tests because of the perception of various factors, including their potential familial and psychosocial impact, their potential predictive character, the fear of discrimination or stigmatisation based on genetic information and their potentially identifying nature. However, these factors are not present in all genetic tests, and many of these characteristics are also present in non-genetic medical tests. In this way, genetic tests do not differ from other medical tests in absolute terms, but rather can be viewed as having characteristics that exist on a gradual spectrum. As a European Commission Independent Expert Group asserted, 'Genetic information is part of the entire spectrum of all health information and does not represent a separate category as such' (McNally and Cambon-Thomsen 2004: 10). As a consequence, we consider most potential benefits and harms related to DTC genetic and non-genetic tests as similar. Specific concerns differ based on the type of test used rather than based on whether the test is genetic. Therefore the following section offers an overview of the potential benefits and harms attributed to DTC testing based on policy documents that specifically address genetic tests as well as those that apply to general health tests.

Various potential advantages have been advanced in relation to DTC tests. Ease and convenience of access are two of the most obvious benefits described in the literature. Consumers are able to order tests when and where it is convenient for them (Ronda *et al.* 2009; Lippi *et al.* 2011; Ryan, Wilson and Greenfield 2010). Moreover, performing a test at home without consulting a general physician or specialist can be quick, confidential and inexpensive (Nuffield Council on Bioethics 2010; Lippi *et al.* 2011). DTC testing may also enable greater consumer autonomy and empowerment, allowing consumers to monitor their health status preventatively and act upon test results by making healthier lifestyle choices, or by undertaking preventive or therapeutic interventions. The right to access one's own health information was also acknowledged in various policy documents. As expressed by the Austrian Bioethics Commission:

> In principle, it can be argued that each individual has the right to obtain information about his or her state of health in order to take action in the interests of his or her own well-being on the basis of this information … In this sense, access to such tests supports the right to self-determination and the right to independent decision-making.
>
> *(2010: 29)*

However, in contrast with this attention to autonomy and self-management, the offer of self-tests directly to consumers has also raised various concerns that have ethical and policy repercussions. As highlighted by the ESHG in a report about DTC genetic testing:

> Individuals are entitled to health information and genetic information about themselves. However, this right to know must be exercised with due respect for the need to protect the same individuals from inappropriate genetic information and testing.
>
> *(2010: 1271)*

Firstly, various concerns are being raised about the quality of many tests available and the appropriateness of offering some tests directly to consumers. As the American Society for Clinical Pathology noted:

> There is concern among the medical community that tests are being conducted to screen for certain conditions (e.g., expensive total body scans to screen for cancer, a cheek swab test to screen for cystic fibrosis DNA, or an inexpensive cholesterol test that does not screen for triglycerides, an important marker for heart disease risk) in DAT [direct access testing] laboratories that would not normally be ordered by a physician. The concern here is that DAT could result in false-positives or false-negatives, possibly leading to increased health care costs as well as adverse impacts on patient health.
>
> *(2005: 2)*

Many policy documents cite the potential overstatement of the actual predictive value and clinical utility of the results (ESHG 2010). Therefore, the risk that consumers might misinterpret their test results was a serious concern for most organizations. The International Society of Nurses in Genetics warned against the misinterpretation of results that are returned without a healthcare provider:

> These risks include misinterpretation of information or distortion of its consequence to the overall health of the person tested due to the complexity of analytical finding implications and the vocabulary use itself. Misinterpretation of results may also lead to the failure to engage in preventive behaviors because the risk is not adequately presented.
>
> *(2009: 2)*

Similar concerns revolve around the quality of test results (including accuracy and precision of measurement), the quality of laboratories (including internal and external quality assurance) and the appropriate qualifications and training of laboratory personnel (ESHG 2010).

Secondly, most policy documents recommend that trained and qualified health professionals be involved in testing to ensure that patients receive accurate information and pre- and post-test counselling. For example, the American Society for Clinical Pathology recommends:

> For optimum patient health outcomes, ASCP recommends that patients consult with their physician for proper interpretation of test results. Laboratory testing helps better identify a patient's health status. Clinicians may have access to the patient's family history and other data that can critically affect test interpretation and can order additional tests to clarify the results or predict risk.
>
> *(2005: 2)*

With regard to genetic testing, the Portuguese National Council of Ethics for the Life Sciences affirmed:

> 10. Genetic tests related to health should not be offered without medical indication and personalised supervision, in respect for the principles of beneficence and non-maleficence.
> 11. In case the test provides or may provide predictive health-related information, it should not be conducted unless genetic counseling is made available before and after the results.
>
> *(2008, p.6)*

Moreover, other organizations discourage DTC testing without the supervision of healthcare professionals. The ACMG recommended that:

> A knowledgeable healthcare professional should be involved in the process of ordering and interpreting a genetic test. Genetic testing is highly technical and complex. A genetics expert such as a certified medical geneticist or genetic counselor can help the consumer determine, for example, whether a genetic test should be performed and how to interpret test results in light of personal and family history. A number of risks can be reduced if a genetics professional is involved in genetic testing. These risks include lack of informed consent, inappropriate testing, misinterpretation of results, testing that is inaccurate or not clinically valid, lack of follow-up care, misinformation, and other adverse consequences.
>
> *(2008: 1)*

Similarly, the ESHG stated:

> The offer of genetic tests providing health-related information, in the absence of clinical indications and individualized medical supervision, may compromise patient health. Key concerns are the provision of sufficient information about the purpose and appropriateness of testing, its possibilities and limitations, as well as the clinical significance of testing. An involvement of independent medical professionals could avoid the waste of money on tests that are clinically irrelevant. In addition, the cost and adverse psychosocial effects of unnecessary follow-up or medical investigations could be avoided.
>
> *(2010: 1272)*

Various documents also acknowledged that healthcare professionals might not always be adequately trained to offer and interpret new tests and, underlined the need for further education. The ASHG, for example, maintained that 'professional organizations should educate their members regarding the types of genetic tests offered DTC, so that providers can counsel their patients about the potential value and limitations of DTC testing' (Hudson *et al.* 2007: 637).

Thirdly, some organizations warned of the potential downstream impact the healthcare system may incur as a result of consumers requesting additional test interpretation, confirmatory testing and further potentially unjustified clinical interventions (e.g. biopsies, radiology, treatments) based on test results derived from DTC testing. For instance, the American College of Obstetricians and Gynecologists cautioned:

> [D]irect-to-consumer genetic testing will create downstream needs for counseling, support, and care for those identified as carriers of genes associated with undesired medical conditions. In many locales, the current health care system is not sufficient to meet those needs. *(2008: 1494)*

The Austrian Bioethics Commission questioned to what extent offering DTC tests raises issues for distributive justice due to this indirect cost: '[a]s scarce resources cannot be available to all in equal measure, the distribution of goods must be governed by criteria that enjoy the broadest possible acceptance' (2010: 31).

Fourthly, a number of documents address the risks associated with testing individuals without their consent or knowledge. The ESHG stated that any 'service that requires a sample to be collected at home runs the risk of samples being submitted for testing without obtaining proper consent or without even the knowledge of the person to whom it pertains' (2010: 1272). Indeed, tests that are performed at home could theoretically be done without the knowledge of the person tested. Given that informed consent is a key requirement to carrying out a medical intervention, various documents consider the practice of non-consensual testing unethical and suggest that the analysis of a specimen from third parties without their consent should be legally prohibited. For example, a Report by the Secretary's Advisory Committee on Genetics, Health, and Society referred to the unclear legal situation in the USA with regard to testing without consent:

> Most States do not have laws restricting surreptitious DNA testing, and those that do generally place restrictions only on nonconsensual health-related testing. Ten States have laws that broadly restrict surreptitious DNA testing for both health- and nonhealth-related purposes, such as parentage determination or ancestry. Even where State laws expressly prohibit surreptitious testing, it is unclear that these laws have ever been enforced. *(2010: 30)*

Moreover, various documents raise concerns surrounding testing of minors or persons unable to give informed consent. The Nuffield Council on Bioethics stipulated clear conditions that must be met before children should undergo genetic testing:

> In the case of children, given our ethical value of the state striving to reduce harm, we recommend that companies should only analyse the DNA of children if (i) a genetic test meets the criteria of the UK National Screening Committee … and (ii) valid parental consent has been given. For such testing to take place, a condition would need to be serious, the test would need to be precise and validated, and there would need to be an effective treatment or intervention available for children identified through early detection. (2010: 161)

Lastly, many policy documents also discuss concerns with regard to inappropriate advertisements. They highlight the need to ensure that advertisements should be accurate and not

misleading and that claims should be transparent and supported by current evidence as well as provide correct information with regard to test limitations, risks and benefits. As expressed by the ESHG:

> Research on DTC advertising of prescription medicine has shown that this has created an inappropriate demand for medications. Moreover, it has shown that various advertisements for drugs have been misleading. Overstatement of effectiveness or minimization of risk has led to inadequate or inappropriate changes in medication, diet or lifestyle by consumers. DTC advertising of genetic tests for health-related purposes runs the same risks as DTC advertising of prescription medicine in this regard. Aggressive marketing strategies and slogans for DTC genetic testing might overstate the potential for predictive information of such tests and overrate its future health implications.
>
> *(2010: 1271)*

Based on the aforementioned concerns, it is not surprising that various organizations have warned against the use of DTC testing. For example, the US Food and Drug Administration (FDA) stated:

> Despite the benefits of home testing, you should take precautions when using home-use tests. Home-use tests are intended to help you with your health care, but they should not replace periodic visits to your doctor … Most tests are best evaluated together with your medical history, a physical exam, and other testing. Always see your doctor if you are feeling sick, are worried about a possible medical condition, or if the test instructions recommend you do so.
>
> *(2010: 1)*

Similarly, the US Federal Trade Commission, aimed at preventing fraudulent, deceptive and unfair business practices in the marketplace and, to increase consumer awareness, also warned against DTC genetic testing on its website: 'Some of these tests lack scientific validity, and others provide medical results that are meaningful only in the context of a full medical evaluation' (2006: 1).

16.3 Regulation

16.3.1 In vitro *diagnostic medical devices legislation*

At the regulatory level, the self-tests described herein usually fall under the statutory regulation of medical devices. In Europe, three directives regulate medical devices, specifically Council Directive 90/385/EEC on the approximation of the laws of member states relating to active implantable medical devices, Council Directive 93/42/EEC concerning medical devices and Directive 98/79/EC on *in vitro* diagnostic medical devices. Directive 98/79/EC, which was published in 1998 and which came into force in all EU Member States in 2003, governs the safety, quality and performance of *in vitro* diagnostic medical devices. Specifically, it outlines the requirements for placing a product on the market (e.g. labelling, analytical and diagnostic performances) and imposes an obligation of post-marketing surveillance. Although generally less burdensome than regimes governing pharmaceutical products, both share a number of key features, including a duty to ensure the safety and performance of healthcare products. Moreover, regulatory authorities may remove existing products from the market should serious problems arise.

The above-mentioned directives regulate the safety and marketing of medical devices in the EU. Each member state must transpose certain provisions of the directives into their national laws. This legal framework is complemented by a variety of non-binding 'guidance documents' and 'implementing measures'. These documents seek to ensure a harmonised approach throughout the EU, and promote a shared approach for manufacturers and notified bodies (typically commercial entities licensed to perform conformity assessments of medical devices) involved in conformity assessments (see below) (Castle and Blaney 2010).

In the current Directive, medical devices are defined as:

> any instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of: diagnosis, prevention, monitoring, treatment or alleviation of disease; diagnosis, monitoring, treatment, alleviation or compensation for an injury or handicap; investigation, replacement or modification of the anatomy or of a physiological process; control of conception, and which does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means.
>
> *(Council Directive 93/42/EEC, article 1(2)(a))*

In vitro diagnostic medical devices are defined as:

> any medical device which is a reagent, reagent product, calibrator, control material, kit, instrument, apparatus, equipment, or system, whether used alone or in combination, intended by the manufacturer to be used *in vitro* for the examination of specimens, including blood and tissue donations, derived from the human body, solely or principally for the purpose of providing information: concerning a physiological or pathological state; or concerning a congenital abnormality; or to determine the safety and compatibility with potential recipients; or to monitor therapeutic measures.
>
> *(Directive 98/79/EC, article 2(b))*

Manufacturers wanting to place a medical device on the market or put it into service must first classify the product according to one of the three risk categories, namely low, moderate or high. Currently, Annex II to Directive 98/79/EC lists a small number of tests that have been classified as high risk (List A) or moderate risk (List B). Only devices listed in Annex II and devices intended for self-testing are subject to a conformity assessment by a third party. These third parties, called 'notified bodies', are private commercial companies licensed by national regulators to perform conformity assessments of medical devices, including *in vitro* diagnostic medical devices (Castle and Blaney 2010: 238; Directive 98/79/EC article 15). During this conformity assessment, medical devices receive a 'CE mark'. The CE mark symbolises that the manufacturer has declared the product to meet all legislative requirements, including safety requirements, and that the medical device has been assessed following the required procedure (French-Mowat and Burnett 2012: S23). The CE mark further indicates that the device 'can be freely marketed anywhere in the European Economic Area (EEA) without further control' (French-Mowat and Burnett 2012: S23). This pre-market review is one way to attempt to ensure truth-in-labelling (i.e. the manufacturer's intended use for the product is supported by the clinical data on the test's performance as set out in the technical file and summarised in the product label and in

promotional material). Unlike devices classified as moderate or high risk, low-risk devices do not go through pre-market review and only need to be registered. Despite these risk category distinctions, Directive 98/79/EC requires manufacturers to report all serious adverse incidents involving devices, regardless of their risk category, as per the mandatory vigilance procedure ensuring post-market surveillance (article 11).

The DTC genetic tests described in the first part of this chapter are considered *in vitro* diagnostic devices. However, technically speaking, they are not considered devices for self-testing as described by the directive because individuals must submit samples to a laboratory that then returns the results to the consumers. This does not change the fact that they are self-tests in the general definition of the term.

In 2008, the European Commission held a public consultation concerning the recast of the Medical Device Directives. Another public consultation was held in 2010. Based on these consultations, in September 2012, the European Commission proposed a new legal instrument to replace the current legislation (European Commission 2012a). An amended version of the Regulation was put to a vote in the European Parliament on 22 October 2013. At the time of writing, the proposed regulation was under discussion at the Council of Ministers.

A number of changes from the original Directive have already received sufficient support and will likely remain in the definitive version of the legislation. Major critiques were made to the existing classification system in the Directive, due to inconsistencies in classifying low risk versus moderate or high risk. For example, some tests listed in Annex II, List B, as having moderate risk raise questions of coherence: chlamydia tests were listed but no other tests for sexually transmitted diseases were included; testing for phenylketonuria (PKU) was also included in this list, but there were no other tests for heritable disorders; and prostate specific antigen (PSA) testing was listed, but no other tests for cancer were included. As a consequence of the current list-based system, most devices were not subject to pre-market review.

In response to these problems, the proposed Regulation suggests the adoption of a four-class risk-based classification system based on the Global Harmonisation Task Force (GHTF) model whereby *in vitro* devices would be divided into four categories ranging from high to low risk, depending on their potential impact on public health and/or the individual patient (European Commission 2012a). All genetic tests (including DTC genetic testing), for example, would fall under class C (i.e. moderate to high risk) and would be subject to pre-market review by a notified body unless they fall under a health institution exemption (European Commission 2012a). This categorisation is significant since most genetic tests to date would generally not fall within Annex II and therefore would not be subject to conformity assessments.

Despite the proposed changes to the Directive, the newly proposed Regulation on medical devices (European Commission 2012b) has been criticised for not sufficiently strengthening the evidentiary requirements on safety and efficiency before market introduction (Storz-Pfennig *et al.* 2013). In 2013, a group of experts submitted a petition to the European Commission, European Parliament and European Council, requesting that they 'enforce the rigorous clinical evaluation of medical devices' (Eikermann *et al.* 2013: 1; Petition 2013), noting:

> Currently, there is no requirement that approval of high and medium risk devices should be based on high quality evidence of benefits that are relevant to patients. We recommended that patient safety should be improved by requiring assessment of short and long term benefits and harms in well designed randomised clinical trials and other high quality clinical studies. Post-marketing surveillance should also be compulsory to ensure that benefits and harms of the device in real world settings are similar to those shown in clinical trials.
>
> *(Eikermann* et al. *2013: 1)*

The debate about these requirements also surrounds *in vitro* diagnostic medical devices in the proposed Regulation regarding the inclusion of the concept of clinical utility. Ultimately, the reason for undergoing (genetic) testing for health-related purposes should be based on the clinical utility of the test. Clinical utility refers to the ways in which the results of testing for a genetic marker (that is known to increase the risk of developing a disease) can be useful in clinical practice (i.e. treatment or prevention options). Moreover, clinical utility informs how results can be utilised to reduce the patient's risk of developing the disease and the extent to which this information contributes to our knowledge of what should be done to prevent disease.

During the 2010 public consultation on *in vitro* diagnostic medical devices, 67 per cent of respondents affirmed that clinical utility should not constitute part of the pre-market assessment process (European Commission 2012c). Rather, they considered it to be a 'moving concept' more effectively regulated at the member state level (European Commission 2012c: 22–3). Respondents also believed 'clinical utility should not be demonstrated by the manufacturer, but should be assessed by the user. The user would have to decide on the clinical utility of a specific IVD [*in vitro* diagnostic] medical device in a specific context or a specific population' (European Commission 2012c: 23). Furthermore, respondents stated that 'it would be impossible to demonstrate the clinical utility and therefore, it will limit the market access for innovative IVD medical devices' (European Commission 2012c: 23).

Despite this controversy, during the vote of the European Parliament in October 2013, clinical utility was introduced as a performance requirement for IVD devices that has to be taken into account where appropriate (Amendment 204). Even though this development could have a positive impact for public health by deterring medically irrelevant tests from reaching consumers, the proposed Regulation does not include a definition of clinical utility or any criteria for its assessment. Consequently, given the existence of different definitions of clinical utility and the subjective dimension these definitions may entail, as well as the lack of sufficient guidance regarding its interpretation, the new Regulation on IVD medical devices might fail, like the previous Directive, to provide a framework in which the quality of tests is sufficiently assessed before these tests are provided to individuals.

An additional concern focuses on the inadequacy of notified bodies to assess devices before market introduction (Cohen 2012a, 2012b; Godlee 2012). For example, the aforementioned petition urged that

> approval of high and medium risk devices (category III and IIb) as well as *in vitro* diagnostic devices should be done by a new public body similar to the European Medicines Agency or that the EMA is given an extended mandate to carry out these assessments.
>
> *(Eikermann* et al. *2013: 1)*

16.3.2 Canalisation of self-tests through healthcare professionals

Currently, Directive 98/79/EC does not permit *in vitro* diagnostic medical devices bearing the CE mark of conformity to be blocked from being placed on the market, but allows national measures to canalise the provision of devices. The Directive does not affect national measures that require a medical prescription for a specific device (Directive 98/79/EC, article 1(6)). However, the proposed Regulation attempts to introduce a change in the provision of genetic tests. During the vote of the European Parliament, a new article was integrated whereby genetic testing would only be performed by a medical professional, after appropriate genetic counselling and informed consent (2013). The approach of canalising genetic tests through healthcare professionals and emphasising the importance of genetic counselling and informed consent seems consistent with the national legislation of several European countries

and the *Additional Protocol to the Convention on Human Rights and Biomedicine, Concerning Genetic Testing for Health Purposes*.

More specifically, in the Netherlands, some self-tests (e.g. for HIV) must be canalised through a doctor or a pharmacist. Only after the user receives certain information (i.e. the possibility of being tested anonymously in the framework of medical supervision, the importance of medical supervision if the test is positive, the correct use of the test and the correct interpretation of test results) may the test be provided (Health Council of the Netherlands 2007). This is not considered the regulation of a 'service', but rather an integral part of the provision of a 'good'. This canalisation procedure provides the framework under which the 'good' can be provided (Health Council of the Netherlands 2007).

Along these lines, various other European countries have enacted legislation stipulating that genetic testing for health purposes may only be available with medical supervision, informed consent prior to testing and genetic counselling (Borry *et al.* 2012). For example, the German *Human Genetic Examination Act* (*Genetic Diagnosis Act* – GenDG) 2009 requires that diagnostic genetic testing be conducted by a physician and that predictive genetic testing be conducted by a certified medical specialist (section 2 §7). The *Act* specifies that these tests can only be conducted after sufficient information is given concerning the nature, meaning and consequences of the test, and after having obtained consent. Similarly, French legislation only permits genetic testing in the context of a clinical relationship and integrates specific requirements relating to genetic counselling and informed consent (see *Code Civil* 2013, article 16-1; *Code de la Santé Publique* 2013, article R1131-1).

The *Additional Protocol to the Convention on Human Rights and Biomedicine Concerning Genetic Testing for Health Purposes* contains similar requirements: '[a] genetic test for health purposes may only be performed under individualised medical supervision' (article 7). The *Additional Protocol* also emphasises the importance of genetic counselling, informed consent, the protection of persons unable to consent, respect for private life and the right to information, as well as the right not to know.

16.3.3 Screening legislation

Some countries have developed screening legislation that may also impact the provision of self-tests. The *Dutch Act on Population Screening* 1992, for example, provides a legal framework which evaluates a test/examination before it is offered to the population: 'population screening is defined as "a medical examination which is carried out in response to an offer made to the entire population or to a section thereof and to detect diseases of a certain kind or certain risk indicators, either wholly or partly for the benefit of the persons examined"' (Borry *et al.* 2012: 718). For such tests, the Dutch Minister of Welfare and Sports issues a permit. If performed without a permit, tests that detect (risk factors of) cancer and (risk factors of) 'incurable' diseases – which can neither be treated nor prevented – are illegal in the Netherlands. Based on article 7, the Minister can refuse a licence if a test is scientifically unsound, if it is not in accordance with the professional medical practice standards or if the potential health risks outweigh the expected benefits. However, problems remain in interpreting and enforcing the *Act*, notably for self-tests available via the Internet.

16.4 Conclusion

In the first part of this chapter, we discussed the main advantages and disadvantages of health tests offered directly to consumers, as expressed in national and international policies. Although we focused on documents specifically addressing DTC genetic testing, many issues are also applicable

to other types of DTC clinical tests. In the second half of this chapter, we discussed European laws that regulate various aspects of self-testing and genetic testing, including the European *in vitro* diagnostic medical devices legislation and the *Additional Protocol to the Convention on Human Rights and Biomedicine*. Together, these two sections provide an overview of the ethical and legal issues surrounding self-testing and, more specifically, DTC genetic testing.

Looking toward the future, what can we expect from self-tests? As patients are becoming more engaged in their own healthcare (Rozenblum and Bates 2013) and an increasing proportion of the population can access the Internet, there is reason to believe that more users will perform self-tests. In fact, some predict that self-tests will become widely used and even more readily available in years to come (Ronda *et al*. 2009).

In the narrower realm of DTC genetic testing, realistic or plausible future predictions are slightly more complicated. In 2010, Wright and Gregory-Jones believed the DTC genetic testing market to be relatively small. In recent years, a number of companies ceased selling DTC genetic testing services (Vorhaus 2012), while others have changed their policies for providing genetic testing to involve healthcare professionals (Howard and Borry 2012). Indeed, certain factors will influence the future of DTC genetic testing including, among others, public demand and general social acceptance, consensus or advocacy among healthcare professionals and other stakeholder groups regarding service models and legal regulations that may limit the activities of DTC genetic testing companies in certain jurisdictions. This last issue was recently highlighted by the FDA when it limited the activities of the DTC company 23andme (FDA 2013).

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Part IV
From bench to bedside

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17

Medical research

Future directions in the genome era

Don Chalmers[1]

Over a decade ago the National Bioethics Advisory Commission (NBAC) declared unequivocally that '[p]rotecting the rights and welfare of those who volunteer to participate in research is a fundamental tenet of ethical research' (2001a: i). This influential report went on to note that 'increasingly, the current system is being viewed as uneven in its ability to simultaneously protect the rights and welfare of research participants and promote ethically responsible research' (NBAC 2001a: i; Chalmers 2004). The first decade of this millennium saw an international reform effort to align the proper protection of human research participants with the accelerating expansion and pace of both academic and commercial research activity. There has been a sustained move to update research ethics and avoid the criticism that 'the philosophy of the state, its ethics – are always yesterday' (Brodsky 1987). This chapter will discuss the development of medical research ethics internationally, and the required future directions for the regulation of medical research and its ability to meet the challenges in the increasingly internationalised context of research in the 'Genome Era'.[2]

17.1 Background to the current governance of medical research

The traditional starting point for an account of the current principles of medical research ethics is the *Nuremberg Code* 1947 and the *Declaration of Helsinki* 1964. Both the *Code* and the *Declaration* were developed by reference to standards of medical ethics and, in the case of the *Code*, the complete failure to respect such standards. The fifth principle of the *Nuremberg Code* – that '[n]o experiment should be conducted where there is an *a priori* reason to believe that death or injury will occur' – derives from the central tenet of the *Hippocratic Oath* to do no harm to the

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2 A term coined by the current Director of the National Institute of Health (Collins 2010).

patient. This principle underlies the centuries of development of medical ethics (Baker 1995)[3] in different traditions (Mendelson 1998)[4] and finds expression in the current *Islamic Code of Medical Professional Ethics* (Universität Jena 1981). The *Oath* was restated in a modern form, reflecting the *Nuremberg Code*, in the World Medical Association's (WMA) *Declaration of Geneva* 1948: 'I will maintain the utmost respect for human life; … I will not use my medical knowledge contrary to the laws of humanity.' The *Declaration of Geneva* became the basis for the *International Code of Medical Ethics* the following year. However, the principles of medical ethics were largely directed to the doctor/patient relationship and the delivery of ethical medical services rather than research (Chalmers 2006).

Medical research was the core focus of the *Nuremberg Code*, which was a watershed in the development of modern research ethics. The *Nuremberg Code* was formulated as a direct response to the failure of professional and humane standards of medical experimentation, namely in the conduct of cruel, lethal and deadly experiments in Nazi concentration camps (Annas and Grodin 1992).[5] Similar revelations later emerged about Japanese atrocities in biological and chemical 'experiments' conducted on prisoners in Unit 731 in China between 1932 and 1945 (Nie *et al.* 2010). Unlike the German Nuremberg trials, many of the scientists in Unit 731 were not prosecuted or evidence was suppressed by US forces. Estimates of between 3,000 and 10,000 prisoners died during these unethical and lethal processes (Harris 1994). The *Nuremberg Code* dealt with universal standards for medical research and with 'matters of ethical significance to humanity' (Leake 1927: 57) in declaring ten principles for medical experimentation, as follows:

1. Voluntary consent of the human subject is essential.
2. The experiment should yield 'fruitful' results for the good of society, unprocurable by other means.
3. The experiment should be designed and based on the results of animal experimentation or natural history as such as anticipatory results justify the experiment.
4. The experiment should avoid all unnecessary physical and mental suffering and injury.
5. No experiment should be conducted where there is an *a priori* reason to believe that death or injury will occur.
6. The degree of risk should never exceed the humanitarian importance of the problem to be solved.
7. Proper preparations and adequate facilities should be provided to protect the subject against even remote possibilities of injury.
8. The experiment should be conducted only by scientifically qualified persons with the highest degree of skill and care in the experiment.
9. The subject should be at liberty to end the experiment where continuation is impossible.

3 See 'The Historical Context of the American Medical Association's 1847 Code of Ethics' (Baker 1995) and also 'Creating a Medical Profession in the United States: The First Code of Ethics of the American Medical Association' (Reiser 1995). This work assessed the work of Benjamin Rush in drawing up the American Medical Association's *Code of Ethics* 1847, which was influenced by the writings of John Gregory (1725–73) and Thomas Percival (1740–1804). Baker has quipped that the American *Code of Medical Ethics* was '… nothing more than self-serving professional etiquettes … to disguise organized medicine's attempt to monopolize medical thought so that, by driving homeopaths and other "irregular" competitors from the medical market place, it could ultimately monopolize medical practice.'

4 See also Rahman (1997).

5 See also Wikler and Barondess (1993).

10. The scientist must terminate an experiment where there is probable cause to believe that injury, disability or death will result to the 'experimental subject'.

(Nuremberg Trial 1949)

The WMA formally developed and adopted these ten principles in the influential *Declaration of Helsinki* in 1964. This *Declaration* has been regularly revised and updated, and establishes the *key pillars* for modern ethical review of medical research which echo the principles of the *Code*, namely:

1. Voluntary consent of the research participant;
2. Independent review of the research project;
3. Assessment of the risk to participants;
4. Conduct of the research by competent researchers of integrity; and
5. Demonstrated merit in the proposed research project.

(World Medical Association 2013)

The *Declaration of Helsinki* influenced national responses to research ethics with the introduction of codes governing ethical research practice (Furrow *et al.* 2000: 979).

Originally, impartial scientific peers were to undertake this ethical review. The idea of any ethical assessment by outside 'non-institutional' or non-scientific 'lay' members of the community had not emerged. Events in the United States were to have a profound and lasting impact not only on the development of modern medical research ethics in America but also on the independent review of human research projects around the world. The introduction of the American formal ethics review system was, in the 1970s, another important watershed in the development of medical research ethics. In America, a 'series of scandals of social science research and medical research conducted with the sick and illiterate underlined the need to systematically and rigorously protect individuals in research' (NBAC 2001a: i).[6] The Tuskegee Syphilis Study was one of the most widely publicised and egregious failures of proper human research standards (Furrow *et al.* 2000: 979). In response, the *National Research Act* 1974 established the National Commission for the Protection of Human Subjects of Biomedical and Behavioural Research and, importantly, required each institution conducting federally supported research involving human subjects to establish Institutional Review Boards (IRBs) (President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research 1983). The following year, the Department of Health, Education and Welfare issued the *Policy for the Protection of Human Research Subjects* (1975), which resulted in the establishment of IRBs in universities, medical schools and hospitals conducting research. This rapid expansion consolidated the IRB as the keystone of the national regulatory system for ethical review of research involving humans.[7] IRBs were required to confirm the voluntary consent of research 'subjects' (more usually now referred to as participants).

Critically, the *Helsinki Code* standard for 'independent review of the research project' was formalised in the IRB. The IRB required the appointment of '… at least one member who is not

6 See also Beecher (1966, 1968), Katz (1993) and Levine (1986).

7 The 'Common Rule' *Public Welfare*, 45 CFR, § 46.101 (a)–(f). The Food and Drug Administration (FDA) has correlative regulations paralleling the Department of Health and Human Services Policy.

otherwise affiliated with the institution' (*Food and Drugs* 21 CFR, § 56.107). This established, for the first time, a systematic procedure for this independent review and approval of research protocols. Monitoring and reporting requirements were also introduced for annual review, approval of changes to a protocol and strict reporting of any risk to participants. A 'light-touch' requirement was added to these procedures, making compliance and IRB approval preconditions for federal research funding. This is not to suggest that the introduction of IRBs was a seamless and uniform process; institutions reported variations, inter alia in professional composition, frequency of meetings, review procedures and access to records.

Reports of research impropriety were not only surfacing in American institutions. In New Zealand, following a Royal Commission into unethical research on cervical cancer patients, major reforms in the institutional basis for ethics committees were introduced (Dawson and Peart 2003). The formalisation of the American IRB system has been influential in the development of research ethics committees around the world and, arguably the most influential American legal export in the regulation of ethical review of research. In the decades following the *National Research Act*, IRB equivalents were introduced around the world in research-active countries. Essentially, research ethics committees were established to review and approve human subjects research for both the voluntary and informed consent of participants, and to ensure the expected benefits of the project did not supersede the interests and safety of the participants. In Australia, for example, the ethics review system traces back to the National Health and Medical Research Council's (NHMRC) ratification of the *Declaration of Helsinki* in 1967. The Council then introduced the *Statement on Human Experimentation*, establishing a system of ethical review for medical research projects and a system of Institutional Ethics Committees (IECs) based on the US model, in 1982. IECs were required to ensure compliance with the *Statement* and their ethical approval were made preconditions to research funding by the NHMRC. The *Statement on Human Experimentation* was replaced by the *National Statement on Ethical Conduct in Human Research* in 1999 (NHMRC 2007)[8] and was significantly revised in 2007.

There was a similar introduction of the research ethics committee system into other research-active countries. These research ethics committees (RECs)[9] were similarly composed of independent and non-affiliated lay members, where these IRB equivalents established a two-tier review system. The first tier continued the researcher's primary ethical and legal duties to the research subjects and the integrity of the project's design. The introduction of IRB/REC equivalents essentially established an independent second tier for the review and approval of research projects involving human subjects as a precondition for public research funding. Some countries have also established a third tier. The National Consultative Committee for Health and Life Sciences in France was a pioneer in its published reports on many aspects of bioethics and medical research. In 1992, the mandate of the Australian Health Ethics Committee (AHEC) set out not only to produce reports on medical research, but also to have sole responsibility for the formulation of guidelines dealing with medical research (NHMRC 1992, section 8),[10] and overseeing the developing national system of research

8 This statement was endorsed by the Australian Vice Chancellors' Committee, the Australian Research Council and the Learned Academies in 1999. It is a national research code of practice governing social as well as biomedical research.

9 'Research ethics committee' is used generically to refer to committees that provide ethical approval for medical and health research projects and that have the primary duty to protect the research participants. They have a variety of national designations: local research ethics committees (UK); human research ethics committees (Australia); institutional review boards (USA); institutional ethics committees (New Zealand).

10 However, these guidelines must be drawn up following a unique two-stage public consultation process under section 14.

ethics review committees. National committees under a variety of titles have been established worldwide to oversee or guide their national ethics review systems (Chalmers 2001a).

17.2 Future challenges in medical research review

17.2.1 Research governance

The governance agenda in research ethics review does not only focus on the central role of the committee, but also considers the wider issues of effective and proper management of research(ers) within the institution. Thus the agenda is a considerable challenge that includes consideration of certification standards for research facilities, risk management in the types of research conducted at the institution, insurance coverage and indemnity arrangements and research training (Chalmers 2001b). Governance borrows from the corporate model and follows the staged analysis of understanding, planning, modifying and implementing changes to improve the research endeavour. The introduction of the IRB system in the USA and its counterparts in other countries was *not* based on a centralised national system of bureaucracy. Essentially, institutions themselves were required to follow a set of general national standards of ethical review.

Perhaps unsurprisingly, different institutions followed the same 'common rule' of review and approval, but not always using the same procedural pathway. Different institutions developed idiosyncratic characteristics. The size of ethics review committees was varied and particularly over-representative of researchers and numbers 'affiliated with the institution' in relation to the non-affiliated members. They also varied in determining boundaries between the scientific and the ethical aspects of the project. In Australia, an inquiry in the mid-1990s noted these and other variations, including workload pressures, lack of scientific expertise, absence of training opportunities for committee members, issues of potential legal liability for ethics committee members, non-pharmaceutical company-sponsored clinical trials and lack of coordination between ethics committees dealing with multi-centre research and project monitoring by ethics committees (Commonwealth of Australia 1996).

Ethics committees were increasingly and commonly united in their complaints about the volume of paperwork to consider, particularly the length and complexity of participant consent forms and the accompanying project information sheets. Gradually, research ethics committees also began to consider social science research projects. The increased work volume of projects motivated procedures for *expedited review*, permitting some projects to be considered by the chair or a subcommittee rather than by the full committee. Research governance reform later introduced a *low-risk* classification for some research, permitting ethics committees to expedite and accelerate approval time of these types of applications while concentrating their expertise on more complex applications. There were continuing concerns, however, about 'excessive workloads for RECs, delays in carrying out reviews … and the risk of important problems being overlooked [in the context] of commercial imperatives and the reality of a global market' (Australian Health and Ministers Advisory Council 2006).

Ultimately, a reform agenda developed for research ethics committees. The international 'governance' (Leblanc and Gillies 2005) agenda for restructuring companies, government administration and civil society itself focused on ethics committees. This governance agenda recognised the centrality of participant consent in research and ethics committee approval, but extended beyond the ethics committee to the whole research endeavour within an institution. At the opening of the new millennium, the NBAC issued a two-volume Report (NBAC 2001a, 2001b) that heralded 'a time for change' in reform of the ethics review system to ensure protection of research

participants in the United States. The Report recommended a range of initiatives to improve the research review system including education for IRB members, accreditation of IRBs, independent risk-benefit assessment, investigator disclosure of interests, additional protections for vulnerable groups, compensation for participants suffering direct harm, review of multi-site research and reduced threats to privacy (NBAC 2001b). The NBAC concluded that 'a comprehensive and effective oversight system is essential to uniformly protect the rights and welfare of participants while permitting ethically and scientifically responsible research to proceed without undue delay' (NBAC 2001b, recommendation 2.2).

This Report noted the need for federal legislation to protect the participants in both publicly and privately sponsored research with: a single independent Federal Office for Human Research Oversight; requirements for education, certification and accreditation of committees; review of IRB membership with the inclusion of members who represent perspectives of participants unaffiliated with the institution; emphasising the informed consent process rather than editorialising documentation; improving and strengthening privacy; investigating the need for compensation programmes; and better resourcing of IRBs (National Bioethics Advisory Commission 2001b, recommendations 2.1–2.2, 3.1–3.4, 3.9–3.10, 5.1, 5.3–5.4, 6.6, 7.1).

These recommendations were echoed in reports from other research countries[11] and were followed by greater scrutiny and organization of ethics review processes. In the UK, for example, Health Authorities were responsible for establishing *local research ethics committees* that centralised guidelines in the Central Office for Research Ethics Committees within the Department of Health (UK Department of Health 2011). This process of continuing review led to a close examination of the regulatory and governance environment in medical research by the UK Academy of Medical Sciences. In their report, a number of recommendations were proposed to increase the speed of decision-making, reduce complexity and eliminate unnecessary bureaucracy and cost in carrying out health research (UK Academy of Medical Sciences 2010a). In this respect, the governance agenda accepted the efficiency as well as the safety aspects of research, although debates are ongoing regarding the use of consent waivers where there is a public benefit interest and the value of the research outweighs to a substantial degree the private interests of personal privacy (Organization for Economic Cooperation and Development (OECD) 2009).

Establishing procedures for single review of multi-centre research, without compromising proper ethical safeguards, is a continuing governance challenge. The Australian *National Statement* in 2007 allowed RECs to accept review by a single ethics review body (National Health and Medical Research Council 2007, chapters 5.3.1–5.3.2). The Harmonisation of Multi-centre Ethical Review is implementing an initiative to recognise a single ethical and scientific review of multi-centre research, which would ensure conformity to the researchers' national as well as local ethical standards of the country in which the research is conducted.

Efficiency may be the declared aim of streamlining ethics approvals systems. An Australian Report noted that a strong incentive for streamlining is the reduction in unnecessary duplication, transparency and consistency, but also acknowledged that these efficiencies could make Australia more attractive for international investment in commercial-sponsored clinical trials. The same Report stated that 'in a global market, it is important that processes for scientific and ethics review do not impede Australian … participation in clinical trials … [but] Sponsors speak of the Australian ethics review process introducing delays that tarnish Australia's reputation as a desirable location for the conduct of multi-centre clinical trials' (Australian Health and Ministers Advisory Council 2006: 14, 17).

11 In the UK see McLean (2004); in Canada, see Llewellyn *et al.* (2003).

The governance agenda is crucial in the face of increased research activity, which suggests enhanced regulation and accountability for the future evolution of the ethics review system that still relies substantially on volunteerism (Chalmers 2011).

17.2.2 The globalised research governance

The modern 'Genome Era' (Sulston and Ferry 2003), as described by Francis Collins and others, has seen an increasing globalisation of research with cross-border collaborations, data linkage and multi-centre clinical trials. In this new era, there has been a vast increase in the funding of medical and genomic research. Technologies, particularly whole genome sequencing (WGS), are becoming cheaper with increasing volume feasibility for large-scale data collection linkage. Increased research funding is not only driving expectations that breakthroughs in health outcomes are on the horizon, but also that these improved outcomes will increase wealth in developing economies. Many nations have adopted national biotechnology strategies to drive biomedical research and encourage private investment. As such, the Academy of Medical Sciences claims that '[t]he UK must grow and sustain its world-class biomedical workforce for our knowledge economy' (UK Academy of Medical Sciences 2010b, 2010c). Significant international collaborations, however, are driven by more beneficent motives. Innovative incentives[12] for multinational pharmaceutical companies to develop drugs in developing countries are being translated into public–private collaborations. Examples include the Medicines for Malaria Venture (MMV) Foundation[13] collaboration with Novartis and the Medicines for Malaria Venture that developed a prophylactic treatment through its collaboration (Novatis Global 2011).[14] Others still are facilitating large-scale research, such as the International Cancer Genome Consortium.

Greater activity and investment in medical research, particularly as international collaborations increase, confirms the need to review international regulatory frameworks. The current ethics review system remains focused on activity within institutions and within national borders. The challenge in the genome era is to develop a more harmonised international regulatory framework for research ethics review. An essential aspect of this challenge will be the development of procedures for the mutual recognition of IRB/REC approvals of cross-border research projects. An internationally harmonised system should be based on an 'equivalent protection' doctrine requiring that the highest standards of research ethics should apply where there may be differences in the ethical research standards between countries (Sugarman 2005; Chima 2006).

These international instruments may be divided into two classes: those of *direct* relevance to medical research; and those that have more indirect *referential* relevance (Pace Mason *et al.* 2010: 572). In the *direct* category, the International Conference of Harmonisation (originally the regulatory authorities of Europe, Japan and the USA) *Guidelines for Good Clinical Practice* were introduced to provide public assurance that the rights, safety and well-being of trial subjects involved in clinical trials are credible and consistent with the *Declaration of Helsinki*. At the regional level, the Council of Europe's *Convention on Human Rights and Biomedicine* 1997 sets out the broad general principles for human subjects research. Also of *direct* influence is the Council of Europe's

12 An idea championed by Thomas Pogge (2002).

13 The Medicines for Malaria Venture was funded through public and philanthropic donations from groups including the government of Switzerland, the UK Department of International Development, the government of the Netherlands, the Bill & Melinda Gates Foundation, the Rockefeller Foundation, US AID and the World Bank (MMV 2013).

14 In collaboration with international organizations, Novartis provides the anti-malarial medicine Coartem without profit for public-sector use in malaria-endemic developing countries.

Directive 2001/20/EC on Research Development for Medicinal Products, which emphasises good medical practice and the ethical and scientific quality requirements for designing, conducting and reporting clinical trials with human subjects. It assures 'that the rights, safety and well-being of prior subjects are protected, and that the results of the clinical trial are credible' (article 1(2); European Commission 2013).

In the *referential* category, the United Nations Educational, Scientific and Cultural Organization (UNESCO) undertook pioneering work in setting standards for human genetic research. Its *Declaration on the Human Genome and Human Rights* declared that '[n]o research … concerning the human genome … should prevail over respect for the human rights, fundamental freedoms and human dignity of individuals or … groups of people' (1997, article 10). The *Declaration* is non-binding but has been widely influential in the revision of some national codes of ethics, such as the 1999 version of the Australian *National Statement on Ethical Conduct in Human Research*. Similarly, the codes of good manufacturing practice issued by the various therapeutic goods administration organizations in different countries reference international standards. In 2011, the World Health Organization (WHO) developed the *Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants* in the way of this *referential* category. In the document, they acknowledge the *International Ethical Guidelines for Biomedical Research Involving Human Subjects* published by the Council of International Organizations of Medical Sciences (CIOMS) and the WHO in 1993. The CIOMS and WHO also collaborated in the publication of the *International Ethical Guidelines for Epidemiological Studies* in 2008. Apart from these, the myriad of international documents that are referred to and may be considered in revisions of national codes and international documents demonstrates a fair degree of national copycatting in setting research ethics standards. For example, the content featured in the 1999 version of the Australian *National Statement on Ethical Conduct in Human Research* was reflective of the United States *Code of Federal Regulations*, the Canadian *Code of Ethical Conduct for Research Involving Humans* (Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada and Social Sciences and Humanities Research Council of Canada 2010) and similar guidelines in the United Kingdom (Royal College of Physicians 2007).

New international collaborations in medical research have increased the need to assess existing ethics review standards and to consider further avenues for harmonising them. In this respect, there have been modest proposals for a framework and platform to facilitate research ethics discussion at an international level, enabling the ethics to catch up with the scientific collaborations that have made research an increasingly global endeavour (Kaye *et al*. 2012). More boldly, there have been proposals for an International Code of Conduct for global genomic research projects (Global Alliance for Genomic Health 2014).

17.2.3 Biobanks and research governance

In the genome era, human tissue and genomic data collection have become essential research tools and have allowed the translation of biomedical innovations to improve healthcare delivery. Biobanks are seen as flagships of the drive to personalised medicine (Chalmers *et al*. 2013). These collections have adopted the neologism of 'biobanks' (Chalmers and Nicol 2008) and depend on advances in sequencing, computational and information technologies. Biobanks are key drivers in new approaches to genomic science that now span large international collaborations of researchers in global networks, such as the International Cancer Genome Consortium (ICGC) (Hudson 2010), The Cancer Genome Atlas (TCGA) (National Cancer Institute 2013) and the Global Alliance for Genomic Health (2014). Large international collaborative cancer studies are

now feasible to identify genetic risk loci and somatic mutations using genome-wide association studies (Easton *et al.* 2007).

Biobanks also appear on governance agendas (Kaye 2011), but with greater urgency not only due to the scale of the endeavours, but also because of how their unique aspects have created new research ethics issues. Previously an individual-specific principle, the protection of research participants in biobanking often considers how the research protocol will benefit the public good. Secondly, consent to participate in one research project is now supplemented with consent for long-term data and tissue storage for future undefined research uses. This controversial idea of broad future consent has been widely debated (Kaye and Stranger 2009).[15] Third, ongoing and dynamic governance that factors in public interest more prominently has largely supplanted traditional institutional governance and accountability processes. Biobank research represents a distinct conceptual shift in research from a 'one project, one centre, one jurisdiction, one point in time' paradigm, to multi-centre group projects and research collaborations crossing national borders.

The proliferation of biobanks around the world encourages an equal proliferation in academic scholarship, debates about policy approaches, and strategies for ethics review and governance of biobanks (Kaye and Stranger 2009; Pascuzzi *et al.* 2013). Before its establishment, community engagement[16] has generally been undertaken and independent bodies established to administer and operate the biobank, such as the UK Biobank. It also requires an Ethics and Governance Council to address ethical concerns and 'to set standards for the project, and to ensure that safeguards are in place for scientifically and ethically approved research' (UK Biobank 2013). Biobanks have also had to develop more sophisticated consent processes that recognise the ongoing nature of participation in research. Similarly, biobanks have equally sophisticated data management and access procedure systems to facilitate research while safeguarding the privacy of participants and protecting confidential and proprietary data. In addition to key biobank governance issues of oversight, security and access, procedures are required in the unlikely case of discontinuing the biobank.

Biobanks have also promoted some reconsideration of the role of the ethics review committee not only as it relates to the institutional governance agenda, but also to wider considerations of the regulatory environment. The UK Biobank Ethics and Governance Council maintains a continuing role in public engagement. In this wider regulatory environment, Brownsword has cautioned that regulatory environments are varied and complex (2013: 43–4). Yet despite this complexity, there is a need to avoid two serious misunderstandings about the characteristics of the regulatory environment. The first misunderstanding, legal exclusivity, is to assume that the only signals in the regulatory environment are formal legal signals. The second misunderstanding, normative exclusivity, is to assume that the only signals in the regulatory environment are normative (that is signals that prescribe what ought, or ought not, to be done). It is easy enough to appreciate why lawyers might be tempted to jump to these conclusions, but why precisely are they in error? In the research ethics and biobank regulatory environment, it cannot be the role of ethics committees, much less lawyers, to police research projects; the ethics review governance system relies on the integrity of all involved in the governance processes and the researchers themselves (Chalmers and Pettit 1989).

15 See also Gibbons and Kaye (2007), Gottweis and Petersen (2008), Mascalzoni *et al.* (2008), Taylor (2008) and Hansson (2006).

16 In some cases this has involved conducting deliberative processes by engaging selected categories of individuals reflecting the 'community' to participate and deliberate on their preferences, judgments, expectations, concerns and values in relation to a proposed biobank (Australian National University 2013).

17.2.4 Privacy and data protection governance

Genetic research can uncover information, not only about the participants but also about their parents, siblings, children and relations. This prophetic potential has prompted many countries to develop codes of practice for ethical conduct in human genetic research. This potential is magnified in the context of biobanking. The research ethics committee must assess the consent aspects of a research protocol, but also the confidentiality and privacy issues of stored genetic information, proposed future research and communication of research results. Arguably, the greatest challenge for research and open genomic data sharing in the genome era is information privacy and security (Greenbaum *et al.* 2011; Global Alliance for Genomic Health 2014). This challenge is emphasised in the modern research regulatory environment in which the scientific community, research funders and governments have promoted and encouraged policies and practices of open access to genomic data for scientific research and medical progress (Greenbaum *et al.* 2011; Birney *et al.* 2009; Walport and Brest 2011). Open access is an accepted norm for large-scale, publicly funded genomic science projects.

At the national level, many privacy or data protection laws were based on the influential OECD *Information Privacy Principles* published in 1980. These principles[17] brought a measure of consistency to national privacy approaches by setting standards for the collection, storage, release, access and accountability for personal information. Later EU privacy directives, particularly the *Directive 95/46/EC* on data protection on trans-border data flow, maintained this principled approach.[18] Privacy or data protection legislation encompasses the collection, storage, release, access to and challenge to personal information.

In the increasingly globalised research environment, the key issue is privacy in trans-border data linkage, particularly in genomic research. Clearly, there are technical requirements for privacy enhancement technologies to shield participant information. In addition, some international projects adopt from the outset procedures to ensure approved access to data. For example, the Data Access Compliance Office (DACO) of the International Cancer Genome Consortium (ICGC) uses 'a tiered access system' (Joly *et al.* 2012) with access to separately classified 'open' and 'controlled' data. The 'controlled' data classification covers sensitive personal data, such as detailed phenotype and health outcome data and genome sequences files. This data, if released at all, requires the consideration and approval of the Data Access Compliance Office under the oversight of the International Data Access Committee. Like other data access processes, all applications for data access are documented, recorded and regularly reviewed. The individual project arrangements for data access and sharing within the ICGC have worked satisfactorily but are not necessarily a template for translation as a model for the future of more widespread data sharing.

There have been justifiable claims that privacy protection is the main challenge to open genomic data sharing (Greenbaum *et al.* 2011). The regulatory theorist Brownsword proposed a 'triple bottom line' test for the adequacy of the privacy and data protection regulatory environment for biobanks during their start-up period: '(i) that both participation and the use of participants' samples and data are based on free and informed consent; (ii) that the privacy, confidentiality, and fair data processing rights of participants are respected; and (iii) that the proprietary rights (if any) of participants are respected' (2013: 42). The latter two continue to apply throughout the duration of tissue and/or data storage (Knoppers 2007: 144).

17 Collection Limitation Principle, Data Quality Principle, Purpose Specification Principle, Use Limitation Principle, Openness Principle, Individual Participation Principle, Accountability Principle.

18 See also *Directive 2002/58/EC on privacy and electronic communications*.

Nevertheless, data sharing is expanding in the big-data genome era and concerns surrounding the actual security of stored data persist. The UK Academy of Medical Science expressed one such concern. It argues that the impact of 'data protection regulation in particular represents a serious impediment to medical research without apparently providing significant benefit to patients. Streamlining and improving current regulation represents a cost-effective approach to creating a more fertile and productive research environment.' There have been concerns within the genomics community that open access 'may not result in greater and more rapid scientific benefits' but may 'result in duplication of effort, cause problems in the peer review system and create incentives for generating more publicly inaccessible databases' (Foster and Sharp 2007).

The balance between open access and data protection is critical to address any privacy concerns participants and the wider community might have. The governance, sharing, design and implementation of revised data access and policies are major challenges in the genome era.

17.2.5 Research governance, conflicts of interest and public trust

Medical research is frequently conducted in a commercialised environment (Chalmers and Nicol 2004: 116). This environment has been supported and promoted by national biotechnology strategies that include medical research as one of the key drivers of commercial and knowledge-based economic development (Sakaiya 1991). Many small, start-up and spin-off companies have their genesis in symbiotic collaborations and partnerships with larger companies as a source for their research funding.

This growing commercialism raises issues of public trust and was the focus of a UK Parliamentary Select Committee. It discussed the crisis of trust in society's attitudes towards science and noted the particular challenges to scientific independence (House of Lords Select Committee on Science and Technology 2000). The Committee argued that 'the concept of independence has become problematic, particularly because of the increasing commercialisation of the research. In our view, scientists must robustly protect and vindicate their independence. Sponsorships and affiliations must be openly declared … [and] research output is submitted to peer review and published in the academic literature' (House of Lords Select Committee on Science and Technology 2000, paras 13–14). Later, the National Institutes for Health adopted a stricter – described as 'draconian'[19] – standard on conflicts of interest in their *Supplemental Standards of Ethical Conduct and Financial Disclosure Requirements for Employees of the Department of Health and Human Services* (2005, § 45.5501) addressing extracurricular activities and interests of their staff.

Detecting and avoiding conflicts of interest by ensuring full disclosure is important for maintaining public trust. In the early development of research ethics reviews, committees were placed in the invidious situation of checking on the ethical integrity of commercial research relations. Research ethics committees were required to examine any business, budget, contractual or other relevant relationships between the researcher and any commercial organization to identify any conflicts with ethical standards (NHMRC 1999, chapters 12.5–12.6).

The NBAC preferred to adopt a governance approach that placed responsibility for checking and auditing potential conflicts of interest on the institution and researchers themselves. The NBAC used the euphemism '*managing* conflicts of interests' (emphasis added) in recommending that sponsors and institutions should 'develop policies and mechanisms to identify and manage all types of institutional, IRB and investigator conflicts of interest. In particular, all relevant conflicts of interest should be disclosed to participants (NBAC 2001a, recommendation 3.8). The

19 These regulations were described as 'punitive and draconian' (Dutton 2005).

proper disclosure of any potential conflict of interest is the established norm[20] and is reflected in international statements.[21]

17.3 Conclusion

In the same year that the Human Genome Project consortium and Celera Genomics made their joint announcement for successfully sequencing the human genome (2001a, 2001b), the NBAC presciently announced a time for change in the regulation and governance of research ethics to meet the demands of the new genome era (NBAC 2001a: prologue). The primary role of the ethics review system remains the protection of the welfare and interests of research participants. In line with this view, the NBAC noted that 'a comprehensive and effective oversight system is essential to uniformly protect the rights and welfare of participants, while permitting ethically and scientifically responsible research to proceed without undue delay' (2001a, recommendation 2.2).

The proper balance between the values of scientific freedom and dignity of the individual research participant remains the dominant theme of research ethics. This theme has seen a shift to informational and privacy concerns in genomic research. In addition, greater international collaborations in research efforts emphasise these issues and the need for change in the proper governance of international projects. In this respect, the research governance agenda has widened the focus of research ethics beyond ethics committees to include researchers and institutions in the entire research endeavour. This is a fundamental requirement in the increasingly globalised research environment and particularly in genomic research. The philosopher, Peter Singer (2003, cited in Kirby 2003) observed the '… science is barrelling forward, but the ethics aren't … I don't want the science to slow down. I want the ethics to catch up.'[22]

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21 For example, the Human Genome Organization (HUGO) Ethical, Legal, and Social Issues Committee, *Statement on the Principled Conduct of Genetics Research* (1996), HUGO Ethics Committee's *Statement on DNA Sampling: Control and Access* (1998), HUGO Ethics Committee's *Statement on Benefit-Sharing* (2000) and HUGO Intellectual Property Committee's *Statement on Patenting of DNA Sequences in Particular Response to the European Biotechnology Directive* (2000).

22 Professor Singer was talking about nanotechnology research but this equally applies to genomics.

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18

The ethical and legal duties of physicians in clinical genetics and genomics

Adrian Thorogood and Bartha Maria Knoppers

18.1 Introduction

Genetics is by no means a new field of medicine, but it is certainly a rapidly evolving one. This chapter explores the ethical and legal duties of physicians in the context of genetic testing. We begin this introduction by comparing genetic information with other types of health information. This comparison will clarify how the traditional ethical and legal duties of physicians apply in the genetic context. First, our genetic make-up is largely inherited. Clinically significant genetic information concerns not just patients, but also their families. Second, genetic information is a powerful predictor of disease in individuals and across generations. Third, our genetic make-up is uniquely identifying: our genes can reveal information about where we come from and to whom we are related. Accordingly, professional norms must reflect these characteristics of genetic information, while being mindful that other non-genetic forms of health information can also exhibit these 'exceptional' qualities. It must also be remembered that both genetic and environmental (e.g. lifestyle, socio-economic) factors play a role in all common diseases. The predictive strength of genetic testing is 'probabilistic,' meaning a positive result does not reveal a condition, but rather a predisposition: an increased likelihood that a condition may arise in the future. It is imperative that medical decision-making reflect the inherent uncertainty of genetic testing as well as its broad social implications.

The scope of this chapter is limited to the use and interpretation of genetic tests in clinical practice. In general, genetic tests have three purposes. Diagnostic genetic testing is used to characterize an existing condition and its genetic cause. It is often used in the paediatric context to diagnose children affected by disorders suspected to be genetic. Carrier status testing is used to inform reproductive decision-making and generally concerns recessive, single-gene disorders. Finally, predisposition testing examines whether an asymptomatic individual is resistant to or at heightened risk of developing a particular medical condition in the future. Predisposition testing may involve common, multifactorial diseases with a genetic component, such as heart disease or diabetes. It also targets autosomal dominant conditions manifesting in adulthood, such as Huntington's disease, and high-penetrance conditions, such as breast cancer.

Section 18.2 of this chapter outlines how the ethical and legal duties of physicians described elsewhere in this Handbook apply in the context of classical genetic testing. First, physicians have

a duty to obtain informed consent for genetic testing. Particular consideration must be given to the types of information included in this process. Second, the duty to treat requires physicians to identify the situations where genetic testing is appropriate. This may be particularly challenging in the paediatric context, where decisions are complicated by the child's temporary inability to consent to testing and parents' shared interest in their child's genetic status. Third, physicians have a 'duty to warn' patients and perhaps their family members of shared genetic risks. The duty to warn, and the tension it may create with the physician's duty of confidentiality if extended to third parties, are also discussed.

With the sequencing of the human genome in the early 2000s (Lander *et al.* 2001), genetic testing is shifting towards a genomics paradigm. New whole-genome and whole-exome sequencing (WGS/WES) technologies allow physicians to generate massive amounts of genetic information about their patients. Section 18.3 discusses emerging duties and challenges for physicians in the genomics age. With a rapidly expanding knowledge base, and the potential to return vast amounts of information, care must be exercised to administer WGS/WES tests under appropriate circumstances, to interpret results correctly, and to handle the communication of clinically significant results unrelated to the initial diagnostic question. Indeed, the physician may not be able to ignore 'incidental' findings, and may face an emerging duty to warn patients of clinically significant results concerning treatable or preventable conditions. Furthermore, the sheer volume of information generated may exacerbate the tension between patient confidentiality and the duty to warn relatives of patients. Section 18.3 concludes with a discussion of the patient's emerging 'right not to know' his or her genetic status. Individuals have an interest in controlling the information they receive, and may have a compelling interest in not knowing certain information about their health. Alternatively, fully respecting patients' informational self-determination and right not to know may put their health at risk.

This shifting normative landscape is particularly tumultuous in the pediatrics context, explored further in section 18.4 (also see Chapter 5). Briefly, many genetic conditions first exhibit symptoms during childhood; some may require immediate intervention. Since children are not considered capable of authorizing genetic testing, their choices about testing should be preserved until adulthood where possible, and interventions should be undertaken where medically actionable during childhood. In addition, newborn screening programmes may also be pressured to expand to include WGS, and even to supply every newborn with a health report card.

Basic bioethics principles inform our discussion of professional norms in medical genetics. They include:

- *Autonomy*. The values and preferences of patients must be respected. Patients should be allowed to exercise meaningful control over when genetic tests are administered (consent), and who has access to their test results (privacy/confidentiality). This autonomy interest encompasses control over the flow of information from the health professional to the patient. Indeed, the patient's 'informational self-determination' is especially important in the genetics context (Andorno 2004). Genetic testing often concerns uncertain results (either because of high error rates of sequencing or the low penetrance of genes) or untreatable conditions. In such cases, a patient may legitimately prefer *not* to know his or her genetic status.
- *Beneficence*. Health professionals have fiduciary obligations to act in the best interests of patients. Genetics poses many questions involving complex weighing of benefits and risks. Beneficence must be considered when deciding to carry out a genetic test. Testing for uncertain or untreatable predispositions may do more harm than good. In some cases,

genetic tests may reveal risks shared by patients' family members. As we discuss below, preventing harm to these third parties is increasingly becoming an ethical imperative for physicians.

- *Privacy*. As with other forms of sensitive health information, patients have a strong interest in limiting access to their genetic test results. A common privacy concern in genetics is discrimination by employers or health and life insurance providers (Pioro *et al.* 2013). Another fear is stigmatization of individuals or ethnicities with 'undesirable' traits. Protecting privacy in healthcare is complicated by the booming availability and connectivity of health data and the myriad third-party interests from researchers, government, and industry in mining that information (Beauchamp and Childress 2008).

As will become evident in the discussion below, decision-making in genetics will often need to strike a balance between a multitude of conflicting and interdependent interests. For this reason, ethical decision-making in clinical genetics requires a proportional, context-specific balancing of interests and ethical principles.

18.2 Traditional professional norms in genetic medicine

18.2.1 Consent

As for any medical procedure, the consent of the patient is required before a physician carries out a genetic test. A detailed discussion of the law of consent to medical treatment can be found in Chapter 3. Briefly, the right of patients to make decisions about their healthcare is internationally recognized (World Medical Association (WMA) 2005, article 3(a); United Nations Educational Scientific and Cultural Organization (UNESCO) 2005, article 5(c)). Physicians must obtain 'free and informed consent' from patients before undertaking medical care or research (UNESCO 2005, article 6(1)), meaning they must provide their patients 'with the information they need to make informed decisions about their medical care' (Canadian Medical Association (CMA) 2004, article 21). For genetic testing, information about the test's purpose, nature, risks, and limitations must be provided. Given the ease with which genetic samples can be obtained (a patient need simply spit in the tube!), the risks of genetic tests are primarily informational. They may provoke, rather than assuage, anxiety, especially where testing for an untreatable condition. For example, positive results for highly penetrant breast cancer genes may leave women with a difficult choice between living with a high but uncertain risk, or undergoing drastic preventative measures. In addition, uncertain results may be succeeded by lengthy, expensive, and unnecessary diagnostic work-ups, only to confirm a negative result. 'Iatrogenic' harm, meaning harm caused by physician activity, is especially worrisome in cases where follow-up testing or increased screening involves invasive procedures.

Genetic tests may also create tension within families when sensitive information about family bonds or shared genetic risks are revealed. For this reason, the implications of withholding (or not) test results from family members should be explained during the informed consent process (British Medical Association 2012). Ensuring that a patient understands the limitations of the genetic test is also important. Individuals without the targeted mutation may still receive a positive result (a 'false positive'). Even a true positive may not tell the patient definitively if, or when, the disease will develop. Finally, in the paediatric context, the consent of a child's parent or guardian is required, and that of the minor when sufficiently mature. However, as we explain in section 18.4, testing in children should only be carried out in the child's best interests.

18.2.2 Treatment

The physician's most evident duty is the duty to treat. Physicians owe their patients 'complete loyalty and all the scientific resources available' (WMA 2006). A physician 'may not discontinue treatment of a patient as long as further treatment is medically indicated' (American Medical Association (AMA) 2008, Opinion 10.01; CMA 2004, article 19). The duty to treat is tied to the principles of beneficence and non-maleficence: medical practice should aim to maximize direct and indirect benefits, and to minimize possible harm (UNESCO 2005). In relation to genetic testing, the duty to treat encompasses the responsible interpretation of test results and, more importantly, responsible decisions about whether or not to carry out a genetic test in the first place. Physicians must 'provide competent medical service' (WMA 2006), requiring them to stay up to date with advances in medical science. The applicable standard of conduct differs between medical specialties and will be higher for medical geneticists (Grubb and Laing 2004: paras 6.28 and 6.40). Failure to meet the standard of care can expose physicians to liability for negligence.

Physicians must also understand, and explain to patients, the predictive capacity of genetic tests. There is a chance that disease may occur even when a test result is negative, and vice versa. The risk status of a patient affects these probabilities (Holtzman and Watson 1998). The gene responsible for Huntington's disease, one of the first sequenced in the 1990s, demonstrates the importance of context. Even though it is a Mendelian autosomal dominant gene, Huntington's exhibits variable penetrance in at-risk individuals, and the time of onset is hard to predict (Miller *et al.* 2008; Miller *et al.* 2010). Uptake of testing in at-risk individuals remains low, not just because Huntington's is untreatable, but also because test results are uncertain (Hayden 2000).

Risk stratification is also increasingly becoming a professional ethical imperative. For example, the US Preventive Services Task Force discourages referral from BRCA counseling and testing for asymptomatic women in the general population (2009). Instead, it recommends a family history assessment to identify candidates for testing (Burke *et al.* 2013; Nelson *et al.* 2013).

One important framework used to evaluate the appropriate use of genetic tests is the 'ACCE' model (Centers for Disease Control and Prevention (CDC) 2013). The ACCE model was the first publicly available analytical process for evaluating scientific data on emerging genetic tests. It was introduced to guide the development of policy in medical genetics and to identify priorities for genetic research. The model takes its name from its four general considerations: analytic validity, clinical validity, clinical utility, and associated ethical, legal and social implications. An analytically valid test result accurately identifies a given genotype. A test is preferred where it is highly sensitive, meaning it gives a positive result when a mutation is present, and highly specific, meaning it will not return a positive result when the mutation is absent. A clinically valid result will consistently and accurately predict a resulting genetic condition. Clinical utility refers to the 'actionability' of a result, whether there is a treatment or preventive measure to improve the patient's outcome. The ethical, legal and social issues considered in the ACCE model include, among others, the possibility of stigmatization, discrimination, breach of privacy or confidentiality, and familial issues (CDC 2013).

18.2.3 Communication

The physician's duty to inform the patient or 'duty to disclose' encompasses four different elements: (1) informing the patient of his diagnosis/medical condition; (2) explaining the nature and objectives of the proposed intervention, and identifying the individual who will be executing the proposed intervention; (3) disclosing the known risks; and (4) identifying the therapeutic options available to the patient (Grubb and Laing 2004: paras 3.112–3.170). The results of any

diagnostic tests ordered by the physician must be disclosed. If a patient is harmed as a result of the physician's incomplete disclosure, liability can arise under the classical rules of tort law or civil responsibility. For example, informing patients of their predisposition to cancer or carrier status may be important to prevent harm. Patients informed of serious genetic predispositions to cancer may be able to increase surveillance to catch the disease in its early stages. Patients informed of their carrier status for a heritable condition can make informed reproductive decisions. Alternatively, patients who are denied prenatal testing and consequently deprived of the decision to terminate a potentially affected child may have recourse in the courts for 'wrongful birth.' In France, the Cour de Cassation awarded compensation for wrongful birth in *Perruche* [2000], Assemblée plénière, no. de pourvoi 99-13701 where a physician failed to diagnose a pregnant woman's rubella infection and her child was born severely handicapped. Public outcry followed the decision. Critics clamoured that such compensation devalued the lives of handicapped individuals. In response, a law banning actions in wrongful birth was passed, leaving the costs of treatment for severely handicapped children to the social support system (Pike *et al*. 2013; *Loi n° 2002-303 du 4 mars 2002*). The French experience suggests that compensation for wrongful birth may eventually be constrained elsewhere, especially in the genetics context, where concerns over identity and dignity are likely to be more pronounced.

The familial implications of genetic risk information raise the question of whether physicians have a duty to warn relatives of patients. For example, diagnosis of a genetic condition in affected children can reveal the carrier status of parents. Here, if the physician fails to inform the parent of a diagnosis, he or she may be liable for injury to both child and parent, or even to other family members. Where the parent is the child's legal guardian, and therefore included in the therapeutic relationship, this duty is relatively clear. Difficulty arises, however, in non-traditional family structures. In *Molloy* v. *Meier* [2003] 679 NW.2d 711, an adopted child with a serious, heritable condition called Fragile X was not properly diagnosed. Neither the adoptive parents nor the biological mother were informed of the diagnosis, leaving the biological mother ignorant of her carrier status. She later gave birth to a second affected child and sued for wrongful birth. The court found 'a physician's duty regarding genetic testing and diagnosis extends beyond the patient to biological parents who foreseeably may be harmed by a breach of that duty' (*Molloy* v. *Meier*, p. 719). The difficulty here is that the biological mother was not the child's legal guardian and was therefore outside the physician–patient relationship.

A similar Canadian case was complicated by divorce. In *Watters* v. *White* 2012 QCCA 257 (Quebec), a physician informed the father of an affected child that his wife was a carrier. The wife was distraught over the marriage breaking down, so the information never reached her. She remarried, left the country, and decades later gave birth to a second affected child. Her niece was also unaware she had inherited the gene. She also gave birth to an affected son, decades after the initial consultation. While the wife's claim for wrongful birth was rejected at trial, her niece brought a successful action. This momentarily established, for the first time in Canada, a duty to warn a third-party family member (*Liss* v. *Watters* 2010 QCCS 3309). However, the Quebec Court of Appeal reversed the trial decision, rejecting the niece's claim and concluding that under the professional norms prevailing at the time (30 years earlier), the physician was only obliged to inform the parent(s) and not other at-risk relatives.

Other cases in the US have addressed the physician's duty to prevent harm to the children of a patient with a heritable genetic condition. In *Pate* v. *Threlkel* [1995] 661 So.2d 278 (Florida), a physician neglected to inform a patient with hereditary thyroid cancer of the risk potentially shared by her daughter, who eventually developed the same cancer. An 'obvious' duty towards the daughter was found, one that could, however, be 'satisfied by warning the patient' (*Pate* v. *Threlkel,* p. 282) The court in *Safer* v. *Estate of Pack* [1996] 677 A.2d 1188 (New Jersey) reached

a similar finding, despite the complication that both the patient and the physician died before the child reached maturity. It was not specified how the duty was to be discharged, just that 'reasonable steps be taken to assure that the information reaches those likely to be affected or is made available for their benefit' (*Safer* v. *Estate of Pack*, p. 627). Courts remain hesitant to recognize a duty to warn biological relatives outside the therapeutic relationship. Not only would such a duty be onerous for physicians, but it would risk conflicting with the physician's duty of confidentiality. We can conclude that physicians have, at a minimum, an ethical duty to prevent harm to family members of patients. This does not mean, however, that physicians have a legal duty to warn these third parties directly; informing the patient of familial implications will most likely be sufficient.

18.2.4 Confidentiality

Physicians must keep health information confidential (WMA 2009: 50–5, 2006; CMA 2004: article 31; also see Chapter 4). Initially, the emergence of genetic information in the 1990s reinforced the legal and ethical duty of medical confidentiality for fear of employment and insurance discrimination. As discussed in the previous section, however, biological relatives may have a legitimate interest in a patient's genetic information. Physicians could have a corresponding ethical duty to prevent harm to these relatives. This can generally be achieved without breaching patient confidentiality by clearly explaining the familial implications to the patient, or by obtaining the patient's consent to communicate the result to family members.

But what if the patient refuses? Some have argued that confidentiality should not prohibit communication to family members, that the family, and not the individual patient, should be treated as the 'unit of confidentiality' (Wertz and Fletcher 2004). Case law, however, firmly rejects the familial solution; as Judge Kasirer concluded in *Watters* v. *White*, individual patient confidentiality remains the 'cornerstone of the doctor–patient relationship' (para. 95).

There are narrow exceptions to confidentiality 'whereby non-consensual disclosure is justified by considerations of public health, urgency or imminent danger' (*Watters* v. *White*, para. 111). For example, many countries legally require physicians to report certain communicable diseases, such as tuberculosis, to the relevant authorities. Physicians may also breach confidentiality to report patients with conditions hindering their ability to drive, or situations where the security or development of a child is in danger (Beskow and Burke 2010). While not every country recognizes a legal obligation to warn identifiable third parties of imminent risk, it is internationally recognized that physicians have a discretionary privilege to breach confidentiality as a matter of moral or deontological conscience (WMA 2009: 51–5). Strict conditions must be met before a physician can exercise this discretion. The expected harm must be considered imminent, serious, irreversible and unavoidable except by unauthorized disclosure, as well as greater than the harm likely to result from disclosure (WMA 2009: 51–4; American Society of Human Genetics (ASHG) 1998). Quebec, a civil law jurisdiction, provides for this discretion in its *Code of ethics of physicians* 1981 (articles 20–21). These articles permit, but do not require, physicians to breach confidentiality 'when there are compelling and just grounds related to the health or safety of the patient or of others'.

It remains unclear whether genetic risk information can fulfill the strict conditions that require (or permit) a physician to breach patient confidentiality. Genetic risk is often uncertain, and disclosure may not be of clear benefit to a third party (Gold 2004). Genetic risk information also rarely qualifies as 'imminent' or urgent (Lacroix *et al.* 2008). Genetic test results tend to be probabilistic. The timing, development, and severity of disease expression depend on many factors such as environment, lifestyle and gene–gene interactions. Genetic risk information may

also fail to justify an exception to confidentiality because the patient is not morally culpable for the threat posed to the third party. Because the patient has not intentionally threatened another person, breaching the right to confidentiality may be less justifiable (Lacroix *et al.* 2008).

18.3 Emerging issues: whole-genome sequencing

The advent of whole-genome and whole-exome sequencing technologies creates new challenges and uncertainties for medical professionals. In a whole-genome approach, all six billion base pairs of an individual patient's DNA are sequenced. A sample is broken down into millions of smaller fragments that are read, sequenced, and ordered along each chromosome (Ng and Kirkness 2010). WGS/WES allow for the exploration of complex gene–gene interactions and sophisticated comparisons between sequences, and have become popular tools in genetic research. Clinical uptake has been slow, but is expected to expand rapidly as costs decrease and our understanding of genomic information advances. Many of the first clinical applications of WGS involve children. WGS/WES can speed up differential diagnosis of rare genetic disorders in newborns suspected of a genetic condition, but not yet exhibiting sufficient clinical symptoms to diagnose (Saunders *et al.* 2012). The genomes of children affected by unknown conditions can be compared with those of their parents to identify *de novo* mutations and diagnose previously unknown genetic causes of disease (Veltman and Brunner 2012). At least in the short term, the primary clinical applications of WGS/WES will continue to be, not exceptionally, in paediatric diagnostics. Particular attention must therefore be paid to the paediatric context, especially concerning the question of when to use WGS/WES, and how to handle the communication of unexpected results to children and/or their parents. Genetic testing in pediatrics will be discussed in section 18.4.

18.3.1 Incidental findings

The controversy surrounding WGS/WES stems in large part from the vast scope of the genetic analysis and the potential of encountering unsolicited findings unrelated to the patient's diagnostic question. How can a physician obtain meaningful patient authorization to test for such a vast range of potential results? Another important caveat for WGS/WES is that laboratories and laboratory medicine specialists, rather than physicians, play a central role in interpretation. Unlike X-rays or other forms of medical imaging, the analysis of WGS/WES results involves complex bioinformatics analysis. The results of this analysis are then pushed to physicians, potentially triggering duties to treat or inform. Laboratory reporting has been the focus of the American College of Medical Genetics and Genomics' (ACMG) recent guidelines on clinical WGS/WES, discussed in detail below (Green *et al.* 2012).

The ethical debate over WGS/WES in both research and the clinic has centered on the duty to inform. WGS/WES returns large amounts of 'unsolicited' or 'incidental' genetic information unrelated to a research or clinical question. This information may be of clinical significance to the individual. This would suggest the researcher or clinician has a duty to return it to the participant or patient. On the other hand, informing individuals of genetic risks they did not know were among those tested may undermine their informational autonomy. This tension is discussed in the next section on the patient's 'right not to know.'

Experience from research with WGS/WES suggests that the informed consent process may be used to establish a plan for the ethical return of incidental findings (Knoppers and Lévesque 2011). In Canada, researchers are required to advise prospective participants of their plan for the overall management of information genetic research reveals (Canadian Institutes of Health

Research *et al.* 2010). Some authors have begun to outline the appropriate criteria for such a plan, taking the form of 'broad consent' models (Wallace *et al.* 2009). Broad consent streamlines informed consent by grouping findings into categories to be returned or not. An example in genomic research is the 'Smart Filter' of the National Cancer Institute (NCI) developed for the biobanking context (NCI 2010). The Smart Filter lists three major criteria for returning a result in the research context, including analytical validity, clinical significance, and clinical actionability. A National Institutes of Health consensus paper on biobank research goes further, suggesting results should only be returned if two additional criteria are fulfilled: the participant has consented to the return of individual findings and the return conforms with applicable law (Wolf *et al.* 2012). Finally, the Network of Applied Genetic Medicine of Québec suggests that approval by an ethics board should also be obtained, and the finding confirmed, before being returned (2013).

The research experience provides an informative platform for developing an ethical return of results policy in the clinic. In many ways, the return of results in the clinical setting may be more straightforward. In research, sequence-based research protocols can be very different, and the researcher–patient relationship is both vague and highly variable (Heger 2012). In the clinic, on the other hand, physicians have a clear responsibility to act for the benefit of their patients. While return protocols must be tailored to specific research studies, a single return of results protocol may be widely applicable across clinical settings. Indeed, there is significant concordance among clinical genetic specialists about what kinds of incidental findings from WGS/WES should be returned to a patient's primary care physician (Green *et al.* 2012).

Berg and colleagues have developed a binning approach to incidental findings in the clinic. Unexpected findings could be organized in 'a clinically oriented manner to facilitate shared decision making by patients and clinicians' (Berg *et al.* 2011: 500). Clinically actionable findings are categorically reported; clinically valid but not directly actionable findings are not returned as a rule, but could be depending on patient preference; and findings of unknown or no clinical significance are not returned. Ayuso and colleagues recently refined this platform. They propose a list of minimum elements to be included in informed consent for clinical WGS testing, including a description of the procedure used to manage incidental findings (Ayuso *et al.* 2013). Incidental findings are grouped according to 'the present or future effect of the variant, their actionability, carrier status, and penetrance' (Ayuso *et al.* 2013: 1057). Whether some groups of findings will be returned is discussed and agreed upon in advance by the patient. For other groups, the authors recommend mandatory return.

Policy in rare diseases research presents considerations similar to the clinical context. The UK10K is a retrospective study of rare genetic diseases involving WGS, which outlines a policy for feedback of clinically significant findings to research participants in its ethics governance framework (Ethical Advisory Group of the UK10K Project 2010). UK10K distinguishes between 'pertinent findings,' relating to the disease under investigation, and 'incidental findings,' relating to diseases outside the original research aims and unforeseen at the time participants gave consent (UK10K 2010: 8). Return of pertinent and incidental findings of a specified clinical utility is contingent on consent for each class of finding. Even in research then, findings are distinguished in relation to the objectives of the sequencing. Why? Pertinent findings are only encountered when participants have been recruited for a specified (rare) clinical condition. This is because individual research studies in rare diseases tend to establish 'robust management pathways for validating potentially diagnostic research data to diagnostic standards' (UK10K 2010: 8). In addition, participants in rare disease research often express a strong desire for information on their condition and readily consent to its return. The UK10K emphasizes that there is no clear duty to return findings in research, especially absent unambiguous demonstration of clinical

utility and participant consent to the specific class of findings (i.e. pertinent and/or incidental of specified clinical utility). The guidelines of the European Society of Human Genetics (ESHG) make a similar distinction in the clinical context between solicited and unsolicited findings (van El *et al.* 2013). Not only should the risk of unsolicited findings be justified before pursuing WGS, but consent practices should also be developed to manage return. The ESHG also encourages categorization of unsolicited findings to facilitate patient expression of informational needs and preferences. Interestingly, the ACMG guidelines for reporting results from clinical WGS make no such distinction between pertinent (i.e. related to the diagnostic question) and incidental findings, but focus instead on the clinical significance of the finding (Green *et al.* 2013).

Many questions remain concerning the handling of incidental findings in WGS/WES. Who will determine the scope of the return/may return/do not return categories? Will the patient sufficiently understand these categories, especially considering the uncertainty and highly probabilistic nature of most genetic information? For patients, more information is not always better. Increasing the scope of informed consent will increase the time and expense of pre-test counseling for the healthcare system, and may result in information overload in patients (Bunnik *et al.* 2011).

When is the use of WGS/WES appropriate? The Canadian Medical Association *Code of Ethics* states that only diagnostic services considered to be beneficial to the patient should be recommended (2004, article 23). The Canadian College of Medical Geneticists endorses the use of WGS/WES in a judicious and cost-efficient manner to answer a clinical question. The administering physician should possess the requisite expertise before recommending WGS/WES testing, interpreting its results, or offering treatment options post-test (Zawati *et al.* 2013). Determining when WGS/WES is beneficial, however, is not always easy. Indeed, examining one part of the sequence may be clinically beneficial, while another may reveal an untreatable condition, or leave a patient with troubling uncertainty.

In this way, WGS/WES blur the boundary between genetic testing and screening, areas traditionally governed by separate normative frameworks (Dondorp and de Wert 2013). The basic principle of screening – the early detection and treatment of disease – is straightforward, but it has long been recognized that this process comes with significant ethical, legal, and social complexity. In 1968, Wilson and Jungner developed criteria for the World Health Organization's (WHO) screening criteria, which remain relevant today. Beyond the basic considerations of genetic testing (analytic and clinical validities, actionability, etc.), there should also be a suitable treatment acceptable to the public, as well as facilities for diagnosis and treatment, and the cost of screening should be justified economically from the health system as a whole (Wilson and Jungner 1968).

Screening targets populations rather than individuals. The benefits of early detection for affected individuals must outweigh the potential of harm to those who do not need treatment. One such potential harm is unnecessary work-up in the case of a false positive. The rate of false positives tends to be higher when testing is carried out in asymptomatic, untargeted populations (Burke *et al.* 2013). Furthermore, classical criteria have to be adapted when screening for genetic disease. First, a population viewpoint may not adequately account for the seriousness of rare genetic conditions. Second, while genetic tests may be cheap and powerful predictors of disease, the related costs of education, counseling, and intervention (if available) may be the true limiting factors (Andermann *et al.* 2008). Finally, the pace of genetic science risks 'out-pacing the ability of professionals and policy-makers to assess the potential benefits and pitfalls of introducing or expanding genetic screening programmes' (Andermann *et al.* 2008). Simply having a test and a treatment is far from enough to justify screening.

The ACMG clinical guidelines for clinical WGS/WES reflect the inevitable blurring between testing and screening (Green *et al*. 2013). The guidelines require mandatory analysis and reporting of a curated list of genetic variants whenever WGS/WES is used in the clinic for newborns, children, and adults alike. In a sense, laboratories are asked to 'screen' for a curated list of mutations, regardless of the patient's original diagnostic question. The curated list includes variants 'for which there is the significant potential for preventing disease morbidity and mortality if identified in the presymptomatic period' (ACMG 2013: 664). Traditionally, medical ethicists have rejected such 'opportunistic initiatives' by physicians (Getz *et al*. 2003). Respect for autonomy requires physicians to focus on a patient's reasons for seeking help, and to honor the patient's right not to be confronted with unsolicited information about biomedical risks. The ACMG policy may be a slippery slope towards population-wide genetic screening. Until now, screening has only been supported for severe metabolic conditions in newborns. If physicians must screen asymptomatic individuals with no family history for certain genetic conditions, simply because they are undergoing WGS, why ignore the rest of the population?

The ACMG's justification to require testing and reporting of a curated list of variants is rooted, perhaps too firmly, in the logic of the duty to inform and fear of subsequent liability. The deliberate search for results not related to the diagnostic question is justified by the health professionals' 'fiduciary obligation' to inform patients of 'unequivocal' pathogenic mutations, especially where treatment or prevention is possible: 'failure to report a laboratory test result conveying the near certainty of an adverse yet potentially preventable medical outcome would be unethical' (ACMG 2013: 664). Even though the list attempts to include only conditions where medical benefit is likely, mandatory reporting has been criticized for failing to respect patients' control over the flow of their genetic information (Burke *et al*. 2013). The ACMG argues that consent to testing meaningfully protects autonomy upstream, while physician discretion during clinician management of the results can reinforce it downstream. Respecting a patient's informational preferences may be infeasible, however, requiring lengthy pretest counseling and consent for the examination of genes unrelated to the clinical question.

The criteria used by the ACMG to establish the list are also controversial. In the ACMG's own words, there is 'insufficient evidence about benefits, risks, and costs of disclosing [the listed variants] to make evidence-based recommendations' (Green *et al*. 2013: 4). This is especially true as the clinical validity of these genetic mutations may have been established in a targeted population, and may be weaker in an unselected population (Burke *et al*. 2013). Net benefit for the healthcare system, an important consideration from a screening optic, is also apparently ignored. The added burden of analysis, interpretation, post-test counseling and follow-up will no doubt have an impact on healthcare resources (Burke *et al*. 2013).

WGS/WES may also amplify the frequency of conflicts between confidentiality and the duty to warn family members of genetic risk. With WGS/WES, the possibility of encountering a genetic finding of potential importance to family members is rapidly increasing (Cassa *et al*. 2012). Under the ACMG guidelines, the duty to inform patients has been intensified to include return of a curated list of pathogenic mutations. This may be fertile ground to argue for an expansion of the physician's duty to inform beyond the patient. In fact, the ACMG explicitly recognizes a new ethical duty towards family members in the paediatric context. It recommends testing and reporting of adult-onset conditions in children, because 'if the child carries a pathogenic mutation, there is a high probability that one parent does as well' (ACMG 2013: 665).

Physicians should not be expected to shoulder all the responsibility for these ethical conundrums. There is a growing need for systematic solutions to improve the clinical utility of WGS/WES (Grosse and Khoury 2006). Decision support tools can help to 'provide clinicians with options for test ordering; indicate the sensitivity, specificity, and positive predictive value of

tests; and aid clinical workflow by providing algorithms to facilitate decisions on the basis of test results' (Mirnezami *et al.* 2012: 491). Risk stratification is also important. Kohane *et al.* call for the development of estimates of disease prevalence by ethnic group (2006). These population reference maps 'will allow the sensitivity and false-positive rate of each individual genomic test to be combined with prevalence to estimate the real overall risk of a positive test result based on approximate ancestry' (Kohane *et al.* 2006). Physicians regularly exposed to WGS/WES test results can familiarize themselves with high-risk and clinically actionable results. Medical schools and continuing medical education can better integrate genomic science into their curricula. From a policy perspective, efforts are needed to clarify the extent to which physicians are expected to understand WGS/WES, and to introduce systemic changes to help cope with the expectations these tests bring (Black *et al.* 2010).

18.3.2 The patient's right not to know

An emerging issue in genetics concerns the patient's 'right not to know.' The right not to know was originally advanced in reaction to expanding predictive genetic testing in the 1990s and is codified in several international normative documents (Council of Europe 2008, article 10.2; WMA 2005, article 7(d)). For example, article 5(c) of UNESCO's *Universal Declaration on the Human Genome and Human Rights* 1997 states that the right of an individual 'to decide whether or not to be informed of the results of genetic examination and the resulting consequences should be respected.' Andorno characterizes the right not to know as an autonomy right, a 'right to informational self-determination' (Andorno 2004: 436). It is not to be confused with waiver of informed consent – patients must always be informed of the purpose and risks of medical tests. Instead, the right not to know protects the patient's interest in not knowing the *results* of a medical test, especially if those results are unrelated to the patient's motives for seeking testing (for a comprehensive introduction, see Knoppers 2014 (in press)).

Choices about genetic information have always been present. A patient can choose whether or not to undergo genetic testing. Indeed, the simplest way for a patient to exercise the right not to know is to refuse diagnostic testing. Patients have an 'established right to refuse unwanted medical tests and the information they might disclose' (Wolf *et al.* 2013: 1050). The informed consent process protects this right. The central aspect of a diagnostic test is that it returns health information. Thus a patient consenting to diagnostic testing is authorizing the physician to seek and report health information. In order for this consent to be informed, however, the patient must understand the nature of the 'health information' sought and the consequences of a positive finding. A patient who considers the informational risk of a genetic test to outweigh its potential benefits is free to decline sequencing.

Many argue that the right not to know is broader than the right to refuse diagnostic testing (Wolf *et al.* 2013). For example, if a physician finds a gene that the patient did not know was being tested for, perhaps for an untreatable condition, should this be categorically reported to the patient? More broadly, the right not to know could be considered a right to refuse health information. An analogy is often drawn between this right and the patient's right to refuse health treatment. The right to refuse health treatment is considered absolute, meaning that even competent patients may refuse life saving treatment (Lemmens 1996).

Is the right not to know absolute? Arguably, patients should not, and cannot practically, be extended the right to refuse potentially life-saving information. Paradoxically, respecting a patient's choice to refuse health information could potentially rob that same patient of an opportunity to exercise a choice about life-saving treatment. The very concept of 'informed refusal to know' is problematic: a decision to refuse information cannot be made without knowledge

of the information one is refusing. While the theoretical justification of the right not to know is compelling, it remains unclear how respect for this right can be implemented. Despite these difficulties, the advent of WGS/WES testing has renewed interest in the right not to know. The clinical meaning of much of the information it returns is highly uncertain. Even where the clinical significance of a genetic variant is known, this information is often probabilistic. Ultimately, knowing you have a predisposition to a disease is not the same as having that disease. Some genetic risk information may be unwelcome or misunderstood by patients, and may lend to the phenomenon of the 'worried well.' Other results may have high penetrance and clear clinical relevance, but offer no treatment or prevention.

Should patients choosing to undergo WGS/WES have the right to refuse potentially life-saving information? Here, understanding the distinction between the 'assay' and 'analysis' of a scientific test is important. A genetic assay is a procedure that identifies the presence of a particular genetic sequence. Many early genetic tests assayed a short genetic sequence. The presence of a mutated sequence would indicate the presence of the genetic condition. By contrast, WGS/WES deciphers much of the individual's genetic code. All possible genetic mutations are simultaneously assayed during WGS/WES. Complex bioinformatics analysis is then used to interpret sequences of interest. The differentiation between assay and analysis makes the ethical characterization of WGS/WES challenging, especially as it concerns the patient's control over the flow of genetic information. When patients undergo WGS, for whatever purpose, they undergo an assay for all disease-associated genes (Green *et al.* 2013). The subsequent bioinformatics analysis can – theoretically – establish any particular unanticipated variant with relative ease. This prompted the ACMG to recommend that genetic laboratories actively seek out and report a minimum list of variants whenever WGS is used in the clinic (Green *et al.* 2013).

The ACMG approach has been criticized for undermining patient autonomy and the 'right not to know.' Patients have an interest in exercising choice over the genes, or at least the types of genes, they are tested for (Wolf *et al.* 2013). Where patients are extended the right to refuse life-saving treatment, should they not also be able to refuse potentially life-saving information? For example, a patient may want to receive genetic findings useful to the diagnosis that prompted WGS/WES analysis, but have no interest in receiving information about his or her risk status for adult-onset Mendelian diseases. The basic solution to ensuring the patient's informational self-determination is to offer comprehensive pretest counseling to inform patients of the types of results WGS/WES may return, and then to apply filters (either during the analysis itself, or before reporting) to respect these preferences. Under the ACMG guidelines, patients are still free to refuse WGS/WES testing. But once they have decided to undergo testing, they will not be able to control what results or types of results are communicated to them (or to their children – see section 18.4). The determination of what results are communicated is instead made by 'expert professional judgment' (McGuire *et al.* 2013). Not allowing patients to refuse reporting of certain results has been criticized as coercive, undermining the shared decision-making process between physicians and patients, and discouraging some patients – potentially to the detriment of their health – from undertaking testing altogether (Ross *et al.* 2013a; Allyse and Michie 2013).

There are compelling justifications for the ACMG's 'all or nothing' approach to WGS/WES. They appeal to the health professional's fiduciary obligation to inform patients of actionable and highly pathogenic mutations (ACMG 2013). Reporting these results would generally benefit the patient's health. These results are also the type that fall under the physician's duty to inform. Physicians could face liability for failing to report a serious and treatable condition that would have been found with a simple modification to the laboratory bioinformatics analysis. Indeed, case law from medical imaging suggests physicians may be liable for failing to identify or to

report an incidental finding for a treatable or preventable genetic condition (Clayton *et al.* 2013). Perhaps the most convincing justification for mandatory reporting is the practical difficulties in administering patient preferences and the 'right not to know.' Even if a binning solution is adopted, establishing patient preferences will require extensive pretest counseling. Physicians holding such results may second-guess even the most 'enlightened refusal' to receive communications about potentially life-saving information. On the other hand, because physicians will feel compelled to return all results they receive – fearing liability for nondisclosure – patient choice may require heightened protection (Ross *et al.* 2013a).

18.3.4 Follow-up

Physicians are required to provide medical follow-up for an examination or investigation (AMA 2008, Opinion 10.01(5); CMA 2004, article 19). WGS/WES leaves doctors in a precarious position with regard to this duty. On the one hand, they may risk liability for negligence if they ignore uncertain genetic results. On the other hand, they may order a battery of alternative, targeted tests to confirm the revelations of WGS/WES testing (Kohane *et al.* 2006). The problem with this defensive medicine approach is that it exposes patients to costly and potentially harmful follow-ups (Kohane *et al.* 2006; Kuehn 2011) and strains already limited primary healthcare resources (McGuire and Burke 2008).

As the WGS knowledge base expands, what happens as the meaning of past WGS/WES test results changes? Currently, in the United States, the United Kingdom, and Canada, physicians are not legally responsible for re-contact, and it is up to the patient to initiate re-evaluation (Thorogood *et al.* 2012). With a large amount of genomic material stored in a patient's health record and susceptible to evolving interpretation, it is difficult to define or delimit the scope of such a duty. In addition, it is hard to imagine how a patient's interest in informational self-determination can be meaningfully respected without allowing him or her to control the terms of follow-up. However, even if the responsibility to follow up is placed on the patient, physicians will still need to respond with care and diligence when approached by their patients for reinterpretation (Pyeritz 2011).

Some suggest that the duty to follow up may one day expand to encompass the re-contact of patients, when consented (Pyeritz 2011; Ali-Khan *et al.* 2009). This would be desirable because genomic information can be stored and treated as an evolving source of health information, rather than a one off test. It remains impractical, however, to expect physicians to monitor every aspect of a patient's health continuously, especially after care has been transferred to another provider or the patient stops making regular visits (Clayton and McGuire 2012). Indeed, the traditional model of the 'single longitudinal relationship' between patient and physician is being displaced. Patients now tend to interact with a 'cascade of providers' (Clayton *et al.* 2013). Intensifying the physician's duty to follow up is more likely to encourage fruitless legal pursuits than it is to enhance the use of genomic test results over time.

18.4 Emerging issues: genetic testing and screening in pediatrics

When is it appropriate to test or screen children for genetic conditions? The central complication in pediatrics is that children are unable to consent. It follows that genetic testing should be carried out if and only if it is in the best interests of the child. Under the UN's *Convention on the Rights of the Child* 1989, children have the right to enjoy 'the highest attainable standard of health,' and to have actions concerning them primarily governed by their best interests (articles 3 and 24). This is affirmed by the ACMG and the American Academy of Pediatrics

(Fallat *et al*. 2013): the best interests of the child should drive genetic testing and screening. While the best interests of the child can be an elusive concept, the central consideration for genetic testing is the potential for timely medical benefit during childhood (Zawati *et al*. 2013). An additional consideration of the *Convention* is that children have the right to be heard (article 12). The decision to carry out genetic testing should give children's views due weight according to their age and maturity (Zawati *et al*. 2013).

Testing children for adult onset conditions is generally discouraged, as they should be allowed to consent to the test once they reach maturity. The Council of Europe states that when, under law, 'a minor does not have the capacity to consent, a genetic test on this person shall be deferred until attainment of such capacity unless that delay would be detrimental to his or her health or well-being' (Council of Europe 2008, article 10). The British Society of Human Genetics recommends that predictive and pre-symptomatic genetic testing normally be delayed until children can decide whether or not to be tested (2010). There is controversy over whether this rule should apply for severe conditions preventable or treatable during adulthood. Here, the likelihood that the child will not be presented with another opportunity to test for the condition must be considered (ACMG 2013). Direct benefits to parents may also be considered where they are continuous with the interests of their children (Ross *et al*. 2013b). According to the ACMG, such indirect benefits may, in some cases, trump the child's future autonomy interest. They challenge the traditional position that genetic testing for late-onset conditions should be delayed until adulthood: 'it may be ethically acceptable to proceed … to resolve disabling parental anxiety or to support life-planning decisions …' (Ross *et al*. 2013b: 238). A fear underlying this position is that failure to test for a genetic condition in an affected child may result in liability towards the child's biological parent.

Newborn screening also relies on the best interests of the child tested, but construes the test more objectively as a duty of the state to protect the vulnerable. The goal of newborn screening is to screen for severe metabolic conditions where immediate medical intervention is available. It is carried out in at least 64 countries without explicit parental consent (Wilson *et al*. 2010). Parents may be obliged by law to screen their child, because no 'reasonable' parent would refuse screening that detects an at-risk child, and because it has become the pediatric standard of care. Because the decision-maker for screening is often a public health agency and not an individual physician, political and economic considerations arise. In addition to analytical validity, clinical validity, and the existence of treatment, one must also consider if there are facilities available to administer that treatment, and if the cost for diagnosis and treatment is economically justifiable in the health system as a whole (Andermann *et al*. 2008).

Screening asymptomatic, at-risk newborns for immediately treatable conditions has long been the professional standard of care in pediatrics (WHO 2011; Wilson and Jungner 1968; Knoppers and Laberge 1990). However, the number of screened diseases has been increasing in the USA, Canada, and Europe (Lindner *et al*. 2011). It is also plausible that newborn screening programs will soon involve WGS/WES (Knoppers *et al*. 2013). Once a newborn's genome is sequenced, the temptation to expand screening to new mutations will be hard to resist. Rigorous application of the ACCE model discussed above may be particularly appropriate here (Lévesque *et al*. 2011; CDC 2010). In the case of rare disease, such an expansion may be desirable. Here, the logic of the emerging 'personalized medicine' paradigm displaces that of screening.

Indeed, newborn screening could provide a future health map for every individual, especially for those with rare diseases (Dondorp and de Wert 2013). The use of such a futuristic report card would need to be tightly regulated in order to serve the best interests of the child. Among the ethical, legal and social issues considered under this model is the interest of newborns in

controlling future choices about their health information, especially when testing can be delayed until adulthood (Dondorp and de Wert 2013). Genetic testing guidelines generally advocate that tests for adult-onset conditions be delayed until adulthood to preserve the child's 'right to an open future' (Hens 2011; Feinberg 1980).

There has been keen interest in using newborn screening samples and dried bloodspots left over from past screening for case-control research. WGS/WES of newborn bloodspots is ideal for genome wide association studies, as they provide an unprecedented, unbiased population reference map. Perhaps the greatest advantage for researchers, albeit a dubious one, is the dispensing of participant consent. Parents are presumed to consent to newborn screening for disease prevention. This presumption does not appear to hold for the storage and research of leftover samples (Association of Public Health Laboratories 2002). Recent outrage and legal action over researchers accessing stored newborn screening samples for research without explicit consent has brought such initiatives into serious doubt (Allen *et al*. 2013).

Incidental findings of WGS/WES add another layer of complexity in pediatrics (Knoppers 2012). First, they significantly complicate the best interests test in deciding to undergo testing. Second, how does a physician determine what findings should be communicated to the representatives of the child who is unable to express his or her informational preferences? Guidelines from the pediatric research context stipulate that researchers are only permitted to report findings (whether individual research results or incidental findings) if they reveal a clinically significant condition that is treatable or preventable during childhood. This is consistent with a position long held in medical genetics: genetic testing should only be performed on children and minors (i.e. prior to legal capacity/mature minor) if the condition under investigation is actionable during minority (American Academy of Pediatrics (AAP) 2009; Canadian Paediatric Society 2003).

This position has been challenged, controversially, by the ACMG guidelines discussed above. Their recommendation for the mandatory reporting of certain genetic conditions applies to all patients undergoing WGS/WES, including children (Green *et al*. 2013). In contrast, the Public Population Project in Genomics and Society (P^3G), while promoting a should-return policy for results actionable in childhood, advocates a no-return policy for results revealing mutations predisposing children to adult-onset conditions. Exceptions are made, however, on a case-by-case basis for situations where a child may benefit by preventing harm to family members (Knoppers *et al*. 2014).

18.5 Conclusion

The issues surrounding WGS/WES are totally absent in international normative guidance except for blanket, general statements on obligations to communicate (or not) results with no mention of WGS (Knoppers and Dam 2011). Even the most recent WHO guidelines mandate only that research participants be informed of the progress of research (WHO 2011). Perhaps this simplicity enables such guidelines to be more universally applicable, but in countries lacking local ethics or professional guidance, more discussion of the options and implications of emerging technologies would be helpful. This is not to say that any one specific technology should be addressed in international normative guidance, as this could well limit the future applicability of international frameworks over time, but that general criteria for evaluation should be provided (Wolf *et al*. 2012). The conflation of the research and clinical contexts using WGS/WES will, however, affect the viability of any guidance provided.

Systematic reforms may be necessary at both the micro and macro levels to ensure the ethical introduction of WGS/WES testing. At the micro level, funders of research and medical

professional organizations may wish to consider revisiting their codes of scientific integrity, or of ethics, to determine if sufficient guidance is provided for their members. In particular, the possible expansion of current duties and responsibilities of physicians to patients across their lifetime needs to be balanced with a corresponding responsibility of the individual patient to request information and make choices. There is no doubt that for genomic information to be understood, education is key. In organizing its health systems and safety oversight of both public and private testing, the state should mandate and control quality assurance at the macro level through oversight and accreditation. Irrespective, one thing is certain: the arrival of whole-genome analysis has blurred the roles of researchers and physicians, of participants and patients, and of local, national and international ethics review. Perhaps it is better to build a system of e-governance that is dynamic, interactive, and international to best reflect this new reality?

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19

Towards precision medicine

The legal and ethical challenges of pharmacogenomics

Gratien Dalpé and Yann Joly

19.1 Introduction

19.1.1 Personalized medicine: from the laboratory to the clinic

Physicians have always explored new ways of making more accurate diagnoses and better drug prescriptions. Since the mid-nineteenth century, evidence-based medicine has supported healthcare decisions by combining the physician's expertise and judgment with the best clinical evidence from scientific research pertinent to a patient's health (Sackett 1997). With such an approach, physicians can obtain more precise diagnoses centered on their patients' personal characteristics. This practice is thought to lead to the discovery of more efficient prognosis markers and to the development of safe and efficient therapeutics.

Modern molecular genetics has the potential to substantially impact many aspects of medicine, including the development of pharmacological treatments. Genetic information enables the identification of individuals through their polymorphisms, small variations in genes related to the inter-individual variability in a given population (Hedrick 2011: 104). It has also increased our understanding of the molecular mechanisms of diseases, allowing genes and their products to become the molecular targets of new pharmaceutical therapies aimed at modulating gene activity (Strachan and Read 1999). As such, the study of genetic biomarkers has been used to foster knowledge and facilitate the prediction of human disease, enable more accurate diagnoses and improve the safety and efficacy of medications tailored to the needs of specific patient groups.

An important element in the success of precision medicine, pharmacogenomics (PGx) is the study of how genomic profile variation between individuals' or subgroups' DNA and RNA influences their response to drugs (Maliepaard *et al.* 2013; Hall 2013). Modern PGx goes beyond the study of single gene mutations and their effect on drug response. It takes advantage of a whole-genome view, using a variety of genomic approaches – such as high-throughput whole-genome sequencing (WGS) and the ability to store and access this data with bioinformatics – to establish a patient's profile and maximize treatment efficacy while lowering the risk of adverse drug reactions (ADRs) (Hall 2013). Between the completion of the Human Genome Project in 2003 and recent advances towards fast and reliable WGS using next-generation sequencing,

it is now possible to obtain an individual's WGS profile for a price approaching $3,000 to $4,000 USD (Green 2013; Yu *et al.* 2012; Crews *et al.* 2012). With the constant decrease in DNA sequencing cost, many have suggested that prices will drop below $1,000 per genome in just a few years (Drmanac 2011; Committee on a Framework for Developing a New Taxonomy of Disease (CFDNTD) 2011; Kedes and Campany 2011; Mardis 2011; Holman 2012). At these prices, WGS has the potential to be used in routine healthcare.

However, epigenetic modifications, proteomics, and microRNA variations can also account for inter-individual variability (Crews *et al.* 2012). Even if the falling cost of WGS makes its clinical use foreseeable, problems such as the complexity of genomic interpretation, our limited knowledge of genes responsible for genetic disease, and WGS's failure to meet quality control sequencing norms such as the *Clinical Laboratory Improvement Amendments* (CLIA) 1988 will need to be resolved prior to implementation in the clinic (US Food and Drug Administration (FDA) 2013a). Nevertheless, this technology might presently be useful for the identification of polymorphisms in genes known to be relevant to drug efficiency and ADR. PGx implementation, combined with affordable and reliable modern sequencing technologies, could result in major healthcare advances by facilitating the identification of new drugs that are safer, more effective, and tailored to patients (CFDNTD 2011).

PGx is often conflated with precision medicine because both disciplines have the same outcome in mind – more personalized healthcare based on the patient's individual characteristics (Poon *et al.* 2013; Katsnelson 2013). Advances in PGx have contributed to an idyllic vision of healthcare practitioners able to quickly determine an individual's genomic profile, and choose the right drug at the right dosage for the specific needs of that patient (Ghosh *et al.* 2010). The promise is a novel, more rational 'precision medicine' which leaves the trial-and-error approach for an evidence-based clinical decision that is 'individualized' and patient-centric (Zineh 2012). Although this chapter will focus on PGx, we do not subscribe to genetic essentialism, and remain conscious of the importance of epigenomic and clinical data in achieving precision medicine.

19.1.2 Regulations, policies and guidelines for clinical pharmacogenomics

In section 19.2 of this chapter, a range of topics related to PGx implementation in drug development will be presented from the point of view of different international regulatory agencies. In Sections 19.3 and 19.4 we analyze some of the major ethical issues perceived as obstructing the implementation of PGx. The role of current and proposed laws and regulatory policies in protecting the public while trying to pave the way for implementation of PGx will also be examined throughout the chapter.

The pharmaceutical industry, governments and non-governmental organizations have shown an increased interest in the sustainable development of PGx. However, there is a need to address significant obstacles faced by stakeholders such as patients' concerns about genetic data privacy and confidentiality; the need for a drug approval process that adequately considers the impact of PGx on patient safety and provides economic incentives during the transition to personalized medicine; and the need for harmonization of drug development regulations at the international level.

PGx tends to stratify a common disease into subgroups based on drug response differences observed in patients. By characterizing this patient stratification with biomarkers, drug developers can design clinical trials that require fewer participants, thereby decreasing cost and streamlining the process (see section 19.2) (Nuffield Council on Bioethics 2006).

One of the most significant impacts of PGx implementation during drug development may be a gradual departure from the current blockbuster model towards a 'nichebuster' model that aims at a higher cost-effectiveness ratio (Brownlee 2011; Outsourcing-Pharma.com 2006). Due to the lower prospect of large profits, it has been predicted by some that the pharmaceutical industry may resist the movement toward PGx. For this reason, reimbursement incentives through third-party payers such as public healthcare agencies or private health insurers could help patients maintain access to affordable drugs while securing stable markets for drug developers (see section 19.3) (National Human Genome Research Institute 2012; Tambuyzer 2010).

Disease stratification due to PGx could also contribute to the identification of more rare conditions in the future (*Orphan Drug Act* (*P.L. 97-414*). Rare diseases are infrequent in the general population and constitute a small market for drug sponsors. The definition of rare disease differs according to the regulatory body. The FDA defines rare diseases as those which affect fewer than 200,000 persons in the United States, or which affect more individuals but still do not occur frequently enough for there to be an economic rationale in trying to develop a medication (*21 United States Code*, § 360bb). Likewise, the European Medicines Agency (EMA) considers the rarity of the condition (less than 5 in 10,000 people) but can also accept life-threatening, debilitating, and chronic diseases if there would otherwise be insufficient expectation of returns to justify the necessary investment (*European Parliament and Council Regulation (EC) No. 141/2000 of 16 December 1999 on orphan medicinal products*, article 3).

Regulatory bodies like the FDA and EMA recognize in their definition of rare disease that current business models present a challenge to orphan drug development (Sharma *et al.* 2010). Therefore 'orphan drug' designations have been created to promote and facilitate the development of medicines for these diseases (see section 19.3) (*Orphan Drug Act*).

In a situation analogous to rare/orphan disease, serious or life threatening conditions (e.g. rare cancers) with unmet medical needs can benefit from programs that facilitate and accelerate the development and approval of new drugs. New regulatory measures have been implemented by different agencies worldwide to allow novel drugs through a faster pathway that manages their risk-benefit elements in a case-by-case manner (Ehmann *et al.* 2013). Since such drugs are generally not destined to the whole public, are subject to continuous regulatory review, and require permission to use, access can be quickly overturned if new data suggest a danger to patient safety. This alternative to the traditional binary licensing approval system is called 'adaptive licensing'. Its step-by-step approval process renders license permission less stringent as long as drug sponsors can demonstrate benefit in the form of milestone accomplishments (see section 19.2).

PGx stratification can occur more easily when patients are segregated by ethnic groups rather than by genotypes. Some genetic variants associated with desired drug responses are thought to be more prevalent in certain ethnic groups, which could have an impact on clinical drug design and healthcare decisions (Tomasi 2012; Otlowski *et al.* 2012). Although the rationale for using ethnicity as a substitute for genotyping is founded on the desire to make drug trials less expensive, safer, and more inclusive, this practice carries significant ethical issues. Poor market prospects could lead companies involved in PGx research and development to exclude individuals with poor drug response from participating in clinical trials, which may lessen their access to safe and efficient drugs for the 'orphan genotype.' It has been suggested that policies should include measures to uphold social equality by preventing financial concerns from limiting patients' access to drugs without lucrative markets (see section 19.4.1) (Tomasi 2012).

In order to use PGx efficiently, a healthcare system should provide patients with access to routine genetic testing services as well as some degree of genetic counseling when indicated. As such, a robust framework of norms and guidelines will be required to ensure and optimize the use of genetic testing, DNA collection, access to patient information, and data confidentiality (FDA 2013a; Zhang *et al.* 2012; Ferreira-Gonzalez *et al.* 2008).

19.2 Regulations, policies, and international outlook

19.2.1 Drug development guidelines proposed by major regulatory agencies

Pharmacokinetics (PK) is defined as the way in which the human body affects the absorption, distribution, metabolism, and excretion (ADME) of a drug, whereas pharmacodynamics (PD) is the way in which that drug affects the human body by acting on biochemical or physiological targets. Genetic differences among human populations can have an effect on the effectiveness of drugs and the possible occurrence of ADRs. The observed clinical variability is partly determined by gene products associated with ADME (Maliepaard *et al.* 2013). Some of the genes encoding drug-metabolizing enzymes are highly polymorphic, and can be used as biomarkers to assess the PK profile of individuals and populations. Indeed, genetic polymorphisms are thought to affect the ADME of about 30 per cent of clinical drugs (Eichelbaum *et al.* 2006). A patient with a 'fast metabolizer' phenotype might break down a drug too quickly and experience low drug efficiency. On the other hand, a 'slow metabolizer' might build up high concentrations of toxic metabolites in their body and experience undesirable side effects. For fast metabolizers, a higher drug dose would be prescribed, whereas the dose of the same drug would be significantly decreased for slow metabolizers.

For instance, cytochrome P450 2D6 (CYP2D6) plays a role in metabolizing 25 per cent of current drugs and has been associated with the occurrence of Risperidone ADRs (Jose de Leon *et al.* 2005). Poor metabolizers lack this enzyme (including 7 per cent of the Caucasian population) and high metabolizers bear two copies of the CYP2D6 gene (including 2 per cent of Northern Europeans, 10 per cent of Southern Europeans and 30 per cent of the African population) (Pirmohamed and Hughes 2013; Bradford 2002).

Many regulatory agencies have assembled data concerning genetic variants associated with ADME. This explains why the emerging policies and guidelines from governing bodies focus on the PK parameter. For instance, 10 per cent of prescription drugs in the United States currently use PGx information in drug labeling, primarily with reference to gene variants and PK (Frueh *et al.* 2008). In this section we review the policies and guidelines of the EMA, the FDA, and the Pharmaceuticals and Medical Devices Agency of Japan (PMDA), pointing out the particulars of each agency's approach and the policy elements they have in common.

Drug clinical trials generally proceed through four phases (*21 Code of Federal Regulations,* § 312.21). Phase I involves establishing a safety profile of the chemical compound, including potential safe dosages and PK/PD parameters, in a sample of 200–400 healthy participants (Organization for Economic Cooperation and Development (OECD) 2009: 50). Phase II evaluates efficacy, with a further focus on safety and broad-range doses in a sample of 200–300 individuals. The results from phase II are used to design the parameters of phase III, which focuses on determining a clinically effective dose. This phase generally involves between several hundred and several thousand participants affected by the condition(s) the drug is likely to treat. The risk-benefit ratio of the drug is evaluated in this phase, and is used as the basis for market approval. Phase IV, or post-market pharmacovigilance, occurs after marketing authorization. Since rare but serious ADRs might have remained undetected due to the low numbers of participants in the

previous clinical trials, this phase involves testing the drug on a high number of participants in the general population.

The use of PGx biomarkers can be beneficial to phased clinical trials if molecular genetics is used to identify markers of efficacy and ADR, thereby determining the participants who are likely to respond well to the drug (OECD 2009: 53). Although clinical trials are generally performed on large samples of randomly selected patients, some believe that PGx could modify this paradigm by altering the aim of each phase. Phase I could try to establish proof of concept; phase II could stratify participants into good responders, non-responders, and adverse responders; and phase III trials could use a much smaller sample of patients if limited to selected genotypes that should respond well to the drug. The obvious benefits of PGx in phased clinical trials include reducing the number of ADRs in participants, accelerating and reducing the cost of trials, and increasing the likelihood of receiving market approval. Drugs unlikely to be approved could also be identified earlier in the process, eliminating the need for further testing.

19.2.1.1 EMA guidelines

The EMA is responsible for the scientific evaluation of applications for marketing authorisation of human drugs in the European Union (EU) (European Medicines Agency 2013). No medical product can be marketed in the European Community without the authorization of the EMA (*Regulation (EC) No. 726/2004 of the European Parliament*, article 3). Its scientific committees, made up of experts from all member states, are responsible for evaluating applications for market authorization.

EMA guidelines provide recommendations for the use of PGx in the evaluation of new medications. Although EMA guidelines cover phases I–IV with a focus on the PK parameter, its mandatory *Guideline on the use of pharmacogenetic methodologies in the pharmacokinetic evaluation of medicinal products* (2011: 6) emphasizes the early phases of drug development by specifying the effect of *in vitro* and *in vivo* cut-off values on subsequent PGx-related trial designs. Drug metabolism studies of candidate human enzymes are recommended prior to phase 1 in order to identify the involvement of known ADME pathways. In the event that an enzyme has a significant effect upon a pathway both *in vitro* and *in vivo* (with cut-off values of >50 per cent and >25 per cent respectively), mandatory DNA testing of research participants is performed in order to identify individuals predicted to have the poor metabolizer phenotype and prevent their exposure to unsafe doses (EMA 2011, section 4.2.2.2).

The EMA (2011, section 4.3) considers population PK studies to be useful during both clinical development and pharmacovigilance monitoring. In its guidelines, it recognizes the importance of PGx in pharmacovigilance methodologies and proposes retrospective analysis of stored samples to link patients' genomes with their clinical information (Harrison 2012; EMA 2011: section 4.3). To this end, the EMA (2010) highly recommends storing DNA samples from all participants in phases I–III and is currently preparing new guidelines concerning pharmacovigilance.

19.2.1.2 FDA guidelines

The US Food and Drug Administration (FDA 2013b) protects public health by ensuring that drugs, biological products, and medical devices intended for the public are safe and effective. The FDA (2010) is responsible for enforcing its regulations as well as laws enacted by the US Congress to protect consumer health. Section 21 of the *Code of Federal Regulations* provides the

relevant regulations on drugs destined for human use (*21 CFR Chapter 1, Subchapter D – Drugs for Human Use*).

The FDA (2013c) released updated guidelines in January 2013 that focus on PGx use in premarket evaluation during early-phase (I and II) clinical studies. The FDA emphasizes the use of early PGx studies to identify populations that should receive lower and higher doses based on inter-individual genetic differences in parameters such as drug exposure, dose-response, effectiveness, and possible ADRs. If significant inter-individual differences are found, PGx information can be used to select patients for trials and stratify them into groups (FDA 2013c: 13). Hence, the information learned about the variability of PK and PD in phase I and II of a clinical trial could be used to improve the design of phase III (FDA 2013c: 8). The goal of these steps is to 'increase the average effect, decrease toxicity, and improve the chances of overall success of the study' (2013c: 13).

The FDA (2013c: 7–8) also considers DNA sample collection important in both exploratory studies and drug development. It recommends that DNA samples should be collected from all clinical trial participants with their informed consent. Furthermore, the FDA (2013c: 19) states that PGx information should be included in drug labels in cases where a link is found between genotype and phenotype during trials. The labels should reflect whether genetic testing ought to be considered, recommended or is necessary before the use of the drug.

Although the aforementioned guidance documents reflect the FDA's current thinking on this topic (2013c: 4), they are not mandatory like the EMA's guidelines (2011) and do not impose a responsibility on the industry. Despite the fact that the FDA does not require the submission of biomarkers and PGx data for market authorization, it nevertheless recognizes that all stakeholders (e.g. academics, drug manufacturers) should cooperate in developing new biomarkers for PGx and share preclinical and clinical data related to drug safety. To facilitate this process, the FDA created the Voluntary Exploratory Data Submission Program, which organizes workshops and expert inputs, and creates a voluntary submission process (FDA 2011a; Amur *et al.* 2008). This program aims to address emerging scientific challenges by fostering robust regulatory PGx science (Anatol *et al.* 2013).

19.2.1.3 PMDA guidelines

Japan's Pharmaceuticals and Medical Devices Agency (PMDA 2013a) is the Japanese regulatory agency responsible for conducting scientific reviews of marketing applications for pharmaceutical and medical devices as well as monitoring their post-marketing safety. Drug sponsors have to submit an application for designation consultation to the Minister of Health, Labor and Welfare, who approves drugs and medical devices in accordance with the *Pharmaceutical Affairs Law*. Based on the PMDA's opinion after preliminary evaluations, the Minister may grant orphan designation to a drug or medical device (Ministry of Health, Labor and Welfare (MHLW) 2009).

In 2001, the PMDA published two guidelines regarding PGx in drug evaluation: *Clinical Pharmacokinetic Studies of Pharmaceuticals* and *Methods of Drug Interaction Studies* (2001a, 2001b). The PMDA recognizes the use of genetic studies to stratify the population when there is a high variability of PK parameters and/or when a drug is mainly metabolized by polymorphic enzymes (2001a, article 3). Moreover, if PK profiles differing from those of healthy volunteers are observed, they should be investigated thoroughly (PMDA 2001a, article 5). As such, the PMDA recommends incorporating information about ADME into the drug investigation. Unlike the EMA, it does not provide concrete criteria for when and how PGx studies concerning the PK

parameters must be performed. For example, the PMDA does not enforce *in vitro* and *in vivo* cut-off values that impose specific PGx testing during phases of clinical trials. But like the EMA and FDA, the PMDA does encourage the collection of DNA samples in clinical trials for retrospective and prospective PGx studies related to the efficacy and safety of drugs (2001a, article 6.1.1; Maliepaard *et al.* 2013).

19.2.1.4 Pharmacogenomics and the problem of phase II/III clinical trial failure

Published studies from life science consultants have recognized that failure in phases II and III of the drug approval process is attributable in major part to efficacy and safety issues. They note that drug developers tend to enter phase III with marginal statistical and proof-of-concept evidence. One way to increase the cost-efficiency of phase II–IV trials without compromising patient safety would be to emphasize the use of PGx and biomarkers (PGx/BM) in early trials. Both allow better identification of the target population and define categories of safe dosage, resulting in improved average effect and decreased toxicity (Arrowsmith 2011a, 2011b). Improving drug approval success rates should also result in better patient outcomes.

PGx/BM designs can be divided into three categories. In cohort design, patient randomization is independent of PGx screening; in stratified design, randomization is performed within the groups identified by PGx screening; and in enriched design, a given biomarker-negative population is excluded in order to focus on biomarker-positive participants. Each type of PGx/BM trial design has its own benefits and limitations (Ishiguro *et al.* 2013).

Policies and guidelines that encourage DNA banking can have a positive impact on the implementation of PGx/BM clinical trial design. However, PMDA guidelines on DNA sample banking seem less stringent than those of the EMA and FDA. Indeed, a study evaluating clinical trials performed on anti-cancer drugs in Japan found that PGx-randomized and PGx-enriched designs were used, but no stratified trials had been conducted. Furthermore, PGx/BM-guided trials were used much less frequently in Japan than in other countries studied (Ishiguro *et al.* 2013).

19.2.2 International harmonization and ethnobridging

19.2.2.1 Global drug marketing

Drug-developing companies seek to develop global strategies for worldwide approval and marketing of their products. Hence they must consider mandatory national policies and globally harmonized policies (e.g. regulatory standards agreed upon at international and regional conferences and adopted at a national level), and develop bridging strategies between national policies and harmonization efforts (Nakashima *et al.* 2011).

Agencies from the major pharmaceutical regions in the world issue their own regulatory documents establishing dose-response standards for safe drug exposure, including risk/benefit management policies which define the lowest safe dose for effective treatment. Studies have shown that countries adopt drug dosage regimens specific to their populations; for example, Japan generally selects lower doses than those seen in the EU and the US. This may be due to their conservative review process and its considerations for the 'uniqueness of Japanese people' (see following section) (Malinowski *et al.* 2008). Hence part of the challenge for global pharmaceutical companies is to obtain regulatory approval in different regions in a cost-effective

manner. International harmonization of these guidelines based on PGx data could facilitate drug development worldwide by providing standard evidence-based criteria for drug approval in different countries. Pragmatic, unified and transparent policies should aid in the development of a globalized drug program (Maliepaard *et al.* 2013).

In 1998, the International Conference on Harmonisation (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH 1998) enacted the *E5* agreement on ethical, scientific, and clinical parameters for the standardization of trial designs and the protection of human participants. Its tripartite guidelines on 'Ethnic Factors in the Acceptability of Foreign Clinical Data' address the intrinsic characteristics of drug recipients (e.g. genetics) and extrinsic environmental factors such as culture and environment that could have an impact upon the outcome of clinical studies. The ICH *E5* objectives are:

- To describe the characteristics of foreign clinical data that will facilitate their extrapolation to different populations and support their acceptance as a basis for registration of a medicine in a new region.
- To describe regulatory strategies that minimize duplication of clinical data and facilitate acceptance of foreign clinical data in the new region.
- To describe the use of bridging studies, when necessary, to allow extrapolation of foreign clinical data to a new region.
- To describe development strategies capable of characterizing ethnic factor influences on safety, efficacy, dosage, and dose regimen.

(ICH 1998)

Thus a regional regulatory authority can assess similarities and differences in PK/PD and the dose-clinical response relationship using clinical data from a foreign country. In a bridging approach, the agency conducts full or partial mirror studies for the purpose of extrapolating foreign clinical data to meet local clinical trial standards (ICH 1998; Nakashima *et al.* 2011). When using external data as the primary source of PGx knowledge, special attention should be given to ethnic biomarker-sensitive approaches in clinical trial design. Ethnobridging (EB) techniques allow evaluation of ethnicity-related differences in PK and PD and their effect on drug efficacy, safety, dosage, and dose regimen (Wang and James Hung 2012).

19.2.2.2 Japanese ethnobridging practices and drug lag

Japan is the second largest pharmaceutical market in the world after the US, with 11 per cent of global sales and a 2.5 per cent growth rate in 2009 despite having less than 2 per cent of the world population (Paek *et al.* 2011; World Population Review 2013). Yet for the period 1999–2007, Japan's approval rate of drugs from the EU and US was fairly low (56.1 per cent and 43.6 per cent respectively) (Tsuji and Tsutani 2010). Approval of Western drugs in Japan requires larger phase II and III studies which take into account the 'intrinsic' PK characteristics of Japanese participants (MHLW 2009; Kelly and Nichter 2012; PMDA 2001a). They may consider data from ethnic Japanese individuals living overseas, but stringent PMDA guidelines (2001a) state that Japanese participants who have spent more than five years abroad are not eligible for EB studies because they do not share 'extrinsic' factors such as diet and exercise. Foreign companies that wish to obtain drug approval in Japan almost always need to repeat the entire clinical drug development process, despite the delay and the enormous cost (Kelly and Nichter 2012).

Although the regulation of EB studies in Japan is meant to protect Japanese patients from inappropriate drugs, it has been suggested that it is also a protectionist measure for the local biopharmaceutical industry (Kelly and Nichter 2012). These regulations created a 'drug lag,' preventing seriously ill Japanese patients from accessing novel foreign drugs that had adequate PGx data but did not make it through the cumbersome Japanese regulatory approval process soon enough (Sinha 2010; Nakashima *et al.* 2011). The drug lag between the US and Japan from 1999 through 2005 was estimated at 40 months (Tsuji and Tsutani 2010). Consequently, some Japanese patients and doctors bought direct-to-consumer (DTC) medications from foreign countries, placing them in a vulnerable position with regard to safety, adequate information and consent to risk (Kelly and Nichter 2012).

The EB approach may also have been used to promote the notion of a pure Japanese bloodline. In attributing special characteristics to the Japanese genome, policy-makers promoted the opinion that the Japanese genome is unique (Kelly and Nichter 2012). This rhetoric may have played a role in justifying and maintaining a separate clinical trial pathway for foreign drugs for many years. However, biological anthropologists and geneticists agree that our established perception of 'race' has no scientific basis (see section 19.4).

The 1998 ICH *E5* agreement and global clinical trial (GCT) guidelines proposed to facilitate foreign drug approval by providing a more compatible framework with international multiethnic PGx studies. GCTs synchronize early-stage drug development by performing simultaneous clinical trials with participants from different ethnic backgrounds in Japan, the EU, and the US (MHLW 2009). These policies helped minimize EB studies and costly reiterations of phase II/III trials. Since 2007, the Japanese Ministry of Health, Labor and Welfare has tried to reduce drug lag by focusing on GCTs. Despite a significant increase in GCT-approved drugs in Japan (13.4 per cent in 2012), most drugs still require some level of EB studies and much more progress is needed in this area (Asano *et al.* 2013; Kelly and Nichter 2012).

The 2013 document *PMDA International Vision* sets Japan's goals for 2020 including the reform of international drug approval regulations (2011, 2013b). The PMDA recognizes that the life cycle of a medical product cannot be achieved only domestically, and states the need to build close international partnerships with foreign regulatory agencies like the EMA and FDA. Therefore the agency affirms its commitment to international harmonization initiatives such as the *ICH* and the International Medical Device Regulators Forum (ICH 2013; International Medical Device Regulators Forum 2013). In order to use resources more effectively, the PMDA also commits itself to accepting foreign clinical data, including PGx studies, and implementing joint GCP (Good Clinical Practice) and GMP (Good Manufacturing Practice) inspections (PMDA 2013b). By removing the dichotomy between national and international standards, the PMDA hopes to enhance its international status and improve domestic healthcare. Faster drug approval should reduce Japan's drug lag by speeding up the delivery of medical products to patients.

19.2.3 Accelerated drug licensing

The traditional drug licensing process generally adopts a binary mode of decision in which the single step of market approval designates a drug as a safe and efficient compound therapy. After long and costly preclinical and clinical trials, an experimental drug either receives marketing approval or fails due to concerns about safety and effectiveness. Problems such as high cost of development, length of time from conception to market, drug lag, and the lack of treatment for orphan diseases are exacerbated by the current binary approval system (Eichler *et al.* 2012). It has also been argued that late-phase drug failures stifle novel pharmacological

development, since each represents a delayed opportunity to develop the next successful drug (Reynolds 2013).

Regulators are looking at novel approaches and opportunities to remove these obstacles. For instance, regulatory agencies around the world are trying to accelerate the approval process by using PGx studies as an early indicator of novel drugs' efficacy and toxicity according to a genetically stratified population (Ehmann *et al.* 2013; Lesko and Woodcock 2002).

19.2.3.1 Expedited drug development programs by the FDA

The *Food and Drug Administration Safety and Innovation Act* was signed into US law on 9 July 2012. It allows drugs to enter an accelerated development and approval pathway if 'preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints' (Reynolds 2013). As such, the development of new drugs targeting serious and life-threatening diseases has seen their development accelerated by approaches based on PGx.

In June 2013, the FDA issued the *Guidance for Industry – Expedited Programs for Serious Conditions – Drugs and Biologics* that describes all expedited programs for drug development in the US, including a novel category, 'Breakthrough Therapies' (*21 USC*, § 356). This document represents the agency's vision for streamlining drug development and should be considered an optional recommendation. When finalized, it will replace the current guidance for industry entitled *Fast Track Drug Development Programs – Designation, Development, and Application Review* and *Available Therapy* (FDA 2006, 2004).

Drug sponsors may only access these programs if the new product addresses 'unmet medical need in the treatment of a serious condition' (FDA 2013d). A serious condition is defined as one that is associated with morbidity and has an impact on day-to-day functioning. The streamlined drug should either constitute a novel treatment or demonstrate improvement over the available therapies (FDA 2013d). Proponents suggest that combining a more flexible regulatory framework with the predicted advantages of PGx approaches could make more new drugs available without compromising their safety and efficacy (Reynolds 2013).

19.2.3.2 Early market entry programs by the EMA

The European Union community code related to medicinal products for human use functions as a single instrument, gathering all provisions for granting authorizations regarding market, production, labeling, classification, distribution, and advertising of medical products. As such, no medicinal product can be put on the market without the authorization of the EMA. If a product sponsor wants to obtain market authorization in more than one member state, the applicant must submit an application based on the same dossier in a process called the decentralized procedure. Likewise, if a product has already been accepted in one member state, an application based on the pre-existing dossier can be submitted to the others. In a second procedure called mutual recognition, the applicant must inform the member state that granted the initial authorization as well as the EMA (*Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use*).

In 2004 and 2006, the EMA introduced two new instruments regulating early drug market entry under exceptional circumstances and through conditional market authorization (*Directive 2001/83/EC of the European Parliament*; *Commission Regulation (EC) No. 507/2006 of 29 March*

2006 on the conditional marketing authorisation for medicinal products for human use falling within the scope of Regulation (EC) No. 726/2004 of the European Parliament and of the Council). The former is used when sponsors are unable to provide PGx data showing efficacy and safety. Faster market access can be granted based on ethical reasons if the drug is needed to treat a rare disease or a life-threatening condition and there is no other efficient treatment (*Directive 2001/83/EC of the European Parliament*, article 4). As with the FDA's expedited programs, failure to provide the required post-market approval studies can result in the withdrawal of an exceptional circumstance market license (*Directive 2001/83/EC of the European Parliament*, article 5). Although the conditional approval license is also intended for products treating unmet medical needs, drug sponsors are expected to provide the relevant clinical data in the immediate future, proving their product has a positive benefit-risk balance for quality, safety, and efficacy (*Commission Regulation (EC) No. 507/2006*, articles 22–23).

Although the EMA's regulations aim at accelerating access to novel drugs, a 2010 study by Boon *et al.* shows that neither of the two regulatory documents helped achieve this objective. For the 1995–2005 and 2006–9 periods, the mean total approval times for drugs submitted under the two early entry regulations were found to be comparable respectively to those of all drugs submitted during those periods regardless of method (Boon *et al.* 2010).

19.2.3.3 The shift to an adaptive licensing paradigm

The accelerated drug approval programs of the FDA, EMA, and other regulatory agencies attempt to depart from the binary approval paradigm through adaptive licensing, a step-by-step process which begins with early marketing authorization and ends with enhanced post-authorization control of a medicine (Eichler *et al.* 2012; EMA 2010; Ehmann *et al.* 2013). Adaptive licensing necessitates many conceptual changes in the critical elements of drug regulations: (1) evaluation over multiple stages rather than the simple dichotomy of pre- and post-licensing; (2) continuous evaluation of the trade-off between the early access risk and enhanced benefits of the novel therapeutics; (3) conversion of uncertain into acceptable risks by educating the public and providing informed consent; and (4) initial licensing to a small group, selected by PGx approaches, with subsequent increases in the group size based on better-defined evidence and risk assessment (Ehmann *et al.* 2013; Eichler *et al.* 2012).

The transition to adaptive licensing raises challenging legal and ethical issues: (1) mandatory drug labeling and prohibition of off-label use for safety reasons; (2) consumer awareness of dangers related to off-label use; (3) waivers for product liability suits during the initial learning period, except in cases of obvious negligence; and (4) longer post-approval studies (Ehmann *et al.* 2013; Eichler *et al.* 2012).

Earlier approval for restricted usage does not necessarily mean a shorter drug development process overall. Since regulatory bodies want to give earlier drug approval without compromising safety, increased pharmacovigilance in the form of longer post-market studies becomes an implicit term of the contract. For instance, newly approved drugs can be prescribed for off-label use under current FDA regulations (Dresser and Frader 2009). However, the acceptance of higher risks under the adaptive licensing paradigm could make these drugs less safe for patients not stratified by early PGx studies. For this reason, there is also a need to convey the information about the drug to patients and physicians, including any prohibition of off-label use. Some medicines approved under adaptive licensing would need to be restricted to certain patient groups until authorization is granted for a wider use.

Evaluation of benefits and risks becomes a complex process involving large amounts of data. Through the use of PGx early on during adaptive licensing drug development, quantification

of benefit-risk and better methods of clinical trial design and analysis can be envisioned. Early stratification of drug efficacy and toxicity could help design and analyze novel drugs and determine if they are suitable for streamlined approval for unmet clinical needs (e.g. life-threatening diseases).

19.3 Implementation of pharmacogenomics

19.3.1 Handling safety and quality

To ensure its proper development, PGx depends on the availability and reliability of genetic test kits to detect specific biomarkers that facilitate the prescription of the right drug at the right dosage while diminishing risks for ADRs.

Under the FDA's regulatory oversight, genetic test kits that are developed and sold to laboratories or direct-to-consumer are considered medical devices named *in vitro diagnostic tests* (IVDs). However, several genetic tests offered directly by clinical laboratories are considered 'home brew' rather than commercial products and fall in the category of laboratory diagnostic tests (LDTs) (Joly *et al.* 2011). Historically, LDTs were not under FDA authority and lacked the oversight given to IVDs. This influenced many companies to commercialise their tests as LDTs. Hence, it has been proposed that LDTs should be reviewed more stringently in order to evaluate their methods, accuracy, and appropriate labeling. Monitoring their safety will be important because LDTs are frequently used to inform critical treatment decisions for high-risk diseases; furthermore, they may be performed outside the supervision of a patient's physician at distant commercial laboratories and may be marketed directly to patients as DTC tests (Gibbs *et al.* 2013).

The Centers for Medicare and Medicaid Services (2013) and the Centers for Disease Control and Prevention (2013) oversee the quality of laboratory testing through the *Clinical Laboratory Improvement Amendments* (CLIA) of 1988, which introduced standards for quality assurance, certification, recordkeeping, and proficiency for laboratory tests (FDA 2013a; Zhang *et al.* 2012). CLIA does not currently enforce proficiency for genetic testing although most labs perform such tests voluntarily at varying levels (Tucker 2008).

Health Canada is the federal regulatory entity responsible for evaluating the safety and efficacy of health products for human use in Canada (Health Canada 2013). For this purpose, Health Canada can grant market authorization under the *Food and Drugs Act*, the *Food and Drug Regulations*, and the *Medical Devices Regulations* which set up criteria for the safety and effectiveness of PGx tests. In Canada, medical devices are graded from class I to IV according to the potential risk they represent to humans, with class IV being the highest risk. IVDs are considered class III medical devices, which represent a moderate potential risk to public health but a high potential risk to individuals (Joly *et al.* 2011). As such, diagnostic manufacturers are required to provide Health Canada with data on drug safety, PD, efficacy, and dose responses. In 2007, Health Canada released a *Guidance Document on Submission of Pharmacogenomic Information* that encourages the submission of PGx data when filing for market authorization in order to support claims about the safety and efficacy of a drug (Health Canada 2008).

19.3.2 Direct-to-consumer testing and medication

One of the most influential developments in personalized medicine has been the sale of drugs and genetic tests over the Internet. $4.3 billion USD was invested in direct-to-consumer advertisement (DTCA) in 2009, representing a quarter of US pharmaceutical expenditure for the period 1996–2005 (Mackey and Liang 2012). Proponents emphasize that 'consumers have been

empowered with additional information to "level the field" with the health care community, contributing to more efficient doctor–patient exchanges' (Paek *et al.* 2011), or that DTC represents 'the patient power revolution' (Kelly 2004). In contrast, opponents are concerned by emerging issues such as safety risks, increased cost, interference in the doctor–patient relationship, lack of analytical validity and clinical utility, false advertising, challenges in interpreting the results, and the psychosocial impact of the results on various communities (Howard *et al.* 2010; Paek *et al.* 2011).

As mentioned previously, some Japanese patients have opted to obtain foreign DTC medicine as a way to compensate for a prevailing drug lag (Kelly and Nichter 2012). These drugs and genetic tests are often associated with insufficient, inaccurate, and/or misleading information and need expert knowledge to be properly understood and used (US Government Accountability Office (GAO) 2010; Mackey and Liang 2012). Furthermore, DTCA is frequently used to market drugs early in their life cycle when there is a lack of pharmacovigilance data with which to determine health risks. Vioxx and Avandia are examples of blockbuster drug recalls following heavy DTCA (Paek *et al.* 2011; Mackey and Liang 2012).

A 2012 study by Borry *et al.* shows that France, Germany, the Netherlands, Portugal, and Switzerland have national laws that can partially or fully regulate DTC genetic testing. However, they are derived from interpretation of legislation that does not specifically address how those tests are advertised (Borry *et al.* 2012). Regulating DTCA for drugs and genetic tests is difficult because their providers can easily bypass national boundaries through the Internet. The *Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine*: *Convention on Human Rights and Biomedicine* 1997 is a binding European treaty, ratified by 29 member states of the European Community, which states that predictive genetic tests should be subject to appropriate genetic counseling (article 12). It also requires that parties provide judicial protection against unlawful infringement of rights and principles, a compensation for undue damage, and appropriate sanctions (*Convention on Human Rights and Biomedicine,* articles 23–35). Moreover, the *Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Genetic Testing for Health Purposes* 2008, which was originally drafted by the EMA, states that genetic testing should always be performed under individualized medical supervision, and that appropriate genetic counseling should always be available for the person tested (articles 7–8).

One proposed solution is the establishment of an international certificate that would force DTC test providers to comply with ethical standards by demonstrating the scientific reliability of their products and meeting the requirements of genetic counseling (Hauskeller 2011). By analogy with the International Organization for Standardization (2013) certification, the rules of this certificate would be voluntary, but would provide a marketing advantage to compliant DTC providers while ensuring consumers a certain degree of protection against exaggerated claims.

19.3.3 Drug labeling and off-label use

The FDA does not prohibit physicians from prescribing off-label drugs to patients who do not have adequate treatment for their conditions (2011b; American Association of Orthopaedic Surgeons 2013). Unless PGx is used to stratify patients with certain predisposing genotypes, off-label use can result in toxicity and ADRs (e.g. increased metabolite overexposure) (Yamashiro *et al.* 2012; Mello *et al.* 2009). Due to these safety concerns, several bodies have called for more stringent risk-benefit assessments. The United States' *Food and Drug Administration Amendments Act* of 2007 imposes 'Risk Evaluation and Mitigation Strategies' on applicants if the FDA considers them necessary to ensure the benefits of a drug outweigh its risks (FDA 2013b, 2013e).

In 2009, French regulators withdrew Mediator (benfluorex), a drug licensed for diabetes but used off-label for weight loss, which caused between 500 and 2,000 deaths over a period of 33 years (Mullard 2011). The recent French law, *Loi n° 2011-2012 du 29 décembre 2011 relative au renforcement de la sécurité sanitaire du médicament et des produits de santé* (*Loi n° 2011-2012 du 29 décembre 2011*), aims to improve risk-benefit management and provide a better regulatory process for off-label prescriptions. Applicants under this law can apply only for diseases with severe prognosis and must follow strict criteria concerning the quality of scientific evidence and drug safety, but they may claim reimbursement from France's public health insurance system if the drug is approved (*Loi n° 2011-2012 du 29 décembre 2011*, articles 15 and 18.2.4). Off-label marketing authorization is granted for a period of three years (*Loi n° 2011-2012 du 29 décembre 2011*, article 18.1).

19.3.4 Orphan drugs

19.3.4.1 Regulations and incentives

Stratification through PGx raises some concerns about the creation of new minority groups. One scenario predicts that for a given drug, PGx research will identity 80 per cent of tested patients who would respond well, 10 per cent who would not show any benefit, and 10 per cent who would likely suffer from toxic effects. The principle of equal access to medicine and medication suggests that all patients should benefit from PGx. However, the market reality dictates that pharmaceutical companies focus on the 80 per cent of good responders and ignore the remaining 20 per cent of so-called 'orphan genotypes' (Rothstein 2003).

The European Organization for Rare Diseases (2013) estimates there are between 6,000 and 8,000 known rare diseases which may affect 30 million European citizens. Most are chronic and life-threatening, and 80 per cent are of genetic origin. Although they affect 6–8 per cent of the world population, orphan diseases have traditionally been neglected by the pharmaceutical industry due to the lack of profit incentive (Sharma *et al.* 2010). This situation calls for economic incentives that aim at promoting research and marketing of orphan drugs (Rothstein 2003). Accordingly, many countries have updated their drug regulatory policies by creating orphan drug designations. These have succeeded in shifting some of the pharmaceutical industry's focus towards orphan drug development.

Orphan drug designation is typically given to products intended to be the first treatment for a rare and/or serious disease. It is estimated that there are between 4,000 and 5,000 rare diseases worldwide for which no treatment is currently available (Sharma *et al.* 2010). In the *Orphan Drug Act* of 1983, the US defines an orphan disease as one affecting less than 200,000 people (approximately 0.06 per cent of the American population). The EU defines a rare disease as affecting 5 per 10,000 citizens (0.05 per cent), while Japan's definition of rarity involves fewer than 50,000 patients (approximately 0.03 per cent) (*Regulation (EC) No. 141/2000*; Japan Pharmaceutical Manufacturers Association (JPMA) 2013). Other conditions also affect the granting of orphan drug status. In the EU, a drug must provide diagnosis, prevention or treatment of life-threatening, seriously debilitating, or serious and chronic conditions such that without incentive-driven policies, the drug would be unlikely to generate sufficient returns to justify the necessary investment and there would be no satisfactory medication for the condition. In Japan, the drug must either treat a disease condition for which there are no other treatments available or be clinically superior to a previously accepted drug (EMA 2011; Sharma *et al.* 2010; JPMA 2013).

Canada currently has no orphan drug designation. However, a draft proposal from December 2012 delineates Health Canada's current position on the development of an orphan drug regulatory framework. The new regulatory framework will probably operate similarly to the US and EU laws for drug designation, which could allow drug sponsors in Canada to collaborate with those jurisdictions and file using a common application process. The objective is also to enhance access to orphan drugs without compromising patient safety (Office of Regulatory and Legislative Modernization 2012: 8; *Food and Drug Regulations*).

Regulatory agencies from the EU, US, and Japan grant a similar package of economic incentives to sponsors with an orphan drug designation, such as 7–10 years of market exclusivity, tax credits for development costs and application fee waivers (*Orphan Drug Act*; JPMA 2013; *Regulation (EC) No. 141/2000*; Thorat *et al.* 2012; Melnikova 2012; Meekings *et al.* 2012; Tambuyzer 2010). These incentives are thought to have a positive impact on drug approval rates. Only ten orphan drugs were approved in the decade before the United States' *Orphan Drug Act*, but 350 were accepted between then and 2010. Likewise, in the EU, the implementation of orphan drug regulations increased approval rates from eight before 2000, to 60 in 2010 alone. Third-party payers such as private insurers and public healthcare agencies have also helped to cover orphan drug costs, making it a very profitable business. With an annual growth of 6 per cent, orphan drug sales have been predicted to reach $112.1 billion in 2014 (Tambuyzer 2010).

19.3.4.2 Access to orphan drugs and reimbursement

Market exclusivity tends to increase medication price and hinder drug accessibility for patients (Murphy *et al.* 2012). This has created tension between different stakeholders. Since orphan drugs constitute a small market for pharmaceutical companies, they claim their drug development efforts should be compensated with some profit margin (Tambuyzer 2010; Sharma *et al.* 2010). Although 7–10 years of market exclusivity are granted to orphan drugs as an economic incentive, pharmaceutical companies claim that a market has to exist in the first place. Even if PGx lowers the cost of drug development, the disease stratification paradigm could also reduce market size so much that: (1) there is no chance of returns at all; and (2) market laws drive drug prices so high that patients are unable to afford them. Moreover, companies tend to maintain high drug prices despite public pressure (Arnst 2006). This economic paradox suggests that public healthcare planners should consider being more supportive of orphan drug development programs.

Member states of the European Community have little power in negotiating orphan drug prices since they are determined by market rarity (de Varax *et al.* 2004). This scenario is familiar in medicine. However, national drug coverage programs for orphan drug testing and reimbursement could help provide patients with access to unaffordable orphan drugs while securing markets for their developers with the promise of long-term profitability (Tambuyzer 2010). A study mandated by the European Commission showed that many EU countries, including France, Germany, Spain, Holland, and Sweden, systematically cover the costs of orphan drugs whose prices are higher than those of regular medicines (de Varax *et al.* 2004).

It has been suggested that a surge of high-priced orphan drugs could overwhelm current reimbursement programs, forcing policy-makers to make difficult ethical choices between allowing high expenditure on a few individuals or using the same amount of money to treat a greater number of patients in other disease categories (de Varax *et al.* 2004; Sharma *et al.* 2010). However, the narrow orphan drug market accounts for relatively little of the total national budget for medicine in most countries, and competition would eventually put downward pressure on drug price (Tambuyzer 2010). Thus, in the context of subsidized orphan drug reimbursement costs, disease stratification could indeed play out in favor of 'orphan patients.'

19.3.4.3 Outlook for adequate orphan drug incentives

There are both proponents and critics of the current incentive system for orphan drug marketing. A 2013 study by Matthews and Glass analysed the adoption process of 13 drugs in five European countries. Their results indicate that countries with stronger social welfare programs tend to pay for orphan drugs, unlike those with more of a free market economy. This suggests that economic incentives and national reimbursement programs could effectively encourage pharmaceutical companies to develop drugs for rare diseases (Matthews and Glass 2013). Another study proposes that economic incentives compensate for the reduced market size, resulting in an orphan drug market as profitable as the regular drug market (Meekings *et al.* 2012). However, concerns about whether PGx stratification could reduce the orphan disease market and its profitability persist (Tambuyzer 2010).

Critics of the current orphan drug programs suggest that economic incentives combined with a period of market exclusivity could create lucrative monopolies that do not necessarily serve all stakeholders. They propose that patients, the industry, and regulatory agencies should be able to better communicate their opinions with respect to the risks and advantages of orphan drug regulation. These critics further recommend public genetic screenings for orphan diseases in young children as a non-economic incentive. They argue that this would allow diagnosis to be linked to an assigned and reimbursed treatment, thus significantly improving children's health and lowering the risk of ADRs while securing orphan drug markets (Tambuyzer 2010).

The industry has also called for a clear and internationally harmonized definition of rare disease that would be accompanied by conditional reimbursement as a way of securing markets (Tambuyzer 2010). It is currently difficult to diagnose a rare disease because the available information is inadequate and healthcare professionals lack training and awareness. Although there are no diagnostic methods available for some orphan drugs, PGx and WGS approaches could contribute to the development of new ones since most orphan diseases have a genetic origin (Sharma *et al.* 2010; Li and Jones 2012). Greater coherence between international regulations would also favor the creation of a globalized market with additional economic incentives for these pharmaceuticals (Tambuyzer 2010).

According to a 2006 study by Ridley *et al.*, '[i]nfectious and parasitic diseases accounted for more than half of healthy years lost in Africa in 2002, but only 3 per cent of healthy years lost in developed countries.' Most people affected by these diseases are from low-income countries, so there is a lack of financial incentives for drug development (Ridley *et al.* 2006). They are called 'neglected diseases' not because there is a lack of scientific knowledge, but because the lack of a lucrative market dissuades pharmaceutical companies from investments and research (Ridley *et al.* 2006; Trouiller *et al.* 2002). Equitable access to innovations in pharmacogenomics and personalized medicine in developing countries appears very unlikely based on their lack of research and development infrastructures, financial resources, economical incentives, and well funded public healthcare plans (Kamal *et al.* 2011). Existing public healthcare systems in these countries simply cannot allocate most of their budget to a few patients with orphan genotypes while leaving aside millions in need of more essential care.

19.4 Ethics of personalized medicine

In addition to those introduced earlier in the chapter, there are a number of core ethical issues which stakeholders need to address in order to facilitate the transition to a more personalized healthcare environment. The advent of PGx could force stakeholders to revisit established bioethics principles such as autonomy, beneficence and justice or even formulate new ones that will

facilitate a more comprehensive ethical assessment of this emerging healthcare model (Ozdemir 2010; Breckenridge *et al.* 2004; Beauchamp and Childress 2001).

Genetically stratifying patients permits the identification of good responders who are also unlikely to experience toxic ADRs. On the other hand, patients that do not share the PK parameters set during drug development could be excluded from clinical trials, meaning little or no data related to drug toxicity would be available for their genotype (Nuffield Council on Bioethics 2006). If clinical trial design for subsequent phases were to include racial or ethnic categories as a proxy for known biomarkers, there is a possibility that a particular ethnic group would be selected as good drug responders whereas another would be excluded as poor responders (Peterson-Iyer 2008; Nuffield Council on Bioethics 2006).

According to its proponents, personalized medicine empowers patients to take their healthcare into their own hands (Paek *et al.* 2011). This rhetoric tends to transfer the responsibility of healthcare from the state and the physicians towards individual citizens. This is particularly troubling in a context where publications from the media, government agencies, and direct-to-consumer advertising companies may not provide access to a clear and balanced representation of emerging health products (Howard *et al.* 2010; GAO 2010). Hence, it is of prime importance that doctors receive the training necessary to advise patients about genetic testing and personalized treatments in an unbiased professional manner.

Although patients are rarely offered genetic testing in the current situation, the introduction of PGx in routine healthcare will mean more frequent genetic testing, possibly including WGS. Healthcare professionals will need to consider important ethical issues such as the type of genetic information that warrants disclosure to patients and its psycho-social impact upon them, including cases involving incidental findings (Nuffield Council on Bioethics 2006: 7). As PGx drugs become part of the medical standard of care for some diseases, patients could be required to undergo genetic testing before the prescription of certain medicines in order to avoid ADRs (Nuffield Council on Bioethics 2006: 3). Reimbursement of PGx treatments by public healthcare or private insurers could become dependent on whether or not the genetic test results indicate a particular drug (van Nooten *et al.* 2012). This is likely to create significant distress for patients suffering from life threatening diseases whose genetic profile does not warrant access to any of the available treatments.

19.4.1 Genetic discrimination

Genetic discrimination has been defined as 'the differential treatment of asymptomatic individuals or their relatives on the basis of their actual or presumed genetic characteristics' (Otlowski *et al.* 2012). If a disease predisposition is disclosed to a third party, the patient risks stigmatization and discrimination in his or her social life, in the workplace, and in obtaining health or life insurance (Rothstein 2003: 330–1). The consequences of genetic testing for disease susceptibility risks were first thought to be different to those of PGx tests for recommended drug types and safe dosages (Roses 2000). A genetic test for PGx purposes could have much narrower effects because it applies mainly to predict drug response (i.e. someone already affected by a medical condition). Yet PGx stratification can provide valuable genetic data about how different subgroups within a population react to drugs. This implies that PGx could promote genetic discrimination if a particular subgroup were to be excluded from phased clinical trials or, later in the process, from access to drugs. For instance, poor responders could experience discrimination by being 'more expensive to treat,' a designation which could affect drug reimbursement by third-party payers (Breckenridge *et al.* 2004). As with disease genetics, discriminatory use of PGx data in the aforementioned scenario could contribute to public fear of PGx testing (Joly *et al.* 2013).

Some PGx studies claim to have identified intrinsically determined drug response differences among racial or ethnic groups (FDA 2005). For example, the Caucasian population in the US has been found more likely to have abnormally low levels of the drug-metabolizing enzyme CYP2D6 that affects antidepressants, antipsychotics, and beta-blockers (Xie *et al.* 2001). Other studies indicate that African-Americans have a poor response to antihypertensive agents (Exner *et al.* 2001; Yancy *et al.* 2001). Moreover, a study of 173 publications in nutrigenetics from 1998 to 2007 shows that a vast majority focused on 'white' participants (Hurlimann *et al.* 2011).

In these types of studies, it is extremely important for reviewers to critically assess the criteria used to place individuals in one group or another, and how the research team actually implemented their stratification protocols. The authors of these studies should also be sensitive to the fact that conclusions formulated too broadly can easily be misinterpreted and used as propaganda by racist organizations (National Alliance News 2008). Detailed information by the authors describing the basis of the stratification and the limitations of their findings could also go a long way in preventing unfortunate incidents associated with the misappropriation of scientific findings.

Admixture between ethnic groups is increasingly common in modern society, and there are more genetic differences between individuals of the same ethnic group than between ethnic groups. As such, it is well argued that race is a social construct and cannot be defined scientifically (Lewontin 1995). Hence it is difficult to justify using the concept of race as a genetic biomarker in PGx drug development. Racial classification reflects an imperfect socio-cultural construct that should not be considered equivalent to scientifically validated genetic biomarkers (FDA 2005). The drug response differences that have been recognized between countries (Malinowski *et al.* 2008) may be caused by extrinsic rather than intrinsic factors, suggesting the use of more transparent and science-based stratification criteria based on socio-cultural and/or geographical ancestry (Ozdemir *et al.* 2008). Furthermore, successful PGx implementation should help identify accurate genetic biomarkers capable of supplanting the use of racial or ethnic stratification altogether (Tucker 2008; Nuffield Council on Bioethics 2006). Scientists and drug sponsors should adopt a PGx approach that includes multiple population groups during research and drug design, and should consult representatives from racial or ethnic minorities regarding their protocol design and participant selection process (Peterson-Iyer 2008). Finally, the development of robust, harmonized guidelines outlining acceptable proxies for PGx stratification would provide more transparency, equity, and accuracy in PGx research and implementation.

Genetic discrimination has also been discussed in the context of personal insurance, where insurers might use this information to determine applicants' eligibility for private life or health insurance coverage. Some employers, primarily in the US, have shown an interest in requiring the disclosure of genetic information as a condition for initial employment or promotion. This could allow them to identify individuals who are more susceptible to developing certain illnesses that would lead to greater absenteeism or pose risks to other workers. In some cases, there may be an argument in favor of testing for public health reasons or to fulfill a legal duty of protecting the health of the workers (Otlowski *et al.* 2012; Roberts *et al.* 2012). Genetic discrimination in insurance and employment is particularly concerning given our limited knowledge of the genomics behind complex disorders. Genetic information, including research data, can be easily misinterpreted or given undue weight by third parties lacking proper expertise. Yet the known instances of genetic discrimination have so far remained mostly limited to a few monogenic dominant disorders (Joly *et al.* 2013).

19.4.2 Instruments protecting against genetic discrimination

PGx implementation relies on the voluntary participation of all segments of the population. Yet multiple surveys have shown that although the public is interested in genetic testing, they fear data misappropriation, discrimination, and breaches of patients' privacy and confidentiality (Haga *et al*. 2012; Armstrong *et al*. 2012; Kobayashi *et al*. 2011). Fear of participating in genetic studies, especially for more vulnerable participants or those belonging to easily identifiable minority groups, could be addressed through education campaigns and best practices explaining the limits of genetic information and the importance of preventing misuse and discrimination outside of the clinical and health research spheres. Legislators around the world have also recognized this problem, resulting in a number of international, regional, and national policies which make explicit requirements to protect individuals from genetic discrimination.

The 1993 *Declaration of Bilbao* was the first to denounce the use of genetic information for discrimination in contexts such as work and insurance (Fundación BBV 1993). The United Nations Educational, Scientific, and Cultural Organization's (UNESCO) 1997 *Universal Declaration of the Human Genome and Human Rights* and 2003 *International Declaration on Human Genetic Data* affirm that no one should be subjected to discrimination based on human genetic or proteomic data, as this would infringe on human rights, fundamental freedoms, and human dignity. The United Nations Economic and Social Council's *Resolution 2004/09 on Genetic Privacy and Non-Discrimination* (2004, article 6) also proposed the development and implementation of standards for protection against misuse of genetic information that might lead to discrimination and stigmatization.

The *Charter of Fundamental Rights of the European Union* (2000, article 1) and the *Convention on Human Rights and Biomedicine* (article 11) prohibit discrimination based on genetic data in Europe. In the US, the *Genetic Information Nondiscrimination Act of 2008* provides some protection against genetic discrimination in health insurance and employment.

No national-level legal documents explicitly prohibit genetic discrimination in Canada (Joly 2006). However, the Canadian Life and Health Association Inc. has adopted a *Position Statement on Genetic Testing* (last revised in 2010), which states that members will not impose genetic testing on insurance applicants but will require access to the results of genetic tests. An individual with a genetic predisposition could be protected through generic dispositions protecting the right to privacy or right to equality in existing human rights laws, although there is currently insufficient case law in Canada to be confident in this type of protection (*Canadian Human Rights Act* 1985, article 3; *Canadian Charter of Rights and Freedoms* 1982, article 4; Otlowski *et al*. 2012). The Canadian *Tri-Council Policy Statement*, a prominent research ethics guideline which is national in scope, considers the risk of genetic discrimination against individuals participating in genetic research and recognizes that equal treatment is fundamental (Interagency Advisory Panel on Research 2010).

In March 2011, *Bill C-508 (Historical), an Act to Amend the Canadian Human Rights Act (genetic characteristics)* was introduced in Parliament 'to protect Canadians from discrimination on the basis of their genetic characteristics.' During the same session, *Bill C-536* was introduced to add the term 'genetic characteristics' to the list of prohibited grounds for discrimination in the *Canadian Human Rights Act*. These are both private members' bills and are unlikely to pass through both houses of Parliament. More recently *Bill S-218*, *an Act to prohibit and prevent genetic discrimination*, was proposed to prohibit the act of forcing a person to undergo a genetic test or communicate its results in order to enter or maintain a contract. If adopted, S-218 would modify the *Canada Labor Code* 1985 and the *Canadian Human Rights Act*.

Although laws have been introduced to offer considerable protection against discrimination in many countries, in others genetic data is not impervious to breaches of confidentiality and data misuse. Indeed, the Internet and data-intensive sciences like PGx have raised considerable privacy threats. Progress in bioinformatics has made it possible, in specific instances, to re-identify individuals through their genetic data, biological samples, or associated clinical data (Lin *et al.* 2004; Homer *et al.* 2008; Gymrek *et al.* 2013). Moreover, privacy laws are often riddled with exceptions that greatly limit their effectiveness (Rozovsky and Inions 2002). Examples include the right to communicate or access personal information with the consent of the individual to whom it belongs, such as for reasons relating to public safety. Given these limitations, PGx researchers and clinicians would be well advised to proceed carefully. This requires adopting robust, up-to-date privacy practices and security mechanisms, and describing the potential limitations of these measures clearly to patients and participants.

19.5 Discussion

Along with the completion of the human genome and the subsequent availability of WGS, progress in pharmacology has led to the discovery of many polymorphic genes that confer individual specificity in ADME. According to proponents of this approach, a healthcare professional could use patient biomarkers to prescribe the right drug for the right condition and at the correct dosage to optimize therapeutic outcomes. Genetic testing for polymorphic biomarkers of drug response should contribute to a more personalized healthcare system, providing a better framework to optimize phased-trial designs, expedite the drug approval process, reduce pipeline costs, and improve safety and efficacy (Tucker 2008). Hence, PGx tests and drugs are likely to improve the success of healthcare systems in addressing many forms of illness, including several life threatening diseases and rare disorders. Yet there are still many obstacles in the transition to personalized medicine. At the scientific level, researchers must still find the most appropriate biomarkers and determine when to use them during drug development.

Current initiatives by various national and regional regulatory agencies aim to harmonize regulatory policy to provide broader and easier access to foreign drug markets. For instance, the FDA and EMA are working towards more coherent regulations and policies for PGx approval within their respective jurisdictions as well as at the international level. In this chapter, we discussed the progressive alignment of drug approval guidelines by the FDA, EMA, and PMDA, suggesting an international harmonizing trend which was not so obvious a decade ago. Global harmonization of regulatory drug policies may be the best way of optimizing resources and fulfilling the needs of most stakeholders. International initiatives such as ICH, voluntary submission of biomarkers, orphan drug incentives, and accelerated drug approval appear to be necessary steps in the establishment of a global PGx regulatory framework. With the proper regulatory incentives and safeguards in place, PGx could contribute significantly to the improvement of global health.

However, well-balanced policy frameworks are needed to address the multiple obstacles on the personalized medicine pathway (Hamburg and Collins 2010). For example, national policymakers must reconcile national research priorities and international human rights norms to promote the application of fundamental bioethical principles such as autonomy, benefice, and justice. The paradigm change towards personalized medicine in healthcare does not warrant setting them aside, but could require new interpretation of these principles, as well as the development of new ones, to fill any existing gap in the international bioethical framework for PGx (Knoppers and Chadwick 2005).

Since personalized medicine relies on accurate and reliable genetic diagnostics, healthcare professionals should be trained adequately to perform PGx-related tasks such as interpreting diagnostics, genetic counseling, and drug prescription. In order to protect patients from overly optimistic claims by vested stakeholders, education policies should also provide the public with impartial, up-to-date and accessible information regarding genetic testing and treatments.

Stratification into smaller markets will likely make PGx treatments more expensive than other blockbuster drugs, at least in the short term. Widespread clinical implementation of personalized medicine will not occur if patients cannot obtain reimbursement for PGx drugs by third party payers, such as private insurers or through public healthcare systems. In the transitional period, improved models will need to be developed to assess the cost, benefit and clinical utility of PGx tools for reimbursement purposes. Policies promoting the development of drugs for rare disease will also need to be revisited to better account for the PGx development model.

19.6 Conclusion

Provided that efficient and safe ethical and legal frameworks are in place, personalized medicine will offer substantial benefits to patients in the future. Hamburg and Collins compared personalized medicine to creating a highway system, writing that '[w]e are now building a national highway system for personalized medicine, with substantial investments in infrastructure and standards. We look forward to doctors and patients navigating these roads to better outcomes and better health' (Hamburg and Collins 2010). We contend that law and ethics will play the important role of traffic signs on the personalized medicine highway system. The right policy balance must be attained so that researchers and clinicians can drive through this exciting new infrastructure at the optimal speed, while accounting for all of the necessary public safety requirements.

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Part V

Public health and international health trends

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20

Public health

Current and emergent legal and ethical issues in a nutshell

Paula Lobato de Faria and João V. Cordeiro

20.1 Public health and public health law

> Everyone has the right of access to preventive health care and the right to benefit from medical treatment under the conditions established by national laws and practices. A high level of human health protection shall be ensured in the definition and implementation of all Union policies and activities.
>
> *(*Charter of Fundamental Rights of the European Union *2000, article 35)*

20.1.1 The importance of health legislation

Health law and legislation have gained significance in the international community for decades, particularly from the World Health Organization (WHO). During the thirtieth World Health Assembly in 1977,[1] the WHO committed itself to several important health goals, including a more efficient organization of health services; the provision of primary healthcare to needy populations; and the improvement and protection of individual and community health. In the same document, the WHO decided to strengthen its program in health law (Khoury *et al.* 2000; WHO 1977; Jennings *et al.* 2003).

This policy formed part of the WHO's program called 'Health for All by the Year 2000' (HFA2000), which sought to 'enable all of the world's citizens to enjoy by 2000 a level of health that would allow them to lead a socially active and economically productive life' (WHO 1977). According to this policy, the importance of investing in the study of health law and legislation under the HFA2000 program was based on the assumption that health legislation is a key element for the formulation and implementation of health policies, along with health education, in order to influence individuals and society to improve health behaviors and lifestyles.

Although written almost thirty years ago, this assumption is still relevant today, as health legislation continues to be the strongest social instrument which has the power, among others, to:

1 In the same period, the Pan American Health Organization, in its recommendations for the ten-year health plan for the Americas (1971–80), encouraged updating health legislation and promoting updated health law publications and compendiums in the member countries (Horwitz 1975; WHO 1972).

create rights and responsibilities; establish principles and standards of healthy behaviors; resolve conflicts of interest between multiple groups in industrialized and globalized societies; and level equity in confrontations between the interests of populations and individual rights often witnessed in public health protection. Health legislation can also promote the required cost control measures and allow a more equitable distribution of resources.

20.1.2 Public health and public health law definitions

Public health is a constantly evolving field that is difficult to define and delimit (Hewitt and Watson 2013). Different classic and contemporary public health definitions have been proposed, from the succinct and yet broad-ranging Institute of Medicine (IOM) definition: 'what we, as a society, do collectively to assure the conditions for people to be healthy' (Committee for the Study of the Future of Public Health, Division of Healthcare Services, Institute of Medicine 1988); to the current definition proposed by the WHO: 'Public health refers to all organized measures (whether public or private) to prevent disease, promote health, and prolong life among the population as a whole' (WHO 2014b). In the first half of the twentieth century, the American public health expert, Charles-Edward Amory Winslow, provided an eclectic definition of public health. Despite all conceptual metamorphosis that ensued, Winslow's definition remains adequate to frame a broad ethical and legal discussion. Winslow defined public health as:

> The science and art of preventing disease, prolonging life, and promoting physical health and efficiency through organized community effort for the sanitation of the environment, the control of communicable infections, the education of the individual in personal hygiene, the organization of medical and nursing services for the early diagnosis and preventive treatment of disease, and the development of the social machinery to ensure everyone a standard of living adequate for the maintenance of health, so organizing these benefits as to enable every citizen to realize his birthright of health and longevity.
>
> *(Winslow 1920)*

This definition is still relevant because it 'accurately depicts the wide range of activities of people who work in the field of public health' and has the benefit of being 'consistent with the broad range of laws enacted in the name of public health' (Mariner 2005, 2006). Hence, public health addresses the power of government to prevent illness and injury and to provide the infrastructure to sustain population health (Wing *et al.* 2007).

Although originally charged solely with preventing infectious disease, the field of public health currently includes matters of environmental protection, occupational health, and food and water safety, as well as epidemic preparedness. These subfields of public health are subject to a battery of legislation and regulation. However, not all enter the scope of public health law, which is distinct (at the same time narrower and more applicable) from the sum of the existing legislation that can directly or indirectly affect the public's health.[2] Otherwise, an all-encompassing

2 On this point see Mariner (2005), who presents several elements that characterize medicine and public health and also a typology of the laws affecting health. Mariner sustains that these 'can be sorted into three categories familiar to most lawyers: (1) laws that target individual conduct – requiring or prohibiting specific actions; (2) laws that set health and safety standards – regulating products or companies that affect health by reducing health risks arising from products or the social or working environment; and (3) laws that affirmatively create benefit programs – offering healthcare, services, or information that individuals are free to accept or refuse' (2005: 268). See also Mariner (2006) for an informative table with a comparison between several elements that characterize medicine and public health.

public health law would result in overlap with already developed branches of law, such as environmental law, consumer law, labor law, and administrative law, to cite a few. The study of these branches of law is often necessary given the multidisciplinary field of public health law, though the two cannot be conflated. Public health law has not yet reached the same recognition in the legal world as the aforementioned branches of law.

Tentative definitions of public health law can be found,[3] but in our opinion, the scope of this branch of law is as difficult to define as public health itself. Nevertheless, the exiguous public health law community shares a consensus. That is, this legal field grants public powers to promote or implement health measures at individual or population levels, though is continuously confronted with ensuring fundamental human rights and liberties in doing so. Anti-smoking and alcohol legislation, as well as confiscation and quarantine to control transmissible diseases, illustrate this dilemma. As these disputes are commonplace in public health law, the use of public powers to promote, defend or improve the health of the population must be tempered with individual rights and liberties.

This tension is central to the ensuing discussion in this chapter. Here, we have selected what we believe are the most relevant classical and emergent ethical and legal topics of public health law, and have aimed to provide a brief but sufficiently grounded base to discuss their unique aspects. However, in such a wide-ranging arena, a legal and ethical analysis is necessarily incomplete. We have attempted to mitigate this in this chapter by informing the reader of relevant informative sources for further analysis whenever we found additional discussion necessary.

20.2 Traditional ethical and legal issues in public health

20.2.1 Transmissible diseases

Although preventing transmissible diseases was the main target of early public health interventions, we have witnessed the reappearance of new infectious disease outbreaks which have renewed the importance of public health legislation as a tool to respond to novel epidemic threats. These include Severe Acute Respiratory Syndrome (SARS), the influenza virus subtype H5N1, Multidrug Resistant Tuberculosis (MDR) and, more recently, Extensively Drug-Resistant Tuberculosis (XDR)[4] (Faria 2008; Martin 2004; Martin *et al*. 2010).

The public health law response to these situations has always required a legal framework that enables health authorities to act quickly and efficiently in a 'public health emergency' (Martin 2006). In such circumstances, national governments and health authorities may need to take exceptional measures which go beyond the normal use of their powers. Sometimes, these measures violate fundamental rights and liberties of citizens, making indispensable the existence of legal instruments that guide and clarify the contents and limits of such interventions. Exceptional measures used in public health emergencies must be ethically and legally grounded. They must balance, on the one hand, the prevention and control of risk and damage to public health and,

3 Namely, Lawrence Gostin's definition of public health law as 'the study of the legal powers and duties of the state, in collaboration with its partners (e.g. health care, business, the community, the media, and academe), to assure the conditions for people to be healthy (to identify, prevent and ameliorate risks to health in the population), and of the limitations on the power of the state to constrain for the common good the autonomy, privacy, liberty, proprietary, and other legally protected interests of individuals. The prime objective of public health law is to pursue the highest possible level of physical and mental health in the population, consistent with the values of social justice' (2008: 4).

4 This reality is exacerbated by inadequate or discontinuous use of anti-tuberculosis drugs and therapies.

on the other, the respect for human rights enshrined in international declarations and national constitutions.

At the peak of the pandemic influenza virus subtype H5N1 threat, there was an international resurgence of interest in public health law and in legislative reform. In the wake of public health threats, a new Portuguese law created a national system of epidemiological surveillance,[5] the *Public Health Act* 2008 was established in the Netherlands, and the Canadian *Quarantine Act* 2005 responded to the SARS menace. Studies comparing pandemic preparedness legislation in Europe urged harmonization (Martin *et al.* 2010) given the detrimental response disparities that the lack of uniform standards could cause in a pandemic scenario. Nevertheless, no European or international legislative body has introduced further harmonization efforts on pandemic preparedness since.

There are, however, some widely recognized elements of effective public health legislation on the prevention and control of communicable diseases. These include the supremacy of protecting fundamental rights in the use of public powers, and the emphasis on standards that facilitate and boost notification to the public in emergency cases (Gostin 2008, 2006; Mariner 2006).

20.2.2 Lifestyles: tobacco and alcohol

Tobacco use and abusive alcohol drinking have been for some time the target of preventive public health measures at the international level. Both are considered by the WHO as main risk factors for a number of chronic diseases, including cancer, lung diseases, and cardiovascular diseases, alcohol use being also associated with an increased risk of acute health conditions, such as injuries, including from traffic accidents (WHO 2011, 2013). Nonetheless, as the WHO (2014) also recognizes, they are 'common throughout the world' and this is what makes the fight against the damage caused to individual and population health by these two substances so extremely difficult for public health professionals and authorities. In addition to the trivialization of the consumption of tobacco and alcohol, public health policies against these highly addictive and toxic substances have to deal with two industries that not only developed subtle and efficient forms of marketing, but are gaining a voice (mainly in the alcohol sector) at the negotiations table (Filho *et al.* 2010).

There are three essential international normative instruments on tobacco and alcohol. The WHO's *Framework Convention on Tobacco Control* (FCTC) (2005) became the first treaty negotiated under the auspices of the WHO, while the World Health Assembly published its *Strategies to reduce the harmful use of alcohol* (2008) and its *Global strategy to reduce the harmful use of alcohol* (2010).[6]

The WHO FCTC (2005) established in reaction to the globalization of tobacco epidemics is an evidence-based treaty that restates 'the right of all people to the highest standard of health.' The main stipulations for tobacco reduction in the FCTC are enshrined in articles 6–14. They include: (1) price and tax measures to reduce the demand for tobacco; (2) non-price measures to reduce the demand for tobacco, namely the protection from exposure to tobacco smoke;

5 Law 81/2009 of 21 August at: http://dre.pt/pdf1s/2009/08/16200/0549105495.pdf (in Portuguese).

6 During the Sixty-third Session of the World Health Assembly, held in Geneva in May 2010, the 193 member states of WHO reached a historical consensus on a global strategy to reduce the harmful use of alcohol by adopted resolution WHA63.13. The adopted resolution and endorsed strategy gives guidance to both member states and to the WHO secretariat on ways to reduce the harmful use of alcohol. The drafting of the strategy was mandated in resolution WHA61.4 from 2008. See: http://www.who.int/substance_abuse/activities/globalstrategy/en/index.html.

(3) regulation of the contents, packaging and labeling of tobacco products; (4) education, communication, training, and public awareness; (5) prohibition of tobacco advertising, promotion and sponsorship; and (6) prevention of tobacco dependence and the promotion of its cessation through counseling and medicine (WHO 2005). In terms of the norms on reduction of supply enshrined in the FCTC, articles 15 to 17 include the control of illicit trade in tobacco products and the prohibition of tobacco sales to, and by, minors (WHO 2005).

The FCTC, which is now closed for signature, has 168 signatories, making it one of the most widely embraced treaties in United Nations history. The European Community is one of the signing Parties. In fact, it is important to mention that article 168 of the *Treaty on the Functioning of the European Union* (or Lisbon Treaty), signed by the EU member states in 2007 and adopted in late 2009, declares:

> The European Parliament and the Council, acting in accordance with the ordinary legislative procedure and after consulting the Economic and Social Committee and the Committee of the Regions, may also adopt … measures which have as their direct objective the protection of public health regarding tobacco and the abuse of alcohol.

The document reveals the influences of WHO efforts to spread the institutional commitment to reduce the public health evidence-based harms of tobacco and alcohol.[7]

The World Health Assembly's (WHA) *Strategies to reduce the harmful use of alcohol* 'urges' member states:

(1) to collaborate … in developing a draft global strategy on harmful use of alcohol based on all evidence and best practices, in order to support and complement public health policies in Member States, with special emphasis on an integrated approach to protect at-risk populations, young people and those affected by harmful drinking of others;
(2) to develop, in interaction with relevant stakeholders, national systems for monitoring alcohol consumption, its health and social consequences and the policy responses, and to report regularly to WHO's regional and global information systems;
(3) to consider strengthening national responses, as appropriate and where necessary, to public health problems caused by harmful use of alcohol, on the basis of evidence on effectiveness and cost-effectiveness of strategies and interventions to reduce alcohol-related harm generated in different contexts.

(World Health Assembly 2008)

More recently, the WHA's *Global strategy to reduce the harmful use of alcohol* 'urges' member states:

(1) to adopt and implement the global strategy to reduce the harmful use of alcohol as appropriate in order to complement and support public health policies in Member States to reduce the harmful use of alcohol, and to mobilize political will and financial resources for that purpose;
(2) to continue implementation of the resolutions WHA61.4 on the strategies to reduce the harmful use of alcohol and WHA58.26 on public-health problems caused by harmful use of alcohol;

7 See the *Consolidated version of the Treaty on European Union*, the *Consolidated version of the Treaty on the Functioning of the European Union*, and the *Charter of Fundamental Rights of the European Union*.

(3) to ensure that implementation of the global strategy to reduce the harmful use of alcohol strengthens the national efforts to protect at-risk populations, young people and those affected by harmful drinking of others;
(4) to ensure that implementation of the global strategy to reduce the harmful use of alcohol is reflected in the national monitoring systems and reported regularly to WHO's information system on alcohol and health.

(World Health Assembly 2010)

The central ethical and legal issues associated with health behaviors such as tobacco and alcohol use are not limited to classical tensions between individual liberty and the exercise of public powers. They involve clashes between competing interests and public health policies, which may severely jeopardize the success of preventative measures. Central to enacting effective public health laws governing health behaviors is recognition of the various sociocultural features of the stakeholder group. If not, such laws risk being easily surpassed. Lobbying, marketing, and other promotional strategies used by the industry reveal strong opposing interests within public health policies, biasing and frequently impeding their efficacy.

20.3 Emergent ethical and legal issues in public health

20.3.1 Patient safety

Patient safety emerged as a major public health concern (Furrow *et al.* 2001: 29–64) in the wake of the American Institute of Medicine's report, 'To Err Is Human – Building a Safer Health System' (Kohn *et al.* 2000). The report found that medical errors (preventable adverse events in healthcare) caused an astounding 44,000 to 99,000 deaths per year, the eighth leading cause of death in the US, surpassing deaths from road traffic accidents (44,458), breast cancer (42,297), or AIDS (16,516) (Kohn *et al.* 2000). A number of different factors contributed to the growing trend, such as the influx of patients and procedures, longer life expectancy, and the current healthcare cost containment politics, the latter exacerbated already by existing scarcities in workforce and material resources, which invited an increase in adverse events and added professional stress (Faria 2010). These factors awakened the world to the need for improving quality assurance in healthcare. In response to *Resolution WHA55.18* adopted at the 55th World Health Assembly, the WHO created the 'World Alliance for Patient Safety' in 2004, urging countries to strengthen the safety of health care and monitoring systems (WHO 2004a).[8]

Patient safety is now an internationally recognized field for public health experts, lawyers, health managers, physicians, nurses, and other health professionals. In the five years following the IOM's report 'To Err Is Human', however, it was clear that quality improvement lagged in US healthcare units (Wachter 2004). As a result, progress in patient safety received a 'failing grade' in the 2009 report 'To Err Is Human – To Delay Is Deadly: Ten Years Later, a Million Lives Lost, Billions of Dollars Wasted', signed by the Consumers Union (2009), lending evidence to the difficulty of achieving patient safety goals and the fact that an efficient strategy in this area is still to be found.

In an effort to generate more creative measures to avoid medical errors (i.e. preventable adverse events), some public health authors have proposed looking to, and perhaps partnering

8 See also the *World Alliance for Patient Safety Forward Programme* (WHO 2004b); the WHO's *Patient Safety* (2014c); and the WHO's *Summary of the Evidence on Patient Safety* (2008).

with, the airline industry for inspiration (Pronovost *et al.* 2009; Romano 2005), although other authors argue the best approaches to preventing medical hazards come from medicine itself, citing the successes witnessed in anesthesia safety in the US (Annas 2010: 165–73).

A July 2013 report from Europe does not bring better news (European Center for Disease Prevention and Control (ECDC)). The European Center for Disease Prevention and Control conducted the first prevalence survey on healthcare-associated infections and antimicrobial use conducted in more than 1,000 hospitals in 30 European countries, and estimated that 'on any given day, about 80,000 patients – or one in 18 patients – in European hospitals have at least one healthcare-associated infection' (ECDC 2013). This report followed the *Council Recommendation of 9 June 2009 on patient safety, including the prevention and control of healthcare associated infections* (Council of Europe 2009) and a 2012 report detailing its implementation (European Commission 2012d). The Report's conclusions are far too optimistic, suggesting most member states have indeed undertaken many of the interventions proposed in the *Recommendation*.[9] Nonetheless, the recent 2013 *Report* indicated these steps were still not enough to stop preventable injury and death in healthcare units.

Even so, there is still 'room for improvement' (European Commission 2012d: 13) in various areas of the EU *Recommendation* at both the member state and EU level. At the member state level, these areas include: to involve patients more actively in safety interventions, in particular to provide more information on safety measures, complaint procedures, and patients' rights to redress; to develop a common understanding of core competencies; to encourage patients and their families to report as well as to collect information on adverse events through further developing systems infrastructures; to ensure a non-punitive context for reporting adverse events; and to evaluate reporting progress (i.e. among health professionals, other healthcare workers, and patients). At the EU level, collaboration is needed: to propose guidelines on how to construct and introduce patient safety standards beyond the *Recommendation*, as well to 'make progress on common terminology on patient safety' (European Commission 2012d); to pursue exchange of best practice; to promote education of health professionals on patient safety, e.g. by integrating education and training of health professionals at all levels; and to further research on patient safety, including cost-effectiveness studies on proposed strategies.

Acknowledging these needs, the European Commission suggested extending the monitoring period an additional two years for implementing the general patient safety provisions outlined in the 2009 *Recommendation*. A second progress report is scheduled for June 2014 (European Commission 2012b).

From a legal perspective, patient safety is still an emerging field where dilemmas surpass solutions. There is no consensus regarding which legal measures can actually improve patient safety in healthcare units. Nonetheless, the legal community is unanimous regarding the urgent need to prioritize patient safety in health facilities both as a public health mandate and as a patient/citizen right (Balsamo and Brown 2007: 187–205; Annas 2004: 337–61, 2010: 165–73). The latter is supported by legal frameworks which consider clinical/medication risk management and prevention in healthcare a human rights issue (i.e. fundamental rights to life and to physical integrity).

The use of incentive laws have also been put forth as legal mechanisms to improve patient safety. Given appropriate security and suitable legal mechanisms, institutions and patients

9 The *Report* states, 'most Member States have embedded patient safety as a priority in public health policies and designated a competent authority responsible for patient safety. Moreover, most countries have encouraged training on patient safety in healthcare settings, though only a few have formally embedded patient safety in education and training programs for health professionals' (European Commission 2012d: 13).

can be better informed of how experience and competence are evaluated among healthcare professionals.

However, it is our conviction that the idea of building a true 'culture of safety' among professionals and institutions depends less on the legal framework and more on a multidisciplinary effort to create effective practices and guidelines to avoid preventable adverse events.

20.3.2 Public health genetics

Different public health fields, such as infectious and chronic disease, occupational health and environmental health can take advantage of data-sharing progress in genomics, leading to what has been described as the 'genetic information for all' era (Gerard *et al.* 2002). The field of genetics is complex in scope and reach, and has expanded dramatically since the completion of the Human Genome Project in 2003 (Green *et al.* 2011). Concomitantly, public health genetics, initially defined as 'the application of advances in genetics and molecular biotechnology to improve public health and prevent disease' (Khoury *et al.* 2000; Jennings *et al.* 2003: 193), poses significant regulatory challenges, many of which have yet to be successfully addressed. Discrete efforts of international law to set broad principles and establish clear limits are nonetheless noteworthy, as are a number of national regulatory initiatives governing important public health genetics projects. Most importantly, the tension between private and public interest is pressing in public health genetics, as in most public health debates. That tension is materialized in specific ethical and legal issues such as privacy and confidentiality protection, the nature and depth of informed consent, individual responsibility for one's own health, the limits of property rights, the appropriateness of quality control schemes, and the notion of genetic discrimination. Next, we discuss some of these issues in the context of genetic databanks and genetic tests.

20.3.2.1 Genetic databanks

Organized collections of biological material and/or associated information, known as biobanks, can assume multiple forms and have distinct aims (Hewitt and Watson 2013). Perhaps as an accurate reflection of the post-9/11 world, the ethical and legal discourse has focused on security biobanks to the detriment of medical research biobanks, both of which raise important public health questions (Knoppers 2003; Annas 2010). Nonetheless, medical research biobanks have also received widespread ethical and legal attention, especially following the historic case in Iceland involving deCODE Genetics and the 1998 *Act on Health Sector Database* (HSD). The *Act* created a nationwide DNA database[10] for medical research purposes allowing a private company such as deCODE Genetics to carry out the licensing and development of the database. The fact that a private company managed the project without defined legal boundaries raised numerous concerns (Masood 1998), many of which have resurfaced following some of the company's financial decisions.

Naturally, informed consent is a relevant starting point for contextualizing a discussion on genetic biobanks from a public health lens. Informed consent has deep roots in biomedical ethics, and is at the core of both doctor–patient and researcher–subject relationships (Beauchamp and Childress 2008). The focus of public health on communities rather than individuals raises the question of whether there is an ethical justification for sidelining informed consent in large-scale

10 Composed of three biobanks – one containing DNA samples covering a significant proportion of the Icelandic population, one consisting of genealogical information, and a third containing health records.

public health projects. Remarkably, Iceland's original *Act on Health Sector Database* 1998 did not include a specific requirement for obtaining informed consent from individuals; instead, an opt-out scheme was adopted (article 8). One could argue that genetic information (especially in the context of medical research) is so particular that its inclusion in large-scale DNA databases should not be regulated by traditional rules, including the classical models of informed consent (McGuire and Beskow 2010; Taylor 2008; Artizzu 2007). Alternatively, to probe the limits set by public health law and ethics, one could ask whether the potential of genetics to advance the common good (more knowledge leading to better health) is so significant that concessions to individual liberty should be considered. Major international law and ethics instruments related to research on genetic data provide, in one way or another, references to the primacy of the human being and consequently to the permanence of informed consent[11] (Karlsen *et al.* 2009). In turn, these principles are inscribed in several national Constitutions (including the *Constitution of Iceland*)[12] and have been transported into different national regulations.

Nonetheless, the inadequacy of current informed consent procedures for genetic databases has been widely debated and relevant arguments about a need for reform have been put forward (McGuire and Beskow 2010; Roche 2009; Lunshof *et al.* 2008; Caulfield *et al.* 2008; Glantz *et al.* 2010). These arguments cite difficulties in delimiting the research context for secondary uses of each sample, the extent to which anonymity can be granted and therefore promised, as well as the property rights retained by biobank donors (Cambon-Thomsen *et al.* 2007; Caplan 2009; Glantz *et al.* 2008; Faria 2009; Hoffman *et al.* 2009). Such obstacles are even more pronounced when we consider that many biobanks are now clustered in networks of significant scale.[13] Accordingly, different consent models have been proposed, including open consent and gift-related models (Lunshof *et al.* 2008; Glantz *et al.* 2010).

However, the values that informed consent aims to protect (i.e. liberty, autonomy, and self-determination) remain fundamental and should be respected, including in public health. Certainly, they must be harmonized with the common good, including the access to results of scientific progress, an officially recognized human right (*Universal Declaration of Human Rights* 1948, articles 29(2) and 27; *International Convenant on Civil and Political Rights* 1966, article 15). Furthermore, according to international law, the characteristics that differentiate genetic information from other health data justify careful ethical and legal analysis and ultimately require particular protection. For example, genetic information relates not only to the individual but also to his/her family (Parker and Lucassen 2004; UNESCO 2003, article 4(a)(ii)). On this point, the issues of privacy and confidentiality in genetics databases become central to recent ethical debates in public health.[14]

Here again, Iceland's *Act on Health Sector Database* provides context. In a case addressing the extent of privacy rights, the Iceland Supreme Court highlighted one of the most fundamental aspects of genetics regulation – the individual nature of privacy rights is extended in the case of genetic privacy to include genetically related family members (Annas 2010: 246–9). Hence, as

11 See as examples the *Convention on Human Rights and Biomedicine* 1997 (article 2); the *Declaration of Helsinki* (WMA 2013, articles 24–29); the *Universal Declaration on the Human Genome and Human Rights* (UNESCO 1997, article 5(b) and 5(e)); and the *International Declaration on Human Genetic Data* (UNESCO 2003, articles 2(iii), 6(d), 8, and 9).

12 Accordingly, the Iceland Supreme Court declared the *Act on Health Sector Database* unconstitutional, which prompted the inclusion of an informed consent procedure (Abbott 2004).

13 See, for example, the Public Population Project in Genomics and Society (P3G 2014), and Biobanking and Biomolecular Resources Research Infrastructure (2014).

14 Policy reviews on the subject are permanently ongoing. See, for example, the *Draft NIH Genomic Data Sharing Policy Request for Public Comments* (National Institutes of Health (NIH) 2013).

individual rights blend into family rights, the lines between private and public interest blur even further. Moreover, downstream of privacy rights, confidentiality rights are also mutating. Despite the fact that most studies show that the overwhelming majority of patients choose to pass information of genetic risk to family members, in some cases confidentiality breaches collide with the carrier's will (Clarke *et al.* 2005). The fact that such heightened risk could be passed on to offspring must also be taken into account when preparing balanced public health regulations and policy, particularly when both parents are carriers and pre-implantation diagnostics could be offered. That brings us to the issue of genetic tests.

20.3.2.2 Genetic tests

The concept of a 'genetic test' is quite broad. It involves testing at different stages – pre-implantation, prenatal, newborn, during childhood or adulthood; by different providers – healthcare units or market companies; and serves different purposes – diagnostic, predictive of disease or response to drugs, forensic, or research. From a legal perspective, a uniform definition in regulatory documents is also non-existent (Sequeiros *et al.* 2012; Varga *et al.* 2012).

The difficulty in finding appropriate legal definitions is just one characteristic of an overly complex regulatory subject. The limitations of regulation in this area are particularly clear in the case of direct-to-consumer (DTC) genetic tests,[15] which have important public health ramifications yet have garnered little legislative attention. DTC genetic tests result from a dramatic decrease in sequencing costs particularly from the second half of the last decade onwards[16] (Mardis 2011). Under the promise of individualized healthcare, international companies – often wrapped in complex marketing, client recruitment, or results communication practices – offer to test for disease predisposition or estimate individual responses to therapies.

Such practices raise several regulatory challenges, starting with analytical validity, a measure of a test's accuracy in detecting the intended genetic marker. Efforts in the US and Europe to license laboratories that perform genetic testing are ongoing. These efforts include requiring appropriate professional training, record-keeping standards, and revision methodologies (Hogarth *et al.* 2008). Where legislation on specific genetic tests is non-existent, adaptating already existent quality control mechanisms (for clinical laboratory or pregnancy tests, for example) must be considered after proper evaluation.

Clinical validity, a measure of how a positive result translates into clinical significance, also requires regulation and is charged with providing accurate scientific notions of probability, risk, or variance during legal proceedings. Finally, clinical utility must be considered as a measure of the test result's usefulness in terms of prevention, diagnosis, or treatment. The utility of a positive or negative result is difficult to estimate, particularly when no therapy or prophylactic measures can be prescribed.

Nonetheless, the limits for DTC genetic testing must be defined (Howard and Borry 2012). Areas that require attention include: the involvement of healthcare providers; premarket reviews; the stringency of advertising and marketing regulations; specific oversight of results reports; provisions from public budgets; and health insurance coverage. Due to considerable public health

15 Genetic tests that are marketed directly to consumers via the Internet, television, or other media without the involvement of a healthcare provider or practitioner.

16 For an overview on the evolution of DNA sequencing costs see *DNA Sequencing Costs: Data from the NHGRI Genome Sequencing Program (GSP)* (National Human Genome Research Institute 2014).

relevance some of these areas have been subject to US and European legislation in recent years (Hogarth *et al.* 2008; Borry *et al.* 2012).

Patients should only be tested for any genetic disease (or risk) once they have been informed and have understood what the test can reveal. Furthermore, privacy of genetic data must be protected always bearing in mind someone's 'right not to know' (Wolf *et al.* 2013). Moreover, professional counseling in DTC genetic tests should be available to help to deal with test results, as with genetic tests offered through a healthcare provider.

Balanced public health regulation that protects the population from inaccurate or invalid DTC genetic tests promotes individual empowerment in healthcare and might limit unnecessary medical tests, self-prescription, failure to take preventive action based on negative test results, elevated anxiety and stress, or unrestricted testing of the most vulnerable.

These features are relevant in an expanding and particularly contested area of genetic tests – Newborn Genetic Screening Programs (NGSP) (Bombard *et al.* 2009; Moyer *et al.* 2008). From a regulatory perspective, the role of parents and legal representatives of newborns in these programs is very important (Tarini and Goldenberg 2012). Arguments favoring the requirement of parental consent for newborn testing include the parents' position as the best proxy for children's own interest, the rarity of most diseases tested and the serious implications of false positive results. In opposition, proponents for mandatory testing argue the overall benefits far outweigh potential individual harms and the burdens of creating bureaucratic procedures are unnecessary when the vast majority of parents agree to the tests. As stated in international ethical and legal documents, parents or legal representatives should consent to individual procedures involving their children.[17]

Establishing the best consent model to implement in NGSP, either voluntary, opt-in, opt-out, or conditional, presents one subsequent challenge. Moreover, ways to resolve disputes should parents disagree on the best course of action should also be found. On the other hand, mandatory screening based on implied-consent models is also sometimes considered (Tarini and Goldenberg 2012; Bombard *et al.* 2009). Ultimately, the context of specific NGSP, their proportionality and whether there are realistic prospects of achieving the proposed public health aims will determine the best consent model to adopt.

In NGSP as in any genetic testing, the results must be confidential. Most national and international legal documents related to human genetics acknowledge the potential for genetic discrimination.[18] Hence, directed targeting of population subsets based on genetic backgrounds for public health reasons should be minutely scrutinized. Different genetic tests pose different regulatory challenges and require dedicated attention (Howard *et al.* 2013). Nonetheless, the fact that consent, privacy, and confidentiality are valuable public health allies, the difficulty in establishing clear risk-benefit analyses and the need for functional, nuanced, and adaptable legal and ethical processes are common conclusions.

17 Additionally, the will of minors who have already the capacity to understand what is at stake should be taken into account even when parents give consent. See, for example, the *Declaration of Helsinki* (WMA 2013, article 27); the *Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Genetic Testing for Health Purposes* (articles 9–12); the *Convention on Human Rights and Biomedicine* (articles 5–6); and the *Universal Declaration on the Human Genome and Human Rights* (UNESCO 1997, article 5).

18 See as examples the *Universal Declaration on the Human Genome and Human Rights* (UNESCO 1997, preamble, article 6); the *Convention on Human Rights and Biomedicine* (articles 1, 11); and the *Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Genetic Testing for Health Purposes* (article 4). See also the *Genetic Information Nondiscrimination Act* for regulation on the matter in the US (110th Congress 2008).

Finally, other public health genetics issues, including gene therapy (Giacca 2010), genetic enhancement (Annas 2010: 251–66), gene patenting (Norrgard 2008; Kesselheim *et al.* 2013) and the use of genetically modified organisms (Lee 2008) deserve legal attention and are the subject of discussion elsewhere (Knoppers 2003; Condit 2010).

20.3.3 Nanotechnology

In broader terms, nanotechnology refers to 'the understanding and control of matter at dimensions between approximately 1 and 100 nanometers, where unique phenomena enable novel applications' (National Nanotechnology Initiative, n.d.). Manipulating matter at the nanoscale can have wide applications, including in agriculture, energy storage, engineering, computer technology, and healthcare. Possible applications of nanotechnology in medicine include drug delivery, *in vivo* imaging, *in vitro* diagnostics, biomaterials, and active implants (Wagner *et al.* 2006). Accordingly, worldwide investment in nanotechnology has been steadily increasing (*Wall Street Journal* 2013; Reportlinker 2013). However, regulatory efforts have not paralleled expansion in the field. Notwithstanding this, considerable public health risks require ethical and legal attention. These include the difficulty of estimating and reducing toxicity levels of materials and particles at the nanoscale[19] and the possible inhalation, dermal exposure, and/or ingestion of nanoparticles that could cross cellular membranes, reach the bloodstream, invade distant organs and lead to unpredictable consequences. Importantly, these risks are common to the public in general and also to workers who manipulate nanomaterials, such as healthcare professionals.

Overall, regulatory efforts should focus on adequate consumer information including known and unknown risks, the development of best workplace practices including rules for handling, transport and disposal, and defining limits to bioaccumulation in ecosystems based on long-term environmental impacts.

In the EU, specific nanotechnology regulation has not been straightforward. In some cases, the EU has backed specific regulation as in its recommendation for a *Code of Conduct for Responsible Nanosciences and Nanotechnology* (European Commission 2008; European Parliament 2009). In other cases, there were proposals that general regulatory rules be adapted to nanotechnology on a case-by-case basis (European Commission 2012b). An important EU document that applies to nanotechnology (although not particularly designed for it) is *Regulation (EC) No. 1907/2006* that deals with the registration, evaluation, authorization, and restriction of chemicals, known as 'REACH' (European Union 2006; European Commission 2013b). This and other general binding documents on chemicals, cosmetics, and food, for example, can also be applied to nanotechnology but require adaptation that is still lacking.

In the US, the *Review of Federal Strategy for Nanotechnology-Related Environmental, Health, and Safety Research* by the National Research Council in 2009, called for appropriate nanotechnology regulation. Subsequently, the Food and Drug Administration (FDA) progressed beyond the creation of a Task Force 'charged with determining regulatory approaches that encourage the continued development of innovative, safe, and effective FDA-regulated products that use nanotechnology materials' in 2007 and released, in 2011 and 2012, draft guidance for industry, cosmetics, and food substances involving nanotechnology. These efforts are in line with the general notion that nanotechnology regulation requires added attention, an idea that has been expressed in an important 2011 White House policy statement (Office of Management and

19 Due to intrinsic properties of these materials or their interaction with chemical and biological systems.

Budget, United States Trade Representative, and Office of Science and Technology Policy, White House 2011).

Despite recent efforts and expressed public health concerns, current nantotechnology regulation is still far from optimal. Nanotechnology combines great potential with high levels of uncertainty and a high-profile safety or health event could undermine public trust and damage the future use of this technology. Therefore precautionary action, based on proportionality and mindful of the best available science, is important.

20.3.4 eHealth

Technological progress is transforming healthcare. Medical diagnosis can now be offered at a distance. As applications of information and communication technologies in healthcare expand, the potential for self-empowerment regarding one's own health becomes considerable. The range of health issues already covered by mobile medical applications is vast and includes viewers of radiologic images, 'expert systems' to help with differential diagnoses, interfaces for medical devices (like ultrasounds and EKG machines), medical simulators,[20] and telemedicine devices. Hence, the right technology allows for the accumulation of considerable qualitative and quantitative health information without the need for additional intermediaries. Furthermore, this information can be uploaded onto dedicated social network platforms where symptoms, treatment, and research can be discussed by a community of patients, doctors, and scientists.

These innovations are transforming medical practice and have considerable public health law and ethics implications. First, self-diagnosis and self-prescription are a cause for concern as we have discussed before in the context of DTC genetic tests. Also, notable challenges to classic notions of consent, personal responsibility, and professional authority can be identified. Therefore legal attention should be paid to specific issues such as clarifying the rules for accrediting health professionals operating in this new system, or specifying quality control norms for software and devices that take into account informed consent or privacy and confidentiality of health data.[21]

As individual and quantified health data accumulates, the possibility that health insurance will be based on a new version of our 'quantified selves' must also be considered and contextualized from a regulatory perspective, and protection from stigmatization and discrimination must be guaranteed. Despite its progress, of which FDA regulation of mobile medical applications[22] and EU efforts to promote and regulate telemedicine are good examples (Callens 2010), eHealth regulation is still lagging.

The public should have access to trustworthy advances in science and technology that can benefit their health. However, that is particularly difficult to assure in a context of scarce public resources. The role of law and ethics in minimizing the impact of economic crises on public health is the subject of the next and final section.

20 For example, advanced cardiovascular life support.

21 Important data protection reform is ongoing in Europe (European Commission 2013a). In the US, two legal documents are of outstanding relevance: the *Health Insurance Portability and Accountability Act* 1996 and the *Health Information Technology for Economic and Clinical Health Act* 2009. For an overview see the US Department of Health and Human Services' *Health Information Privacy* section on their website (2013).

22 See the FDA's *Medical Devices* web page (2013) and the *Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions – eHealth Action Plan 2012–2020 – Innovative Healthcare for the 21st Century*, COM (2012) 736 (European Commission 2012a).

20.4 Economic crises and public health

It is fundamental to estimate the impact of economic crises on public health and to ascertain how best to defend and promote public health during these periods. Significant pressures on public health resulting from the socio-economic changes seen during economic downturns have been observed in the past.[23] More recently, the 2008 financial crisis, which began in the US and later spread to Europe, confirm these pressures (Stuckler and Basu 2013).

As a result of unemployment and reduction in household income and social safety nets, public health indicators such as mental health, suicide, substance abuse, and incidence of infectious disease are exacerbated, while overall access to healthcare deteriorates (Karanikolos *et al.* 2013; Stuckler *et al.* 2009; Suhrcke *et al.* 2011). The role of law, and public health law specifically, in providing protection from such effects, can be best understood through an analysis of different European responses to economic crises. During the Eurozone Crisis, austerity packages[24] included cuts to social welfare programs and a reduction in health budgets (Fahy 2012). These measures varied from country to country and cut the salaries of health professionals, reduced public hospital beds, increased user charges for healthcare, and decreased family support, dissolved childcare benefits and implemented other social welfare cuts. In Greece, where austerity measures were first implemented and have had the strongest impact, mental health has deteriorated significantly. Suicide rates have peaked, HIV and malaria outbreaks have been reported, and access to healthcare has been significantly constrained (Economou *et al.* 2012; Madianos *et al.* 2010; European Center for Disease Prevention and Control (ECDC) 2012). Similar effects are also emerging[25] in Portugal, Ireland and Spain. These effects include, a rising number of winter deaths among the elderly, increasing mental disorders, suicide rates, alcohol-related disorders, and worsening child malnutrition (Mazick *et al.* 2012; Thomas *et al.* 2012; WHO Regional Office for Europe 2012).

Therefore it is important to understand whether these detrimental public health effects are direct consequences of the economic crises, or if they also result from the drastic reduction (and in some cases the complete abrogation) of crucial social safeguards that defend the population during trying economic times. In contrast, however, Iceland was not affected by such deletrious public health effects following its own economic crisis in the last decade (Stuckler and Basu 2013: 57–75). One key reason for this was investment in social protection and reemployment programs, as opposed to strict austerity measures, proposed at the time by the International Monetary Fund (IMF). Promoting a healthy diet based mainly on local fish supplies, restricting alcohol access and fostering strong social cohesion ultimately mitigated the impacts of the crisis on population health (Stuckler and Basu 2013: 57–75). Similarly, states that furthered social welfare programs during the Great Depression in the US avoided the worst public health effects and, in some cases, actually improved health indicators (Stuckler *et al.* 2010).

One question that remains essential: can law and ethics protect public health from becoming collateral damage in the tense ongoing confrontation between financial markets and rights-based

23 For example, the American Great Depression in the 1930s; the post-Soviet era in Eastern Europe in the late 1980s and early 1990s; or the Asian economic crisis in the late 1990s.

24 Some countries, like Greece, Ireland, and Portugal, were subject to official bailouts by the so-called *troika* (composed of the International Monetary Fund (IMF), the European Central Bank (ECB), and the European Commission (EC). Other countries, such as Spain and Italy, despite avoiding this regime, also included austerity measures in their budgets.

25 Some of which are still disputed. See Ayuso-Mateos *et al.* (2013) for examples.

approaches? Three examples deserve mention. First, measures enacted by the *troika* in Greece limited spending on health to no more than 6 per cent of its GDP (Fahy 2012), effectively diminishing the role of the Greek government in defining its health budget. Second, Spanish legislation approved by a royal decree bypassing parliament led to the privatization of the previously universal Spanish health system (Rada 2012). Finally, Portugal's continued approval of unconstitutional annual budgets has impacted its health sector, where the legislative branch challenged limits that were set to protect social safeguards.[26]

Despite the existence of specific constitutional norms for states of emergency that allow for extraordinary measures while protecting against arbitrariness and disproportionate action, none of these countries have formally declared a state of emergency as a consequence of the financial crisis. As we have discussed above, public health law is important to set rules and limits to extraordinary interventions during emergency situations. Therefore the prolongation of informal states of economic emergency, during which violations of constitutional rights and principles are justified seemingly under arbitrary discretion, can be cause for concern, particularly when severe public health effects are difficult to avoid. Therefore, in order to endure economic crises, public health must lean on its strongest allies – ethics, law, and human rights – combining that alliance with innovative action and nonconformism by members of society and the public health authorities.

20.5 Conclusion

Any text on public health legal and ethical issues is necessarily incomplete. As we have discussed throughout this chapter, public health encompasses a variety of issues that are considerably complex, all of which demand attention and appropriate regulation in order to balance the many (and sometimes conflicting) interests. The law, with its unique powers, is an exceptional tool for the implementation of public health policies. In fact, it is the only social instrument that can simultaneously impose sanctions and set rules, procedures, and requirements, as well as define competencies and establish rights and duties. As corollaries of this power, the law imposes duties on public institutions or individuals, and empowers the authorities to impose exceptional actions within some limits that protect citizens against abuses of those same powers. The law can also influence the way people think and act, allowing a change in behaviors and attitudes. Although the vocation of the law as a modulator of human behavior is a very complex issue, time has lent evidence to the ways in which the law's lifestyle model, mainly if it is accompanied by sanctions, inculcates 'good' behavior among a majority of people.

Emergent issues in public health are continuously and simultaneously posing new challenges while demonstrating great potential. Arguably, it is also in the interest of public health that the results of scientific progress and innovation reach the widest public possible. That aim, which is not only an aspiration but also a recognized human right, must be confronted with the inherent economic costs of intervention and the current asymmetries in access to basic human needs, such as food, shelter, and healthcare. Therefore public health can only benefit from clear and precise rules governing the just allocation of resources. In order to achieve this, and regulate such

26 Rulings of the Portuguese Constitutional Court (PCC) were based on interpretations of fundamental public law principles, such as the principle of trust and the principle of proportionality. Relevant rulings can be found here (in Portuguese): http://www.tribunalconstitucional.pt/tc/acordaos/20120353.html; http://www.tribunalconstitucional.pt/tc/acordaos/20130187.html; http://www.tribunalconstitucional.pt/tc/acordaos/20130602.html; http://www.tribunalconstitucional.pt/tc/acordaos/20140413.html.

a broad range of issues as the ones that compose the field of public health, individual liberties and public interest must coexist as harmoniously as possible. We must be mindful that neither can completely overshadow the other as they are both fundamental in a fair and modern society.

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21

The role of international organizations in promoting legal norms

Obijiofor Aginam[1]

> We meet as we fight to defeat SARS, the first new epidemic of the twenty-first century … Globalization of disease and threats to health mean globalization of the fight against them … The events of the last few weeks also prompt us to look closely at the *instruments of national and international law*. Are they keeping up with our rapidly changing world?
>
> *(Brundtland 2003a)*

21.1 Introduction: the relevance of legal norms

Brundtland's observation in the wake of the SARS epidemic in 2003 underscores the relevance of 'the instruments of national and international' legal norms in global health governance. It is now widely accepted in academic literature, national health polices, and policy frameworks of relevant international organizations that 'globalization of public health'[2] is afoot. In an interdependent world, public health raises globalized challenges that require innovative legal and ethical norms to guide the actions of nation-states and non-state actors. Public health, especially at the global level, is now 'comprised of numerous and varied actors with competing values, interests, and motivations' (Zacher and Keefe 2008: 135; Cooper *et al.* 2007: 3–14). To effectively address these competing values, interests, and motivations, nation-states have cooperated to establish intergovernmental organizations with clear mandates. This chapter explores the mandate of the World Health Organization (WHO) to promote legal and ethical norms relevant to international medical and public health issues.

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2 The 'globalization of public health' refers to the cumulative impact of the cognitive, spatial, and temporal dimensions of global interdependence on public health across various regions and societies of the world. In the infectious disease context, the globalization of the world's political economy creates opportunities for disease pathogens to travel transcontinental distances with the speed of a jet. On globalization of public health, see Lee and Dodgson (2000), Lee *et al.* (2002), Yach and Bettcher (1998a, 1998b), Brundtland (2001, 2003b), Woodward *et al.* (2001), Fidler (1997a, 2004).

21.2 The mandate and legal and normative authority of the World Health Organization

The WHO was established at the International Health Conference when 61 representatives of participating nation-states officially ratified its constitution in New York on 7 April 1948 (WHO 2001: 1; Burci and Vignes 2004). With 194 current member states, the WHO is a specialized agency of the United Nations (UN) with a mandate to 'act as the directing and coordinating authority on international health work' (International Health Conference (IHC) 1948, articles 2(a)–2(v)). As an inter-governmental organization, the WHO's normative and legal parameters are firmly rooted in a state-centric international system.[3] The WHO *Constitution* permitted the organization to use innovative instruments to create ethical and legal norms – treaties, legally binding regulations, and non-legally binding declarations (soft law) to pursue its public health mandate. Despite well-founded criticisms that the WHO did not fully utilize these legal mechanisms during its six-decade history, two landmark events in 2005 marked significant improvements: the adoption of the *International Health Regulations* (IHR) and the operationalization of the WHO *Framework Convention on Tobacco Control* (FCTC) in 2005.

The legal and normative authority of the WHO falls into three categories: (1) treaty-making powers analogous to conventional treaty negotiation, adoption, and ratification by states in international law; (2) the authority to adopt legally binding regulations analogous to legislative or quasi-legislative process in domestic law; and (3) the authority to adopt non-binding recommendations analogous to 'soft law' in international law.

The WHO's conventional treaty-making authority – similar to that of most multilateral institutions in the international system – is covered by article 19 of its *Constitution* which provides that:

> [T]he Health Assembly shall have the authority to adopt conventions or agreements with respect to any matter within the competence of the Organization. A two-thirds vote of the Health Assembly shall be required for the adoption of such conventions or agreements, which shall come into force for each Member when accepted by it in accordance with its constitutional processes.
>
> *(IHC 1948)*

Although article 19 is a conventional treaty-making authority that most international organizations derive expressly from their constitutions, charters, or other constituent instruments, in the case of the WHO, some scholars argue that, when combined with its ambitious objective '[for] all peoples [to attain] … the highest possible level of health,' and its equally ambitious definition of health as 'a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity' (IHC 1948, preamble), article 19 provides the Organization with virtually limitless treaty-making power. Moreover, it surpasses any treaty powers possessed by the WHO's precursors, including the Pan American Sanitary Bureau, the International Office of Public Health, and the Health Organization of the League of Nations.[4]

3 Only states can be members of the WHO, as provided for by article 3 of the WHO *Constitution*: 'membership in the Organization shall be open to all States' (IHC 1948).

4 David P. Fidler was the leading exponent of this argument in the late 1990s (Fidler 1998). Fidler argued that the WHO is facing an international legal tsunami that will require a sea change in its attitude towards international law; that the WHO's lack of interest in international law does not reflect the historical experience of states and international health organizations prior to World War II; and that while the WHO has been accused of focusing too little on international law, international relations prior to World War II were plagued by too much international health law.

Article 21 of the WHO *Constitution* authorizes the World Health Assembly (the WHO's highest policymaking organ) to adopt legally binding regulations concerning:

(a) Sanitary and quarantine requirements and other procedures designed to prevent the international spread of disease;
(b) Nomenclatures with respect to diseases, cause of death and public health practices;
(c) Standards with respect to diagnostic procedures for international use;
(d) Standards with respect to the safety, purity and potency of biological, pharmaceutical and similar products moving in international commerce;
(e) Advertising and labeling of biological, pharmaceutical and similar products moving in international commerce.

(ICH 1948)

Regulations adopted by the World Health Assembly under article 21 are legally binding for all WHO member states, except for those that invoke the 'contracting out' procedure provided for at article 22 of the *Constitution*. Such regulations come into force for all WHO member states after the Health Assembly gives due notice of their adoption, except in cases where members notify the WHO Director-General of a rejection or reservation(s) within the period specified in the notice. Articles 21 and 22 of the WHO *Constitution* have been described as creating a quasi-legislative procedure that constitutes a radical departure from the conventional international treaty-making practice in the late 1940s when it was first established (Sharpe 1947).[5]

Article 23 of the WHO *Constitution* gives the World Health Assembly the authority to adopt non-legally binding resolutions (soft law) with respect to any matter within the competence of the organization. Although soft-law instruments, like recommendations and declarations, are not automatically legally binding, international law scholars agree that such instruments nonetheless catalyzed the evolution of rules in international law (Gruchall-Hesierski 1984, cited in Szasz 2001: 26–7; Chinkin 1989). Soft-law instruments 'operate in a grey zone between law and politics' (Malanczuk 1997: 54), and are considered a special characteristic of international law, especially on emerging economic and environmental issues (Malanczuk 1997: 54). In sum, the legal and normative authorities of the WHO fall within the three categories of conventional treaty-making authority (articles 19–20); regulatory authority (articles 21–22); and non-binding soft-law authority (article 23).

Medical and public health experts, including physicians and epidemiologists, have historically dominated the WHO. In its first five decades (1948–98), the WHO did not significantly elaborate legal norms in the pursuit of its mandate. In the 1990s, the WHO's under-utilization of its enormous legal and normative authority became the subject of intense debate among (international) legal scholars. Tomasevski (1995: 859),[6] Taylor (1992: 302), and Fidler (1998) criticized the increased 'medicalization' of the WHO as a result of the organization's reluctance to use international legal mechanisms. According to Fidler:

5 For a study of international legislative processes of international organizations 'by which an increasingly substantial amount of international law is steadily being created,' see Szasz (2001) and Kwakwa (2002).

6 Tomasevski strongly critiqued the WHO's overt bias in favor of non-binding and non-legal norms built upon ethical rather than legal principles. She also observed that an important reason for the WHO's bias for non-binding rules is the traditional reluctance of the medical profession to submit itself to the rule of law. Beginning in the eighteenth century, medical associations developed codes of professional behavior. Self-regulation presumes the exclusion of lay persons, thus reinforcing the traditional paternalism of the medical profession, dating back to the Hippocratic Oath, the assumption that whatever a physician decides is, by definition, correct.

> [The] WHO was isolated from general developments concerning international law in the post-1945 period. This isolation was not accidental but reflected a particular outlook on the formulation and implementation of international health policy. WHO operated as if it were not subject to the normal dynamics of the anarchical society; rather, it acted as if it were at the center of a transnational Hippocratic society made up of *physicians, medical scientists, and public health experts*. The nature of this transnational Hippocratic society led WHO to approach international public health without a legal strategy.
>
> *(1999a: 15)*

Similarly, Taylor observed:

> [The] WHO's traditional reluctance to utilize law and legal institutions to facilitate its health strategies is largely attributable to the internal dynamics and politics of the organization itself. In particular, this unwillingness stems, in large part, from the organizational culture established by the conservative medical professional community that dominates the institution.
>
> *(1992: 303)*[7]

The WHO's 'medical' approach was understandably influenced by science through proving the germ theory correct. Once physicians and epidemiologists understood how humans were infected by disease, they automatically turned to diagnosis and healing rather than to international legal norms for solutions. International legal scholars who are critical of WHO's non-legal approaches to global health work recognize this viewpoint. As Fidler observed:

> The common argument used to explain WHO's antipathy towards international law is that WHO is dominated almost exclusively by people trained in public health and medicine, which produces an ethos that looks at global health problems as medical-technical issues to be resolved by the application of the healing arts. The medical-technical approach does not need international law because the approach mandates application of the medical and technical resource or answer directly at the national or local level.
>
> *(1998: 1099)*

Science arguably catalyzed the development of international health law in the 1890s by providing the breakthrough needed to facilitate agreement by nation-states on common rules and values codified in the *International Sanitary Conventions*.[8] However, the contemporary antibiotic revolution in the wake of affirming the germ theory impeded the WHO's sustained deployment of international legal strategies. The propensity for doctors and public health officials to combat infectious agents directly largely diverted efforts from seeking legal recourse through treaties and regulatory regimes that can also serve as effective tools in solving medical and health problems.

Situating this discourse in the post-1945 world order, the international system has undergone a significant and dynamic transformation. The expanded definition of health in the WHO *Constitution* as 'a state of complete physical, mental and social well-being and not merely the

7 For a discussion of this theme in other seminal writings, see Fidler (1997b: 788, 1999b), Aginam (2005), Lakin (1997), and L'Hirondel and Yach (1998).

8 For a discussion of the science and politics of the international sanitary conferences in the nineteenth century, see Howard-Jones (1975), Goodman (1977), Fidler (2001), and Aginam (2005).

absence of disease or infirmity' meant drawing linkages between public health, and poverty, underdevelopment, human rights, food (in)security, food safety, climatic and related environmental changes, natural disasters, wars and the use of weapons of mass destruction, international trade agreements, and other multi-faceted dimensions of the globalization phenomenon. On almost all of these issues, legal and ethical norms are relevant and important tools in the mandate and work of international organizations. In retrospect, the post-1945 decades since the establishment of the United Nations witnessed the evolution of international legal norms on human rights (including the right to health), global environmental issues (multilateral environmental agreements), international humanitarian laws, food and agriculture, and trade-related health concerns, among many others (Fidler 1999b; Aginam 2005). The WHO, largely due to the 'medicalization' of its public health mandate, did not play any active role in the negotiation and adoption of these legal norms.

21.3 WHO, norms, and norm entrepreneurship: locating the linkages

In political theory, 'norms' are generally understood as a 'standard for appropriate behavior for actors with a given identity' (Finnemore 1996, cited in Finnemore and Sikkink 1998: 891; Katzenstein 1996: 5; Klotz 1995). Norm entrepreneurs are individuals, NGOs, states, or international organizations, which actively promote a norm and seek its acceptance by all the relevant actors, especially nation-states. Although the categories of norms differ across disciplines, 'the most common distinction is between regulative norms, which order and constrain behavior, and constitutive norms, which create new actors, interests, or categories of action' (Ruggie 1998, cited in Finnemore and Sikkink 1998: 891). Finnemore and Sikkink identified the three stages of the norm's adoption: emergence, acceptance ('norm cascade'), and internalization (1998: 895). Norm entrepreneurs play a critically important role in augmenting norm emergence through persuasion in their 'attempt to convince a critical mass of states (norm leaders) to embrace new norms' (Finnemore and Sikkink 1998: 895).

There are two pre-conditions for a norm to successfully emerge: *norm entrepreneurs* (agents with strong notions about appropriate or desirable behavior in their community), and *organizational platforms* (where international norm promoters advocate for the adoption of their norms). While individuals – such as Swiss national Henry Dunant – are often credited with norm entrepreneurship, modern-day norm entrepreneurs would most likely work within international organizations to facilitate norm emergence. As Finnemore and Sikkink affirmed:

> [O]ne prominent feature of modern organizations and an important source of influence for international organizations in particular is their use of expertise and information to change the behavior of other actors. Expertise, in turn, usually resides in professionals, and a number of empirical studies document the ways that *professional training of bureaucrats in these organizations helps or blocks the promotion of new norms* within standing organizations.
>
> *(1998: 899)*

In over sixty years, only two legally binding normative instruments have served as analytical benchmarks for exploring the WHO's role as either a norm entrepreneur or organizational platform: the *International Health Regulations* and the *Framework Convention on Tobacco Control*.

21.3.1 International Health Regulations (IHR 2005)

The IHR (then known as 'International Sanitary Regulations') was adopted by the WHO in 1951 pursuant to article 21 of its constitution. The WHO renamed the regulations the *International Health Regulations* in 1969 and has slightly modified them twice in 1973 and 1981. The IHR represent one of the earliest legally binding regulatory tools for global management of certain infectious diseases. As of 1997, the IHR became legally binding for virtually all WHO member states. The IHR function as regulatory surveillance mechanisms for the sharing of epidemiological information on the trans-boundary spread of cholera, plague, and yellow fever. The fundamental principle of the IHR was to ensure 'maximum security against the international spread of diseases with minimum interference with world traffic' (WHO 1983: 5). To achieve this purpose, the IHR obliged the WHO member states to notify the Organization of any outbreaks of cholera, plague, and yellow fever in their territories. Any notification sent by a member state to the WHO was transmitted to all other member states in order to mount an appropriate response to such outbreaks.

The IHR call for maximum public health measures applicable during outbreaks and outline rules for international traffic and travel. They require, among others, health and vaccination certificates against these three diseases for travelers from infected areas, as well as mandated detailed containment measures at airports and seaports. Measures listed in the IHR are the maximum measures allowed in outbreak situations and aim to protect the country against the risk of overreaction and unnecessary embargoes between contiguous neighbors, trading partners, and other countries. These embargoes are often economically damaging and have severe consequences for tourism, traffic, and trade.

By the 1990s, it became evident the IHR were largely unsuccessful in regulating global health. Chief among the reasons for their ineffectiveness was the fear of outbreak, specifically if the potential remained for other member states to take excessive measures if an outbreak did occur and was reported to the WHO. Such was the case during the cholera epidemic in South America – first reported in Peru in 1991 – which is estimated to have cost over $700 million in trade and other losses. Similarly the 1994 plague outbreak in India led to $1.7 billion losses in trade, tourism, and travel as a result of excessive embargoes and restrictions imposed by other countries (Taylor 1997: 1348; Garrett 1996: 73–4).[9]

The economic costs of disease outbreaks that are not subject to reporting obligations under the IHR were high in certain countries. The SARS outbreak, which first emerged in Southern China and spread rapidly to other countries, was reported to have 'rocked Asian markets, ruined the tourist trade of an entire region, nearly bankrupted airlines, and spread panic through some of the world's largest countries' (Lemonick and Park 2003: 13). In Canada, the economic cost of the SARS outbreak was estimated at $30 million daily. It was estimated that China and South Korea each suffered $2 billion in SARS-related tourism and other economic losses. Visitor arrivals dropped drastically in Singapore, while Hong Kong carrier Cathay Pacific cut its weekly flights by 45 per cent (Lemonick and Park 2003: 13). Apart from the negative effects of costly embargoes, other reasons often cited for the ineffectiveness of the IHR include its relative inexperience in the creation and enforcement of norms and legal regimes, inability to adapt to changing circumstances in international traffic, trade, and public health, and limited protection against only three diseases.

9 Taylor states that in the case of plague outbreak in India, such excessive measures included closing airports to aircrafts that were arriving from India, barriers to importation of foodstuffs, and in many cases the return of Indian guest workers even though many of them had not lived in India for several years. Garrett also states that India lost almost two billion dollars as a result of excessive measures following the plague outbreak.

Recognizing its inefficacy, the 48th World Health Assembly passed a resolution calling on the Director-General of the WHO to revise the IHR in May 1995. Pursuant to this resolution, the WHO held an informal consultation of experts in December 1995 (WHO 1995). The expert group proposed a range of amendments to the IHR, and in February 1998, the WHO circulated a provisional draft of new regulations to member states. The proposed amendments focused on expanding disease surveillance to include immediate reporting of syndromes, as well as epidemiological information for their emergence, prevalence, and control. A number of other reliable sources were central to providing the WHO with disease surveillance information, including the WHO Collaborating Centers, non-governmental organizations, mass media, other international organizations, and non-member states. Whereas previously the WHO depended on member states to report outbreaks, the sheer volume of information provided by these other sources was unprecedented. Few, if any, disease outbreaks can be hidden thanks to extensive global media networks, and innovations in communications technology spawned independent global outbreak monitoring sources. Examples of these include: the Global Public Health Information Network (GPHIN), an electronic surveillance system developed by Health Canada; Pro-MED, a private initiative of the Federation of American Scientists' Program for Monitoring Emergent Infectious Diseases which creates a global system of early detection and response to disease outbreaks; and PACNET, an Internet-based information provider on disease outbreaks in the Pacific region. The implication of these innovations, therefore, is that disease outbreaks can no longer be hidden under the veil of state sovereignty.

The new (revised) *International Health Regulations* (2005) have been described as innovative (Fidler 2005; Baker and Fidler 2006; Lo 2010) and officially entered into force on 15 June 2007 as a normative tool for global disease outbreak control. The emergence of the revised IHR was largely catalyzed by the outbreak and global spread of Severe Acute Respiratory Syndrome (SARS), a new deadly and terrifying infectious disease.

21.3.2 Framework Convention on Tobacco Control

The WHO *Framework Convention on Tobacco Control* (FCTC) directly implicates the WHO as a norm entrepreneur in global health governance. In May 1999, the World Health Assembly adopted (by consensus) Resolution WHA52.18 urging the Director-General of the WHO to enter into multilateral negotiations for the FCTC. The FCTC negotiation process was the WHO's first use of its treaty-making authority under article 19 of its *Constitution*.

As a governance/regulatory tool, FCTC was based on the evidence that tobacco use is one of the leading causes of preventable deaths and a leading contributor to the global burden of disease (Murray and Lopez 1996, 1997). There are over 1 billion smokers in the world, and it was then estimated that about four million people die yearly from tobacco-related diseases. Although tobacco use is a leading cause of premature death in industrialized countries, the epidemic of tobacco addiction, disease and death is rapidly shifting to developing countries (Murray and Lopez 1996, 1997).[10] Powerful and influential tobacco multinational companies targeted growing markets in Latin America in the 1960s, the newly industrialized economies of Asia (Japan, the Republic of Korea, Taiwan and Thailand) in the 1980s, and women and young persons in Africa in the 1990s (Connolly 1992). Tobacco use is medically associated with a range of diseases and

10 Taylor (1996) also states that the absence of effective domestic regulation of tobacco in developing countries has created a lucrative opportunity for transnational tobacco companies to target such countries. In many of the poorer states, aggressive tobacco promotion by the tobacco industry and Western states simply overwhelms underfunded national tobacco control efforts.

fatal health conditions including lung and bladder cancers, heart diseases, bronchitis and emphysema, and increased antenatal and prenatal mortality.

In May 1999, the World Health Assembly established an initial working group and an Inter-Governmental Negotiating Body (open to WHO's 191 member states) to discuss proposed drafts of the WHO *Framework Convention on Tobacco Control* and related protocols. The Tobacco Free Initiative of the WHO prepared background documents for the working group, enumerating possible elements to be covered by the *Framework Convention* and other elements of subsequent protocols. Draft elements of the *Framework Convention* included a preamble, principles and objectives, obligations, institutions, implementation mechanisms, lawmaking processes and final clauses (signatories, reservations, ratification and withdrawal). Potential elements for subsequent related protocols would include cigarette prices and harmonization of taxes, measures against smuggling, duty-free tobacco products, tobacco advertising and sponsorship, reporting of toxic constituents of tobacco products, packaging and labeling, and tobacco and agricultural policy.

The FCTC negotiating process comprised different phases: Working Groups (1999–2000); Public Hearings (2000); and Intergovernmental Negotiating Body Sessions (2000–3). The Intergovernmental Negotiating Body (INB) finalized its work on the first public health treaty under the auspices of the WHO in February 2003. The WHO FCTC was adopted by the 56th World Health Assembly in May 2003, and was open for signature until 29 June 2004. The FCTC was signed by 168 states during this period, which also expressed their willingness to subsequently become a Party to the Convention. In accordance with article 36 of the WHO FCTC, the FCTC entered into force on 27 February 2005, 90 days after the 40th state acceded to, ratified, accepted, or approved it (WHO 2014). With over 170 states parties, the FCTC was widely accepted by WHO member states within a relatively short period. Regular sessions of the Conference of the Parties (COP) for the WHO FCTC are held every two years, when it authorizes the COP to adopt protocols to the Convention (WHO 2003, article 33). After four years of negotiations, the first Protocol to the FCTC – the *Protocol to Eliminate Illicit Trade in Tobacco Products* – was adopted by the Parties to the FCTC at the 5th session of the COP on 12 November 2012.

As the WHO member states continue to accept the FCTC and its protocol(s), embedding the terms of the Convention in the legislative, legal, institutional, and policy frameworks of these states, serious trade and investment questions will likely be raised in the years ahead, particularly for developing countries where tobacco conglomerates exert influence and continue to exploit poverty and underdevelopment. The WHO should devise effective policy strategies to counter this.

21.4 Postscript: the WHO, norm dynamics, and emerging legal and ethical issues

As an international organization, the WHO's role and relevance as the 'directing and coordinating authority on international health work' has been challenged in complex ways by the dynamics of the globalization of public health. While the organization remains essentially an intergovernmental institution with membership exclusively composed of nation-states, the trends, realities, and dynamics of the phenomenon of globalization prove the emerging and re-emerging medical and public health issues defy the territorial boundaries of individual nation-states. As such, the WHO must devise innovative normative (legal and ethical) strategies and tools to tackle these issues. The effects of economic globalization have permeated public health, mobilizing communicable and non-communicable diseases and related medical and public health threats. The globalization of public health has led to the concept of 'global health governance'

that looks beyond state-centrism to identify the emerging and other relevant non-state actors and stakeholders in the global health arena. The relevance of legal and ethical norms in the relationship between WHO as an international organization and these emerging actors, whether proliferating public-private partnerships or other networks, is both intriguing and complex. However, most scholars agree that innovations are needed. As Cooper *et al.* observed:

> These innovations will need to come in the realm of ideas, as the prevailing principles and norms that guide global health governance are redefined and reinvented for a comprehensively and instantaneously interconnected, complex world. They will be needed in the realm of institutions, where new rules, decision-making procedures, resources, and participants are required if the expectations and behavior of the world's countries and citizens are to converge on the reality, rather than just the ideal, of health for all. In both cases, the still dominant Westphalian model – now almost half a millennium old – of sovereign territorial states engaging in limited international cooperation for particular purposes is fast approaching the end of its useful life.
>
> *(2007: 4)*

Looking beyond the Westphalian (state-centric) model, the successor system will be carefully crafted to accommodate all the emergent relevant actors and stakeholders. According to Cooper *et al.*:

> Designing, developing and delivering the successor system will require the talents of many from national and sub-national governments, international institutions, healthcare professionals, philanthropists, the private sector, local communities, nongovernmental organizations (NGOs), faith groups, committed groups and victims from around the world.
>
> *(2007: 4)*

In both the contemporary (dominant) state-centric model and the imagined successor system with multiple actors and stakeholders, the WHO, as an inter-governmental organization, will continue to play a key role in the elaboration of legal and ethical norms.

21.5 Conclusion

The WHO, a specialized agency of the United Nations, is mandated to 'act as the directing and coordinating authority on international health work' (ICH 1948, articles 2(a)–2(v)). As an inter-governmental organization, the WHO's normative and legal parameters are firmly rooted in a state-centric international system. The WHO's Constitution permits the organization to use innovative instruments to create ethical and legal norms – treaties, legally binding regulations, and soft law – to pursue its public health mandate. In the contemporary dynamic and evolving international system, the effectiveness of the WHO as a norm entrepreneur largely depends on how the Organization manages the two interlinked challenges of (1) innovatively deploying its legal and constitutional authorities to initiate new norms in a dynamic international/global system; and (2) crafting a symbiotic and cooperative relationship with the new (non-state) actors in the global health arena. These challenges are critically important for the WHO's continued relevance and legitimacy as a norm entrepreneur for emerging and re-emerging medical and public health issues. To effectively address them, the WHO must collaborate with other relevant international organizations, within and outside the United Nations system, whose mandates touch

on public health, including the Food and Agriculture Organization of the United Nations, the World Trade Organization, and the World Organization for Animal Health.

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22

The law and ethics of access to medicines in developing countries

Paul Ogendi and Peter Munyi

22.1 Background

Lack of access to essential medicines has led to untold suffering and loss of many lives, particularly in developing countries (Yamin 2003), and was rightly termed by Yamin as a 'horrific injustice' (2003: 370). Notwithstanding this, *the World Medicines Situation* report continues to identify inequality and discrimination in access to essential medicines as the key public health challenge of our time (Hogerzeil and Mirza: 2011). The situation is exacerbated by the increasing demands for existing and new medications to mitigate the HIV/AIDS, tuberculosis (TB), and malaria burden in developing countries. Today, the World Health Organization (WHO) estimates about one-third of the world's population lacks access to essential medicines (Hogerzeil and Mirza 2011: 1; UN Human Rights Council 2011: 4). In some areas, the figures project that more than 100 million people endure high financial burdens to fund their healthcare due to high costs (UN Human Rights Council 2011: 4). In developing countries, patients pay approximately 50 to 90 per cent of the cost of medicines, while 20 to 60 per cent of these costs are accounted for in the country's healthcare budget (UN Human Rights Council 2011: 4). Therefore, increasing access to affordable medicines in resource-poor settings and finding new ways to promote the development of new medicines and vaccines to treat diseases of the poor remain a top priority (Leach *et al.* 2005).

Indeed, measures to address the current public health challenges of access to medicines, particularly in developing countries, must be sustainable (Klug 2008). These measures must take into account the complex interplay of macro-economic development, disease patterns, and healthcare needs and provision (Attridge and Preker 2005). Notably, the recognition of access to medicines as a fundamental human right under the right to health is the foundational argument for universal access to essential medicines (Kenyan Constitution 2010, article 43(1)(a); South African Constitution 1996, section 27).

22.2 Legal framework regarding access to medicines

22.2.1 Overview of the right to health and access to essential medicines

In 1946, the preamble to the WHO Constitution was the first document to recognize the fundamental right to health. It defined health as 'a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity' (WHO 1946, preamble).

Arguably, the WHO Constitution paved the way for the recognition of the right to health in various international treaties and instruments (Torres 2002). In the recent past, the regional and national protection of the right to health has also gained traction among WHO actors.

The right to health is extensively protected at the international level. Article 25 of the *Universal Declaration of Human Rights* 1948 (UDHR) enshrines, amongst other socio-economic rights, the right to health. This is important since the UDHR is the first universal authority and statement on human rights (Dimitrijevic 2006). In fact, some parts of the UDHR are believed to be customary law, meaning they are legally enforceable (Dimitrijevic 2006).

The UDHR provision on the right to health was subsequently incorporated in article 12 of the *International Covenant on Economic, Social and Cultural Rights* 1966 (ICESCR). Unlike the UDHR, the ICESCR is legally binding and enforceable. Other binding and enforceable international instruments include article 12 of the *Convention on the Elimination of All Forms of Discrimination against Women* 1979 (CEDAW), and article 24 of the *Convention on the Rights of the Child* (CRC) 1989. The CEDAW and the CRC are predominantly concerned with the rights of women and children respectively.

Notwithstanding the importance of each instrument enshrining the right to health, the ICESCR is of particular importance since it led, through treaty-body interpretation, to the classification of access to essential medicines as a core obligation under the right to health (UN Economic and Social Council 2000, para. 43(d)). Thereby a state party to the ICESCR cannot derogate from this obligation whatsoever. Currently, there are 160 state parties to the ICESCR and 70 signatories (UN Treaty Collection 2013). It is also in the context of the protection of the international right to health that the UN Special Rapporteur on the Right to the Highest Attainable Standards of Physical and Mental Health[1] has been able to publish various reports on this issue. In particular, the Special Rapporteur's report entitled 'Expert Consultation on Access to Medicines as a Fundamental Component of the Right to Health' is significant, as it asserts that since 'access to medicines is an integral and fundamental part of the right to health, Governments and the international community as a whole have a responsibility to provide access to medicines for all' (UN Human Rights Council 2011, para. 44).

Recent news indicates that the UN Human Rights Council may actually consider a resolution on access to medicines as a human right, to be submitted to it by India, Brazil, South Africa, Egypt, and Thailand upon recommendations from the Special Rapporteur (Don't Trade Our Lives Away 2013). This would expand the access to medicines discourse beyond the list of drugs to the 'essential medicines' in use for decades (Don't Trade Our Lives Away 2013).

Secondly, regional instruments have also contributed to the protection of the right to health. In Africa, article 16 of the *African Charter on Human and Peoples' Rights* 1981 (*African Charter*),[2] article 14 of the *Protocol to the African Charter on Human and People's Rights on the Rights of Women in Africa* 2003,[3] and article 14 of the *Protocol to the African Charter on the Rights and Welfare of the Child* 1999[4] all provide for the right to health. At the regional level, the African Commission on Human and Peoples' Rights put in place a resolution on access to health and needed medicines (Resolution 141 2008). On the legislative front, the Pan-African Parliament called for the

1 The mandate emanated first from the Commission on Human Rights Resolution 2002/31 of April 2002 and later Human Rights Council Resolution 6/29 of 14 December 2007.

2 Kenya acceded to the *African Charter* on 23 January 1992. South Africa ratified the *African Charter* on 9 July 1996.

3 Kenya signed the *Protocol* on 12 December 2012 but has yet to ratify it. South African ratified it on 17 December 2004.

4 Kenya acceded to the *Protocol* and ratified it on 25 July 2000. South Africa ratified it on 7 January 2000.

'development and/or review of national medicines policies to ensure that all the key elements that ensure access to medicines are covered …' (2011: 2).

With regard to the Inter-American human rights system, article 26 of the *American Convention on Human Rights* 1969 requires the progressive realization of the socio-economic rights provided for under the *Charter of the Organization of American States* 1948, as amended by the *Protocol of Buenos Aires* 1970. The *American Convention on Human Rights*, however, does not specifically provide for enforceable socio-economic rights in its text. Similarly, the *Charter of the Organization of American States* only commits its members to certain socio-economic goals including '[u]rban conditions that offer the opportunity for a healthful, productive, and full life' (article 34(1)).

In 1999, the Inter-American human rights system adopted the *Additional Protocol to the American Convention on Human Rights in the Area of Economic, Social and Cultural Rights* [*Protocol of San Salvador*]. Article 10 of the *Protocol of San Salvador* enshrines the right to health. This article has been relied on by litigants, in addition to article 4 of the *American Convention on Human Rights*, to demand access to antiretroviral medications (*Jorge Odir Miranda Cortez et al.* v. *El Salvador* 2001). Finally, the *European Convention for the Protection of Human Rights and Fundamental Freedoms* 1950, like its counterpart, the *American Convention on Human Rights*, does not explicitly mention the right to health. However, the *European Social Charter* (Revised 1996) was later adopted in 1961 and provided for socio-economic rights, including the right to health under article 11. These rights are not legally enforceable and rely on 'a supervisory mechanism based on a system of collective complaints and national reports' to ensure their respect and the implementation of the *European Social Charter* (Secretariat of the European Social Charter 2009: 1).

Third, there is an increasing protection of the right to health at the national level. Kenya and South Africa are leading the way, codifying a justiciable right to health in their respective Constitutions. Kenya guarantees the right to health under article 43(1)(a) of its 2010 Constitution, while South Africa protects the right to health by virtue of article 27(1)(a). As a result of this constitutional protection of the right to health, both the Kenyan and South African constitutional courts have been able to enforce access to medicines. In *Patricia Asero Ochieng and others* v. *The Attorney General*, Petition No. 409 of 2009 (popularly known as the *Patricia Asero* case), the Kenyan Constitutional Court addressed access to generic drugs in the context of national anti-counterfeit legislation. In *Minister for Health and others* v. *Treatment Action Campaign and others* 2002 (5) SA 703 (popularly known as the *TAC* case), the South African Constitutional Court discussed expectant mothers' access to Nevirapine for the prevention of mother-to-child-transmission of HIV. Both cases upheld the government's obligation to provide access to essential medicines unconditionally.

These cases add to the growing list of authorities on access to essential medicines, particularly in developing countries. India is leading the world in protecting the right to health through judicial interpretation, even though the right to health has been listed outside of the country's enforceable fundamental rights pursuant to article 37 of Part IV (Directive Principles of State Policy) of the Indian Constitution 2007.[5] India has also developed progressive access to medicines jurisprudence as in *Novartis* v. *Union of India and others*, Civil Appeal No. 2606-2716 of 2013. In this case, the Supreme Court of India rejected Novartis' patent renewal application for a popular cancer drug on the grounds that it did not meet the patentability criteria set out under the patent laws of India. In rejecting the appeal by Novartis, the judges, at para. 195 of the judgment, posited that the new invention claimed 'fails in both the tests of invention and patentability as provided under clauses (j) and (ja) of section 2(1)

5 The 1970s fundamental rights case *Kesavananda Bharati* v. *State of Kerala* AIR 1973 SC 1461 ushered in a new era of judicial protection of Directive Principles of State Policy alongside other fundamental rights.

and section 3(d) respectively' of the *Patent Act* 1970. This decision has been lauded by various public health actors because of its potential impact in curbing the problem of 'evergreening' of pharmaceutical patents, which delays access to affordable generic medicines in the market (MSF Access Campaign 2013a).

22.2.2 WTO rules and access to medicines

The inclusion of intellectual property under the World Trade Organization (WTO) through the *Trade Related Aspects of Intellectual Property Rights* (TRIPS) *Agreement* 1995 marked a new era of intellectual property (IP) rights protection globally, within a set of minimum standards. Unlike before, IP could now be treated as a trade commodity under international trade, meaning material interest in an intellectual creation is protected through an international property-based IP system (Yu 2007).

However, the main concern in developing countries currently under the TRIPS Agreement is the protection of public health, and economic and technological development generally (Commission on Intellectual Property Rights 2002). In particular, developing countries are concerned that by introducing patent protection, medicine prices will increase while the choice and supply of pharmaceuticals will decrease (Commission on Intellectual Property Rights 2002). In August 2000, Resolution 2000/7 of the UN Sub-Commission on the Promotion and Protection of Human Rights on intellectual property rights and human rights was the first international resolution to acknowledge the conflict between human rights and intellectual property (Sub-Commission on Human Rights Resolution 2000/7, para. 2). However, it was quick to also declare that the TRIPS Agreement is not equivalent to human rights, which are fundamental in nature and indivisible (Sub-Commission on Human Rights Resolution 2000/7, para. 2). The Resolution also sought to remind the governments of the primacy of human rights obligations over economic policies and agreements (Sub-Commission on Human Rights Resolution 2000/7, para. 3). In responding to the above report, Pakistan noted that developed countries were benefiting more from the TRIPS Agreement than developing countries. According to Pakistan's reply, the cost-to-gain ratio borne by developing countries is disproportionate:

> The experience of many developing countries with the implementation of the intellectual property agreements indicates that the fundamental objectives of these agreements are not being realized. There may perhaps be reasons to believe, at best on theoretical grounds, that in the long term, benefit could accrue in the form of increased investments, innovation and transfer of technology. However, it is painfully evident that in the short and medium term, the costs being borne by developing countries are higher than the gains, and that the balance between the rights holder (mostly from the developed countries) and the user of intellectual property has shifted dramatically in favour of the former.
>
> *(UN Sub-Commission on the Promotion and Protection of Human Rights 2001: 3)*

Pakistan goes on to provide detailed reasons. Notably, the government of Pakistan posits that stronger intellectual property protection undermines the right to health, the right to education and the right to food (UN Sub-Commission on the Promotion and Protection of Human Rights 2001: 4). The government of Pakistan also argued that stronger intellectual property rights protection promotes monopolistic and anti-competitive practices (UN Sub-Commission on the Promotion and Protection of Human Rights 2001: 4). Lastly, the government of Pakistan further asserted that some developing countries have been unable to quickly respond to

epidemics such as HIV and AIDS (UN Sub-Commission on the Promotion and Protection of Human Rights 2001: 4). Notwithstanding the current stand-off, the TRIPS Agreement avoided the defects of the World Intellectual Property Organization (WIPO) and other IP treaties by insisting on 'balance' as the multilateral objective (He 2011: 831). In this regard, the 'rules v. flexibilities' dichotomy embodies an unprecedented level of international will (He 2011: 831). This is because the concrete and enforceable TRIPS Agreement flexibilities are also meant to give effect to the objectives and principles of articles 7 and 8.1 of the Agreement (He 2011: 832). Nevertheless, a 'one-size-fits-all' approach to IP protection is unadvisable since it is 'unreasonable and unrealistic' and may actually hamper rather than facilitate the achievement of an appropriate legal balance (He 2011: 833).

Recently, the TRIPS Council extended one of the flexibilities under the TRIPS Agreement to the least developed countries (LDCs), granting them a transition period. Article 66.1 of the TRIPS Agreement initially required LDCs to comply with the TRIPS Agreement's minimum standards within a period of ten years. In 2005, the TRIPS Council extended this initial transition period to another seven and a half years. With regard to pharmaceutical patents, an extension was granted in 2002, until 1 January 2016, pursuant to para. 7 of the *Doha Declaration on the TRIPS Agreement and Public Health* 2001. The *Doha Declaration* is an important instrument in the access to medicines discourse since it grants developing countries the right to utilize the TRIPS Agreement's flexibilities to promote public health initiatives. In June 2013, the transition period for LDCs was again extended to 2021, eight years away, in order to further promote innovation and technological development. This new extension received popular support from the UN, developing countries (including China, India, Brazil, and South Africa), academicians, and civil society organizations across the world (Saez 2013). Since the extension on pharmaceutical patents has yet to expire, LDCs will need to seek a separate extension in 2015.

This new extension of the transition period may have implications on access to medicines, according to UNAIDS, in that it will preserve the policy space for LDCs. Particularly, the extension will 'conserv[e] the autonomy of LDCs to determine appropriate development, innovation, and technological promotion policies, according to local circumstances and priorities' (UNDP and UNAIDS 2013: 4). A press release by Médicins Sans Frontières (MSF) stated that LDCs are 'now in a position to roll-back existing level of IP protection to meet domestic policy objectives, and should do this in the years ahead' (2013: 1a). However, while acknowledging that pharmaceutical patents were covered by this extension generally, MSF recommended that LDCs should insist, in 2015, on a 'more comprehensive extension,' which is not time bound and without any other conditions (2013b: 1). Notwithstanding, the EU pointed out that the 2021 extension is conditional on the country remaining an LDC and not gaining developing country status (Permanent Mission of the European Union to the World Trade Organization 2013). The EU further asserted that LDCs 'have committed themselves not to reduce or withdraw the current protection that they give' (Permanent Mission of the European Union to the World Trade Organization 2013: 1). From the above, it appears that the exact meaning of the 'no-roll-back' clause is contested and will form the basis of future engagement, particularly in the implementation of the decision in LDCs.

22.2.3 Threats to access to medicines

Free trade agreements (FTAs) animate a number of threats in the access to medicines movements by the impracticability of some amendments in the TRIPS Agreement and the *Anti-Counterfeiting Trade Agreement* 2011 (ACTA).

22.2.3.1 FTAs

Despite the TRIPS Agreement, international communities perceive a failed enforcement of IP in developing countries given the prevalence of counterfeiting and piracy (Kur 2009). In particular, members of the WTO have been accused of not adequately implementing the provisions of the TRIPS Agreement, and/or not investing enough resources to enforce the provisions enacted nationally in compliance with the Agreement (Kur 2009). The above reasons, coupled with unwillingness at the multilateral level to upgrade substantive obligations under IP law, led to the revival of bilateral strategies (Santa-Cruz 2007). In response, the United States, the EU, and Japan are offering favorable market conditions to specific trading partners for stronger IP protection. According to Musungu and Dutfield, this concession becomes critical when applied to areas such as public health, the promotion of domestic industries, and access to knowledge (2003: 4). For example, the presently negotiated EU-India FTA may restrict access to generic drugs for HIV/AIDS, while Indian manufacturers supply 80 per cent of these generic antiretroviral drugs to MSF for treating patients (MSF 2013b). In addition, 'due to deficiencies of procedural fairness and equal standing of negotiating parties,' the resultant IP provisions in FTAs are 'ill-adapted to a member's individual situation' (Kur 2009: 33).

According to Correa (2006), FTAs generally require stronger protection of IP rights than what is internationally sanctioned under the TRIPS Agreement. In some cases, FTAs surpass the interests of the developed countries promoting them (Correa 2006). Ultimately, Correa concludes that the impact of these FTAs is to limit the capacity of states to realize their human right to health and to negate the *Doha Declaration* (2006: 402). FTAs may include what is often referred to as 'TRIPS-plus' provisions for requiring protection beyond the minimum requirements under the TRIPS Agreement. These provisions so far extend to the following: broadening patentability; restricting patent oppositions; extending patent duration; introducing test data exclusivity and a patent-registration linkage; and, lastly, IP enforcement requirements (UNDP and UNAIDS 2012: 3–4). According to UNAIDS and UNDP, countries should avoid entering into FTAs that contain TRIPS-plus provisions in order to benefit from the TRIPS Agreement flexibilities (2012: 5).

22.2.3.2 TRIPS amendments impracticability

The most contested flexibility seems to be in the area of compulsory licensing, where there has been considerable flip-flopping from WTO members. In particular, the *Doha Declaration* identified the difficulties WTO members experience in having insufficient or no manufacturing capacities to utilize the compulsory licensing provisions under the TRIPS Agreement (*Doha Declaration*, para. 6). Therefore the *Doha Declaration* instructed the Council for TRIPS 'to find an expeditious solution and report to the General Council before the end of 2002' (para. 6). On 30 August 2003, the General Council reached a decision on this issue and dubbed the 'Implementation of Paragraph 6 of the Doha Declaration on TRIPS Agreement and Public Health' (the Decision) (WTO General Council 2003). The Decision allowed for limited importation and exportation in countries with little or no manufacturing capacities. Baker described this outcome as a 'cumbersome, but potentially important mechanism for allowing trade in low-cost generic medicines' (2004: 7). In effect, both LDCs and developing countries are allowed to benefit from the Decision. For LDCs, they are automatically eligible, but eligibility for non-LDCs or developing countries is conditional on 'insufficient or inefficient capacity in the pharmaceutical sector' (Baker 2004: 16). Compulsory licensing is allowable where there is a patent in place to benefit from the Decision (WTO General Council 2003). In 'good faith,' all WTO

members can export under the Decision following stringent conditions (WTO General Council 2003). In practical terms, the real difficulties of the Decision concern post-1994/5 discoveries. It expands the 2005 product-patenting rights for countries like India that must become fully TRIPS compliant and must provide patent protection both for post-1994/5 pipeline/mailbox patent applications and for all post-2005 inventions. Of course, the Decision also applies to countries like Brazil, where most medicines are patented and intended to be exported under a non-competition-based compulsory license (Baker 2004: 30).

The complexities described above are arguably responsible for the limited number of countries adopting legislation implementing the Decision as an exporting country. These countries include Norway, Canada, India, the EU, Hong Kong, Switzerland, the Philippines, Singapore, Albania, Croatia, China, the Republic of Korea, Jordan, and Japan (WTO 2011). Similarly, only one importing country, Rwanda, has used the system to import drugs from Canada for its HIV patients despite the availability of similar drugs in India (South Centre 2011: 8). The overarching issue is the continued failures of the current system to improve access to essential medicines in developing countries because it is 'unnecessarily burdensome and complicated' (South Centre 2011: 8).

22.2.3.3 ACTA

Anti-counterfeiting is discussed under Part III 'Enforcement of Intellectual Property Rights' of the TRIPS Agreement. Thereby members are urged to apply border measures to combat, among other things, trademark counterfeits (TRIPS Agreement, article 51). With regard to willful trademark counterfeiting, criminal procedures and penalties are preferred in order to enforce IP rights (TRIPS Agreement, article 61). Nonetheless, industrialized countries appear dissatisfied with the enforcement provisions under the TRIPS Agreement: they are convinced that the current enforcement provisions cannot combat counterfeiting, urging for strategies beyond the TRIPS Agreement (Kur 2009). However, the problem lies in expanding anti-counterfeiting measures beyond what is provided for under the TRIPS Agreement as it has little benefit to the consumer: only willful trademark counterfeiting is potentially dangerous to the public since willful counterfeit medicines are not registered with the national drug regulatory authorities (Maybarduk 2010: 4).

This dissatisfaction with the enforcement mechanisms in the TRIPS Agreement is manifest in the proceedings, negotiations, and signing of the *Anti-Counterfeiting Trade Agreement* 2011 (ACTA). ACTA sought to fight counterfeiting, but failed to distinguish criminal activity and civil infringement by extending enforcement to patent and ordinary trademark infringements (Maybarduk 2010: 3). Consequently, it was believed that ACTA would create legal uncertainty, impose costs, taint commercial disputes with 'the air of criminality,' and 'divert resources and attention away from more direct and comprehensive measures to protect the public from unsafe products' (Maybarduk 2010: 3–4). Specifically, from an access to medicines standpoint, the following proposed measures are undesirable:

- *Border measures requirements* that expand the scope of authorized seizures to any case where a border agent 'suspects' a medicine's label of being 'confusingly similar' to a brand.
- *Injunction provisions* that require all ACTA members to put in place the basic legal elements that were used in the 'Dutch seizures' cases in the EU, enabling authorities in one country to issue injunctions preventing goods from entering commerce in a third country without that third country's officials ever passing on whether the item would infringe its own laws.

- *Third-party liability rules* that increase risks of erroneous injunctions and seizures of property from distributors, shippers, procurement agents, and component suppliers of any generic product suspected of having a 'confusingly similar' label.
- *Damages provisions* that over-deter lawful conduct by encouraging determinations of damages in poorer countries based on the 'market price' or 'suggested retail price' of a branded product, even where that price is intentionally set at a level that excludes the great majority of a population from access to the product.
- *Information disclosure requirements* that could be used by right holders to discover details on distribution chains of generic companies and mount aggressive and expensive litigation against suppliers and intermediaries to deter generic entry into key markets.
- *Expansion of criminal liability* to cases where a supplier did not intentionally create or use the counterfeit label itself, thus raising the (over-)deterrent effect of trademark law for importers, including those of generic medicines.
- *Expansion of seizure and destruction rules* to require that, for example, absent 'exceptional circumstances,' a medicine found to have a minor trademark infringement on a label be destroyed rather than re-labeled and re-sold.

(Flynn and Madhani 2011: 2–3)

In terms of the implications of ACTA, Flynn and Madhani contend that:

> On the whole, ACTA negotiators created an agreement that shifts international 'hard law' rules and 'soft law' encouragements towards making enforcement of intellectual property rights in courts, at borders, by the government and by private parties easier, less costly, and more 'deterrent' in the level of penalties. In doing so, it increases the risks and consequences of wrongful searches, seizures, lawsuits and other enforcement actions for those relying on intellectual property limitations and exceptions to access markets, including the suppliers of legitimate generic medicines.
>
> *(2011: 1)*

In this regard, numerous health actors have opposed the issue of anti-counterfeiting and patent linkage; for example, under the TRIPS Agreement, the subject of IP for which the term 'counterfeiting' is used is limited to trademarks and copyright, and is not extended to patents. According to Baker, if patents are excluded, the health risk under ACTA will be reduced (2010: 2). The effects of the anti-counterfeiting measures proposed in ACTA are evident, especially in Europe. In 2008 and 2009, Dutch customs officials detained multiple drug shipments, based on Council Regulation (EC) No. 1383/2003, applying a manufacturing fiction doctrine (Baker 2010: 3). The risk in linking patents to counterfeiting is not limited to border seizures alone. Baker argues that injunctions may be used against active pharmaceutical ingredients manufacturers, international shippers, and other participants in the global trade of medicines, thereby effectively crippling the trade of generic medicines (2010: 4). Because of the potential risks that ACTA portends, it is not surprising that the European Parliament rejected the Agreement *in toto* (European Parliament 2012).

In Kenya, some of the arguments above were borrowed and utilized successfully in the *Patricia Asero* case, dating back to when Kenya first enacted its *Anti-Counterfeit Act* 2008. In 2009, the three petitioners living with HIV and AIDS opposed the law on the grounds that it violated their constitutional right to health, life, and human dignity. The UN Rapporteur argued for the right to the highest attainable standard of physical and mental health, and some civil society organizations joined the case as *amici curiae*. The petitioners singled out sections 2, 32, and 34 of

the *Anti-Counterfeit Act* as potentially restricting access to generic medicines in the country. In particular, they argued that section 2 on the definition of counterfeiting conflated 'counterfeits' with 'generics.' The petition was granted, but the decision has yet to be implemented. In response to the decision, UNAIDS observed that the ruling will safeguard access to affordable and quality life-saving generic medicines (UNAIDS 2012). The decision of the Kenyan High Court seems to have contributed to the delayed enactment of anti-counterfeiting legislations in the African region.

22.2.4 Domestic application of access to medicines concepts in developing countries

This section examines the domestic application of access to medicines concepts in developing countries, focusing on pre-grant opposition in India, parallel importation and anti-counterfeiting in Kenya, compulsory licensing in Indonesia, and compulsory licensing in Latin America.

22.2.4.1 Pre-grant opposition in India

Depending on the country's intellectual property system, a pre-grant opposition and/or a revocation (also known as post-grant opposition) may be exercised by concerned parties to challenge a patent duly filed with the relevant government department. One reason may be due to, *inter alia*, failure to meet the patentability criteria. According to article 62(4) of the TRIPS Agreement, revocation, opposition, and cancellation of patents should be governed by the principles set out in article 41(2) and (3). Article 41(2) provides for fair and equitable procedures. Article 41(3) requires that all decisions be reasoned and in writing. Lastly, article 32 of the TRIPS Agreement allows for judicial review of any decision to revoke or forfeit a patent. Arguably, a post-grant opposition procedure is preferable in an incentive patent based system to a pre-grant opposition that may lead to unnecessary delays in patent protection (Tripathi 2013).

India provides for both pre- and post-grant opposition. Opposition of patents in India is provided for under section 25 of the *Patents Act* 1970. Section 25(1) deals with pre-grant opposition generally. Similarly, section 25(2) addresses post-grant opposition. There are various grounds to base an opposition, including obtaining an invention wrongfully (sections 25(1)(a) and 25(2)(a), *Patents Act*) and if the invention was published before the priority date (sections 25(1)(b) and 25(2)(b), *Patents Act*). In the case of a post-grant opposition, it must be filed within one year from the date of publication of grant of the patent (section 25(2), *Patents Act*).

In early 2013, India won a case it had successfully filed against the pharmaceutical giant, Novartis, with regard to its cancer drug Gleevec. The case was initially filed as a pre-grant opposition and was later decided by the Supreme Court of India. In *Novartis AG* v. *Union of India and others*, Civil Appeals Nos. 2706-2716 2013, the Appellant, Novartis, had filed a patent renewal grant on 17 July 1998 for Imatinib Mesylate in beta crystalline form at the Chennai Patent Office (para. 8). The Appellant claimed that the application was valid because the 'new' product had '(i) more beneficial flow properties; (ii) better thermodynamic stability; and (iii) lower hygroscopicity than the alpha crystal form of Imatinib Mesylate' (*Novartis*, para. 8). However, due to section 3(d) of the Indian *Patents Act*, the Appellant was ultimately unsuccessful: the application for patent renewal failed. Section 3(d) of the *Patents Act* is part of the amendments adopted by Parliament and which came into effect on 1 January 2005 (Patents (Amendment) Ordinance 2004). According to this section, a higher patentability criterion was introduced, requiring that

any new form of a known substance must also enhance the known efficacy of that substance. If this criterion is not met, the application for patent renewal must fail, as in *Novartis*. As stated by the Supreme Court of India:

> Thus, in whichever way section 3(d) may be viewed, whether as setting up the standards of 'patentability' or as an extension of the definition of 'invention', it must be held that on the basis of the materials brought before this Court, the subject product, that is, the beta crystalline form of Imatinib Mesylate, fails the test of section 3(d), too, of the Act.
>
> (Novartis, *para. 190)*

Novartis expanded access to medicines by addressing the problem of patent renewals known as 'evergreening'. The decision has been praised worldwide: according to MSF, it was a major victory for 'patients' access to medicines in developing countries' (2013c: 1). Indeed, this would have not been possible without the patent reforms of 2004/5. Novartis failed in its attacks against section 3(d) of the *Patents Act*, which aims at safeguarding the public health system in India (MSF 2013c). Other developing countries can learn from India's example and provide better protection in their public health system by amending their patent laws.

22.2.4.2 Parallel importation and anti-counterfeiting law in Kenya

By definition, parallel imports/trade 'occurs when products produced under the protection of a patent, trademark, or copyright in one market are subsequently exported to a second market and sold there without the authorization of the local owner of the intellectual property (IP) right' (Matthews and Munoz-Tellez 2007: 1429). Parallel importation in Kenya is provided for under section 58(2) of the *Industrial Property Act* 2001 (IPA). This section provides for an international exhaustion principle opening the widest avenue possible to exploit this flexibility in the country. This utilization of the TRIPS Agreement parallel importation flexibility by Kenya constitutes best practice (Lewis-Lettington and Munyi 2004). Some tangible benefits of utilizing parallel importation include 'lower pricing, improved stability of supply, and generally enhanced competition' (Lewis-Lettington and Munyi 2004: 18). Nonetheless, others have noted that the utilization of parallel importation flexibility in Kenya has failed to promote access to essential medicines to the general public (Pharmacy and Poisons Board (Kenya) 2006). However, not in doubt is the steady growth of parallel importation in Kenya since its inception in 2002 (Nyaga 2009).

The anti-counterfeiting situation in Kenya is nuanced. In 2008, it enacted the *Anti-Counterfeit Act* 2008 amid opposition from civil society actors working around access to medicines locally and abroad. The basis of the opposition was that the definition of 'counterfeiting' under the law was TRIPS-plus.[6] Of particular concern was the inclusion of patent linkage for generic medicines, as well as the ambiguous 'counterfeiting' definition under section 2. This led to a High Court petition, the *Patricia Asero* case, where the three petitioners argued that sections 2, 32, and 34 of the anti-counterfeiting legislation violated their constitutional rights to health, life, and human dignity, as they relied on generic medicines which would be restricted if the anti-counterfeiting legislation was enacted as drafted. Ultimately, the case was decided in favor of the petitioners, affirming important principles. First, it determined that human rights (life, human dignity, and health) supersede intellectual property rights. Secondly, it established that the right to health also encompasses access to affordable generic medicines. Lastly, it confirmed that international law applies directly to Kenya.

6 This term is used to mean that the standard adopted is higher than what is found under the TRIPS Agreement.

22.2.4.3 Compulsory licensing in Indonesia and Latin America

Compulsory licensing is permitted under article 31 of the TRIPS Agreement. As such, several countries, including Indonesia, have managed to intervene in HIV and AIDS treatment programs. In 2004, for example, the President of Indonesia issued a decree enabling a local manufacturer of antiretrovirals to offer affordable prices in Indonesia (2004). Similarly, Brazil followed this example for the AIDS drug Efavirenz. After amending its laws (Decree No. 3,201 1999), Brazil appealed to the public interest as another ground for issuing a compulsory license under article 71 of *Brazil Law 9.279* 1996. The introduction of this new ground allowed the Minister for Health to declare that Efavirenz was a public interest drug for HIV and AIDS (Minister of Health, 2007), enabling the President to decree a compulsory license for Efavirenz (Presidential Decree No. 6.108 2007). The decree was extended in May 2012 for another five years. In conclusion, compulsory licenses work elsewhere in promoting access to essential medicines, particularly in fighting HIV and AIDS.

22.2.5 Some threats to access to medicines at the national level

National budgetary allocations for health and unreliable bilateral funding and unsustainability of funding from the Global Fund pose formidable threats to access at the national level and each are discussed in turn in the following sections.

22.2.5.1 National budgetary allocation for health

The allocation of public resources in most countries is predominantly decided by way of a national budgeting process. The importance of health budgeting lies in its direct effects on service delivery, particularly to the poor and the vulnerable segments of the society who depend heavily on the public health system (Save the Children 2012). All health services, including doctors, medicines, and hospitals, have a cost (World Health Report 2010: 4). In fact, the government pays both directly to the health sector and indirectly through addressing the social determinants of health (WHO 2010: 23). Total external assistance is usually minimal in most cases. In 2007, for example, external assistance to the health sector for low-income countries was less than 25 per cent (WHO 2010: 23).

In 2001, African Union (AU) members pledged to commit at least 15 per cent of their national health budgets to improve the health sector (Abuja Declaration on HIV/AIDS, tuberculosis and related infectious diseases 2001). To date, only South Africa and Rwanda have achieved the set target (WHO 2011). Despite a 9.9 per cent increase in the government budget from 2009 to 2011, the Kenyan health budget witnessed a 13.5 per cent reduction in the same years (Sealy and Rosbach 2011). Consequently, most AU member countries, including Kenya, are not on track to achieve the health-related millennium development goals, such as that of eradicating HIV and AIDS. Moreover, access to essential medicines has also suffered due to lack of adequate health financing.

22.2.5.2 Unreliable bilateral funding

The past half-century has seen unprecedented public attention paid to global health. Increased funding, among other things, has assisted in the effort to 'successfully eradicate smallpox, decrease AIDS mortality, and raise average global life expectancy from forty to sixty five' (Council on Foreign Relations 2013: 1). However, in a recent report published in *Health Affairs,* the study

results show that as a result of the global financial crisis, the development of assistance for health has slowed down from 17 per cent in 2007/8 to 4 per cent in 2009 to 2011 (Leach-Kemon *et al*. 2012: 230). Similarly, the growth rate of health financing from bilateral agencies has decreased from 12 per cent in 2009/10 to 4 per cent in 2010/11 (Leach-Kemon *et al*. 2012: 231). This situation is precarious considering that development assistance for health from bilateral agencies was the major driver of a 14 per cent annualized growth rate in health initiatives (Leach-Kemon *et al*. 2012: 231). The current slow-down is a result of the US decision to slow its development assistance for health due to the global economic crisis (Leach-Kemon *et al*. 2012: 232). In order to maintain growth, the World Bank's International Bank for Reconstruction and Development increased its development assistance by 128 per cent in 2010/11 (Leach-Kemon *et al*. 2012: 230).

22.2.5.3 Unsustainability of funding from the Global Fund

Equally affected by the global economic crisis is the Global Fund, namely because health assistance channeled through it decreased by 16 per cent between 2010 and 2011 (Leach-Kemon *et al*. 2012: 232). Disbursements from donors also continued to decrease with tides of the global economic crisis. In 2009, donors disbursed about 94 per cent of their commitments, but only disbursed about 78 per cent of their commitments in 2010. In response, the Global Fund scaled back its funding (Leach-Kemon *et al*. 2012: 232).

22.2.6 Current and emerging legal and ethical issues pertinent to access to medicines

The following analysis discusses access to medicines as an emerging issue. In particular, it reviews recent developments through a financial and research lens, respectively.

22.2.6.1 Financing side

Generally speaking, research and development is driven by market forces. The market for medicinal development in developed countries is supported either through private consumption or public funding (Lexchin 2010: 1). Consequently, developing countries are bearing the brunt of developing medicines for neglected diseases. We discuss briefly three solutions suggested by Lexchin: paying for innovation; priority review vouchers; and public-private partnerships (2010).

Paying for innovation entails an 'advanced scheme to promote research into neglected diseases that are based on paying the innovator from a prize fund,' such as the Health Impact Fund (Lexchin 2010: 6). The idea is to 'incentivize the development and delivery of new medicines by paying for performance' through an alternative registration mechanism that would promote access to essential medicines, particularly in developing countries, through a system of reward based on the actual health impact of the drug and not profitability (Lexchin 2010: 6). Despite slight differences, other countries share the same idea by basing 'their payments on the therapeutic value of the new products' (Lexchin 2010: 6).

Secondly, the priority review voucher system was initiated by the United States in September 2008 to promote research in neglected diseases. The US Food and Drug Administration (FDA) gives priority (up to six months priority period from the previous 12 months standard period) to a company's products presented for registration, provided that it also conducts research and development on new drugs for neglected diseases (Lexchin 2010: 7). In 2009, for example, the FDA granted its first voucher to Novartis for its combination product (artemether/

lumefantrine, trade name Coartem) (Lexchin 2010: 7). The priority review is usually worth millions of shillings because it depends on the sales potential of the product, which is a sufficient incentive for research and development on drugs for neglected diseases (Lexchin 2010).

Lastly, public-private partnerships (PPP) do not predominantly engage in drug development but 'integrate multiple industry and academic partners and contractors along the drug development pipeline; allocate philanthropic and public funds to the "right" kinds of R&D projects; and manage neglected disease R&D portfolios' (Lexchin 2010: 8). Despite its successes, one major challenge is the lack of representation of developing countries on relevant boards (Lexchin 2010).

Other strategies include: advanced market commitments (AMCs); patent buy-outs; and patent pools. To begin, AMCs mean advance donor commitment to purchase drugs or vaccines for poor-country diseases as a way of spurring research and development on these diseases and ensuring that, if developed, these drugs or vaccines reach those who need them (Kremer and Glennerster 2004). The central pillar is to provide incentives through guaranteed economic returns at the time of investment and not at the time of the sale (Basheer 2012). Second, patent buy-outs can potentially promote greater access to medicines, particularly where they are purchased and put in the public domain, becoming available for public use, or are licensed to generic manufacturers (Outterson 2006).

Lastly, patent pools have also been proposed to create new combinations and formulations of needed medicines, as patent holders voluntarily offer, under certain conditions, the IP related to their inventions to the pool. Any company wanting to use the IP to produce or develop medicines can seek a license from the pool against payment of royalties (Bermudez and 't Hoen 2010). A good example is the UNITAID patent pool financing mechanism established in 2010. The project is dedicated to scaling up treatment, particularly for AIDS, tuberculosis, and malaria.[7] The first agreement was signed in July 2011 between the Medicines Patent Pool and Gilead Sciences for HIV and Hepatitis B medicines for developing countries (UNITAID 2011).

22.2.6.2 Research side (global frameworks to support medical R&D)

Another important development in access to medicines is the discussion at the WHO on global frameworks to support medical R&D. In 2006, the WHO Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH) brought to the fore the need 'for an international mechanism to increase global coordination and funding of medical R&D' in its report on Public Health Innovation and Intellectual Property Rights (2006: 91). In adopting the CIPIH Report, the WHO also put in place a Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property to which are anchored elements for prioritizing and promoting medical and R&D needs. Whereas discussions and negotiations towards actualizing the Global Strategy and Plan of Action have been mired by differences of opinion among countries, recent World Health Assembly resolutions reveal consideration for a three-pronged approach towards its fulfillment: the establishment of a global health R&D observatory; the setting up of demonstration projects; and the development of norms and standards to better collect data on health R&D. The ultimate wish for most developing countries is the negotiations and adoption of a medical R&D treaty for it is believed that such a treaty would provide a concrete and tangible plan on which frameworks for promoting and supporting medical R&D would rest.

7 For more information, see http://www.medicinespatentpool.org/who-we-are2/partners/.

22. Conclusion

Throughout this chapter, we have canvassed the issue of limited access to essential medicine in developing countries. The legal framework on the right to health and access to medicines was discussed. The ICESCR General Comment No. 14 2000 is crucial in that it recognizes access to essential medicines as a compulsory obligation of states parties to the ICESCR. The next part addressed WTO rules including the *Doha Declaration*, which codified a right for WTO members, particularly from developing countries, to avail themselves of the TRIPS Agreement flexibilities for intervening in public health cases like HIV/AIDS, tuberculosis, and malaria. The third part of the paper focused on threats to access to medicines including ACTA. ACTA has been discredited, particularly because it introduces a number of controversial provisions that limit the ability of developing countries to utilize TRIPS Agreement flexibilities, and will hamper access to essential medicines. The subsequent section discussed the domestic application of access to medicines concepts, including the granting of compulsory licenses in Brazil on public interest grounds. Some threats to access to medicines were also discussed with the global economic crisis affecting a significant number of health programs. Lastly, this chapter reviewed contemporary developments in the area of access to essential medicines. The current discussion on global frameworks to support medical research and development at the WHO is of tremendous importance.

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23

Traditional, complementary, and alternative medicine

Terry S. H. Kaan

23.1 Scope

In any survey of traditional and alternative medicine, the threshold problem is the most intractable and difficult. It is that of definition. Aside from the polemics that often attend discussions in this area, even the most objective commentators on the subject have had little success in formulating a universal definition broad enough to encompass the great diversity of practices and disciplines without also lapsing into impractical vagueness. A clear, objective and neutral (but not neutered) definition of the field is the first requirement for any reasoned debate and discourse for both commentators within and outside the field, and on different sides of the debate.

Few effective tools for engagement have emerged from the available literature and the available literature is very disparate. Where Traditional Chinese medicine or Indian *ayurvedic* medicine is practiced outside their familiar societies and cultures, commentators fluent in only Western European languages must not only grapple with the interpretation of relevant cultural perspectives and beliefs, but must also accept that the body of published discourse on these systems is published in languages foreign to them. That is, if they are published at all, considering that the common mechanism in many such societies for the transmission of beliefs, perspectives, and rituals that comprise these approaches is generally oral tradition. Thus for the most part, Western commentators must rely on the odd translations and interpretive accounts of traditional medicine approaches that occasionally emerge. The objectivity, reach, and accuracy of perspectives built up from such marginal snippets may thus be open to challenge.

23.1.1 Classification, nomenclature, and taxonomy

There is little agreement on the terminology for many practices, disciplines, and traditions, and even less on how they are to be classified: should they be grouped together by history or in terms of allied traditions; according to functional principles; or according to how they are used in relation to 'conventional' medical therapy? Of the various labels such as 'traditional medicine,' 'complementary medicine,' 'alternative medicine' (or what appears to be fashionable in recent years, 'complementary *and* alternative medicine' (CAM)), herbal medicine and so forth, the clearest group is arguably the systems of traditional medicine and bodies of beliefs and perspectives

in relation to healing practiced in South and East Asia. These ancient, yet highly developed, belief systems are so deeply ingrained in the traditions of the relevant societies that they are an integral part of their socio-cultural identities. In any discussion about 'alternative' medicine (in contradistinction to 'conventional' medicine that is practiced and prevalent in developed countries), it bears remembering that these traditional systems of healing practice and beliefs were ancient before the rise of modern 'conventional' medicine following the Industrial Revolution in Europe. They rank among the original medical systems of humankind. They are still referred to by their ancient names in native languages today, such as the Indian *ayurveda*, Korean *hanbang*, or Javanese *jamu*. The name and connotation inevitably loses much of its power when described or directly translated into a Western language, as it is then couched in terms familiar to a Western mind, such as 'Traditional Chinese medicine.'

The starting point of reference for those trained in the prevalent system for healthcare delivery of medical services in developed countries is what has been variously described as 'conventional medicine,' 'orthodox medicine,' 'allopathic medicine,' 'mainstream medicine,' 'biomedicine,' or 'Western medicine,' depending on the comparison (World Health Organization (WHO) 2001: 1–2) sought to be made. This is the dominant system of medicine espoused by public health authorities as the general standard in most countries. A term such as 'conventional medicine' is not free of subjective perspectives, but it is one that most people in developed countries will at least understand as a general concept, even if they are fuzzy on the details. There are variations, however. Health Canada, for example, uses the term 'conventional health care' in contradistinction to 'complementary and alternative health care' (CAHC) (Smith and Simpson 2003: 3–5). In this chapter, we use the term 'conventional medicine' if for no other reason than that it is readily understandable and is recognized as a concept by most in the English-speaking world, even if there is disagreement as to its significance.

The bedrock of conventional medicine is an insistence on the scientific method, and the use of drugs, therapies, and interventions whose safety, efficacy, and effectiveness are backed by empirical data. The touchstone of the scientific method for drugs is the randomized controlled trial (RCT). For the US Department of Health and Human Services, by 'definition, CAM practices are not part of conventional medicine because there is insufficient proof that they are safe and effective' (Barnes *et al*. 2008: 1). For most patients in developed countries, 'conventional medicine' is *the* 'conventional' medicine simply because it is the dominant system of medicine in their national healthcare systems.

If 'conventional medicine' is to be defined largely in terms of its dominance in developed countries, then the prospects for a sound working definition of other systems of practice and beliefs about healing and health are made even more difficult. The main problem in attempting to define all of the therapeutic disciplines and traditions falling outside the scope of conventional medicine is the sheer diversity, range, and heterogeneity of the inquiry. Traditional, complementary, and alternative medicine is simply what conventional medicine is not. Mertz gives a good account of the problem by starting from a negative premise in defining traditional, complementary, and alternative medicine as essentially an 'extensional definition' rather than an 'intensional one' (2007: 329–30). He notes that there are those who consider a universal definition of complementary and alternative medicine as impossible 'because CAM is mainly historically and culturally constituted (a "social construct") like "traditional medicine,"' and that the term must be 'sensitive to the situation in different contexts' (Mertz 2007: 330).

Because conventional medicine dominates in developed countries, and because of the ubiquity of its associated institutional and political structures (such as hospitals, public healthcare systems, healthcare financing systems and professional guilds and associations), critiques of traditional or CAM medicine tend to emerge from the context of the accepted paradigms and

cultural vocabulary of conventional medicine. In practical terms, if proponents of a particular traditional or CAM discipline seek admission or inclusion of their discipline in hospitals or a national healthcare system, justification generally must be made in accordance with the standards and accepted paradigms of conventional medicine.

When the UK House of Lords Select Committee on Science and Technology reported the results of an inquiry on complementary and alternative medicine, it failed to settle on a definition, noting that it was 'beset by questions of definition which are hard to resolve,' and that even the 'CAM community has been struggling for fifteen years to come up with a single definition of CAM agreed by all, but with no success' (2000: paras 1.11–1.13). In the end, the Committee settled on a list of traditional, complementary, and alternative medical therapies or therapeutic disciplines in three broad – and controversial – groupings (2000: paras 2.1–2.3, table 1).[1]

The strained and indefensible result is a classification in which Traditional Chinese medicine and *ayurvedic* medicine are lumped together with crystal therapy, dowsing, and radionics in a catch-all list of three groups under the general rubric 'Alternative Disciplines.' Acupuncture, likewise, is classified under two entirely different groups (House of Lords Select Committee on Science and Technology 2000: paras 2.1–2.3, table 1).

In one influential article presenting data on the use of 'unconventional medicine' in an American mainstream medical journal, it was reported that 34 per cent of respondents to a telephone survey 'reported using at least one unconventional therapy' in 1990, and that 'a third of these saw providers for unconventional therapy' (Eisenberg *et al.* 1993).[2] But an examination of the kinds of 'unconventional therapy' used by the respondents revealed that the most popular included relaxation techniques, massage, imagery, commercial weight loss programs, lifestyle diets (e.g. 'macrobiotics'), megavitamins therapy, and self-help groups – some of which would not generally be considered complementary or alternative medicine (Eisenberg *et al.* 1993: 248). Of the 'mainstream' CAM disciplines, only chiropractic therapy ranked within the top ten, at second place (10 per cent) after relaxation techniques (13 per cent). A report by the Centers for Disease Control and Prevention on the use of CAM in the US in 2007 revealed a different picture – but using a similar approach – and showed that the most commonly used CAM therapies were 'nonvitamin, nonmineral, natural products (17.7%), meditation (9.4%), chiropractic or osteopathic manipulation (8.6%), massage (8.3%), and yoga (6.1%)' (Barnes *et al.* 2008: 3).

The chief consequence of an exclusionary definition is that the lumping together of so many different disciplines, traditions, perspectives, and worldviews under the auspices of traditional or CAM medicine makes it difficult for proponents of individual traditional, or CAM disciplines to mount an effective defense or justification of their own discipline. As a result, disciplines different and unrelated to traditional or CAM medicine are treated as an indivisible whole, when their only source of commonality is that they are all by definition *not* part of conventional medicine.

Whatever the substantive merits of the individual therapeutic philosophies, traditions, and practices that make up traditional medicine and CAM, it is a great disservice to conflate and lump them together. Even from the scientific perspective, or from that of conventional medicine, conflating these two systems has the unfortunate effect of obscuring the objective assessment of the worth of individual disciplines, particularly if both national laws and national public health systems alike apply the same lumping policy. Disentangling the good or worthy from the bad or fraudulent is thereby made so much more difficult.

1 Compare with McIntyre's (2001) critique of the House of Lords Select Committee's Report.

2 As of 25 September 2013, the article had been cited 1,755 times, according to the record of citations on the entry for the article in the *New England Journal of Medicine* – there may be well many more in publications not assayed for the citation record system, particularly in journals outside of the scientific mainstream, or not in English sources.

23.1.2 Functional classifications

What then, might be a better approach? The World Health Organization offers the following somewhat diffident definitions of traditional medicine, complementary medicine, and alternative medicine:

> Traditional medicine is the sum total of the knowledge, skills, and practices based on the theories, beliefs, and experiences indigenous to different cultures, *whether explicable or not*, used in the maintenance of health as well as in the prevention, diagnosis, improvement or treatment of physical and mental illness.
> The terms 'complementary medicine' or 'alternative medicine' are used inter-changeably with traditional medicine in some countries. They refer to a broad set of health care practices that are not part of that country's own tradition and are not integrated into the dominant health care system.
>
> *(2000: 1, emphasis added)*[3]

Careful readers will not have missed the caveat 'whether explicable or not,' gingerly slipped into the middle of the definition of traditional medicine. The import of this will be one of the themes explored later in this chapter. But even within the WHO, the use of these definitions is by no means entirely consistent. In another report published a year later by the WHO, the relationship between traditional, complementary, and alternative medicine was defined in the following terms:

> The terms 'complementary medicine' and 'alternative medicine' are used interchangeably with 'traditional medicine' in some countries. Complementary/alternative medicine often refers to traditional medicine that is practiced in a country but is not part of the country's own traditions. As the terms 'complementary' and 'alternative' suggest, they are sometimes used to refer to health care that is considered supplementary to allopathic medicine. However, this can be misleading. In some countries, the legal standing of complementary/alternative medicine is equivalent to that of allopathic medicine, many practitioners are certified in both complementary/alternative medicine and allopathic medicine, and the primary care provider for many patients is a complementary/alternative practitioner.
>
> *(WHO 2001: 1)*

Nonetheless, the WHO definitions are more nuanced than many used by national agencies in developed countries, which tend to draw a starker distinction between conventional medicine and all other kinds of medical disciplines, traditions, and approaches. A couple of examples of this may be useful. The National Centre for Complementary and Alternative Medicine (NCCAM), part of the National Institutes of Health of the United States Department of Health and Human Services, defines complementary medicine as generally referring 'to a non-mainstream approach *together with* conventional medicine,' while alternative medicine is defined as referring to 'using a non-mainstream approach *in place of* conventional medicine' (2008: 1, emphasis in original).

This perspective is therefore firmly rooted in conventional medicine philosophies, and is entirely consistent with the NCCAM's description of its role as the US 'Federal Government's lead agency for scientific research on health interventions, practices, products, and disciplines

3 These definitions are an elaboration of shorter definitions given in the World Health Organization's *General Guidelines for Methodologies on Research and Evaluation of Traditional Medicine* (2000a).

that originate from outside mainstream medicine' (NCCAM 2008: 4). The same lines are drawn by Health Canada, which defines 'complementary and alternative health care (CAHC)' and 'complementary and alternative medicine' in terms of 'diagnosis, treatment and/or prevention that complements mainstream medicine by contributing to a common whole, by satisfying a demand not met by conventional approaches, or by diversifying the conceptual framework of medicine' (Health Canada 2003: 2).

This different approach to functional classification has its advantages. In developed societies where conventional medicine dominates, it is justifiable to classify the different strands of traditional, complementary, and alternative medicine according to *how they are used by persons seeking healthcare*, rather than according to the substantive worth of each based on the standards and paradigms of conventional medicine. This approach does of course run the danger of being turned on its head in some Third World countries where traditional, complementary, and alternative medicine may be the only or main form of medical services of any kind available to the overwhelming majority (see below for a fuller discussion). That being said, it may be argued that the proposed approach nonetheless holds true even for these countries, because the national public health authorities are likely to accept the same conventional medicine-centric approach to public health policies. More fundamentally, conventional medicine is likely to be sought after as the preferred kind of healthcare, even by people who cannot afford it.

This functional approach to classification also makes the distinction between traditional, complementary, and alternative medicine disciplines clear. A valid criticism of this approach, however, is that classification by function in relation to conventional medicine can also be used to carve up the whole in different and self-contradictory ways. For example, it is entirely possible for a discipline like Traditional Chinese medicine to be regarded (not necessarily by the same users) as traditional medicine, as well as complementary medicine, or alternative medicine.

So generalizations must be accepted – the reality is that in most developed countries, all three non-conventional approaches are often readily available, in addition to conventional medicine, as a matter of choice for the consumer. Most consumers accept the dominant role of conventional medicine: the use of alternative medicine to the exclusion of conventional medicine (where the latter is readily available) is rare. Most patients in developed countries choose conventional medicine as their main medical resource, and use traditional, complementary, or alternative medicine as adjuncts (NCCAM 2008: 1; Eisenberg *et al.* 1993: 249; Druss and Rosenheck 1999). Healthcare consumers may be more critical in making choices than was previously assumed, as they select from both conventional and 'unconventional' medicine according to their personal assessment of the most effective therapies. They may not know, or are indifferent, to debates about classification, but many consumers are aware of what services are offered by each discipline, and how they align with their personal preferences. As a result, 'alternative' systems of medicine are perhaps best regarded not as parallel systems to conventional medicine (few alternative medicine disciplines would claim this), but as alternative solutions for specific health problems.

23.1.3 Assimilation

But classifications can also change over time. One notable phenomenon is the tendency of the more popular strands of traditional, complementary, or alternative medicine to be assimilated or integrated into the accepted body of conventional medicine. They become so mainstream that they cease by definition to be merely complementary or alternative, and become part of the conventional. In some societies, this occurs as a result of explicit national policies directed at the integration of conventional and traditional medicine indigenous to that particular culture or society (such as Traditional Chinese medicine in China, or *hanbang* traditional medicine in

South Korea). In others, particularly in the West, the process of assimilation and integration is usually somewhat more fiercely confrontational:

> Historically, orthodox medicine fights these practices vigorously by denouncing and attacking them, restricting access to them, labeling them as antiscientific and quackery, and imposing penalties for practicing them. When these therapies persist and even rise in popularity despite this, mainstream medicine then turns more friendly, examining them, identifying similarities they have with the orthodox, and incorporating or 'integrating' them into the routine practice of medicine … Today the overwhelming effort is towards attempts at 'integrating' alternative medicine into the mainstream.
>
> *(Jonas 1998: 1616)*

Nonetheless, the result is the same. In China, public health bodies deliver an integrated form of conventional and Traditional Chinese medicine (especially specific subdisciplines such as acupuncture, which have also gained a foothold in the West and in some Asian countries). In the West, disciplines such as chiropractic, osteopathy, and homeopathy have been partially integrated into national health systems, especially in Europe, and notably in Germany. An assessment of how these formerly 'alternative' or 'complementary' disciplines may have been affected or changed by their assimilation into the mainstream has yet to be explored. The answer to this question will be of great relevance and interest to those disciplines still excluded from the conventional medicine classification.

23.2 Patterns of use

23.2.1 Developing countries

The WHO offers a sobering reminder that for a large proportion of humankind, traditional and CAM medicine is not just only the main form of medicine, but it is essentially the *only* kind of primary medical care readily available. It estimates that '80% of the population living in rural areas in developing countries depend on traditional medicine for their health care needs' (WHO Regional Office for Africa 2000a), although commentators note that the WHO has 'since backed away from the 80% estimate, settling for the safer position that most of the population of most developing countries regularly use traditional medicine' (Bodeker 2001: 164). This does not detract from the conclusion that for most of the developing world, only a minority has access to conventional medicine. The WHO Regional Committee for Africa reports that the 'African Region is facing difficulties in ensuring equitable access to health care and only about half the population in the Region have access to formal health services' (WHO Regional Office for Africa 2000b: 164). However, its recommendation for the integration of traditional medicine into national health systems for their improvement should not be necessarily viewed as the counsel of desperation, for as the Report observes, 'traditional medicine … maintains its popularity for historic and cultural reasons' (2000b: 2).

Nevertheless, there is no denying that in developing countries, there is often a very strong correlation between poverty and the use of traditional medicine. A report (referred to in this chapter as the 'WHO Strategy Report') prepared for the WHO in 2002 offers valuable insights into the pattern of use of traditional medicine and CAM around the world (WHO 2002). It highlights that traditional medicine is often the only kind of medicine available to the poorest. Conventional medicine is expensive in terms of required skills, infrastructure and equipment, and drugs. It is not surprising, therefore, that in countries like Tanzania, Uganda, and Zambia, the

ratio of traditional medicine practitioners to patients is in the order of 1 : 200–400. In contrast, the ratio of conventional medicine practitioners in those countries is 'typically 1 : 20,000 or less,' most of whom tend to practice in urban areas, further disadvantaging the patient majorities living in rural areas (WHO 2002: 12). A 1987 paper estimated that only roughly 20 per cent of the health services in Nigeria (by far the most populous country in Africa) were located in rural areas (Chiwuzie *et al.*). Nor is this picture confined to Africa. For more than half of India's population, traditional medicine is the only healthcare available (Chiwuzie *et al.* 1987: 13). For poor people in developing rural areas, the choice of healthcare systems is constrained simply by the cost and unavailability (two mutually reinforcing factors) of conventional medicine. Traditional medicine is much cheaper, its practitioners more numerous, and its methods and principles are culturally familiar.

23.2.2 Developed countries

But what if cost and availability were less of an issue, or not an issue at all? The experience of developed countries with national universal healthcare systems provides an interesting contrast. It might be assumed that the same correlation between poverty and the use of traditional medicine and CAM might also hold true in the developed world. Not so. In fact, 'virtually all surveys' in this area show the opposite correlation: economically better-off and better-educated people tend to use *more* traditional medicine (or CAM), not less (Ernst *et al.* 2004). In 1990, Eisenberg *et al.* reported that the highest use of 'unconventional medicine' in the United States was among 'non-black persons from 25 to 49 years of age who had relatively more education and higher income' (1993: 246–8, table 1). Barnes *et al.* reported that, 'consistent with results from the 2002 NHIS [National Health Interview Survey], in 2007 CAM use was more prevalent among women, adults aged 30–69, adults with higher levels of education, [and] adults who were not poor' (2008: 4 and 14–16). However, the authors do note that where worry about costs delayed access to conventional medicine, or when respondents were simply unable to afford conventional care, then the respondents were more likely to resort to CAM than if cost or affordability were not a concern (Barnes *et al.* 2008: 5). This positive correlation between education, income, and use of CAM also holds true in Canada: in 1998–9, the use of 'alternative practitioners' rose in a linear relationship with education, from 12 per cent of adults with less than high school education to 20 per cent of those with a college or university education (Millar 2001: table 3).

One simple explanation for this apparent contradiction in the data may be that in developed countries, access to traditional medicine or CAM is generally restricted (or not available at all) under universal healthcare programs, or is similarly limited or restricted under private health care insurance. This means that if patients want traditional medicine or CAM, they will have to pay out of their own pockets for such services (Millar 2001: 17). Likewise, if a patient has inadequate coverage for conventional medicine under public healthcare or private insurance, the obvious alternatives are traditional medicine, or CAM, or simply self-medication with over-the-counter herbal remedies.

Practitioners of conventional medicine may be surprised by the frequency of use of traditional medicine and CAM in the West. The United States witnessed an increase in these levels over the last two decades. In 1990, 34 per cent of survey respondents used at least one unconventional therapy. By 2007, this percentage rose to nearly 40 per cent (four in ten adults) (Eisenberg *et al.* 1993: 246–8, table 2; Barnes *et al.* 2008, table 1; NCCAM 2008: 1). In 2002, the WHO offered the following estimates for the percentage of the 'population who had used

CAM at least once in selected developed countries': 31 per cent for Belgium, 42 per cent for the US, 48 per cent for Australia, 49 per cent for France, and 70 per cent for Canada (p. 11).

The data, of course, is not all strictly comparable. For instance, the data provided by Eisenberg *et al.* and Barnes *et al.* relate to different years. There is also no consensus between the various studies and national agencies as to what falls within the classification of traditional medicine or CAM. In Canada, it emerges that high utilization rates are at least in part due to the inclusion of the use of 'natural health products' (NHPs) regulated under the *Natural Health Products Regulations* 2004 – including vitamins – which many traditional medicine and CAM practitioners would regard as alien to their own traditions and disciplines (regulation 1, schedule 1). If access to traditional medicine or CAM is defined in terms of actual consultations with alternative medicine practitioners, then the rate of use drops to between 17 and 22 per cent, depending on the time frame of the survey. Annual surveys present challenges in capturing the episodic nature of medical needs, as people may not feel the need to resort to CAM services (or indeed, conventional medicine services) at all in any given year (Millar 2001: 12–13).

23.2.3 Balance between traditional and non-traditional medicine

The pattern of use of traditional medicine and CAM in developed countries also differs significantly from that in developing countries. Whereas developing countries tend to favor traditional medicine and traditional herbal remedies, users of CAM in developed countries (and particularly in Western Europe) tend to especially favor non-traditional CAM disciplines such as chiropractic, homeopathic, and osteopathic medicine. These are relatively new disciplines, which have developed in parallel to modern conventional medicine and have, in many developed countries, become at least partially integrated into national healthcare systems. The singular exception to this preference for relatively new and non-traditional medicine in developed countries is acupuncture. According to WHO reports, developed countries with state-sponsored traditional medicine or CAM include Japan, Australia, Germany, Norway, the United Kingdom, Canada, and the United States (WHO 2002: table 3). A further survey of the degree to which traditional medicine or CAM is integrated or included within national health systems is presented below.

23.2.4 Migrant populations in the developed world

An interesting question is what happens when people migrate from lower-income, less-developed countries with strong traditions of traditional medicine to developed countries with universal public healthcare systems. Does their pattern of use and preference change? This question forms the basis for substantiating the claim that people make do with traditional medicine or CAM when they have no choice, but abandon it when given ready access to conventional medicine. The empirical evidence is that the answer to this question is a particularly complex one.

A study of Korean migrants to the United States showed that only half (53.7 per cent) used conventional medicine exclusively. More than a quarter (26.3 per cent) reported that they used both conventional medicine and traditional Korean *hanbang* medicine; a very small minority (3.9 per cent) opted exclusively for traditional medicine; and a larger group (16.1 per cent) reported that they did not require any medical attention within the last six months (Kim *et al.* 2002: 115). The authors observed that for elderly Korean Americans who used both systems, traditional medicine did not play a central role, but assumed a complementary one to conventional

medicine (Kim *et al.* 2002: 118). This demonstration of loyalty to traditional medicine and its complementary role to conventional medicine are also confirmed in separate studies of migrant Korean populations in Australia (Han and Ballis 2007). In both studies, the authors identified one fundamental difference between providers of traditional medicine and those of conventional medicine. Patients report spending far more time in clinical consultation with the traditional medicine provider than with the conventional medicine provider.

In contrast, the rates of utilization of Traditional Chinese medicine by ethnic Chinese immigrants from China, Hong Kong, Taiwan, and Southeast Asian countries are much higher. In a small study of ethnic Chinese immigrants in Houston and Los Angeles, less than half (44 per cent) of the respondents reported using conventional medicine within 12 months of landing in America. Twenty per cent of the respondents never resorted to conventional medicine in the US at all, with a remarkable 32 per cent having sought medical care in China or Taiwan within the last two years (Ma 1999: 429, table 3). A quarter (25.3 per cent) used Traditional Chinese medicine clinics as their primary medical providers, compared to 21.3 per cent who used conventional medicine clinics, while 45.3 per cent used both conventional medicine health facilities as well as Traditional Chinese medicine clinics (Ma 1999: 429–30).

Broadly, the same conclusions were drawn from a larger study of 2,167 elderly ethnic Chinese immigrants in seven Canadian cities, with over two-thirds (65.4 per cent) reporting the use of Traditional Chinese medicine in combination with conventional medicine, and 32.5 per cent reporting the use of conventional medicine only (Lai and Chappell 2007: 61). Over half (50.7 per cent) used over-the-counter Chinese herbs, while slightly fewer (49.1 per cent) used processed Chinese herbal formulas in pill or powder form. But there were markedly fewer reported consultations with Traditional Chinese medicine practitioners, with herbalists (24.1 per cent) and acupuncturists (8.3 per cent) being the most popular (Lai and Chappell 2007: 61). An interesting finding of this study was that despite the fact that no less than 96.8 per cent of the respondents reported that they had a conventional medicine family physician they could consult, as many as two of three older Chinese immigrants still resorted to Traditional Chinese medicine (Lai and Chappell 2007: 62).

While accepting the dominant role of conventional medicine, immigrant ethnic Chinese patients often appear to regard conventional medicine as not being complete on its own. This attitude further underlines the complementary 'holistic health' function that users of traditional medicine seem to especially value (Ma 1999: 432; Kim *et al.* 2002: 118).[4] For conventional medicine healthcare providers treating such populations, these conclusions have practical implications. What might be the cultural expectations of the patients? What might they feel is missing from the services that conventional medicine providers offer? And, importantly, what kind of traditional Chinese medication or herbal remedies might such patients use concurrently with their conventional medicine prescriptions? What are the risks and implications of adverse interactions between these two completely different medicinal regimes (Lai and Chappell 2007: 62–3)?

Finally, the legal, ethical, and social paradigm of conventional medicine is focused mostly on the individual and on individual autonomy. The Western conception of autonomy dictates that an individual adult patient make decisions for her or himself. Only when the patient is incompetent to make clinical decisions do proxies and families weigh in on the decision, particularly at the end of life. But this approach may be less applicable in communitarian Asian cultures, as many traditional medicine practices allow for greater familial participation in decision-making, and the role and influence of the family may loom larger (Rhodes *et al.* 2008).

4 Han and Ballis (2007) observe that 'complementary medicine thrives and expands in the gaps of conventional medicine' (Conclusion, para. 1).

23.3 Approaches to legal regulation: toleration, inclusion, or integration?

23.3.1 Models

There is a paucity of empirical and comparative data on the use of traditional medicine and CAM globally. There is even less comparative data on the kinds of regulatory or legal regimes under which traditional medicine and CAM must operate in different countries. This is not surprising, given the scope of the inquiry. Again, the lack of consensus on common terminology precludes this systematic investigation. The experience of the Association of South East Asian Nations (ASEAN) regional bloc of countries is instructive. Despite the close proximity of its member nations, their common historical ties, and ancient traditions of reliance on traditional medicine (especially traditional herbal medicine), terminology remains a challenge. In an attempt to harmonize the regulation of traditional medicine and health supplements among member countries, the regional bloc initiated a project to establish common terminology (ASEAN Consultative Committee for Standards and Quality (ACCSQ) Product Working Group on Traditional Medicines and Health Supplements 2006).

In a series of papers, the World Health Organization surveyed the international regulatory landscape on the use of traditional medicine and CAM in countries around the world. Several documents in this series are noteworthy: the aforementioned WHO Strategy Report (2002), the WHO's 'Regulatory Situation of Herbal Medicines: A Worldwide Review' (Herbal Medicine Review) (1998) and the WHO's 'Legal Status of Traditional Medicine and Complementary/Alternative Medicine: A Worldwide Review' (TCAM Review) (2001). These documents form the basis for the general survey of traditional medicine and CAM patterns of use internationally.

23.3.2 The principle of respect for traditional medicine

Politically at least, the international community has committed itself to the principle of respect for traditional medicine. In 2008, the WHO Congress adopted the *Beijing Declaration*, declaring that 'knowledge of traditional medicine, treatments and practices should be respected, preserved, promoted and communicated widely and appropriately based on the circumstances in each country' (article 1). Subsequently, the World Health Assembly (the governing body of the WHO) passed a resolution urging member states to adopt and implement the principles of the *Beijing Declaration* (WHO Congress on Traditional Medicine 2008).

Various approaches have been proposed for the classification of regulatory responses to traditional medicine.[5] One useful approach is to define what the WHO Strategy Report maintains are the 'three types of health systems to describe the degree to which TM/CAM is an officially recognized element of health care' (2002: 8–12, tables 2–3). The underlying premise is, of course, that *all* member states already acknowledge the centrality of conventional medicine in public healthcare policy. Thus the only question is to what extent, and how, traditional medicine and CAM are to be regarded – if they are to be permitted at all – within the dominant conventional medicine framework. But the documents seem to effectively give member states interpretive flexibility with qualifying phrases such as 'in accordance with national capacities, priorities, relevant legislation and circumstances' (World Health Assembly 2009, resolution 1(1)) and 'appropriately based on the circumstances in each country' (WHO Congress on Traditional Medicine 2008, declaration 1). The injunction to 'consider, where appropriate,' the inclusion of traditional

5 A useful analysis may be found in Gray's 'Four Perspectives on Unconventional Therapies' (1998).

medicine into national health systems is carefully qualified by the phrase 'on the evidence of safety, efficacy and quality' (World Health Assembly 2009, resolution 1(4)).

The WHO Strategy Report categorizes the responses of governments and national public health authorities into three general groups: integrative systems, inclusive systems, and tolerant systems (2002). These categories are not mutually exclusive, and necessarily overlap to some extent. Individual countries may also incorporate specific elements within the broader traditional medicine and CAM disciplines. For instance, some countries may integrate chiropractic, osteopathy, and homeopathy, but merely tolerate traditional medicine. Again, caution must be exercised against conflating every known 'unconventional' discipline or practice into a single category of 'unconventional' medicine.

23.3.3 Integrative systems

In *integrative systems*, 'TM/CAM is officially recognized and incorporated into all areas of health care provision' (WHO 2002: 8.). This means that the *particular* traditional medicine or CAM discipline which has been approved is fully integrated into national healthcare systems. They are treated as aspects or approaches to medical care in much the same manner as conventional medicine, and national healthcare systems dispense both kinds of medical treatment. The practical effect is at least some blurring of the distinction between the two. Both systems of medicine are given co-equal status. The approved traditional medicine discipline is formally regulated, and the state funds training and research. But the WHO concedes that true integration is rare: only China, North Korea, and Vietnam satisfy this definition (2002: 9, table 2). Significantly, all three jurisdictions integrate only one single discipline – traditional medicine based on or derived from the corpus of Traditional Chinese medicine – including traditional herbal medicine and acupuncture. These countries effectively elect to admit only their own indigenous medical traditions into the body of conventional medicine. The regulatory responses of several Asian societies (including China) with dominantly ethnic Chinese populations to Traditional Chinese medicine will be examined further as a case study.

23.3.4 Inclusive systems

In *inclusive systems*, conventional medicine is dominant, but legal or executive provision is made at governmental levels for some degree of accommodation of traditional medicine or CAM disciplines or practices. This seems to be the predominant model reported by the WHO for countries that permit traditional medicine or CAM a role in national healthcare systems (WHO 2001).

It is striking that both developing and developed countries apply this model, but in different ways. Developing countries tend to apply this model in the context of the inclusion or integration of indigenous traditional medicine. In contrast, developed countries use it to include either elements or entire disciplines of non-traditional complementary or alternative medicine from relatively recent origins (post-Industrial Revolution) such as chiropractic, osteopathy, and homeopathy. In this category, too, are 'natural health products,' as is the case in Canada.

The WHO notes, 'in many developed countries, certain CAM therapies are very popular … the percentage of the population that has used CAM is 46% in Australia, 49% in France and 70% in Canada' (2002: 11). In some developed countries, there is a surprising degree of CAM inclusion. Nearly 46 per cent of Swiss doctors responded positively to a survey when asked 'Avez-vous déjà utilisé des médecines alternatives pour vous-même?' Of these, 55 per cent used homeopathy and 45 per cent acupuncture (Domenighetti *et al.* 2000). The separation out of the subdiscipline

of acupuncture from the general body of Traditional Chinese medicine and its adoption in at least 78 countries by the year 2000 is especially remarkable – the areas from which the practice of acupuncture is most conspicuously absent are not in the developed world, but in Africa and the Middle East (WHO 2002: figure 4).

23.3.5 Tolerant systems

The last category, which the WHO diplomatically refers to as *tolerant systems*, comprises countries in which conventional medicine is exclusively and legally dominant, but in which 'some TM/CAM practices are tolerated by law' (WHO 2002: 9). The WHO does not provide any examples and is silent on a logical fourth category, which would include countries that do not tolerate any form of traditional medicine or CAM at all.

23.3.6 Case study: China, Hong Kong, and Singapore

In this section, we examine how the integration and inclusion models of the WHO are applied in three predominantly ethnic Han Chinese populations in three jurisdictions (China, Singapore, and Hong Kong)[6] in determining how ancient systems of traditional medicine are integrated, assimilated or otherwise accommodated within their respective national healthcare infrastructures. These jurisdictions offer useful insights for countries (particularly developing ones) seeking to accommodate indigenous traditional medicine.

23.3.6.1 China

A pedigree of over 2,000 years is claimed for the body of Traditional Chinese medicine (TCM), with literature in the field dating from *c.*220 BCE, and with the first TCM school being founded in China in 624 CE (WHO 2010).[7] However, the current form of TCM's co-existence and close integration with conventional medicine in China dates back only to the postwar period. The Chinese government implemented policies that integrated all available medical resources – including TCM – into the national healthcare system. An early Western observer noted in 1971 that, among the major changes brought about by the Chinese government in the wake of the Cultural Revolution, 'was the requirement that *Western* or modern medicine as we know it must be fully integrated with *traditional* Chinese medicine' and that 'fully 90% of the medical care is dispensed through the traditional system' (Dimond 1971: 1558). This integration came about with the establishment of modern China's most famous icon of their postwar medical revolution: the barefoot doctor.[8]

6 Hong Kong is politically a part of China. Formerly a British Crown Colony, Hong Kong has since 1997 been a Special Administrative Region (SAR) of China when it reverted to the sovereignty of China, but retains considerable autonomy in its self-governance, with the exception of defense and foreign relations, in accordance with its constitutional framework guaranteed under the Basic Law. Also formerly a British Crown colony, Singapore has been an independent country since 1965.

7 The WHO is not entirely consistent. It states elsewhere that the earliest records of TCM date back to the eighth century BCE (2001: 2). A bolder statement is made by the US Department of Health and Human Services' NCCAM, which states that TCM is 'rooted in the ancient philosophy of Taoism and dates back more than 5,000 years' (2009: 1). The basis for this assertion is unclear, given that Laozi 老子, generally regarded as the founder of Taoism, lived (assuming that he was in fact a historical figure) no earlier than the sixth century BCE.

8 A recent account of China's barefoot doctor may be found in Zhang and Unschuld (2008). For a description of the organization of primary healthcare in rural China in the 1970s, and of the social context in which the barefoot doctors operated in a system that closely integrated conventional medicine and TCM, see Chen and Tuan (1983).

These barefoot doctors were essentially paramedics with no more than a secondary school education (Chen and Tuan 1983: 1412). Barefoot doctors were given medical training at the county or community hospital level for between three to six months, and largely took the place of physicians trained in conventional medicine in rural areas. They were by far the dominant (and often sole) providers of primary medical care to rural populations in China for over two decades, dispensing integrated medicine unique to China.[9] By 2002, the WHO Strategy Report estimated that over a half million Traditional Chinese medicine doctors and an additional 72,000 associate TCM doctors and 83,000 TCM pharmacists were practicing in China (2002: table 2). The equal status of conventional medicine and TCM is now enshrined in article 21 of China's *Constitution* 1982, which provides that:

> The State develops medical and health services, promotes modern medicine and traditional Chinese medicine, encourages and supports the setting up of various medical and health facilities by the rural economic collectives, State enterprises and institutions and neighborhood organizations, and promotes health and sanitation activities of a mass character, all for the protection of the people's health.

A full account of the regulatory mechanisms and participating institutions of this integration is given in the WHO TCAM Report (2001: 148–52). Among its salient features is a national system of professional training, education, and accreditation for TCM practitioners. As health services move toward consumer-centered systems, insurance covers both TCM as well as conventional medicine services (WHO 2001: 152).[10] The barefoot doctors and state-ordained integration of TCM and conventional medicine was born out of necessity as a result of the shortage in conventional medicine doctors, particularly in rural areas. Given the fundamental differences in the philosophical bases of the two systems, tensions inevitably arise (Skolnick 1996).

But perhaps the true significance of China's program and policy of integration from a historical context may lie not so much with the integration of conventional medicine and TCM, but the institutionalization, formalization, and regulation of TCM at every level of the organization of the state. Whereas historically TCM has generally been practiced at the level of consumers by individual practitioners with no tradition of any professional peer organization (beyond that of master and disciple in the transmission of knowledge and skills), each generally practicing on their own and for their own account, the paradigm of the organization of TCM has shifted in most countries to a completely different but very familiar model: organized conventional medicine (Wang 2011a). What effect this drawing of a traditional medicine discipline into a formal centralized hierarchy of state regulation and control may have on its development is not yet clear, and may not be known until many years down the road.

In traditional medicine systems, the individual practitioner, whether *sinseh*, *guru*, or traditional healer, is respected for her or his spiritual and professional achievements and skills, and not because she or he holds a particular position in a state system. The 'guild' model of organization of conventional medicine with its origins in the guilds of medieval Europe is in many respects antithetical to those traditional medicine cultures that celebrate the skilled individual healer. In the rush towards a centralized and formalized system, bodies of traditional beliefs may become distorted, or inconvenient aspects or branches allowed to wither. This is a consideration that

9 It was only in January 1985 that the term 'barefoot doctors' was abolished – they were renamed 'countryside doctors' if they passed a qualifying examination, or 'health aides' if they failed (Cheng 1988; WHO 2008).

10 Which is only practical, given that the services are integrated. It would be difficult to dissociate costs attributable to one or the other from each other.

should not be ignored by international agencies in their push towards the 'capture' of traditional medical systems.

23.3.6.2 Hong Kong and Singapore

If the story in China is one of determined, and largely successful, integration (if evaluated from an organizational perspective), the situations of Hong Kong and Singapore may well be described as cautious moves towards inclusion rather than full integration, and differ from China in two critical respects. The first is in population demographics: 100 per cent of the population in Hong Kong and Singapore is urban, compared to China's 50.6 per cent, and both jurisdictions host some of the highest population densities in the world (UN Department of Economic and Social Affairs 2011). Second, both jurisdictions have highly developed economies with high levels of human development. Nominal GDP per capita in 2012 reached US$36,667 (Hong Kong) and US$51,161 (Singapore), compared to China's US$6,075. In comparison, the figures for the United Kingdom and the United States are US$38,588 and US$49,922 respectively (International Monetary Fund 2013). Given their state of economic development, both Hong Kong and Singapore have highly developed national healthcare delivery systems which, until recently, were largely dominated by conventional medicine. Moreover, the statutory regulatory regimes in both jurisdictions mainly addressed the organization of conventional medicine.

In the case of Hong Kong, the place of TCM is protected and enshrined in article 138 of its Basic Law Constitution, a provision clearly modeled on that of its parent jurisdiction, China:

> The Government of the Hong Kong Special Administrative Region shall, on its own, formulate policies to develop Western and traditional Chinese medicine and to improve medical and health services. Community organizations and individuals may provide various medical and health services in accordance with law.

The inclusion of the directive '*shall*, on its own,' in the imperative mood is perhaps significant. It makes clear that, whatever the antecedents or model for the provision, Hong Kong is free to develop its own health policies independently of China. A British Crown Colony until 1997, when it reverted to the sovereignty of China, Hong Kong was not affected by China's push towards the integration of TCM and conventional medicine. Under the *Chinese Medicine Ordinance*[11] 1999, comprehensive legislation governing TCM was enacted. The *Ordinance* provided for the establishment of the Chinese Medicine Council which was given regulatory oversight of, among other things, the registration of Chinese medicine practitioners loosely based on the model established for conventional medicine practitioners in Hong Kong. The *Ordinance* provides that no person shall be entitled to recover in court any fees or charges for TCM consultations, services or herbal medicines unless the person is registered under the *Ordinance* (section 76). Those unable to meet the registration requirements are therefore marginalized in the new system (Wang 2011b).[12] At the practical level, a significant inducement for members of

11 The long title of the *Ordinance* is *An Ordinance to make provision for the registration of practitioners in Chinese medicine; the licensing of traders in Chinese medicine; the registration of proprietary Chinese medicines; and other related matters*.

12 There are grandfather clauses: section 90 of the *Chinese Medicine Ordinance* makes provision for a TCM practitioner to be a 'listed Chinese medicine practitioner' and to use the title of 'Chinese medicine practitioner' or its equivalent in the Chinese language if he was practicing TCM on 3 January 2000, while sections 92 and 93 provide for exceptions to be made in particular cases to the Licensing Examination requirement for qualification as a registered Chinese medical practitioner (effectively the 'full registration' status under the Ordinance), notably on the basis that the applicant has practiced TCM in Hong Kong for a continuous period of 15 years or more prior to 3 January 2000.

the public to consult only registered TCM practitioners is the fact that medical certificates for sick leave issued by registered TCM practitioners are to be accepted by employers in Hong Kong on the same basis as those issued by conventional medicine practitioners (*Employment Ordinance*, section 33).

The situation in Singapore is somewhat different: a different model of accommodation is adopted compared to Hong Kong's. Instead of aiming for broad inclusion, the legislative approach in Singapore is targeted at bringing in specific subdisciplines of the larger body of TCM one by one into a framework of compulsory registration, much as is required for conventional medicine practitioners. Under section 14(1) of the *Traditional Chinese Medicine Practitioners Act* 2000 (TCM Act):

> [the] Minister may … declare any type of practice of traditional Chinese medicine as a prescribed practice of traditional Chinese medicine if he is of the opinion that it is in the public interest for that type of practice of traditional Chinese medicine to be regulated under this Act.

To date, only two TCM activities have been declared under the regulatory remit of the TCM Act: acupuncture, and acting as a TCM physician.[13]

Despite very high incomes and the universal availability to Singapore citizens of high-quality conventional medicine healthcare services, the level of public support for TCM remains high. The estimate given in the Singapore Parliament on the Second Reading of the Bill for the TCM Act was that about 45 per cent of the population had at some time or other consulted a TCM practitioner. The statement was also made that there 'is also the popular belief that TCM is milder and has fewer side effects, thus making it a preferred modality among older persons. As the population in Singapore ages, it is likely that there would be an increased demand for TCM treatment' (Singapore Parliamentary Reports 2011: col. 1126).[14]

The rationale given by the Singapore Ministry of Health for starting first with the regulation of acupuncture under the TCM Act was that:

> [A]cupuncture is an invasive procedure that carries risks of injury and infection. It is estimated that there are about 1,070 acupuncturists in Singapore. This will then be followed by the registration of TCM general practitioners in about 3 to 4 years' time, and the TCM herbal dispensers at a later date.
>
> *(Singapore Parliamentary Reports 2011: col. 1128)*

The registry excludes, however, TCM herbalists and herbal dispensers who are widely favored by Chinese in Singapore. It is relatively common for Singaporeans to purchase herbal medicine over the counter (Singapore Parliamentary Reports 2011: col. 1133). Most Chinese medicine shops (or 'medical halls,' as they are known in Singapore) are small, family-run businesses, and are found in all parts of the country. Imposing registration requirements would effectively prohibit Chinese

13 The specific content of the prescribed TCM practice includes '(b) the diagnosis, treatment, prevention or alleviation of any disease or any symptom of a disease or the prescription of any herbal medicine on the basis of traditional Chinese medicine, and (c) the regulation of the functional states on the basis of traditional Chinese medicine' (*The Traditional Chinese Medicine Practitioners (Prescribed Practices of Traditional Chinese Medicine) (Consolidation) Order*, 01, GN No. S63/2001).

14 An assumption not as unwarranted as it may seem to proponents of conventional medicine, given reports that adverse drug reactions may have ranked between the fourth and sixth leading causes of death in the United States in 1994 (Lazarou *et al.* 1998; Bates 1998).

medicine shops from selling traditional Chinese herbs without properly registering their herbal dispensers. Assuming that there would be sufficient registered herbal dispensers to meet the demand, or that a majority of the medical halls could afford to employ one, registration requirements would significantly increase prices for loyal consumers, which is most likely why herbal dispensers have so far been exempt from the obligatory registration stipulated in the TCM Act.

In all three jurisdictions, there is a common theme of traditional Chinese medicine being drawn into the fabric of a formal structure of centralized state regulation. In the case of China, this has resulted in the integration of TCM and conventional medicine as co-equal systems of medicine (at least from the political policy perspective), while Hong Kong appears to be moving towards integration much more cautiously with more carrot than stick in its attempts to raise the general standards of the TCM community, and by establishing a universal legal framework for TCM. But a vital difference between China's and Hong Kong's systems is that the intent and effect of the regulatory framework for TCM is to set TCM up as a parallel (or alternative) system of medicine, and not so much to integrate TCM with conventional medicine. One advantage of such a dual system is that patients can continue to choose services from two distinct and independent systems.

The parallel system approach from Hong Kong is mirrored in Singapore. There remains, however, some reluctance in Singapore to give TCM practitioners a status equal to that of practitioners of conventional medicine. Unlike China and Hong Kong, no special constitutional protection is afforded to Traditional Chinese medicine in Singapore. In the same Parliamentary session discussed above, there was some debate about whether employers (especially government departments, agencies and schools) should recognize medical leave certificates issued by registered TCM practitioners. The government accepted that it was not prepared to recognize such certificates issued by TCM practitioners, and this decision holds today (Singapore Parliamentary Reports 2011: cols 1141–2).[15] As a result, TCM practitioners are severely disadvantaged, for, in effect, a patient who feels unwell enough to require sick leave must consult a conventional medicine practitioner in order to legitimize their leave.

23.4 Ethics

23.4.1 The perspective of ethical judgment

This most difficult part has been left for last. There is an abundance of serious and important issues requiring urgent resolution. None admit of an easy solution. Within the perspective of conventional medicine, moral judgments have to be made in relation to choices of courses of action. These judgments apply only to human conduct: it is misconceived to speak of particular drugs or kinds of treatment as being 'unethical.' The drugs or treatment cannot have any moral content in themselves. Moral judgment can only attach to what people do or want to do with them. Within the context of conventional medicine, it is customary to examine the moral content of decisions made by physicians and other healthcare providers. But even in such a system, physicians are not the only ones responsible for ethical decision-making. Others have responsibility for making moral judgments too, particularly the patient. In the context of traditional medicine or CAM, these responsibilities (and rights) in ethical judgment may have to be (or are customarily) articulated according to different paradigms, particularly those that focus not so much on the individual alone, but on the individual as a person inextricably connected and

15 There is no provision equivalent to that in section 33 of Hong Kong's *Employment Ordinance* 1997, nor is there any specific constitutional guarantee relating to TCM or traditional medicine.

bound to the context of her or his family or community. So it is in the context of some societies, particular Asian ones, that the family may have a prominent role. And finally, over larger issues that affect all, the state, too, necessarily occupies a role that cannot be delegated.

In the medical literature of the West and developed countries, there is no shortage of commentators offering insights and proposals on the kind of value system that ought to be applied in making such ethical judgments in the context of the practice of traditional medicine or CAM. Unsurprisingly, most of these commentaries focus on the moral and ethical obligations of the physician or practitioner, although she or he is but one of the two parties in the physician–patient relationship. There is much less examination of the process of ethical decision-making by patients, or the ethical values to be applied from the patient's perspective. There is even less on ethical judgments by the family, which is not surprising given its relegation to the utter margins by most legal systems in developed countries in the name of individual autonomy, except at the end of life, when there is often a decisional vacuum. Patients and families do not generally write articles on ethics and decision-making in medical care. So it is important when examining the literature on medical ethics to bear in mind the inevitably distorted perspective of the lens applied by many contributors in the arena of medical ethics.

In the assessment of ethical issues in relation to traditional medicine and CAM, ethical judgment acquires an added dimension. The fundamental question is from whose perspective ethical judgment is to be made. Or, to put it another way, the question is: from whose perspective or according to which system of medicine should ethical judgment be made? In the medical and ethical literature of the Western world, and certainly of that in the English language, the predominant perspective is naturally that of its dominant system of medicine, conventional medicine.

This is not unnatural. Indeed, it would be unnatural if it were otherwise. The difficulty is, of course, that in a human world, there can be no such thing as a truly objective and neutral perspective from which to make ethical judgments. Judgments must be made on the basis of one set of values or another. Conventional medicine champions science and its methods as the touchstone for truth, but even the most cursory reflection will reveal that even in the most developed countries, there is no social consensus that science and its methods have any particular monopoly on immutable truths, let alone the higher ones. It is sufficient to remind physicians working in the famous hospitals originally established by religious foundations (and perhaps still run by them) of their antecedents. And there may still be a place in these institutions for a chapel or a place for quiet reflection, and for the appointment of chaplains and other religious advisors.[16] For many people, there is no particular difficulty in accepting a perspective that admits a plurality of systems that deal with different kinds of truth: one might look to science for insights into the laws of the natural world, but one might equally look to religious convictions for insight. Even doctors and scientists are permitted to believe in both.

23.4.2 Values in ethical judgment

The usual approach of commentators on ethical judgment in traditional medicine or in CAM is to extrapolate from their own perspectives and to apply the body of fundamental values applied in their own tradition. In most cases, this will be one flavor or another of the Belmont Principles

16 It is instructive to note how 'prayer' is treated by Eisenberg *et al*. in their seminal survey of the use of 'unconventional medicine' in the US in 1990: 'prayer' together with 'exercise' appear to be regarded as falling within the ambit of the definition of 'unconventional therapy,' although 'prayer' and 'exercise' are carefully excluded from the final result (1993: 248–50, table 2). Were 'prayer' and 'exercise' 'unconventional' only because these were not therapies prescribed by physicians?

(National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research 1979)[17] or of the Georgetown Mantra: autonomy, beneficence, non-maleficence, and justice.[18] These commentaries are offered in good faith, but the authors note the difficulties in translating these concepts across perspectives and worldviews.

The central concern of most commentators is the possibility of harm from therapies of unproven safety and efficacy. The standard principles of ethics in conventional medicine demand that drugs and therapies should not be offered to patients unless there is clear empirical evidence (preferably from results of the gold standard of the randomized controlled trial) that the therapies are reasonably safe (or offer an acceptable return of potential benefit for the risk) and reasonably effective, and, where possible, that there is a reasonable understanding of the likely mechanism or basis for the therapeutic effect. To this end, the objectivity of the scientific method is the key (Jonas 1998: 1617). The absence of or the failure of one or more of these make rational defense of a given therapy difficult from the perspective of conventional medicine. Unfortunately, this is often a difficult thing to do in relation to traditional and complementary medicines because there is little in the way of empirical research on traditional medicine and CAM compared to the vast output of research for conventional medicine (Ernst 1996: 178–9).

At its bluntest, the proposition for conventional medicine has been put thus by Fontanarosa and Lundberg:

> There is no alternative medicine. There is only scientifically proven, evidence-based medicine supported by solid data or unproven medicine, for which scientific evidence is lacking. Whether a therapeutic practice is 'Eastern' or 'Western,' is unconventional or mainstream, or involves mind-body techniques or molecular genetics, is largely irrelevant for historical purposes and cultural interest. We recognize that there are vastly different types of practitioners and proponents of the various forms of alternative medicine and conventional medicine, and that there are vast differences in the skills, capabilities, and beliefs of individuals within them and the nature of their actual practice … Nonetheless, as believers in science and evidence, we must focus on fundamental issues – namely, the patient, the target disease or condition, the proposed or practiced treatment, and the need for convincing data on safety and therapeutic efficacy.
>
> *(1998: 1618)*

Criticisms from the perspective of conventional medicine in good faith deserve respectful consideration as they have at heart the well-being of the patient. Few in traditional medicine or CAM would argue against such a premise. But how much space should be left for the principle of autonomy of the competent patient? People make choices in life, and sometimes not very sensible ones. Some people make choices that are patently unsafe, not only for themselves, but also for others, such as smoking. But in most of the developed world, both the bodies of law and ethics demand that we respect such choices, even if they may be harmful to us, for the first principle is one of respect for the person as an autonomous individual.

17 It may be useful to remind readers that the current accepted fundamentals of bioethics in conventional medicine are of surprisingly recent provenance, and were originally formulated for the context of research.

18 For a critical commentary, see Takala (2010).

23.4.3 Autonomy – the individual perspective

Autonomy is especially problematic when applied to judgments in relation to traditional medicine and CAM. To what extent is an individual free to choose medical therapy or a medical system which is unproven from the perspective of science (or conventional medicine), and for which the risks are unknown? In Canada, the United States, and England, and in countries in the English common law system, it is clear that medicine must give way to personal autonomy in decisions relating to choices of treatment. In the case of *Malette* v. *Shulman et al.* [1990] OJ No. 450, the Ontario Court of Appeal held that a doctor who administered a blood transfusion during an emergency to a Jehovah's Witness, in violation of her express wishes as recorded on a card found on her person, was liable for battery. This was despite the fact that the court found that the doctor had acted in good faith, 'in an honest exercise of his professional judgment,' doing an act that 'may well have been responsible for saving her life' (*Malette* v. *Shulman et al.*, para. 12). The Court of Appeal in *Malette* made reference to the 'classic statement' of Justice Cardozo in *Schloendorff* v. *Society of New York Hospital* [1914] 211 NY 125: '[e]very human being of adult years and sound mind has a right to determine what shall be done with his own body; and a surgeon who performs an operation without his patient's consent commits an assault, for which he is liable in damages' (para. 17).

The *Malette* case and Justice Cardozo's statement were taken up by the then highest court of law in England in the case of *Airedale NHS Trust* v. *Bland* [1993] AC 789, which further elaborated on the extent of individual autonomy in the following terms:

> The first point to make is that it is unlawful, so as to constitute both a tort and the crime of battery, to administer medical treatment to an adult, who is conscious and of sound mind, without his consent … Such a person is completely at liberty to decline to undergo treatment, even if the result of his doing so will be that he will die.
>
> *(p. 857)*

The House of Lords went on, stating:

> First, it is established that the principle of self-determination requires that respect must be given to the wishes of the patient, so that if an adult patient of sound mind refuses, however unreasonably, to consent to treatment or care by which his life would or might be prolonged, the doctors responsible for his care must give effect to his wishes, even though they do not consider it to be in his best interests to do so.
>
> *(*Airedale NHS Trust *v.* Bland, *p. 864)*

Here are two quite distinct propositions. The first is that, whatever the situation in the past might have been, there is no place in the practice of modern medicine for medical paternalism where decisions are made 'for the benefit of the patient' without the competent patient's consent. Second, a competent patient is entitled to make decisions in relation to health choices which may not objectively (or scientifically) be in the patient's interest, and which may be actually harmful. If these propositions represent the current approach of the law to patient autonomy in at least some developed countries, then there are fundamental implications for ethical arguments against traditional medicine or CAM. The law places autonomy above empirical evidence of benefit. Or to shorten the equation even more fundamentally: the law places autonomy above benefit, for otherwise logically, no patient could ever refuse the direction of a physician prescribing in good faith based on scientific evidence.

But if we are to make public space for patients to make choices in favor of traditional medicine or CAM on the premise of individual autonomy and the right of the individual to self-determination, what limits are there to this principle? For the conventional medicine practitioner, practical ethical issues arise mostly in relation to patients who are also concurrently accepting (or contemplating) traditional medicine or CAM therapies. Ernst observes that the principle of autonomy requires that patients make informed decisions on the basis of adequate information on benefits and risks (1996). However, as Ernst argues:

> [In] the area of [complementary medicine] this is a difficult, in certain cases even an impossible, task simply because our knowledge is too incomplete. In this particular situation the best approach may be to be truthful to the patient, communicate the known facts and point out where our present knowledge is incomplete.
>
> *(1996: 197)*

23.4.4 The internal perspective

As Ernst's comments illustrate, much of the debate and concern in the literature centers on ethical issues arising from the interface of conventional medicine and traditional medicine or CAM. There is much less available literature, at least in English, on *internal perspectives* on ethics as applied to traditional medicine systems, from the viewpoint of those practicing it. This is a valid and important question. And it needs to be remembered again that the disciplines and systems of traditional medicine and CAM are not a homogenous entity. While it is far beyond the scope of any one single work (let alone within the limits of this chapter) to investigate the internal ethical underpinnings of individual traditional medicine or CAM disciplines, there is a compelling case for the responsibility of traditional medicine and CAM practitioners to clearly and transparently articulate the ethical bases and values of their own disciplines, if nothing else so that that their own patients can make choices on the basis of better information. Practitioners of conventional medicine would also add that traditional medicine and CAM also have the responsibility to demonstrate scientific safety and efficacy through scientific trials, but this may not be a premise accepted by some traditional medicine or CAM disciplines. But in fairness to their own patients, the practitioners of these traditional medicine systems or CAM should make this objection explicit. If patients understand their chosen therapy may not be supported by empirical data, then that is an informed choice which they make, and which they are entitled to make. But likewise, if they accept the premise of proof through scientifically controlled RCTs, then both national public health authorities and conventional medicine agencies are under a moral duty to commit themselves to helping such traditional medicine or CAM disciplines in such research and investigations. Although it must be observed that, by definition, if the safety and efficacy of traditional medicine or CAM treatment is proven in this way, the treatment in question (or even that branch or discipline of traditional medicine or CAM) will be necessarily subsumed into the canon of conventional medicine! Effectively, they cease to be traditional medicine or CAM. Traditional medicine and CAM practitioners wary of the hierarchy and organizational structure of conventional medicine cannot be unaware of this irony.

23.4.5 The social and public perspective

Some of the ethical concerns of conventional medicine about traditional medicine and CAM, however, assume greater cogency when applied to the social and public sphere. A simple example

is that of the treatment of an infectious disease, which is a threat to public health if not controlled. In the case of a disease like cancer, the consequences of making permitted choices about treatment (or non-treatment, as *Airedale* v. *Bland* makes clear) are limited to the individual making that choice, so there is little issue about the application of the principle of individual autonomy and the right to individual self-determination.

But suppose a patient with an infectious disease like SARS or MERS, with serious implications for public health, should decide to (a) opt for a course of traditional medicine treatment which from the viewpoint of conventional medicine is useless; or (b) refuse any kind of treatment on the grounds of religious beliefs? The reader may observe that (a) is more likely to arise in developing countries, and (b) in developed ones. But again, the consequences will be exactly the same, and the underlying justification is the same, if the patient in (a) believes that the treatment is culturally and spiritually appropriate.

Public health authorities must draw a line here. But based on what ethical justification? The proposed justification is an entirely *external* one – it has nothing to do with judgment that one system of medicine is better or more efficacious than another, or that conventional medicine is better than traditional medicine or CAM in this respect. It is simply that from the public perspective (specifically the public health perspective), public health policies must be founded on one or other system of medicine. Preferably, the choice is one subscribed to by the majority of its citizens. To do otherwise would run the danger of contradictions and inconsistency in public health policies. In most, if not all countries, the official system in this case would be primarily that of conventional medicine.

Thus the justification for forcing conventional infection control measures or treatment on a SARS or MERS patient who would prefer traditional or CAM treatment is *not* made on the basis that conventional medicine is better for the patient (although it may be), but on the basis that infection control measures be carried out according to the selected official perspective (usually that of conventional medicine). This will come as no comfort to the discombobulated patient with *Malette* v. *Shulman* still ringing in his ears, but it represents the compromises that we have to make in living together in a human society.

Perhaps this, too, is the best argument for what the WHO has been advocating as the best approach to engaging with traditional medicine and CAM practitioners: raise the standards of professional training and organization in traditional medicine and CAM disciplines, help them carry out research, and help them work out the central practice and ethical and social values of their chosen discipline (WHO 2002: 4–5). Only then can traditional medicine and CAM practitioners attract patients to their cause, offer them truly informed choices, and persuade governments to integrate or include their disciplines in their national healthcare systems and public health philosophies.

23.5 Conclusion

It is not the objective of this chapter to persuade practitioners of conventional medicine to accept the perspectives and methods of those who practice complementary, traditional, and alternative medicine, or vice versa. But as is clear from this account, there is international agreement among governments that traditional medicine systems should be promoted, while the reality is that traditional medicine is the main and often the only kind of healthcare available to a significant majority of people in some countries in the developing world. Yet when conventional medicine is available, people may still choose to avail themselves of complementary, traditional, or alternative medical therapies. If the paradigm of individual autonomy is to be given effect, then practitioners of conventional medicine must respect such a choice, even if they may not

agree with it. Logically, the same argument must also apply with similar force to practitioners of non-conventional therapies. But given their fundamentally different premises, the uncomfortable truth may be that there is unlikely to be any solution to the tension between the perspectives of conventional and unconventional medicine in the near future.

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24

The domestication of stem cell tourism

Douglas Sipp

24.1 Historical background of stem cell marketing

The rise of international marketing for putative stem cell products and procedures, commonly referred to as 'stem cell tourism,' is a well-documented phenomenon that dates back to the early 2000s (Lau *et al*. 2008; Kiatpongsan and Sipp 2009; Regenberg 2009; Ryan 2009; Sipp 2011a). The modern commercialization of unregulated cell or tissue biologics traces its origins to transplants of fetal brain or adrenal tissue for neurological diseases in the 1980s and 1990s (LeVay 2008). Further, commercialization practices gained widespread popularity in Europe and in the United States where xenogeneic transplants of lyophilized cells, tissues, or extracts harvested from sheep, rabbits, goats, and monkeys, and described variously as *Frischzelllen* (fresh cell), live cell, or Sicca cell therapy, began in the 1920s and continues today (Last 1990; Van Dyke *et al*. 1990). These nascent examples demonstrating the unregulated sale of cell- or tissue-based products displayed many of the hallmark features of present-day stem cell marketing: extraordinary claims of medical efficacy or rejuvenating power of living cells or cell extracts, widespread use of media innovations, and mention of required overseas travel for patients. In one well-known example, John Brinkley, known as 'the goat gland doctor,' pioneered the use of commercial radio in the 1920s, and later established the first 'border blaster' station in northern Mexico to reach American listeners while evading federal laws (Brock 2008). Despite the popularity of Paul Niehans' 'fresh cell' approach across German-speaking Europe, and a brief public fascination with fetal tissue transplants in Asia and Latin America in the 1980s, the demand for cell and tissue medicinal products has historically been a niche market.

Unlike its antecedents, however, contemporary stem cell tourism has developed into a global industry. It comprises hundreds of companies across dozens of countries offering supposed 'stem cell' products and services advertised for medical, nutritional, cosmetic, anti-aging, and veterinary applications; some websites list over 100 distinct 'treatable conditions' (Repair Stem Cell Institute (RSCI) 2013). Consensus among the scientific and medical communities remains that stem cells, of any kind, have only been shown to be safe and efficacious for non-experimental use in the treatment of hematologic cancers and other blood/immune diseases using hematopoietic stem cells (HSCs), and the repair of corneal damage using limbal stem cells (Daley 2012). In both of these stem cell-based treatments, the demonstrable therapeutic effect is attributable to

homologous use, i.e. the cells function as they ordinarily do in the body (HSCs generating blood cells, limbal cells generating corneal epithelium). In contrast, many businesses that advertise putative stem cell interventions make claims about 'non-homologous' uses, such as HSCs to generate heart tissue, or of mesenchymal stromal cells – which ordinarily give rise to bone, cartilage, and fat cells – in the repair of the nervous system. Additionally, stem cell clinics often advertise products that are clearly manipulated and capable of altering the biologic activity of cells, such as through long-term culture or treatment with exogenous growth factors or hormones. (The concepts of 'homologous use' and level of *ex vivo* 'manipulation' have legal implications in the United States and other countries, as described below.) The operation of such clinics in extralegal settings further places them beyond effective oversight or independent scrutiny. As a result, a number of companies and individuals have been found mislabeling slurries of mixed tissues (Jandial and Snyder 2010), animal cells (Trossel 2010), dead cell fragments (60 Minutes 2012), and even inert vehicles such as saline for direct sale to patients (*Campbell* v. *Immunosyn Corporation et al.*, case no. 692711 (complaint filed in 2009, but case has yet to proceed) (Texas Southern District Court)). Notwithstanding the lack of evidence or scientific consensus on the safety and utility of these companies' medical offerings, and the great potential for exploitation, fraud, and abuse, the industry continues to boom.

24.2 Convergent factors

Resistance to human embryonic stem cell (hESC) research on religious or ethical grounds triggered an immediate search for alternatives, prompting strong enthusiasm among some groups for the development of adult (somatic) stem or progenitor cells, such as umbilical cord blood- or adipose-derived mesenchymal multipotent stromal cells (commonly referred to as mesenchymal stem cells, or MSCs), olfactory ensheathing glial cells, and endothelial progenitor cells (Prentice 2003; Prentice and Tarne 2007; Focus on Family 2009). This enthusiasm for adult stem cells as a viable clinical alternative to hESCs led in some cases to a misunderstanding (and occasionally to deliberate misrepresentation) of the clinical utility of stem cell-based interventions, spurring demand in advance of evidence to suggest their safety and efficacy (Sipp 2013a).

The reluctance or refusal to fund hESC research in various national jurisdictions, including, importantly, the US (for eight years, the National Institute of Health (NIH) limited funding for such research to a small number of preexisting cell lines), motivated numerous Asian countries to invest heavily in stem cell research of all kinds. Notable in this regard were China, South Korea, Singapore, Thailand, Taiwan, and India. The failure of the US to capitalize on its traditional strengths in biomedical research and development in this area was apparently perceived as an opportunity for such countries to gain a foothold, or a lead, in the development of advanced biomedicine, at a time when much of East Asia was seeking to diversify away from heavy industry and manufacturing (Sipp 2009a, 2009b). Additionally, several countries in the region, of which Thailand, India, and Korea are prominent examples, simultaneously invested in establishing 'medical tourism' as an important economic sector. In the early days of unchecked optimism about the broad-spectrum clinical efficacy of stem cells, government agencies directly supported this investment, or promoted the operation of private companies that would come to be recognized as stem cell tourism operators (Thai Board of Investment 2005; Korea Tourism Organization 2013).

The presumption of efficacy was further amplified by a trend commonly witnessed in areas of leading-edge science: hyperbolic reports in the media and overenthusiastic speculation on the part of scientists. Media coverage of both stem cell science and of patient travel to obtain putative stem cell therapies has also contributed to uncertainty over the safety and clinical benefit of

stem cell interventions. Examples of major print, broadcast, and online media outlets running stories suggesting that stem cells are 'the future of medicine' or 'a miracle' are too numerous to list. Media coverage of direct-to-consumer marketing of stem cell-based interventions has been remarkably positive. Analyses of English-language (Zarzeczny and Caulfield 2010) and Chinese-language (Ogbogu *et al.* 2013) media reports on this phenomenon suggest that the trend has been increasingly to cast these procedures in a sympathetic light, and frequently to assist in fundraising for specific patients to travel overseas.

Much has been written about the pressures on basic scientists to suggest applications for their findings even at the earliest stages of research (Fang and Casadevall 2010; Levenson 2013). This is certainly the case in stem cell biology, which has become an area of science used as a yardstick of national research competitiveness, as evidenced by reports that the US had fallen behind Asia in the stem cell race (Einhorn *et al.* 2005), or that EU prohibitions on hESC patenting would hamper the ability of European labs to keep up (Kemp 2011). In 2013, an international group of scientists published a commentary on how the pressure to rush fundamental science into translational research has led the state to overestimate clinical development in stem cells, fueling patient demand, public urgency, and the premature marketing of stem cell 'cures' (Bianco *et al.* 2013). Stem cell clinical studies, many of which are conducted by academic or government organizations with little experience in conducting clinical trials, have been found to use potentially misleading language suggesting 'therapeutic intent' to describe research protocols much more frequently than comparable studies involving small molecule drug candidates (Scott *et al.* 2010).

The system's vulnerability to abuses in scientific integrity and quality assurance is also highlighted in the marketing practices of many stem cell clinics. The rise of 'predatory' publishers has made it simple to publish superficially peer-reviewed articles describing poor-quality or overly-speculative studies that may be indistinguishable from legitimate science to non-specialist readers (Beall 2012). Patent filings and penny stock listings are also readily obtained and useful in creating a veneer of legitimacy. Surprisingly, registration of clinical trials, particularly those using cell types such as MSCs, with which the drug regulatory authority may have some familiarity, is also apparently straightforward; numerous companies have successfully registered studies for single indications while actively marketing identical stem cell treatments for a myriad of other medical conditions. In 2011, for example, the US Food and Drug Administration (FDA) issued a warning letter to TCA Cell Therapeutics for treating multiple patients outside the indications listed in their five registered clinical trials (FDA 2011a). Groups of physicians engaged in the marketing of unapproved stem cell interventions have banded together to form societies which lobby for the deregulation of stem cell biologics, issue accreditations, and share business practices (Kuehn 2009). Meanwhile, individual practitioners may seek membership or submit presentation abstracts to societies not typically associated with the commercial promotion of spurious stem cell interventions, which can then be used in marketing as tokens of credibility.

One unifying thread among these practices is the reliance on the Internet as a relatively unregulated, inexpensive, and effective medium for targeting marketing messages to patients. The nature of online business provides the low startup and operating costs, mobility, anonymity, extraterritoriality, and broad reach that enable clinics located even in poorly resourced countries to communicate directly with users. Users search for combinations of keywords relevant to their conditions that are supported by search engine optimization and paid placement of advertisements through programs such as Google's AdWords. The Internet has also had an undeniably positive effect on patient empowerment and activism, allowing individuals to educate themselves about their medical conditions and treatment options, and to network with others affected by the same or similar diseases. However, it has also served as an inexpensive and extraordinarily effective marketing and recruitment forum for predatory stem cell clinics (Ryan *et al.* 2009).

Patient communities and blogs are a rich resource of information on individuals' disease status, and have occasionally been aggregated by clinics for use as a promotional tool.

Normalization of medical travel, lack of adequate health care insurance (particularly in the US), and generalized frustration with the medical system have also provided fertile soil for the growth of the illicit stem cell industry. Medical tourism, as mentioned above, has become an important sector in many developing economies, and patients in rich countries are accustomed to the idea that affordable quality care may be available beyond their national borders. Millions of people in the United States still have no or inadequate medical coverage, which, coupled with unusually high healthcare costs, fuels public disaffection and willingness to travel overseas for care. However, while potentially improving access, affordability, and speed of treatment, this phenomenon is not without its issues. It may be difficult for seriously ill patients to travel, which can leave patients without emergency medical care or legal recourse following an adverse event, and may make it difficult to access or retrieve medical records post-treatment (Turner 2010).

The growing popularity of so-called complementary and alternative medicine (CAM) (also referred to as 'integrative medicine') is a symptom both of dissatisfaction with conventional medicine, and preferences for minimally invasive, 'natural,' or holistic approaches to care (Eisenberg *et al*. 1993). Many businesses engaged in the sale of ostensible stem cell products offer combinations of stem cells with acupuncture, traditional folk medicine, homeopathy, or other alternative modalities (Sipp 2011b). The marketing of herbal or nutritional supplements purporting to boost stem cell function or increase the number of stem cells circulating in the bloodstream has also grown over the past decade.

The religious underpinnings that motivated further research into hESCs as therapeutic alternatives for adult stem cells illustrate how ideology can play an important part in shaping public perception. A small but vocal movement to rally opposition against the notion that autologous stem cells can be regulated as biologic drugs has arisen amid a more general opposition to government regulation of healthcare. The latter was first organized by free-market think-tanks such as the Heritage Foundation, Manhattan Institute, and Cato Institute in alliance with groups of physicians seeking to defeat federal oversight and disaffected patient groups (Sipp 2013a).

It is clear from this brief overview of contributing factors that the rise of direct-to-consumer stem cell marketing seems overdetermined nearly to the point of inevitability. The convergence of social, economic, political, legal, and ideological undercurrents led first to the emergence of clinics located on the fringes – in medical tourism hubs, island resorts, and towns bordering major developed markets. In the following section, I review what appears to be the largest growth area for the industry in recent years. Using the United States as the leading example, I discuss the emergence of scientifically dubious stem cell clinics practicing regulatory brinkmanship or openly defying the law in developed nations with well-established regulatory infrastructure.

24.3 Reborn in the USA

Although international travel is now considered the hallmark of 'stem cell tourism,' one of the first documented 'stem cell' clinics (Biomark International, which claimed to use umbilical cord blood-derived stem cells in the treatment of neurological conditions) was based within the United States and primarily targeted American patients (Zarembo 2005). After a federal investigation for medical fraud, the proprietors of the company fled the country. They subsequently established a similar company, Advanced Cell Therapeutics, which operated briefly in Europe and later in South Africa, as well as a separate outfit, Tissü, in the Seychelles. The globetrotting impunity of BioMark's owners – a South African man and his American girlfriend – highlights

not only the difficulty in regulating international businesses, but also the ready portability of the business model.

Many other early businesses engaged in the promotion and sale of unproven or under-regulated stem cell interventions, which have also been closely linked to individuals or companies from the United States. Theravitae, a Thai-Israeli joint venture based in Bangkok, was established by an American businessman and marketed an unvalidated transplant technique introduced by an academic cardiologist based in the US. Theravitae also served as the model for one Florida cardiologist who established a company, Regenocyte, that sent patients to a partner stem cell clinic in the Dominican Republic; he later lost his medical license when two patients he treated domestically in the US died after or during procedures (Freeman 2013). Beike Biotechnology, a large Chinese public-private company based in Shenzhen, served as a cord blood bank and a recruitment and referral service for patients seeking stem cell injections in China. It was established by a Chinese scientist-entrepreneur and an American businessman who was previously reported to have been involved in trafficking and harvesting organs from executed prisoners (Spencer 2005; BBC Panorama 2009). A Ukrainian scientist and an American businessman/artist jointly operated the Institute of Regenerative Medicine, a Bahamas-based clinic, and also putatively used fetal cells from Eastern Europe (Thompson 2006). Medra was a clinic located in the Dominican Republic, but was owned and operated by a California psychiatrist claiming to use fetal stem cells imported from Eastern Europe to treat serious medical conditions (BBC Panorama 2009). (Medra has since been renamed Stem Cell of America and now sends its patients to Mexico.) The Institute for Cell Medicine in Costa Rica (now the Panama-based Stem Cell Institute), which advertises interventions using various somatic stem cell types for the treatment of neurological and autoimmune diseases, was launched by a US entrepreneur in close collaboration with the publicly traded stem cell company Medistem, a company of which he was also chairman. Clearly, from its earliest days, the 'stem cell tourism' industry has not been limited to locally owned companies in developing economies with poorly developed regulatory systems.

The opening of Regenerative Sciences by a Colorado-based physician, businessman, and activist marked a turning point in stem cell tourism, from clinics relying on outbound travel to clinics operating within US borders. Regenerative Sciences was accompanied by the establishment of the International Cellular Medicine Society (ICMS) (originally named the American Stem Cell Therapy Association), a coalition of like-minded practitioners that actively lobbied for the deregulation of autologous stem cell products. For example, members of the ICMS Board are required to affirm statements that appear to be in direct contravention of current federal regulations:

> … minimally culture expanded stem cells are 1). Part of the practice of medicine and used as part of a physician practice in one state and through the state practice of medicine, 2). Do not constitute the creation of a new biologic drug or product that would fall under any part of FDA regulation on new drugs or biologics and 3). Exempt from any US Food and Drug Administration regulations …
>
> *(International Cellular Medicine Society 2013)*

In 2007 Regenerative Science began marketing a processed autologous stem cell product under the trade name Regenexx, and the following year received an untitled letter from the FDA informing them that they appeared to be promoting the '… use of mesenchymal stem cells under conditions that cause these cells to be drugs …' under relevant federal law. This prompted a series of suits and countersuits between Regenexx and the FDA that were decided by the District Court in 2012, and are currently under appeal (Sipp and Turner 2012).

The law in question is the *Code of Federal Regulations* (Title 21, Part 1271), which defines the regulations over human cell and tissue products (HCT/P). These products are broadly defined as any human cell, tissue, or derived product that is introduced into interstate commerce and that meets any one of the following criteria: (1) more than minimally manipulated; (2) intended for non-homologous use; (3) systemic in effect; or (4) shows metabolic activity. Important exceptions to these rules include blood and blood products, vascularized tissues or organs, human reproductive cells intended for immediate transfer to an intimate partner (all of which are regulated separately) and, importantly, establishments that harvest 'HCT/Ps from an individual and implants such HCT/Ps into the same individual *during the same surgical procedure*' (*Code of Federal Regulations*, Title 21, Part 1271) (emphasis added by author). For its part, Regenerative Sciences insisted that the harvesting and transplantation of autologous stem cells should be considered part of medical practice, a state-regulated activity in the US, rather than the federally regulated manufacture of a biologic drug.

US-based clinics were quick to note and take advantage of the same-surgical-procedure exemption. In effect, the exemption removes from federal oversight the marketing of stem cell-based interventions in the absence of rigorous evidence of safety, purity, and efficacy that would typically be required of a drug, medical device, or biologic. Regenerative Sciences itself was one of the first to exploit this regulatory gap, introducing a number of alternatives to its cultured cell product (Regenexx-C) that are delivered in what is described on the company website as the same surgical procedure.

The fields of aesthetic plastic surgery, orthopedic repair, and anti-aging medicine were quick to awaken to the possibilities of selling weakly regulated autologous stem cell interventions on a direct-to-consumer basis without the need to go through the time-consuming, expensive, and uncertain validation process required for other medicinal products. One of the most popular forms of autologous cell treatments available is a combination procedure that harvests a small amount of fat from the patient; this fat is then spun in a centrifuge to obtain the MSC-rich stromal vascular fraction, which is then re-injected into another site in the same patient's body for medical or cosmetic purposes. The scientific evidence supporting the efficacy of such procedures remains equivocal at best, and the absence of accepted standards of care makes it certain that there is wide variability in clinical practices. Indeed, the American Society of Plastic Surgeons and American Association of Aesthetic Plastic Surgeons have jointly issued a position statement that, based on current scientific evidence available, it is premature to market stem cell interventions (Eaves *et al*. 2011). Similarly, the American Association of Orthopaedic Surgeons (AAOS) maintains that 'stem cell procedures in orthopaedics are still at an experimental stage' (AAOS 2007).

Therapeutic claims about autologous stem cells harvested and transplanted in the same surgical procedure are not limited to cosmetic surgery and joint repair. A growing number of domestically operating clinics now claim to treat more serious medical conditions on an experimental, but for profit, basis. In past years, a small number of naturopathic clinics made similar claims for putative stem cell products, but this practice has now moved into mainstream medicine. The Cell Surgical Network (2013) established by the California Stem Cell Treatment Center now has practice affiliates in Hawaii, California, Arizona, Nevada, Colorado, Texas, Iowa, Illinois, Indiana, Mississippi, Florida, Georgia, North Carolina, New York, Connecticut, and Massachusetts, offering experimental same-day injections of autologous cells for neurologic, cardiovascular, urologic, autoimmune, ophthalmologic, and orthopedic conditions, as well as hair restoration. Regenerative Sciences has also introduced a Regenexx Provider Network licensing program, and a number of companies have begun to offer courses in stem cell harvesting and transplantation.

One increasingly popular trend in clinics both overseas and in the US is to provide services as part of 'clinical trials' or 'on an experimental basis,' so that patients who wish to participate in 'research' must pay the costs. By wording websites and informed consent documents in ways that indemnify the providers not only against unforeseen adverse effects but also against lack of efficacy, these 'pay-to-participate' marketing schemes blur the already fuzzy lines between experimentation and care in this area of biomedical development, and place an undue burden on patients willing to volunteer as test subjects at some physical risk to themselves (Sipp 2012). Conservative organizations have begun to promote the notion that the regulation of stem cell products is overly stringent, and safety studies should be sufficient to bring products to market after surveillance and outcome databases can be used to determine efficacy (Gottlieb and Klasmeier 2012). If enacted, these requirements would seem to achieve the same end result: transferring the financial responsibility for research costs from for-profit companies to vulnerable patients.

In addition to the commercialization of procedures with therapeutic intent, many companies sell nutritional supplements or cosmetics alleged to boost the function of the body's endogenous stem cells. Although the FDA regulates both supplements and cosmetics, such products undergo a much lower level of scrutiny. The *Dietary Supplements Health and Education Act* of 1994 placed severe limits on the FDA to require premarket safety and efficacy testing for nutritional supplements, so long as their makers confine their labeling to so-called 'structure/function' claims and disclose that the product has not been reviewed by the FDA (Hurley 2007). Thus supplement makers are at liberty to assert their products, for example, 'support liver function' or 'enhance metabolic activity' by 'stimulating stem cells,' but cannot claim to treat, cure, or mitigate any disease. One of the most popular such products, StemEnhance, is sold as part of a distributed marketing scheme and claims to have earned more than $1 million USD in revenue in its first month on the market (although it appears that a very similar product, Cell Enhance, created by the same individual, was on the market for more than a decade prior to its rebranding). Several individuals affiliated with medical stem cell clinics have also developed proprietary brands of stem cell supplements (such as Stem-Kine and Regenexx). To date, the FDA has not taken action against the manufacturer of a stem cell nutritional supplement.

Cosmetic manufacturers are also at much greater liberty in labeling their products than are makers of drugs and devices. The FDA's primary role in the regulation of conventional cosmetics is monitoring for adulteration, misbranding, and post-market safety issues; premarket testing is not required, and claims are evaluated with an eye to whether they are likely to be more or less 'exaggerated' (Liang and Hartman 1999). With the advent of new bioactive cosmetic products (i.e. those products whose function is not merely to conceal or enhance superficial features, but to effect changes in some physiological process or function) are calls for the creation of a regulatory category between cosmetics and drugs, often referred to as cosmeceuticals. However, the law in this area remains controversial and unevenly applied. Thus sunscreens, antiperspirants, and antidandruff shampoos manufactured in the US are regulated as drugs, while topical theophylline and retinol can be sold as cosmetics (Elsner and Maibach 2005). Major cosmetics manufacturers use highly suggestive claims to boast the regenerative effects of the product or the inclusion of stem cells in their formulae. A subset of these products claims to use 'stem cells' from plant species, including edelweiss, bilberry, argan, butterfly bush, Echinacea, apple, and grape, among others, and typically places a strong emphasis on their supposed 'natural' and 'rejuvenating' properties. In 2012, the FDA issued a warning letter to L'Oréal over claims made about the properties of several of its products, the first such enforcement activity against a stem cell cosmeceutical (FDA 2012). Thus it appears that the majority of companies selling 'stem cell' medical treatments, nutritional supplements, and cosmetics have found exceptions, exemptions,

and lacunae within the law that enable them to operate with little fear of federal intervention and little need to support their claims with scientific evidence prior to (or after) entering the market.

Removing the necessity of overseas travel for patients seeking stem cell interventions has also had clear implications for the industry. On the positive side for consumers, the expansion of choices on the market, which now encompasses both foreign outfits and US clinics marketing 'same surgical procedure' transplants, appears to have brought about price competition, resulting in lower prices for consumers. This is a good thing overall, as even in the event that the products turn out to be spurious or inefficacious, the financial harm is mitigated to some extent. However, it must be noted that the economics of this industry remain poorly understood due to the lack of transparency and, paradoxically, a number of clinics now appear to be charging more than the former industry average of around $20,000 USD per treatment (possibly seeking to differentiate themselves on the basis of 'quality' as reflected by price).

The downsides to the domestication of what was formerly a touristic phenomenon have been subtler, but perhaps over the long term more profound. The erosion of the scientific integrity of medical practice in the United States, as typified by the ascent of complementary and alternative medicine as independent modes of healthcare, and their increasing integration into mainstream practice and academia, is well documented (Chaterji *et al.* 2007; Gorski 2008). This appears to be a partial consequence of the deprofessionalization and subjection of healthcare to market forces over the past four decades. In free-market medicine, patients are free (as they should be) to make decisions about their treatment options. Likewise, providers are free (ill-advisedly) to make claims based not on scientific research, but 'whatever the market will bear.' A discussion of the perils of the free-market model for scientific integrity and progress in medicine is beyond the scope of this article, but excellent reviews of the subject from medical and economic perspectives are available (Relman 2007).

24.4 Regulatory responses

Despite the rapid ascendancy of stem cells across multiple pseudomedical product categories, the domestic healthcare and regulatory systems are not entirely defenseless against such unsupported claims and business practices. Since 2011, the FDA has stepped up its enforcement activities, conducting inspections and issuing a half-dozen warning letters to clinics and companies (Sipp 2013b). This regulatory response appears to have been timed not only to the growth of the domestic industry, but to the resolution of the *U.S.* v. *Regenerative Sciences* [2012] 878 F. Supp. 2d 248 case which, had it been decided in favor of the defendants, could have overturned the FDA's authority over a broad swath of cell biologics. State and federal law enforcement have also taken action against fraudulent stem cell claims. In 2011, two men in Nevada were charged with conspiracy to commit mail fraud and wire fraud over stem cell treatments that they had been marketing since 2005 (FDA 2011b); both entered guilty pleas in 2012. More dramatically, a group of people, including an academic researcher, involved in a fraudulent stem cell business exposed by the television news program 60 Minutes, were arrested and convicted for their parts in the scheme (US Attorney's Office 2012; Glenn 2013).

State medical boards could also potentially play an important role in reining in the more egregious claims of physicians advertising unproven stem cell treatments. To date, only the Florida Board of Medicine has taken disciplinary action, and then only after two fatal complications of stem cell transplants performed within the state (Freeman 2013). The failures of state medical board systems to discipline practitioners, even in cases of serious breaches of professional and ethical conduct due to lack of resources, fear of litigation, and unwillingness on the part of fellow

doctors to report their colleagues are not however limited to the area of stem cell marketing, (Eisler and Hansen 2013). Thus it appears unlikely that state boards will take action in any but the most serious and ironclad of cases. In the state of Texas, where the governor (himself the recipient of an unvalidated stem cell injection) prompted the State Medical Board to enact a rule protecting physicians from disciplinary action in the event that they deliver stem cells on an experimental basis, that likelihood would appear to be even lower still (Kaiser 2012).

The civil courts have been underutilized for litigation against stem cell companies and providers who have made ostensibly spurious or misleading claims. A group of Korean-American patients who were treated by clinics affiliated with Human Biostar, the US affiliate of Korean stem cell firm RNL Bio (now K-Stem Cell), filed suit against the company, alleging that it 'defrauded elderly Plaintiffs through false representations that experimental stem cell therapy … would cure not only all known ailments, but would also reverse aging' (*Ben Hang Lee et al.* v. *Human Biostar Inc. et al.* (complaint filed in 2012, but the case has yet to proceed) (California District Court)). Several law firms are now actively soliciting plaintiffs for lawsuits against fraudulent stem cell clinics (Schmidt Firm LLP 2012) and even a potential class action suit against Lancôme for its promotion of misleading health claims associated with some of its 'stem cell' cosmetics (Blankinship 2013). But given the sophistication of the marketing claims for unproven stem cell products and interventions, frequently accompanied by disclaimers that they have not been reviewed by the FDA, they remain experimental. That is, such products and interventions offer no guarantee of safety or efficacy, and the widespread use of informed consent documents serve to indemnify providers against litigation and insulate them against malpractice claims. Therefore it remains to be seen whether courts will look on such suits favorably. The depiction of stem cell treatment as an area of complementary and alternative medicine may work to the advantage of providers, as it is more difficult to win malpractice cases against CAM practitioners, given their highly limited scope of practice and non-reliance on conventional standards of care (Jesson and Tovino 2010).

24.5 Conclusion

The United States and other countries have seen a stem cell invasion in recent years. If unsupported medical claims for stem cells are allowed to remain unchecked, it may have serious consequences not only for public health and patient safety, but for the future of legitimate stem cell research as well. Over the past half-century, American patients and consumers have grown accustomed to a market in which the safety and efficacy of medicinal products must be demonstrated prior to being approved for distribution. They are growing less accustomed, unfortunately, to the notion that medicine is not a business, but a profession guided by codes of conduct that prioritize patient care. Efforts to shift the oversight of these interventions from the stringent regulatory framework for cell biologics to the more liberally regulated practice of medicine reflect this new reality. Emphasis on freedom of choice resonates with patients, especially those with intractable conditions who may be disillusioned with the current system. However, many gloss over the basic guarantees of quality and reliability that make such freedoms worth exercising. It has been noted that the history of medicine, which until very recently has been unregulated with respect to premarket evidence of efficacy, is the history of the placebo: free markets are notorious for their inability to distinguish safe and effective products and services from ones that are merely safe and attractively presented. By making the case for clinical uses of stem cells through marketing pitches rather than rigorous and reproducible scientific studies, companies engaged in direct-to-consumer marketing of these interventions do their customers and the field a deep disservice.

The opening of the domestic market to companies that take shortcuts around the FDA regulatory pathway also leads to significant market distortion to the disadvantage of companies that seek to introduce products via the established route. Costs for the clinical development, testing, and authorization of a stem cell product for a single indication are estimated around $100 million USD and take a decade or more to approve for commercial use. But when companies, clinics and individual providers are able to begin earning nearly instant profits, then clearly they will financially outcompete traditional companies at least in the near-to mid-term. Low startup and running costs as well as direct-to-consumer marketing that includes promotional texts, albeit it without promises or evidence of efficacy, have enabled companies to do so. The profitability of the direct-to-consumer stem cell marketing model is undeniable, and has not gone unnoticed within the industry – many companies with registered clinical trials now partner with clinics in neighboring countries to which they send patients who wish to buy into a research study as a paying subject (a practice that is typically not permitted in the US and which raises serious ethical issues). My future work will examine the serious issue of publicly traded companies that either engage directly in such practices or act as direct suppliers. For now, regulators and consumers must become more vigilant to the unsupported claims of medical utility among stem cell therapeutics if public trust in the field is to be maintained.

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