CHAPTER 6

Legal Aspects of Health Applications of Genomics

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INTRODUCTION

Much has been written about the ethical issues raised by the incorporation of new genomic technologies into clinical practice, issues that have been addressed elsewhere in this book (see Chapter 5). But the limits of what is permissible in practice are defined by law, which delineates what people can and cannot do at the risk of other penalties or liability. The law, however, is complex and comes from a variety of sources. In much of the world, a country's constitution defines the outer limits of what the government can do. Within those limits, governing bodies enact laws. In many countries, legislative bodies are the primary entities that have the power to pass laws. In other cases, the executive branch, such as the president, can directly set policy as well, albeit often in a more limited way. In either case, laws and executive directives frequently do not spell out all the details necessary for their enforcement but rather delegate authority to regulatory bodies to create final rules or regulations. The courts play a role as well. In some countries, the role of the courts is simply to interpret the

Genomics and Society
DOI: http://dx.doi.org/10.1016/B978-0-12-420195-8.00006-9

laws, directives, and regulations either for enforcement or to adjudicate claims for relief by plaintiffs, people who claim that they were injured because the laws and regulations were not followed. In federal systems that have governments at both the national, state, or more local levels, law, regulations, and adjudication occur at multiple levels, at times coming into conflict. In common law countries, moreover, some courts may also apply judge-made law to analyze claims that plaintiffs were inappropriately injured and so were entitled to damages.

FRAMING THE ISSUES

The discussion that follows is organized in the order in which legal issues arise in the process of implementing clinical genomic testing. The first is what clinicians are permitted to order and use, since clinical practice is highly regulated in most countries, especially in civil law jurisdictions. The second is what genomic information patients can access. This involves two parallel inquiries: (i) what medical records they can obtain and (ii) what genomic information they can acquire outside the clinical setting, for example, through direct-to-consumer genetic testing, and what they can expect their clinicians to do with these results. The third is reimbursement or coverage, what tests payers will reimburse. The last is the role of potential liability in shaping physician behavior regarding the use of genomic testing. We will not, however, address legal issues posed by reproductive genetic testing or state-run newborn screening.

Because constitutions, statutes, regulations, and case law vary from country to country, this chapter will apply this framework primarily in two different settings, the United States, which is a federal and common law country, and Quebec, which is a civil law province in another federal country, Canada. References will be made to other jurisdictions, where appropriate. Our purpose is to illustrate some of the legal issues that must be explored in order to implement genomic testing effectively in the clinic. This discussion is not intended to be interpreted as legal advice nor does it purport to be comprehensive, especially given the rapidly changing legal landscape around the world, so that the reader is strongly advised to seek advice from local counsel for any legal concerns.

THE UNITED STATES

What genomic information clinicians can order and use

The practice of medicine is heavily regulated in the United States, which can be challenging in an environment where genomic technologies are rapidly changing [1]. Probably the most important law in the area of genomic testing is the Clinical Laboratory Improvements Amendments of 1988 (CLIA) [2]. This law was enacted after a scandal revealed that poor laboratory procedures in reading Pap smears caused

many women to receive inaccurate results, including results that were not theirs. This law requires detailed procedures to ensure that samples are not mixed up and that test results are accurate and interpreted appropriately. Clinicians are mandated to use CLIA-compliant laboratory results in caring for patients. Recently, however, some scholars have argued that these regulations impermissibly violate the clinician's right to free speech under the US Constitution's protection of commercial speech [3]. How the courts would respond to such a claim were it ever to be litigated remains to be seen, especially since such an interpretation would substantially undermine the basis for regulation in the United States. In any event, however, as will be demonstrated later in the discussion about patients, the impact of CLIA has been substantially reduced by new regulation in another area.

The US Food and Drug Administration (FDA) have long asserted their ability to regulate genomic technologies, but until recently, has not chosen to do so. Recently, however, the FDA has proposed to require that new laboratory-developed tests (LDTs), which are commonly used in genomics, require an Investigational Device Exemption (IDE) "if test results are returned to the patients without confirmation by a medically accepted diagnostic product or procedure" [4]. At this early stage of genomics, confirmatory tests are often not available. The process of obtaining an IDE is an onerous one and would be a major disincentive to innovation. Here, some argue that this proposal is impermissible regulation of the practice of medicine, which is precluded by the FDA's authorizing statute, as well as a violation of commercial speech rights [5], how the courts would address these arguments were they to be raised remains to be seen.

Some states impose additional requirements on genetic testing as well. New York, for example, requires that DNA testing services for its residents must take place in a laboratory accredited by its Department of Health [6]. California imposes additional requirements as well [7].

Notably, all of these laws in the United States address issues of process that must be met before results can be returned. Some other countries, by contrast, decide centrally which specific tests will be available for clinical use and under what circumstances.

Returning to the United States, another issue is to whom clinicians can disclose patient information. Physicians are bound ethically by norms of protecting patient's confidentiality. A long-standing ethical consensus holds that clinicians should not inform patients' relatives about particular genetic risks they may share except in the most unusual situations and then only after the clinician has counseled the patient about the importance of sharing the information and has offered to help the patient to do so [8]. The major law about protecting patient information on the national level in the United States is the Health Insurance Portability and Accountability Act (HIPAA), which has recently adopted a different, and more permissive, position. The so-called privacy rule, which generally prevents clinicians from disclosing patients'

personal health information, has a number of exceptions for such purposes as payment for clinical care, public health, and criminal prosecution. Recently, the Office of Civil Rights (OCR), which enforces HIPAA, stated that "*[p]roviders may share genetic information. . .with providers treating family members. . .who are seeking to identify their own genetic health risks,. . . provided the individual has not requested. . .a restriction on. . .disclosure*" [9]. The OCR then went on to say that clinicians need not agree to their patients' request for confidentiality. Thus, patients whose information was disclosed are left to state law for protection of their privacy, a topic addressed in the section on liability later.

Notably, countries differ widely in their protection of medical records and their willingness to permit physicians to disclose their patients' genetic information to relatives [10]. Thus, this is an issue for which local legal advice is particularly important.

What genomic information patients can obtain

The trend in the United States is to expand patients' rights to review information in their medical records. Driven in part by HIPAA, which mandates that patients have broad access to their records, many healthcare institutions now provide patient portals to enable patients easily to obtain laboratory and imaging results. New regulations issued under the Health Information Technology for Economic and Clinical Health (HITECH) Act expand this access dramatically [11], by providing patients with access directly from the laboratory to any information in a "designated record set," which is defined as "(1) A group of records maintained by or for a covered entity that is: (i) The medical records. . .about individuals maintained by or for a covered health care provider;. . .or (iii) Used, in whole or in part, by or for the covered entity to make decisions about individuals" [12]. The OCR explicitly stated that "[t]his final rule is intended to remove barriers in the HIPAA Privacy and CLIA regulations to individual access to test reports maintained by laboratories subject to or exempt from CLIA" [13]. Thus, patients will have access to non-CLIA-compliant data, as well as any data that states had regulated under their own CLIA-type laws, even though clinicians may not be allowed to use such results to treat patients.

This rule poses particular issues with regard to multiplex data, such as genomic data, because this regulation requires that patients be able to obtain all the data generated on request so long as the test is complete [14]. Thus, it appears to mean that patients have access to *all* genomic data from a broad-based genome test if any part of the data is used for clinical care or if a third party payer is billed electronically for its generation.

This rule, however, conflicts with significant efforts over many years to create evidence-based processes to decide which data are useful clinically and to develop decision support strategies to ensure that clinicians and patients know how to use the results for prevention and treatment [15,16]. Admittedly, the concepts of clinical

utility and actionability and who decides them are hotly debated [17], but most of the discussion assumes that at least some genomic data should not be returned because their meaning or what can be done with the data to improve health outcomes are not known.

What the impact will be for patients of having access to broad genomic data is unclear. The HITECH regulations state specifically that laboratories are not required to provide any interpretation of the data. The OCR leaves the responsibility for interpretation to clinicians, the vast majority of whom lack these skills. Until better support systems become available in the healthcare system, patients in the future may need to turn to commercial entities that are currently developing interpretation protocols.

Direct-to-consumer genetic testing raises a different set of concerns. People have been able to get a variety of tests outside the healthcare system, such as blood pressure measurements as well as blood glucose and cholesterol. Direct-to-consumer imaging became popular in the early 2000s, only to fall into disfavor [18]. In the last decade and a half, a number of companies have offered direct-to-consumer genetic testing, for a whole array of purposes, including determining paternity and ancestry, but some focused on providing genetic-risk information to purchasers, a move that has been quite controversial [19,20,21]. Here as well, the FDA has asserted authority to regulate, and on November 22, 2013, issued a warning letter to 23andMe instructing it to stop its Personal Genome Service until it obtained marketing approval from the FDA, which required, inter alia, demonstrating analytical and clinical validity [22]. New York, California, and other states had previously regulated these entities as well [23]. If these tests become available again, questions still remain about whether physicians are willing to use their data in their practices [24,25] and if they can do so in ways that improve healthcare outcomes [26].

Coverage and reimbursement

The United States has a complex "system" of healthcare coverage, with coverage by governments under Medicare and Medicaid and a wide variety of private payers, including health insurers and self-insuring companies. Medicare and most Medicaid programs cover some genetic tests, the latter varying widely among states. Other than state-run health newborn screening programs, the only genetic tests that are required to be covered by private insurers under the Patient Protection and Affordable Care Act are those for BRCA1 and BRCA2 for high-risk women [27]. This requirement exempts already existing or so-called grandfathered plans. Otherwise, private health insurers differ widely in their coverage of genetic tests, often requiring precertification and specific clinical features that indicate an elevated risk that the person carries a pathogenic variant [28].

Issues of coverage and reimbursement, obviously, are quite different in countries where the government is the only or the primary payer for health care and so makes decisions about coverage centrally.

Liability

Medical practice in the United States is shaped in no small part by the fear of liability, which is no surprise since it is one of the most litigious societies in the world. Anyone can go to the courthouse, although they are unlikely to get help from a lawyer unless they have a reasonably strong claim. In this section, we will discuss the realistic claims that patients can bring against clinicians and healthcare institutions.

None of the federal laws discussed earlier—CLIA, HIPAA, and FDA—create a so-called private right of action, which would allow patients to seek to enforce the law or to obtain damages if the laws were not followed. Thus, patients are largely left to pursue claims based on common law theories. The most important of these is the law of negligence, in which claimants must prove that the defendant(s) breached a duty of care proximately causing compensable injuries. One major issue, then, is the scope of the duty of care, which in the healthcare context is generally defined by what reasonably prudent, similarly situated practitioners would do. This is how federal laws may become pertinent even though they are not directly enforceable by patients because their goal is to shape the standard of care by setting the standards for, for example, how laboratories should run or what information should be released. Evolving practice patterns and professional guidance also affect the scope of the duty. As noted previously, much effort is being devoted to determining which results ought to be returned and how best to do so [29], which will shape practice and hence what providers and institutions will be expected to do. If failure to meet these obligations causes a patient to suffer physical harm, providers may well be liable for damages.

The use of multiplex technologies like genomic testing has the potential to reveal findings that are not pertinent to reason testing was undertaken, the so-called incidental or ancillary findings, raising questions about whether clinicians have a legal duty to return them. A recent review found no reported case in which patients have argued that they were harmed by not receiving incidental genomic results [30]. The few cases that have been reported in the context of medical imaging point out the importance of having a physician–patient relationship and defining the standard of care for the particular physician in order to impose liability. An additional issue in the context is whether there is a duty to hunt [31] for ancillary findings by examining all the genomic data, whether the clinician can examine only those parts of genome specific to the patient's clinical issues, or whether some subset of additional genes should be analyzed, as was recently recommended by the American College of Medical Genetics and Genomics [32,33]. Even limited inquiries will likely reveal pleiotropic or

ancillary findings [34]. How far these duties to identify and return these additional findings will extend will depend upon how practice patterns evolve unless legislative bodies intervene to define the scope of liability.

One particularly challenging issue may arise when patients have access to more genomic test information than clinicians are prepared to interpret and rely upon, particularly information that is not included within practice guidelines for use. The standard of care should be an adequate defense for uses outside standard practice, but physician reluctance to do what the patient wants is the type of situation that leads to unhappiness, a major determinant of litigation. Referral will not always be an option due to the paucity of geneticists or other knowledgeable clinicians.

Obligations to family members are more complex. For the most part, clinicians do not have a physician–patient relationship with relatives and so arguably have no duty. Two cases in the United States in the 1990s, *Safer v. Pack* [35], and *Pate v. Threlkel* [36], raised questions about whether physicians have a duty to warn relatives. The more far-reaching case, *Safer*, which held that a physician could be required to warn his patient's young child specifically about her genetic risk, was overturned by that state's legislature, and a general consensus emerged that, with few potential exceptions, physicians were ethically required only to warn their patients about the importance of sharing genetic-risk information with relatives and to offer to assist them in doing so. No lawsuits asserting failure to warn relatives of genetic risk have been filed since that time, but this may change with the recent changes in HIPAA, described earlier, which permit physicians to warn the physicians of at-risk family members. Questions about whether the patient's physicians owe a legally enforceable duty to their patients' family members would still remain, but the regulatory change evinces a policy of informing relatives, which could lead to lawsuits if relatives were not warned and became ill.

COMPARATIVE ISSUES IN QUEBEC

When it comes to how legal traditions address the above-framed issues, the Canadian province of Quebec provides an interesting contrast to the United States. Being a civil law jurisdiction, Quebec puts much more emphasis on the role of laws, regulations, and codes in providing guidance. This, however, does not mean that these jurisdictions take diametrically disparate stances on the common issues facing the orderly implementation of genomic testing in the clinic.

What clinicians can do?

Quebec, being one of 10 provinces in Canada, finds itself governed by both provincial and federal laws and regulations. Currently, genomic testing is indirectly regulated by various sources, and a sharing of power occurs between the provincial and federal jurisdictions on regulatory matters. Indeed, Canada's Constitution endows both the

federal and provincial legislatures with competence to regulate diagnostic tests. The federal government, through Health Canada, is empowered to regulate medical devices under its prerogative over criminal matters [37]. As for the provinces, their jurisdiction over the management of hospitals [38] provides them with the authority to regulate tests locally [39]. The regulatory process at the federal level can be stringent but allows for the marketing of the product across the country. In contrast to the United States, Canada recognizes four classes of medical devices (regulated by federal authorities) based on the level of control required to ensure safety and efficacy [40]. A similar classification can be found in the European Union [41].

According to Canada's *Medical Devices Regulations*, genetic tests are considered *in vitro* diagnostic tests and are classified as class III (Schedule 1, rule 4). "Genetic testing" is defined as "the analysis of DNA, RNA or chromosomes for purposes such as the prediction of disease or vertical transmission risks, or monitoring, diagnosis or prognosis." (see USA section, pp. 121) Genetic tests that are not sold as test kits but developed only for and in one laboratory will fall under the general category of LDTs, which are regulated provincially. LDTs can only be performed locally and "cannot be commercially marketed to consumers or sold to other laboratories" [39].

Section 31 of the *Medical Act* (chapter M-9) provides that the prescription of diagnostic tests generally must be done by a physician. The obligations to be carried out by these clinicians are outlined in the *Code of Ethics of Physicians* (chapter M-9, r. 17), which states that a physician's duty is "to protect and promote the health and well-being of the persons he attends to" (section 3), while practicing in a "manner which respects the life, dignity and liberty of the individual" (section 4), and which is "in accordance with scientific principles" (section 6). A physician must be sensible "in his use of the resources dedicated to health care" (section 12) and must "make his diagnosis with the greatest care, using the most appropriate scientific methods and, if necessary, consulting knowledgeable sources" (section 46). A physician must use diagnostic technologies that are proven and medically necessary (sections 48–50). However, he must respect the patient's diagnostic choices, all the while ensuring that sufficient information is provided to the patient concerning risks or disadvantages that could result (sections 48–50). The next section will address the nature of the information that will be disclosed to patients and the level of protection surrounding them.

What patients can get?

Section 38 of the *Civil Code of Quebec* states generally that "[. . .] any person may, free of charge, examine and cause the rectification of a file kept on him by another person." Additionally, the information contained in such a file should be made accessible in an intelligible transcript. According to the *Act Respecting Health Services and Social Services* (chapter S-4.2), every patient 14 years of age and over has a right to access

his/her records held in a health institution (section 17). However, such a right is not absolute and patients could be denied access temporarily if the communication of the record "would likely be seriously prejudicial to the user's health" (section 17), among other limitations. It is safe to say that results from genetic tests found in the medical record will be made available to patients, even if not immediately.

What about results from whole-genome (WG) or whole-exome sequencing (WES)? Given the complexity of such information, can they be accessed by patients? If made available in the medical records, all indications point to the right of access of patients to such information based on the above-mentioned provisions of the *Act*. As a practical matter, no Canadian normative document exists on the type of information that should be made available in the medical record of a patient following WG or WES. Recently though, a statement endorsed by the Board of Directors of the Canadian College of Medical Geneticists (CCMG) has suggested that competent adult patients should be given an option to receive clinically significant and actionable results following clinical WGS/WES [42], which would mean that such information would be made available in the patient's medical records. "Medically actionable" and "clinically significant" have yet to be specifically defined, but in this document, a clinically significant finding is understood as being "of potential health or reproductive importance" and medically actionable results are broadly characterized as revealing "preventable or treatable conditions." Overreporting could potentially harm patients by creating undue anxiety and could be used as a justification to temporarily deny them right of access to their medical records, according to the *Act*, although this has yet to be tested in administrative courts. In any case, the *Act Respecting Health Services and Social Services* specifies that a health institution that provides a patient with information contained in his/her medical record, shall, at the request of the patient, "provide him with the assistance of a qualified professional" (section 25), something that online direct-to-consumer companies usually fail to do.

Like the United States, patients in Quebec and Canada have access to online services provided by direct to consumer (DTC) companies. Very recently, 23andMe has begun operating in Canada, even though Personal Genome Service was blocked by the FDA in the United States for lack of marketing approval [43]. According to 23andMe, after extensive discussions with the federal health authority in Canada (Health Canada), the latter has determined that given the nontherapeutic nature of their product, it falls outside the purview of the *Food and Drugs Act* [44], as well as the *Medical Devices Regulations*, and so needs no federal premarket approval.

This, however, will not protect them from eventual regulation in the provinces, especially when it comes to the expertise required for the interpretation of the results. Currently, the Quebec *Medical Act* provides that only physicians are allowed to diagnose illnesses (section 31(1)). While some DTC companies assert that their services are not for diagnostic purposes, Quebec courts have broadly defined the term

"diagnosis" to include opinions and observations by a person on the health status of another individual [45]. Provincial medical colleges could eventually pressure provincial legislatures, such as Quebec's, to stop direct-to-consumer genetic testing companies from bypassing the involvement of a licensed physician during the interpretation process.

Costs and reimbursement

In Quebec, the universal Health Insurance Plan covers healthcare services that are medically necessary and that have been rendered by a licensed general practitioner or medical specialist [46]. The costs of any genetic test meeting this definition will be covered. Any healthcare service that is not medically necessary is not covered by the Plan. Patients are expected to pay for such services, which include most laboratory services, unless provided in a hospital [47].

Reimbursements can be made when the insured service is not available in the province of Quebec (Health Insurance Act, section 10) or when the individual did not present his/her health insurance card when receiving the service (section 13.1). In both cases, only covered medical services will be reimbursed provided the patient submits his/her claim within 1 year of the date on which he/she received the service (section 14.2).

Liability

Physicians in Quebec have four duties toward their patients: (i) duty to inform, (ii) duty to treat, (iii) duty to follow-up, and (iv) duty to uphold professional secrecy [47]. This section will focus on the duty to inform as well as the duty to uphold professional secrecy.

The essentials of the therapeutic duty to inform in Canada can be characterized as the provision of sufficient information (material risks, as well as, in the common law provinces, special or unusual risks) to patients in order for them to make the best decision possible when consenting to treatment. In the landmark common law *Reibl v Hughes* case [48], Judge Laskin of the Supreme Court of Canada wrote: "What 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" (paragraph 16). In *Hopp v Lepp* [49], the same Court further specified the scope of the duty to inform of physicians, to include answering "any specific questions posed by the patient as to the risks involved without being questioned, disclose 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" (paragraph 29). This

has since become the minimum standard with which physicians are expected to comply in the common law provinces.

In Quebec civil law however, courts have tended to reject the "reasonable patient" threshold proposed in *Reibl v Hughes* and upheld a test focused on what a reasonable physician would disclose in the circumstances [50]. In civil law jurisdictions more generally, the duty to inform has been advanced through civil codes. In Quebec, the duty to inform has been incorporated in both the *Civil Code of Quebec* and under professional norms, such as the *Code of Ethics of Physicians*. The latter enshrines the legal duty to provide the patient 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" (section 29). The physician–patient relationship, which is classified as a contractual relationship, is bound by the *Civil Code of Quebec*'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" (section 2102).

In France, the duty to inform is enshrined in the French *Code de la santé publique*. This law states that every person has the right to be informed about his/her state of health (section L1111-2), which would also include information pertaining to the proposed treatment, investigation, the potential benefits, and the foreseeable risks. In both jurisdictions, if a patient undergoes genetic testing prescribed by the physician, the latter is obligated to provide the patient with the results as well as how it affects his/her overall health assessment (e.g., diagnosis). But, is the clinician obligated to inform patients of incidental findings? A comprehensive answer to this question is made difficult by the lack of normative guidance on the topic although some argue that providing unverified and nonvalidated information to the patient is counterproductive and will most likely fail the standard of prudence and diligence required by the courts [51]. That being said, if a finding is validated and reveals a clinically significant and actionable condition, does the physician have a duty to return it? A recent proposal endorsed by the Board of Directors of the CCMG suggests that physicians should offer patients the option of receiving such findings [42]. Contrary to the position taken by the American College of Medical Genetics and Genomics, however, this proposal did not establish any duty to hunt for such findings.

Similar to common law jurisdictions, a breach of the duty to inform in civil law could result in the liability of clinicians 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 (i) fault, (ii) injury, and (iii) a causal link. Plaintiffs must prove the existence of each of these components: "[e]very person has a duty to honor 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" [52]. This same standard applies in France, where section 1382 of the French *Code civil* states, "Any act whatever of man [sic], which causes damage to another, obliges the one by whose fault it occurred, to compensate it." Section 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."

As for the duty to uphold professional secrecy, it is based on the right of every individual to nondisclosure of their confidential information. The Quebec *Charter of Human Rights and Freedoms* (chapter C-12) (a quasi-constitutional normative document) states that: "no person bound to professional secrecy by law may, even in judicial proceedings, disclose confidential information revealed to him by reason of his position or profession" (section 9). This duty, however, is not absolute and can be breached by the physician if he/she is authorized to do so by the patient or by an express provision of the law (section 9).

What about family members? Similar to the United States, clinicians in Quebec do not have a physician–patient relationship with the patient's relatives and, consequently, have no duty toward them. However, the law allows physicians to breach their professional secrecy when "there are compelling and just grounds related to the health or safety of the patient or of others" [53] or if someone's life is in peril and requires immediate physical assistance (duty to rescue) [54]. The "compelling and just grounds" authorization is discretionary and not an obligation. As for the duty to rescue, most authors argue that it does not apply to genetic conditions [42]. In any case, until clear legislative guidance is made available, one cannot conclude that a physician has a duty toward the relatives of patients. A recent Quebec case, *Watters v White* [55], tackled this issue more specifically and arrived at the conclusion that physicians only owe a duty to inform to their patients. The facts of the case, however, dated back to the 1970s and may not be pertinent to today's standards. The recent proposal endorsed by the CCMG suggests that when "results reveal clinically significant and actionable conditions for identifiable family members, physicians should, on a case-by-case basis, encourage patients to communicate such results." Moreover, physicians are encouraged to make themselves available to discuss such matters with the family members.

CONCLUSIONS FOCUSING ON WHAT THIS WILL MEAN FOR NEXT GENERATION SEQUENCING

This brief comparison reveals the complexity of the legal issues raised by implementing new genomic technologies in the clinical setting, both within any particular country and among countries. The legislative and regulatory process is complicated, with jurisdiction often being spread among different levels of government. In many instances, legislators and regulators have failed to address issues raised by new

technologies, especially in a comprehensive manner. When they have spoken, their actions are not always consistent. Direct-to-consumer genetic testing, for example, currently is treated differently in the United States and Canada. Privacy rules also differ widely around the world, as do which technologies are covered by healthcare systems. To make matters even more challenging, the relevant laws and regulations continue to change over time. Another source of diversity is in the scope of liability, a factor known to drive clinician behavior, which is defined differently in civil law and common law jurisdictions, the judge-made law in the latter injecting an additional element of uncertainty. Thus, those who are working in this field are advised to obtain expert legal advice about the legal landscape in the jurisdiction(s) in which they operate, recognizing that the law simply defines the outer limits of what is permissible and mandatory and that many of the most challenging issues will turn on ethical norms well within these legal boundaries.

This chapter was supported in part by 1R21HG00612-01 and by Genome Canada through the *Innovative chemogenomic tools to improve outcome in acute myeloid leukemia* project.

REFERENCES

[1] Katz G, Schweitzer SO. Implications of genetic testing for health policy. Yale J Health Policy Law Ethics 2013;10(1):90–134.
[2] 42 U.S.C. § 263a (2014).
[3] Evans BJ. The first amendment right to speak about the human genome. University of Pennsylvania. J Constitut Law 2014;16.
[4] 21 C.F.R. Part 812 (2014).
[5] Evans BJ, Dorschner MO, Burke W, Jarvik GP. Regulatory changes raise troubling questions for genomic testing. Genet Med 2014;16(11):799–803.
[6] N.Y. Comp. Codes R. & Regs., tit.10, § 58-1.7 (2014).
[7] Cal. Bus. & Prof. Code § 1288.5 (2014).
[8] ASHG statement. Professional disclosure of familial genetic information. The American Society of Human Genetics Social Issues Subcommittee on Familial Disclosure. Am J Hum Genet 1998; 62(2):474–83.
[9] 78 Fed. Reg. 5566 at 5668 (2013).
[10] Dupras C, Ravitsky V. Disclosing genetic information to family members: the role of empirical ethics. eLS. Chichester: John Wiley & Sons; 2013.
[11] 45 C.F.R. § 164.524 (2014).
[12] 45 CFR §164.501 (2014).
[13] 79 Fed. Reg. 7290 at 7296 (2014).
[14] 45 C.F.R. § 493.1291(l) (2014).
[15] Pulley JM, Denny JC, Peterson JF, et al. Operational implementation of prospective genotyping for personalized medicine: the design of the Vanderbilt PREDICT project. Clin Pharmacol Ther 2012;92(1):87–95.
[16] PharmGKB. CPIC: Clinical Pharmacogenetics Implementation Consortium. <http://www.pharmgkb.org/page/cpic> [accessed 9.5.2015].
[17] Eckstein L, Garrett JR, Berkman BE. A framework for analyzing the ethics of disclosing genetic research findings. J Law Med Ethics 2014;42(2):190–207.

[18] Goldrich MS. Direct-to-consumer diagnostic imaging tests, Report of The Council on Ethical and Judicial Affairs; 2005.
[19] Roberts JS, Ostergren J. Direct-to-Consumer genetic testing and personal genomics services: a review of recent empirical studies. Curr Genet Med Rep 2013;1(3):182–200.
[20] Caulfield T, McGuire AL. Direct-to-consumer genetic testing: perceptions, problems, and policy responses. Annu Rev Med 2012;63:23–33.
[21] Borry P, Cornel MC, Howard HC. Where are you going, where have you been: a recent history of the direct-to-consumer genetic testing market. J Community Genet 2010;1(3):101–6.
[22] Food and Drug Administration. Warning Letter to 23andMe, Inc.; 11/22/2013.
[23] Dick HC. Risk and responsibility: state regulation and enforcement of the direct-to-consumer genetic testing industry. J Health Law Policy 2012;6(1):167.
[24] Mainous III AG, Johnson SP, Chirina S, Baker R. Academic family physicians' perception of genetic testing and integration into practice: a CERA study. Fam Med 2013;45(4):257–62.
[25] Goldsmith L, Jackson L, O'Connor A, Skirton H. Direct-to-consumer genomic testing from the perspective of the health professional: a systematic review of the literature. J Community Genet 2013;4(2):169–80.
[26] Bloss CS, Schork NJ, Topol EJ. Direct-to-consumer pharmacogenomic testing is associated with increased physician utilisation. J Med Genet 2014;51(2):83–9.
[27] Public Health Service Act § 2713 (2010).
[28] Michael DG, Needham DF, Teed N, Brown T. Genetic testing insurance coverage trends: a review of publicly available policies from the largest US payers. Pers Med 2013;10(3):235–43.
[29] ACMG policy statement: updated recommendations regarding analysis and reporting of secondary findings in clinical genome-scale sequencing. Genet Med 2014.
[30] Clayton EW, Haga S, Kuszler P, Bane E, Shutske K, Burke W. Managing incidental genomic findings: legal obligations of clinicians. Genet Med 2013;15(8):624–9.
[31] Holm IA. Clinical management of pediatric genomic testing. Curr Genet Med Rep 2014;1–4.
[32] Green RC, Berg JS, Grody WW, Kalia SS, Korf BR, Martin CL, et al. ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing. Genet Med 2013; 15(7):565–74.
[33] Incidental findings in clinical genomics: a clarification. Genet Med 2013;15(8):664–66.
[34] Kocarnik JM, Fullerton SM. Returning pleiotropic results from genetic testing to patients and research participants. JAMA 2014;311(8):795–6.
[35] 677 A.2d 1188 (N.J. App. Div. 1996).
[36] 661 So.2d 278 (Fla. 1995).
[37] Section 91(27) *Constitution Act*.
[38] Section 92 (7) *Constitution Act*.
[39] Joly Y, Koutrikas G, Tassé AM, Issa A, Carleton B, Hayden M, et al. Regulatory approval for new pharmacogenomics tests: a comparative overview. Food Drug Law J 2011;66(1):1–24.
[40] *Medical Devices Regulations*, SOR/98-282, section 6.
[41] 98/79/EC; 93/42/EEC; 90/385/EEC.
[42] Zawati MH, Parry D, Thorogood A, Nguyen MT, Boycott K, Rosenblatt D, et al. Reporting results from whole-genome and whole-exome sequencing in clinical practice: a proposal for Canada? J Med Genet 2014;51(1):68–70.
[43] Picard A. Controversial genetic self-testing kits coming to Canada. Globe and Mail online: <http://www.theglobeandmail.com/life/health-and-fitness/health/genetic-self-testing-kits-to-come-to-canada/article20885678/> [accessed 9.5.2015].
[44] R.S.C., 1985, c. F-27.
[45] Zawati MH. Les conseillers en génétique et les professions médicales et infirmières au Québec: des frontières brouillées ? MJLH 2012;137–87.
[46] *Health Insurance Act*, chapter A-29, section 3a.
[47] Régie de l'assurance maladie du Québec (RAMQ) (Quebec Health Insurance) website: <http://www.ramq.gouv.qc.ca/en/citizens/health-insurance/healthcare/Pages/medical-services.aspx> [accessed 9.5.2015].

[48] Reibl v Hughes, [1980] 2 SCR 880, 114 DLR (3d) 1.
[49] Hopp v Lepp ([1980] 2 SCR 192, 112 DLR (3d) 67.
[50] Pelletier c Roberge, 41 QAC 161, [1991] RRA 726 (Qc CA).
[51] Philips-Nootens S, Lesage-Jarjoura P, Kouri R. Éléments de responsabilité civile médicale: le droit dans le quotidien de la médecine. 3rd ed. Cowansville: Yvon Blais; 2007.
[52] *Civil Code of Quebec*, section 1458.
[53] *Code of Ethics of Physicians*, section 20(5).
[54] *Charter of Human Rights and Freedoms*, section 2.
[55] *Watters v White*, 2012 QCCA 257.