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Overview of Law and Policy Challenges

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I will set the context for the next day and a half for the three particular topics that we will address. However, first I will take you through four phenomena that are affecting how population health, how pharmacogenomics and the Haplotype Map will be received, and how policies will or will not be crafted.

The four phenomena, drawn from experience over the last fifteen years, may be described as (1) reductionism, (2) overgeneralization, (3) exceptionalism, and (4) commercialization. These four phenomena affect how policy is made and how the public perceives genomic advances.

The most troubling of these phenomena is the first, the phenomenon of reductionism, which I refer to as "genes are us." This phenomenon has been driven by the perception that you are your genes, and you are fatally determined and predisposed by your genetic code. In the United States, this perception has led lawmakers to adopt genetics-specific laws—for example, to prohibit employer and insurer discrimination based upon genetic information. The premise for this legislation is that additional statutory protection is necessary because genetic information is different from other medical information—i.e., genetic information will not be understood, and you will be perceived by employers and insurers as already ill based upon your genes.

Reductionism is not particular to the U.S., where there is no universal health care system. European countries also have been adopting this "genes are us" reductionist or determinist approach, because they see life insurance as a social good.[1] Life insurance is

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1. Trudo Lemmens et al., *Génétique et Assurance Vie: Analyse Comparative*, GenEdit, March 2004, *available at* http://www.humgen.umontreal.ca/int/GE/fr/2004-2Fr.pdf.

a requisite to buy a car, have a mortgage, or take out a loan.[2] Many Europeans are concerned that, should insurers get hold of genetic information, they probably will misinterpret it and use it against the candidate by driving up fees or put life insurance totally out of citizens' hands. The resulting legislative approach undermines the potential of genetics, and actually serves to exacerbate possible discrimination rather than normalizing genetic information as medical information that may be highly sensitive.

The second phenomenon is overgeneralization, and this is what I call the "spill-over effect"—the view that nature is immutable, nature is static, and genes should not be touched. And so, coming from a totally different field, nothing to do with genetic diseases, are genetically modified organisms, or GMOs. Now, this country in particular has been spared some of the ravages of the movement against GMOs that is playing itself out in Europe, but we are beginning to see the effects in Canada with calls for labelling on anything that has been genetically modified.[3] Well, I would predict that, if you are really going to be honest in this labelling, you are going to find it extremely difficult if not impossible to implement. In Europe, where they have adopted this approach, they have not been able to put the labelling into effect yet. The Europeans are discovering that virtually everything, somewhere along the line, has been genetically modified. Nevertheless, this view of nature as static, as immutable, and the idea that companies, such as Monsanto, are harming the environment, harming genes, harming people, has further diminished public trust in the future of genetics.

The third phenomenon, exceptionalism, is my favorite because this is how I get through customs. When people ask me, "What do you do? Why are you going down to the United States?" if I say,

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2. Bartha Maria Knoppers et al., *A Comparative International Overview*, *in* Genetics and Life Insurance, Medical Underwriting and Social Policy (Mark A. Rothstein ed., 2004).

3. *See, e.g.*, Canadian General Standards Board, Voluntary Labeling and Advertising of Foods That Are and Are Not Products of Genetic Engineering, http://www.pwgsc.gc.ca/cgsb/032_025/standard-e.html; Canadian Food Inpection Agency, http://www.inspection.gc.ca/english/corpaffr/newcom/2004/20040415e.shtml; The Campaign to Label Genetically Engineered Foods, http://www.thecampaign.org/canada/index.php.

"Biotechnology and ethics," their eyes sort of get bigger and they say, "Well, what is that?" So now I just say, "Well, you know, Dolly . . . ."[4] Everyone knows Dolly. Dolly, the icon, not only gets me through customs, but also has served, if you like, as a target for cloning technology and has helped to inspire an international movement to promote a ban on, and adopt an international convention against, human reproductive cloning.[5]

Now, this is one of the areas where we do find, in spite of different norms, ethics, cultures, and worldviews around the globe, quite a lot of consensus. But the inability to adopt a United Nation's convention over the last three years is attributable to usurpation of Dolly in the political domain. Dolly has been used in political rhetoric to say that, in addition to banning human reproductive cloning, we should ban all forms of cloning, including therapeutic cloning which uses stem cells from pre-embryos.[6] The net effect of "Dolly" is laws and protection mechanisms crafted for anything in the area of gene therapy or research and, like the previous phenomenon, technology becomes "genetic" and suspect. Consequently, the possibility of creating the first international instrument in the area of biotechnology, an instrument that will manage to achieve some consensus, looks quite dim, at least over the next few years.

The fourth phenomenon is commercialization. I have been interacting with geneticists for about fifteen years now—going to their labs and trying to understand a science that I am not trained in. In the early 1980s, it was common for samples to be shared and for people to call each other up and say, "Do you have a pedigree for this? Can I have some DNA on that? I hear Finland has a few interesting families," and so on. That era of collaboration and sharing in basic research is coming to a rapid end, and this is not unique to the U.S. The demise of the collaboration era is

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4. Schnieke I. Wilmut et al., *Viable Offspring Derived from Fetal and Adult Mammalian Cells*, Nature, Feb. 1997, at 810; Keith H. Campbell et al., *Cloning: Eight Years after Dolly*, Reproduction in Domestic Animals, Aug. 2005, at 256.

5. United Nations Declaration on Human Cloning, G.A. Res. 59/280, U.N. GAOR, 59th Sess., U.N. Doc. A/RES/59/280 (Mar. 23, 2005).

6. *See, e.g.*, World Health Organization, *Cloning in Human Health*, Report by the Secretariat, 52d Assembly (Apr. 1999).

attributable to the alliance between academia and industry that is promoted by the universities and by governments who say that the private sector should pull its own weight, and that the public sector alone cannot shoulder the full costs of basic research.

This shift has led to perceived and actual conflicts of interest, and we find "gag clauses" in the contracts that are drawn up for researchers working in labs dealing with health issues and looking for therapies for humans. These clauses say things like, "You cannot publish, you cannot talk at a meeting, you cannot submit an abstract, you cannot do anything in the public domain until you have the approval of a commercial sponsor."[7] This has caused many student researchers under the level of post-doc to opt-out of working in labs to ensure that they will still have the freedom to get their thesis through without being slowed down by this kind of process. This situation is not as dim and dismal as I make it out to be; it is the reality, if you like, of a new kind of funding. Nevertheless, this new reality demands more transparency and perhaps calls for rules that ensure freedom of basic research while promoting research support.

Patents and proprietary interests under commercialization have received tremendous world attention. Access to AIDS drug treatments, the imposition of patent norms on developing countries, and tensions between the holders of proprietary interests in the breast cancer gene test and universal health care systems are the subject of worldwide debate.[8] There are countries that have said that they do not think the gene in any form should be patentable, obviously showing a misunderstanding of the patent system, as well as the gene, in terms of what is actually going on. And there are researchers who have patented their innovations, and who have actually done it purposely in order to put the knowledge into the public domain so it could be used, and have ensured very broad licensing arrangements to make sure patent interests do not

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7. Geneviève Cardinal & Bartha Maria Knoppers, *Lorsqu'en Recherché Génétique, Financement Privé ne Rime Plus Avec Santé, in* Les Pratiques de Recherché Biomédicale Visitées par la Bioéthique (Chrisitan Hervé et al. eds., 2003).

8. Yann Joly, *Accès Aux Médicaments: Le Système International des Brevets Empêchera-t-il les Pays du Tiers Monde de Bénéficier des Avantages de la Pharmacogénomique*, Les Cahiers de Propriété Intellectuelle (2003).

adversely affect the health care system. In Europe, there is still opposition to the breast cancer gene test put out by Myriad for many reasons.[9] The current worry is that the debate we have had over patents through the last decade will be repeated in an even broader, potentially endless debate over the legitimacy of copyright in genomic databases.

To conclude then on these four phenomena and on the subject of commercialization, the one issue that has not been squarely faced in Europe, Japan, and Canada is the impact of the large number of patents issued, each with exclusive rights and licenses, on a universal health care system. Now, in a universal health care system such as Canada's, to give you an example, when the BRCA1 and BRCA2 genes were patented by Myriad, the exclusive license was given to one company in Canada. Of course, that allowed one company to set the price at a rate they desired. The resulting inequitable access by women with breast cancer across Canada was a first for the Canadian universal health care system.[10] Some supported offering the test to patients on a case-by-case basis, each to be approved by the Ministry of Health. Others said, "No, we have a test that we're going to use that is not as good but at least everyone will get access to it." And others said, "No, we're going to contest the patent."[11] Variations of this scenario are taking place in many other countries with universal health care systems.

Keeping these four phenomena in mind, let us move to how these perceptions, social representations if you like, of human genetics and advances therein will affect the three topics we will be looking at tomorrow and the next day. Such consideration was

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9. Sabine Steimle, *Critics Question BRCA2 Patent Decision in Europe*, Journal of the Cancer Institute, Sept. 21, 2005, at 18.

10. Laura Eggertson, *Ontario Defied U.S. Firm's Genetic Patent, Continues Cancer Screening*, Canadian Medical Association Journal, Feb. 19, 2002, at 166.

11. T. Caulfield et al., *Genetic Technologies, Health Care Policy and the Patent Bargain*, Clinical Genetics, Jan. 2003, at 15; Richard Gold et al., *Gene Patents and the Standard of Care*, Canadian Medical Association Journal, Aug. 6, 2002, at 167; Jinisi Paradise, *European Opposition to Exclusive Control over Predictive Breast Cancer Testing and the Inherent Implications for United States Patent Law and Public Policy: A Case Study of the Myriad Genetics' BRCA Patent Controversy*, 59 Food and Drug L.J. 133 (2004).

directly integrated into the Human Genome Project ("HGP") when it put a percentage of its budget aside to contemplate ethical, legal, and social implications under worldviews.[12]

In other words, HGP planned that ethics would be part of the advances in genetic research. Therefore, before looking specifically at population health, pharmacogenomics, and the Haplotype Map, we have to ask ourselves whether these endeavors fully integrate and conceptually constitute a solid triangle depicting the advancement of science or, rather, a more surreal painting depicting Darwin, Dali, and science. In other words, we must ask ourselves whether these three very important endeavors will be able to contribute to the advancement of science in a tangible, meaningful manner.

Currently, population health has three sources of policies that will protect human subjects, protect or advance population health, or obstruct it. The first is that of personal data legislation. A lot of personal data legislation originated in the 1980s from fears of state surveillance, the creation and use of information banks for commercial marketing, and access to personal financial data by credit card companies and other entities. So there are very strong personal privacy concerns surrounding the elaboration of these particular laws.

Consider that, at the same time these concerns arose, we also had the emergence of forensic banks, including forensic databanks on violent criminals and recidivists.[13] Here, there are socially carved exceptions to personal data legislation to promote public security and public safety interests. But these new personal data laws lost a traditional exception, which has existed since the 1950s, for public health concerns. No longer was there an opportunity for the state to intervene on behalf of the population and legitimately

12. The Human Genome Organisation, http://www.hugo-international .org/committee_ethics.htm.

13. The Federal Bureau of Investigation in the United States operates the Combined DNA Index System, which is available at http:// www.fbi.gov/hq/lab/codis/index1.htm; The Royal Canadian Mounted Police operates the National DNA Databank, which is available at http:// www.rcmp.ca/security/index_e.htm. *See also* Donald Crosby, Protection of Genetic Information: An International Comparison (2000).

access personal data. These provisions were reduced, except in the forensic or national security areas.

At the same time, the protection of medical records *per se* increased with the popularity of the notion that the confidentiality of such data is important and that genetic data should also be protected.[14] But should genetic information be protected under personal data legislation, under medical data legislation, or should it have its own sphere of protection carved to fit this kind of data? Well, I have argued that the best approach would be to increase protection of medical data and integrate genetic data therein so as to avoid the deterministic approach and avoid the kind of discrimination that comes when you think genetic data somehow is different—that it is not part of the normal human condition.

Medical data, and the protection thereof, has also been influenced by the codes of ethics that have emerged since the Nuremberg Code of 1947. These codes, specifically aimed at protecting research subjects, have grown and multiplied over the years. I could easily do a good Ph.D. study comparing these codes and their sometime contradictory statements which, perhaps, is good because of cultural differences. But one common thread runs through all of the ethical codes involving medical and biomedical research, and that is the protection of the individual, the autonomy of the individual.[15]

So, pulling together personal data legislation, medical protection, and the principle of autonomy, one must ask herself, "How can we still do population health research? How can we build a philosophy, if you like, of populations?" Maybe genetics will get us there because genetics transcends the individual. It is necessarily familial; we are going to have to rework those codes with an eye towards families. Genetics is also communities and, in

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14. *See generally* Genetic Secrets: Protecting Privacy and Confidentiality in the Genetic Era (Mark A. Rothstein ed., 1997); Genetic Ethics: Do the Ends Justify the Genes? (John F. Kilner et al. eds., 1997).

15. *See, e.g.*, World Health Organization, Genetic Databases: Assessing the Benefits and the Impact on Human & Patient Rights (2003); World Medical Association, Declaration of Helsinki (2002), *available at* http://www.wma.net/e/policy/b3.htm; U.N. Education, Scientific, & Cultural Organization [UNESCO], International Declaration on Human Genetic Data, Art. 1(a) (Oct. 16, 2003).

some regions, it is ethnic groups. We have known this for quite a while, but we have not really done much applied medicine with that knowledge, except through specialized screening programs. And now, as we will see starting tomorrow, genetics is encompassing whole regions and countries through establishment of biobanks; populations are learning to think of their genes and their records as resources for research.

Potential collective benefits rather than immediate, individual benefits are driving this trend. It is not as if participants were in a clinical drug trial for cancer, obesity, or hypertension. How do we change the mindset of people to participate in these necessarily longitudinal studies? The problem is that, even if we get citizens to participate, and even if things go well, the language used to identify the samples—to take but two examples: coded, anonymized, de-identified schemes under the Health Insurance Portability and Accountability Act ("HIPAA"),[16] and double-coded, reversibly anonymized schemes in the United Kingdom biobank[17]—will make it impossible to collaborate and share these samples on an international level. The taxonomy or the nomenclature, whatever you want to call it, is the vocabulary that could thwart necessary international collaboration and sharing.[18]

What about pharmacogenomics? The alchemist during the Middle Ages had two goals, one was to find immortality and the other was to turn gross metals into gold. Well, some have likened this new era of pharmacogenomics and individual life medicine, molecular medicine, and so on to a new era of alchemy. But in 2003, the *American Journal of Pharmacogenomics*, in an article entitled *Pharmacogenomics and Individualized Drug Therapy: High Expectations and Disappointing Achievements* concluded, "For the next five years or longer, we do not expect that tests based on these approaches will become available to the practicing

16. Health Insurance Portability and Accountability Act of 1996, Pub. L. No. 104–91, 110 Stat. 1936.

17. The Wellcome Trust, Medical Research Council and Department of Health, U.K. Biobank Ethics and Governance Framework, http://www.ukbiobank.ac.uk/docs/egf-comment-version.doc.

18. Bartha Maria Knoppers & Madelaine Saginur, *The Babel of Genetic Data Terminology*, Nature Biotechnology, Aug. 1, 2005, at 925.

clinician."[19] Now, I do not want to be a prophet of doom. I think what they mean is that pharmacogenomics is going to stay largely in the research sphere for the foreseeable future. In fact, some would argue that there are certain dangers in disease stratification and patient stratification. I do have some positive, immediate hopes, however, for pharmacogenomics. At a minimum, it will probably be used in terms of genotyping to exclude people from Phase 1 trials, people who would be at risk for adverse effects such as death from toxicity and so on. So pharmacogenomic probably will make a meaningful debut in clinical trials rather than clinical care, and in terms of ensuring safety and exclusion rather than inclusion and treatment.

Now, a few words to place the Haplotype Map into the context of the four phenomena. Here we are, rather than doing candidate genes and dealing with families with rare, inherited conditions, we are looking at assembling a resource, a research tool, that will allow us to build ancestral blocks and a better understanding of genetic variation and the role that genetic variation plays in the expression of genetic diseases. So it is not really a genetic map, it is a genomics map. You will hear much during this conference about the implications of shifting from traditional population health to haplotype mapping. For example, the haplotype mapping people have their hands full because people say, "It's okay, you're not identifying people; you are using anonymized samples." But these samples are taken from populations, such as the Yorubans in Nigeria, the Han Chinese in China, the Japanese, and the Mormon population of Utah. So people will be profiled, albeit collectively. The more we know, the more we will associate risks and diseases with the Chinese, the Yorubans, and so forth. And so we will attribute, if you like, genetic characteristics based on such origins; we will be labelling.

What if we find out that people who thought they were from one ethnic origin, people who have built countries and established land ownership and cultural history tied to ancestral beliefs, who have relied on their beliefs about their identity when in fact these

19. D.W. Nebert et al., *Pharmacogenomics and "Individualized Drug Therapy": High Expectations and Disappointing Achievements*, 3 Am. J. Pharmacogenomics 361, 370 (2003).

beliefs have no biological basis and, in fact, the biology runs against their beliefs? The social-political constructs that we have built up over time in history might prove to be unfounded, biologically speaking. So these are some of the challenges facing this very important effort, and one that I think, in the long run, will serve not only as a research tool, but also as a resource for the validation of other genetic tests.

In conclusion, we are talking about new policies, legislation, regulations, guidelines, or a combination thereof in response to the genomics revolution. We must consider our options and chart an approach. I talked about genetics-specific legislation, and the dangers of adopting genetics-specific laws that usually prove to be inadequate. When Dolly was born, several countries enacted legislation to ban cloning but the science was so specifically described in the definition sections that the technique used in Dolly was not covered.[20] So there are specific laws, there are self-regulatory codes and codes of conduct, and guidelines.[21] There is also the free-market approach.[22] Finally, there is the approach that I favor, which is that of human rights.

I would argue that privacy, liberty, security, integrity, and, perhaps, new human rights will emerge. How we interpret human rights can incorporate understandings of the new biology, of the new genomics. We should adapt human rights to frame these technologies. If we increase the protection of medical records, if we are more transparent about commercial partnerships, if we increase their accountability, if we have more oversight by accredited, knowledgeable IRBs (independent review boards), incidentally, a real challenge in the population domain, if we move away from "What's in it for me"—the notion of personal benefit above all—and towards more of a citizen approach, if we stop equating tissues with humans and genes with persons, then I think we might have some possibility in the next decade of having a

20. George J. Annas et al., *Protecting the Endangered Human: Toward an International Treaty Prohibiting Cloning and Inheritable Alterations*, 28 Am. J.L. & Med. 151 (2002).

21. Bartha Maria Knoppers, *Reflection: The Challenge of Biotechnology and Public Policy*, 45 McGill L.J. 559 (2000).

22. *Id.*

more international approach, more harmonization, and, thus, collaboration.

One of the first slides shown today mentioned the word "epigenesis," and if you look at physics, you see an epigenetic approach—a complex systems approach that brings in all the interactive elements. We are really in a complex system of networks. These intersecting domains will allow a systems approach if we can handle the complexity and stay away from the polarization, the black and white, the polemic, and the rhetoric. If we arrive at this approach, I think we can handle the future that these three promising areas bring. One thing for sure is that if we tone down the rhetoric and the hype, and if we truly believe that these public endeavors are equally important to any other individual intervention, we may restore public trust and, I hope, increase public participation in these population endeavors.