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Implications of Genetic Testing for Health Policy

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Implications of Genetic Testing for Health Policy

Gregory Katz* and Stuart O. Schweitzer†

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INTRODUCTION

Genetic testing has created both opportunities and dilemmas for personal health care as well as public health systems. The sequencing of the human genome and advances in areas such as genomics and bioinformatics have brought about new diagnostic and therapeutic procedures. These rapidly arising innovations have created policy challenges to providers and other stakeholders, such as employers, insurers, and the legal system. In 1990, the United States National Institutes of Health (NIH) created a taskforce focusing on the ethical, legal, and social implications of human genome research and diagnostic testing. Similarly, the United States and some European countries have enacted legislation addressing discrimination that genetic testing might cause. As genetic testing technologies advance, national and international guidelines attempt to prepare and educate health professionals to prescribe genetic tests and interpret their results.

This paper addresses the apparent divergence between the advances in genetic-based medicine and the guidelines concerning quality standards for genetic tests and the appropriate use of those test results. The integration of genetic medicine into primary care has spread rapidly thanks to the availability of affordable diagnostic tests for an increasing number of diseases. In this paper, we focus on four aspects of genetic testing that present particular dilemmas for health policymakers both in the United States and abroad:

1) The diffusion of genetic testing and its impact on medical practices;

2) The tension between confidentiality and transparency related to health insurance;

3) The expansion of genetic testing for embryo selection; and

4) The evolution of regulatory frameworks for the assurance of quality of genetic tests.

1. Muin J. Khoury, Genetics and Genomics in Practice: The Continuum from Genetic Disease to Genetic Information in Health and Disease, 5 GENETICS MED. 261, 261 (2003).
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In Part I, we discuss the rapidly expanding use of genetic testing and how Internet access has accelerated this process. The Internet has also had the effect, however, of allowing genetic testing to bypass the physician entirely, which brings another set of issues to the forefront, including the need for interpretation and counseling.

Part II discusses the dialectics of confidentiality and transparency of genetic information. There are important public health and legal issues involving responsibility to inform others when specific genetic information impinges on their well-being. The decision to take a genetic test and the decision to disclose its results may create asymmetries of information that eventually disrupt the equilibrium between insurers and policyholders. Furthermore, even when legal protections prohibit genetic discrimination in the workplace, few trust that all parties will fully comply with these laws.

Beyond the issues of transparency, Part III analyzes how the expansion of genetic tests to in vitro fertilization is offering parents the possibility of selecting embryos based on genetic traits. Pre-implantation genetic diagnosis (PGD) uses genetic tests to screen human embryos for genetic predispositions to rare disorders as well as prevalent and treatable diseases, including breast cancer. For medico-economic reasons, will couples with genetic predispositions one day be invited by health authorities to seek assisted reproduction to test their embryos before having children?

In the last Part, this Article examines the state of regulatory authority concerning test validity and reliability. The status of regulation for test quality differs widely between the United States and European countries. Meaningful and harmonized regulation on a global scale is difficult to implement because over-regulation could limit innovation, while under-regulation may lead to commercial abuse, consumer confusion, and distrust of this promising health care revolution.

I. THE DIFFUSION OF GENETIC TESTING AND ITS IMPACT ON MEDICAL PRACTICES

According to a 2003 survey of eighteen OECD members, the expansion of genetic testing is staggering: between 2000 and 2002, the number of genetic tests

6. The Organisation for Economic Co-operation and Development (OECD) is composed of thirty democratic governments (including twenty-three European countries, Australia, Canada, Japan, Korea, Mexico, New Zealand, and the United States) who work together to compare policy experiences and address economic, social, and environmental challenges of globalization in order to identify good practices and coordinate domestic and international policies. The OECD promotes policies designed to achieve sustainable economic growth and employment and a rising standard of living in member and non-member countries. See ORG. FOR ECON. CO-OPERATION & DEV., ANNUAL REPORT 2009, at 9 (2009), available at http://www.oecd.org/dataoecd/38/39/431255523.pdf.
conducted in 827 hospitals nearly doubled. During 2001, 18,000 tissue samples crossed OECD country borders for laboratory testing in other countries. As of October 2009, genetic tests for predispositions to 1819 diseases, including type 2 diabetes, Alzheimer's disease, obesity, and breast cancer, were registered by GeneTests, an NIH sponsored think-tank. The number of laboratories performing those tests has remained stable since 2003 (Figure 1). On the other hand, the number of diseases for which a test is available has grown at an average annual rate of twelve percent since 2002. These two trends illustrate that laboratories are increasingly engaged in genetic testing and, as a result, are significantly shaping medical practices both nationally and globally.

A. Medical Practices and National Disparities

In 2003, only fifty-seven percent of laboratories in OECD countries required written informed consent prior to testing. In the United States, no harmonized federal requirements for informed consent regarding genetic testing exist. At a state level, Delaware, Nevada, New Jersey, New York, and Oregon laws require researchers to obtain individual informed consent before retaining genetic information. The absence of such an informed consent could conflict with the need to retain biological samples for quality assurance reasons. A New York State Civil Rights Law requires testing laboratories to obtain written informed consent prior to conducting certain genetic tests. Similarly, laboratories operating in Arkansas and Oklahoma must preserve patient privacy through the use of written informed consent forms prior to conducting genetic testing and research on biological tissue and blood. Other states require informed consent for genetic testing but do not require consent for research as long as patient

8. Id. at 13.
10. This calculation is based on the 2002-2008 data presented in Figure 1.
11. OECD, GENETIC TESTING, supra note 7, at 46. Such a written informed consent would describe the genetic test and its limitations and risks and would be used to protect patient privacy and rights.
12. See id. at 125.
15. See HAKIMIAN ET AL., supra note 13, at 7.
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identities are not disclosed. New Jersey is the strictest on the use of samples for research. The state's Genetic Privacy Act requires that samples used in genetic research be destroyed upon completion of the project.16 In most European countries, patients must provide written informed consent prior to genetic testing. However, according to the OECD survey, even in the absence of informed consent, only thirteen percent of laboratories declined to perform the test. Almost half of genetic testing laboratories in OECD member states are not accredited or certified.17 In the United States, all clinical laboratories must be certified under a common licensing law, whereas few European OECD countries impose licensing requirements.18 For instance, in Finland, Ireland, Sweden, Turkey, and the United Kingdom, laboratories are not required to obtain a government issued license for genetic testing.19

These data reflect significant regulatory disparity across countries, within countries and between hospital laboratories. Without adapted regulation and medical training programs, genetic tests and services have developed erratically, with poor clinical reliability, thus fostering the distrust of practitioners and patients. The difficulty of adopting harmonized medical training for the use and interpretation of genetic tests is partly due to the rapid growth in genetic testing availability. This difficulty is exacerbated by the pace of scientific breakthroughs in bioinformatics and sequencing technologies, which complicates designing updated training programs for laboratory technicians and medical practitioners. At a laboratory level, the OECD reported that "74% [of laboratory directors] were certified or registered to practice clinical laboratory medicine by an officially recognised body, and 67% had received formal training in molecular genetics."20 Furthermore, the majority of laboratories employed technicians, ninety-one percent of whom had minimum education and training, to perform the genetic tests.21

The challenge of regulating genetic testing is to create an adequate framework that enables patients to access health care and targeted treatment without fear of misuse or discrimination based on their genetic profile.22 Many countries therefore recognize the need for tighter regulation regarding access to

16. See id.
17. See OECD, GENETIC TESTING, supra note 7, at 87-88.
19. See OECD, GENETIC TESTING, supra note 7, at 88-90.
20. Id. at 37.
21. Id. at 125.
genetic testing and subsequent health care. Standardized medical training and laboratory accreditation are also considered as possible ways to harmonize testing procedures and reliability of results. In its guidelines on genetic testing, the OECD stresses that genetic tests should be delivered by a health care professional and within a quality assurance framework.

National and international organizations recognize the need to develop harmonized international best practice policies for quality assurance and accreditation of genetic tests. Many OECD countries also identified the need for national gatekeepers, such as health authorities and organizations, to oversee testing availability, quality, and procedures. Both the U.S. Food and Drug Administration (FDA) and the U.K. National Health Service (NHS) have issued guidance documents for industry, regulatory, and medical staff promoting best practice guidelines and procedures for the development and use of genetic diagnostic tests. In the United Kingdom for instance, the government-supported U.K. Genetic Testing Network (UKGTN) aims to increase oversight awareness among laboratory directors. Providing laboratories with incentives to comply with standards on genetic testing safety, effectiveness, and quality improvement would promote the harmonization of public policy.


26. See OECD GUIDELINES, supra note 24, at 19.


28. See OECD, GENETIC TESTING, supra note 7, at 88.
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Definitions

- **Clinical validity** is the ability of a test to detect or predict the associated disorder. 29 The clinical validity of a test measures the precision with which a test identifies a condition or a predisposition to a condition. Validity is defined in terms of specificity, sensitivity, and predictive value on a clinical basis.

- **Clinical utility** is determined by the risks and benefits associated with a test’s introduction into routine practice. 30 Clinical utility expresses the value of test results in order to guide the tested individual in his/her choices regarding preventative strategies or treatment.

B. Online Distribution

Some medical laboratories take advantage of regulatory loopholes to circumvent health authorities, enabling the commercialization of genetic tests in a poorly controlled market. Commercial websites use the loose regulatory framework to increase their market share through various forms of retailing services. Retailers such as DNAdirect sell genetic tests manufactured by other companies. For example, the test for cystic fibrosis is sold for $260. 31 Another retailer, 23andMe, commercializes medical tests 32 as well as tests for eye color transmission, manufactured by DNAPrint Genomics, Inc., 33 and for muscular performance for sports professionals, manufactured by Genetic Technologies. 34 In 2007, Google invested $3.9 million into 23andMe and, in parallel, decided to launch Google Health, a web-based medical record repository aimed at creating a personal, digital future for health-related data. 35 Google Health allows individuals to correlate their medical history and genetic test results with their treatments in order to minimize drug interactions and prevent adverse reactions.


30. See id.


32. 23andMe, http://www.23andme.com (last visited Nov. 11, 2009).


Other retailers such as Clinical Data Online sell genetic tests to physicians to better predict response rates to a particular drug. Clinical Data Online is a direct-to-practitioner platform, whereas 23andMe is a direct-to-consumer website.³⁶

Other websites such as Navigenics or deCODEme analyze their customers’ genetic profile and update results as soon as new tests are commercialized.³⁷ In other words, these firms do not offer single tests, but rather offer a continuing service as new tests become available. Registration fees are around $2500 and the annual cost is $250.³⁸ Similarly, companies such as Spain-based Labgenetics offer couples undergoing artificial reproductive technology the opportunity to use genetic tests to screen embryos through pre-implantation genetic diagnosis (PGD).³⁹ With the same genetic testing technology, Navigenics offers secondary prevention through early diagnosis, while Labgenetics offers primary prevention through embryo screening. In both cases, the revolution of consumer genomics has created a shift away from a physician-controlled approach towards a patient-empowered system.⁴⁰

C. Bypassing the Physician

Bolstered by the growing availability of commercialized tests on the Internet, genetic tests are thriving in an unregulated market. By turning to the Internet to purchase a genetic test, consumers bypass the doctor-patient relationship, together with its personalized genetic advice and counsel.⁴¹ Direct-to-consumer advertising of genetic tests does not encourage consumers to contact their health care provider.⁴² A recent study found that direct-to-consumer marketing of genetic tests increased consumers’ awareness about diseases, but failed to accurately convey risk information.⁴³ Until recently, the physician decided whether to prescribe a genetic test and would subsequently adapt the patient’s medical intervention according to the test results. Genetic test results are usually difficult for the layman to interpret because they are often imprecise and

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36. See 23andMe, supra note 32.
37. deCODEme, http://www.decode.me.com (last visited Nov. 11, 2009).
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Diseases commonly result from a combination of environmental factors and genetic factors. In weighing the genetic factors, it is important to know whether a disease is monogenic (caused by a single gene) or polygenic (caused by several genes). In addition, mutations in some genes have a strong impact on the development of a disease. These mutations, such as those that cause cystic fibrosis, are known as highly penetrant, where a patient who has the mutation almost surely will develop the disease. Mutations in other genes, such as those that are linked with hypercholesterolemia or autism, are not highly penetrant. In these cases, having the mutation may not mean that a patient will develop the disease.

For patients, attempting to interpret the complex results of genetic tests without any medical assistance could be a risky task. The results from a self-prescribed test can be all the more anxiety-provoking if the patient discovers that no treatment exists for the disorder, such as in the case of Huntington’s chorea, which is fatal. The announcement of the results of a positive genetic test could produce a violent emotional impact and disturb the patient’s psychological balance. A positive test for Huntington’s could also impact family members who may discover themselves to be carriers of the disease and who may unknowingly have passed the genetic mutation to their offspring. Additionally, the reliability of tests is in most cases questionable, creating additional distress for patients. For instance, genetic testing for BRCA1 and BRCA2 misses an estimated fifteen percent of mutations. Such false-negative test results may discourage patients from seeking further examination, leading to possible detrimental consequences. On the other hand, false-positive results for breast cancer testing could subject patients to further stressful and costly medical examinations, sometimes leading to unnecessary prophylactic mastectomies. Prenatal diagnosis to determine chromosomal or genetic disorders in the fetus,

known as Chorionic Villus Sampling, has a higher rate of false-positive results (1–1.5%) compared to amniocentesis (0.5%). Although useful as medical devices, genetic tests alone could interfere both with patients’ emotional stability and the quality of medical care they receive.

D. Duty to Inform?

In some cases, the duty to inform third parties about genetic test results has been interpreted as a duty to prevent foreseeable harm. When a patient refuses to disclose genetic information to relatives, it poses an ethical dilemma to health care professionals. When test results are kept confidential, which may be more likely when a patient orders the test directly, other persons at risk are not warned and lose the chance to receive preventative treatment. The French case is illustrative: in 2003, the French national bioethics advisory committee considered whether informing a patient’s relatives of a potential health risk should take precedence over protecting individual privacy. The 2004 French bioethics law states that if tests reveal a serious genetic predisposition, “the physician should inform the patient about the potential consequences of his or her silence: putting vulnerable family members at risk, who could otherwise benefit from preventative medical attention.” In the United States, there have been legal cases in which patients’ relatives have sued physicians for not warning them of their risk. The Safer v. Estate of Pack case illustrates this: a daughter sued her father’s physician for breaching his duty to warn her about a hereditary colon cancer risk.

In 2001, bioethicists Doukas and Berg proposed an original solution known as the “family covenant,” to overcome some of the ethical dilemmas brought

50. Godard et al., supra note 45, at S70.
52. R. Beth Dugan et al., Duty to Warn At-Risk Relatives for Genetic Disease: Genetic Counselors’ Clinical Experience, 119C AM. J. MED. GENETICS 27, 27 (2003).
55. CODE DE LA SANTE PUBLIQUE art. L1131-1 (Fr.).
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about by genetic testing. An agreement is established prior to genetic testing between the patient, their family, and the physician regarding which genetic information should be shared and with whom. This contract seeks to strike a balance between the need to respect the privacy of patients undergoing genetic testing, the rights of family members to be informed of genetic disorders that could affect them, and the responsibility that both relatives and physicians have in communicating genetic test results. Genetic test results may disrupt the patient-physician relationship; this contract contributes to stabilize this relationship by anticipating what decisions should be made before and after the test results are known.

Nonetheless, the legal situation remains unclear regarding disclosure against a patient's will. In 2003, Falk and her colleagues surveyed medical geneticists, all members of the American Society of Human Genetics and the American College of Medical Genetics. Their findings indicated that over two thirds of the surveyed geneticists considered themselves to be responsible for warning the relatives of their patients when discovered to be at-risk for a genetic disease. Faced with a patient who refuses to notify at-risk family members, one quarter of the geneticists contemplated disclosing the information to the at-risk relatives without their patient's consent. Four respondents only took the liberty to warn at-risk relatives about their genetic profile.

However, is it the physician's or the individual's responsibility to disclose medical information? Advocating the idea that the patient should inform other family members, the French medical statistician Adolphe Bertillon proposed in 1876 that each family should update a record of their medical history that is then made accessible to descendants. In present times, this opinion is supported by the National Society of Genetic Counselors. The American Society of Human Genetics, however, defends the position that information should be disclosed only if a high penetrance disease is preventable or treatable. Although they diverge on this point, both are leading organizations promoting the role of

59. See id.
61. See Patterson et al., supra note 56, at 2102.
genetic counselors in health care to ensure the quality of genetic services and the best application of those services to society. Additionally, the National Society of Genetic Counselors and the American Society of Clinical Oncology have both published formal statements opposing the ethical duty to warn.65 However, if genetic transparency provides a chance for prevention, does lack of disclosure from one family member hinder adequate treatment for another? Fundamentally, the underlying ethical dilemma consists in assessing whether the harm due to failure of disclosure outweighs the harm that may be caused by disclosure.66

II. BALANCING CONFIDENTIALITY AND TRANSPARENCY

A. Confidentiality and Discrimination

In 2003, nearly half of the hospitals in OECD countries used genetic tests without prior patient consent, and thirty-seven percent did not have a written confidentiality policy regarding test results.67 But what is really at stake when genetic data are disclosed to third parties such as health insurers68 or employers?69 A simple DNA sample represents an encrypted medical record containing statistical information, whose nature is radically different from that found in classic medical data.70 Before consumers entrust their biological samples to companies performing genetic tests, they should enquire about the confidentiality clauses provided by the firms that collect DNA samples in hospitals or through the Internet.71 Some of the firms offering genetic tests sell the clinical data to other laboratories or other companies.72 The confidentiality agreements of companies such as deCODEme, Myriad, or 23andMe may include certain contractual clauses allowing them, in some cases, to transfer their clients’ genetic data to third parties, much as credit card data is shared between commercial entities. However, an individual’s genetic code presents far more exposure to one’s personal state of well-being than a credit card number. While a

65. See Patterson et al., supra note 56, at 2103.
67. OECD, GENETIC TESTING, supra note 7, at 46, 81.
72. See Roche & Annas, supra note 70, at 546.
compromise of one’s credit card number can be mitigated, in part, by cancelling and replacing the credit card, one cannot simply change one’s set of chromosomes or genotype. When a third party comes into possession of a genetic sample, it can discover information that we ignore, discover information that we would prefer to ignore, and discover information that we wish others to ignore.

What should we worry about? The view that we have nothing to fear from genetic transparency has been suggested by its proponents, including James Watson shortly after publishing the sequence of his genome. We know, however, that Watson refused to allow one part of his genotype to be analyzed (the area implicated in the predisposition to Alzheimer’s disease (Apolipoprotein E)). His grandmother died of this serious neurological disorder, and for his own peace of mind, he does not wish to know of his predisposition to this disease. Besides personal reasons, social arguments could also dissuade people from taking genetic tests. Indeed, the fear of genetic discrimination may discourage some patients from using genetic tests, thus depriving themselves of appropriate treatment. Some people may not want to know about late-onset and incurable diseases, particularly if the information might lead to discrimination. Others attempt to persuade their physicians not to write their genetic test results in their medical records. Individuals might also avoid disclosing test results to their physician for fear of discovery by insurance companies. Upon discovery of genetic test results, some might give up purchasing more comprehensive health insurance, while others might decide to increase their coverage.

In the employment context, in order to avoid genetic information impinging on public freedom, the United States adopted several anti-discrimination laws. In 1990, Congress enacted the Americans with Disabilities Act (ADA), a civil

73. See id.
74. See id.
75. See Meredith Wadman, James Watson's Genome Sequenced at High Speed, 452 NATURE 788, 788 (2008).
78. See Nancy Kass & Amy Medley, Genetic Screening and Disability Insurance: What Can We Learn from the Health Insurance Experience?, 35 J.L. MED. & ETHICS (SPECIAL SUPPLEMENT) 66, 70 (2007) (discussing a risk that insurance companies might discriminate against individuals genetically disposed to disease).
80. See id. at 126.
rights law prohibiting discrimination based on disability. The ADA Amendments Act was signed into law in 2008, giving broader protections for disabled workers. In 2000, an executive order was issued by President Bill Clinton, prohibiting discrimination in employment based on genetic information and imposing a duty of confidentiality regarding genetic data outside an employee’s company. However, this law does not prevent the employer from using the information internally as a decision or human resource management tool. Once the employee is hired, medical exams can be performed, including genetic tests. Refusing to comply with these genetic tests might lead to job loss or denial of a promotion. Furthermore, in order to enforce the law, employees need to prove that their employers have discriminated against them on the basis of their genetic information. American case law has addressed various such instances: a medical laboratory that tested its own employees for genetic predispositions or the 2001 case in which the Burlington Northern Santa Fe Railroad (BNSF) company used genetic tests on train drivers without their consent to detect their predispositions to Carpal Tunnel syndrome. Under the ADA, however, employers are not permitted to run genetic tests on their employees without their consent once they have become disabled. Thus the actions of BNSF were widely criticized and led to demands for bans on genetic discrimination in the workplace. A lawsuit arose in response to six employee complaints and the litigation was settled out of court: the railroad company agreed to pay $2.2 million in damages to thirty-six of its employees and to terminate the collection of blood samples for genetic


84. See id. at 6879.


86. Ellen Wright Clayton, Ethical, Legal and Social Implications of Genomic Medicine, 349 NEW ENG. J. MED. 562, 566-67 (2003).

87. Sally Lehrman, Medical Tests Cost Lawrence Berkeley $2.2 Million, 405 NATURE 110, 110 (2000). In 1995, seven employees of the Lawrence Berkeley National Laboratory (LBNL) sued the company, claiming it had performed genetic tests, using stored blood samples, to test its workers for pregnancy, sexually transmitted diseases, and sickle-cell trait without their consent, and made decisions to lay off employees based on these results. Following this class action, LBNL agreed in 2000 to a provisional $2.2 million settlement. See WEIR & OLICK, supra note 85, at 191-92.


89. See Clayton, supra note 86, at 564.
testing.\textsuperscript{90}

In the private insurance market, the Health Insurance Portability and Accountability Act (HIPAA) was passed in 1996 in order to help individuals benefit from continuous health coverage, particularly following job moves.\textsuperscript{91} One objective was to improve access to long-term group health coverage by waiving pre-existing condition exclusions for individuals.\textsuperscript{92} It addresses the security and privacy of health data by regulating, but not altogether excluding, the use and disclosure of information concerning an individual's medical record or payment history held by health insurers and medical service providers.\textsuperscript{93} Though its aim is to protect individuals, HIPAA has limitations: for instance, HIPAA cannot prevent an insurance company from raising the premiums for group health plans as a whole, based on the genetic information of one individual in that group.\textsuperscript{94} Based on genetic information, the insurance provider can refuse to insure potential customers, potentially leaving them without health insurance coverage.

The private health insurance market is not as widespread in Europe as in the United States, but the possible use of genetic information in insurance and employment is increasingly generating debate and causing concern.\textsuperscript{95} The European Convention on Human Rights and Biomedicine, also known as the Oviedo Convention, was approved by the Council of Europe in 1997 and was signed by thirty-four of its forty-seven member states,\textsuperscript{96} with the principal objective of protecting individuals from genetic discrimination.\textsuperscript{97} The Convention prohibits any form of discrimination based on a person's genetic heritage and limits the use of genetic tests for health and research purposes by mandating that appropriate genetic counseling be provided.

\textsuperscript{90} See Weir & Olick, supra note 85, at 188.
\textsuperscript{93} See George J. Annas, HIPAA Regulations—A New Era of Medical-Record Privacy?, 348 NEW ENG. J. MED. 1486, 1486-90 (2003).
\textsuperscript{94} Genetic(al) Correctness, 17 NATURE GENETICS 363, 364 (1997).
\textsuperscript{95} See Godard et al., supra note 79, at 124.
Among the member countries is Denmark, who signed the Convention in 1997 and ratified it by Parliamentary decision in 1999. Genetic testing in Denmark is "regulated through the legal framework that applies to the Danish national health care system as a whole." However, because the Danish Constitution states no rules regarding genetic discrimination, the Oviedo Convention was incorporated into Danish national law in 1992 in order to address these issues. The nondiscrimination rule in Article 14 of the Oviedo Convention prohibits the use of predictive genetic tests by insurance companies and employers. Although insurance companies and employers are not allowed to demand or make use of an individual’s genetic information, they are authorized to inquire about disorders or diseases which have already manifested in the individual or a family member. Individuals with a family history of breast cancer, for instance, could therefore be considered at-risk even in the absence of genetic test information.

Another example is Spain, in which the Constitution of 1978 and the General Health Care Act of 1986 guarantee the right to health care. Spain’s national legislation does not prohibit the use of predictive genetic tests. Nevertheless, in accordance with the Spanish Constitution, the Oviedo Convention supersedes national legislation and can be applied in Spain, thus protecting individuals from genetic discrimination, as outlined in Article 11 of the Convention. Over a dozen European countries have published Ethical-Legal Papers describing patients’ rights in Europe. Their aim is to contribute to a vaster five-year EU funded program, the EuroGentest, to build adequate frameworks and guidelines in order to achieve harmonization of genetic testing services across Europe.

The Convention has not, however, been signed by some of Europe’s leading countries, such as the United Kingdom and Germany. In Germany, the government issued a draft legislation in 2004 that would enable employers to perform genetic tests on job candidates in order to identify existing or potential

100. See Nys et al., supra note 98, at 40.
103. See Council of Europe, supra note 97.
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genetic disorders.104 In the United Kingdom, a Discrimination Law Review was proposed in February 2005 to create a clearer framework on the protection against genetic discrimination, but has not been adopted.105 Although most European countries do protect individuals from genetic discrimination, the European Group of Science, Ethics and New Technologies released a study in 2003 conducted on behalf of the Institute of Directors revealing that, out of 353 interviewed corporate managers and directors, thirty-four percent were in favor of genetic screening for heart diseases if the employee consented.106 This figure suggests that many European health systems, traditionally based on universal coverage, might shift their model from a mutualistic paradigm to a more individualized approach, based on genetic risk assessment. With the availability of genetic tools, employers—rather than policymakers—could provoke a shift in health care coverage systems.

Employers’ fear is met by the companies’ pragmatism: can they take the risk of signing a work contract with an employee whose health is questionable? An employee’s health insurance represents a significant expense, and the group’s premium can increase if an employee becomes seriously ill. In addition to the costs of higher health insurance premiums, employers are also responsible for indirect costs of illness such as the cost of replacing a sick employee. Employers might contemplate using genetic tests to prevent workplace accidents and their associated liabilities through the application of tests to detect altered sleep patterns, allowing them to match an individual’s sleep profile to the nature of his work.107 Another issue could arise from identification of a rare but debilitating disease. Could an applicant for auto insurance be turned down on the basis of his genetic profile, despite the fact that the applicant has never had the slightest accident or suffered from any of the disease symptoms?108 All these examples illustrate the potential of using genetic testing to assess risk factors for conditions that have not yet (and may never) appear. Under what circumstances, if any, should increased risk factors be used to affect current employment?

International organizations have also expressed concerns about the misuse of genetic testing data. For example, the United Nations Educational, Scientific and

104. See Barclay & Markel, supra note 22, at 958.
Cultural Organization (UNESCO) enacted a declaration on the protection of genetic data to protect employees from discrimination on the basis of genetic tests. The aim of this declaration is "to ensure the respect of human dignity and protection of human rights and fundamental freedoms in the collection, processing, use and storage of human genetic data." However, this declaration is not a convention and, as such, the United Nations cannot sanction member states that infringe the declaration's ethical principles.

In order to strengthen existing state laws on genetic discrimination, the U.S. Congress enacted the Genetic Information Nondiscrimination Act (GINA) in May 2008. Following thirteen years of deliberations and revisions, this act was put forward by then-Senator Barack Obama and subsequently unanimously adopted by both houses of Congress. GINA prohibits the use of genetic tests by recruiters and insurers. Companies using genetic tests to recruit, fire, or re-grade employees face fines of up to $500,000. Despite the law's intended goal of protecting employees, there is concern regarding the bill's effectiveness. Enforcement will remain difficult because a dismissed worker cannot easily prove that he or she is a victim of genetic discrimination because of loopholes in the law. For instance, a company can request a medical history of the employee's family and incidentally discover family genetic disorders. A company can also include genetic tests in health programs it offers its employees and access the results. How then can one prove that a company has used this genetic information to re-grade or lay someone off?

B. Implications for Health Insurers

Personalized medicine is becoming the central argument to convince people to disclose their genetic information for medico-economic reasons. The GINA regulations prohibit discrimination on the basis of genetic information by insurance companies. However, refusing to take a genetic test could be
interpreted by the insurer as a refusal of transparency, one that exposes the patient to medical risks and the insurer to excess health costs.\textsuperscript{118} Although preserved, the right to refuse disclosure of genetic information is facing growing economic pressure.\textsuperscript{119} For instance, in 2000, genetic testing manufacturer Myriad entered into a multi-year agreement with Kaiser Permanente, a managed care organization, to provide its breast and ovarian cancer genetic tests to Kaiser Permanente's customers.\textsuperscript{120} With this agreement, Kaiser joined well-known insurers, health maintenance organizations (HMOs), and managed care organizations (MCOs) such as Aetna, US Healthcare, and Empire Blue Cross and Blue Shield, all of which cover genetic diagnostic services for their members.\textsuperscript{121} Some patients might regard this information disclosure as an opportunity to benefit from preventive treatment earlier and at a lower cost than they would without the test.\textsuperscript{122} Others, however, might refrain from taking the test for fear of losing health coverage. Two costs are at stake: the cost of the additional premium the policyholder would have to pay in case of a genetic disorder, and the cost of the treatment of this disorder if not covered by the insurance policy. Although difficult to assess, this economic dilemma could induce an asymmetry of information between policyholders and insurance companies.\textsuperscript{123} In such cases, a policyholder could be denied health coverage altogether if the withheld information eventually becomes uncovered, despite having paid regular premiums.

A second form of asymmetry concerns moral hazard. An individual who is protected by an insurance policy may behave in a less prudent way than an individual who is not covered for certain risks. Hypothetically, insured individuals predisposed to type 2 diabetes might unconsciously neglect an appropriate diet if they pay for comprehensive health care coverage and receive adequate treatment. In such a case, insured and insurer have the same level of information; however, the policyholder's insurance coverage may reduce his incentive to avoid risky behavior. Hence, the level of genetic information the


\textsuperscript{120} Judy Mouchawar et al., \textit{Impact of Direct-to-Consumer Advertising for Hereditary Breast Cancer Testing on Genetic Services at a Managed Care Organization: A Naturally-Occurring Experiment}, 7 GENETICS MED. 191, 191 (2005).

\textsuperscript{121} Myriad Genetics Signs Agreement with Kaiser Permanente, \textit{5 ONCOLOGIST} 175, 175 (2000).


\textsuperscript{123} See Godard et al., \textit{supra} note 79, at 126; \textit{see also} Hoy & Ruse, \textit{supra} note 68, at 224.
policyholder possesses could have a direct correlation with his insurance status as well as his behavior and lifestyle.

In 2000, the recommendations of the U.K. Genetics and Insurance Committee (GAIC) stated that the genetic test for Huntington’s disease was sufficiently reliable and accurate for insurance companies to use the results when assessing applications for life insurance. Insurers could therefore continue to impose a genetic test for this highly penetrant monogenic disease. However in 2001, the Association of British Insurers (ABI) signed a five-year moratorium with the British government suspending all requests for DNA tests by potential insurers. This moratorium, which allows customers with adverse genetic test results to obtain significant levels of coverage (up to $800,000), has been extended to 2014. Its purpose, prompted by a concern regarding test accuracy, is to preserve consumer access to insurance as well as insurer access to information on the health risks of potential customers.

British insurers cannot require their clients to undergo genetic tests before offering an insurance policy, but they can require that prior genetic test results be disclosed before agreeing to cover an individual. The objective is to reduce the asymmetry of information between the client and the insurer, a situation that can lead to a phenomenon known as “adverse selection.” Again, insurers encourage customer transparency through premium incentives and test reimbursement.

Patients can also take advantage of asymmetric knowledge regarding genetic risk. It has been observed that individuals who know that they are carriers of Alzheimer’s disease genetic predispositions are six times more likely to modify their insurance. The insured knows of a health risk that the insurer does not, therefore the premium does not reflect true genetic information. Hence, asymmetric information regarding genetic risk affects both parties to a contract.


126. See generally U.K. DEP’T OF HEALTH, CONCORDAT AND MORATORIUM ON GENETICS AND INSURANCE 6 (2005) (discussing the extension of the moratorium until November 1, 2011); Sowmiya Moorthie & Carol George, Moratorium on the Use of Genetic Test Results Extended, PHG FOUND., June 18, 2008, http://www.phgfoundation.org/news/4249 (discussing the decision by the ABI to further extend the moratorium to 2014).

127. See U.K. DEP’T OF HEALTH, supra note 126, at 3.


Access to genetic tests may enable insurance companies to substantially reduce the asymmetries of information that threaten their financial viability, but they are aware that individuals who know they are at high risk are more likely to purchase health insurance.

In France, the Belorgey regulation was signed in 2001 between patient associations, insurance companies, banks, and the ministries of health and finance. This convention was designed to guarantee patients the ability to take out a bank loan despite serious health risks. In practice, however, this convention was not uniformly adhered to by banks and insurers, and in 2004, out of 35,000 cancer survivors using this procedure, 9000 did not obtain the loan for which they had applied. Failing, therefore, to fulfill its objectives, the regulation was replaced in 2007 by the *s'Assurer et Emprunter avec un Risque Aggravé de Santé* or AERAS convention. The strengthened regulation increases the chances for a person presenting a health risk to obtain a bank loan. For instance, the cut-off age for eligibility is increased to 70 years, the maximum housing loan is increased to €300,000 ($450,000), and tighter deadlines are imposed to process loan applications. Additionally, a mediator can be designated to verify whether the AERAS procedure is adequately implemented to prevent any form of discrimination against the applicant.

Discrimination dilemmas arise in two ways. On the one hand, an individual has the ability to go to court to defend his rights if he feels he is a victim of discrimination. On the other hand, an unborn fetus does not have the legal or
physical capacity to do the same. The market for genetic tests, applied to birth screening for the purpose of primary prevention, could soon attract the interest of health care providers, manufacturers, and insurers looking to minimize prospects of litigation.

III. THE EXPANSION OF GENETIC TESTING TO EMBRYO SELECTION

A. Preimplantation Genetic Diagnosis

During the next decade, health care professionals will increasingly become involved in discussing reproductive options when providing genetic testing to patients and their families affected by hereditary cancer syndromes. This trend will be driven by several factors, including the expanding clinical availability of genetic tests that predict risks for many conditions, including those for pediatric and adult cancers. In vitro Fertilization (IVF), the process of combining egg and sperm to create an embryo outside of the body, and genetic testing are converging technologies. Already, substantial literature exists regarding the use of Preimplantation Genetic Diagnosis (PGD) for prenatal diagnosis. Following IVF, this technology consists of extracting a single cell from the embryo and testing it for pathogenic genetic mutations. Only embryos not carrying these mutations are implanted into the womb.

By 2005, about 5,000 PGD applied to IVF cycles were reported worldwide. Depending on which of the models is chosen, the cumulative cost of PGD and IVF for single-gene disorders can be as high as $12,000 to $15,000 per cycle. The availability of PGD is increasing as hundreds of IVF centers in the United States and worldwide acquire expertise in the micromanipulation of embryos and gain access to laboratories to which specimens can be sent for single-cell genotyping. Because of the growing number of IVF cycles associated with PGD, extensive genetic data collection might soon help define a large-enough distribution of cases to permit statistically significant stratification

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of genetic profiles in the population.\textsuperscript{142}

This genetic stratification might have important policy implications for health care systems.\textsuperscript{143} Will health authorities cover health care expenditures for deleterious genotypes depending on the extent of genetic screening that was undertaken before birth? Will couples seeking assisted reproduction be advised to test their embryos before having children? As for couples with genotypes carrying few deleterious mutations, will parents be encouraged to reproduce in order to spread healthy chromosomes throughout the population?

\textit{B. The U.K. Experience}

In 2006, a British couple hesitated to procreate because the husband carried a genetic predisposition to a rare and incurable disease: neurofibromatosis type 1. In 2007, the couple resorted to IVF and PGD to select their future child’s genotype.\textsuperscript{144} To avoid covering a lifetime of expensive treatment, the National Health Service agreed to compensate the parents £7,000 ($12,000) for having taken the precaution of birth screening.\textsuperscript{145} Government coverage of PGD is not limited to incurable genetic disorders. In the spring of 2006, the United Kingdom’s regulatory authority, the Human Fertilisation and Embryology Authority (HFEA),\textsuperscript{146} approved PGD for breast cancer mutation carriers. The HFEA periodically updates the list of genetic diseases for which preimplantation diagnosis is licensed by the HFEA, without indicating whether the full cost is covered by the National Health Service (NHS).\textsuperscript{147} The six public and private centers that offer PGD in the UK are licensed by the HFEA.\textsuperscript{148} Twenty-nine diseases were listed by the HFEA as being approved for PGD in 2004. In 2009,
this number quadrupled to 116 genetic disorders, including breast, colon, and ovarian cancers, many of which are treatable, poorly penetrant, and late onset diseases (Figure 2). The HFEA table illustrates that, even for treatable disorders, embryo selection with PGD is indicated by the U.K. health authorities. In the case of breast cancer screening, “the first license application to perform PGD for BRCA1-linked hereditary breast and ovarian cancer was made in 2007.” In January 2009, the first baby selected through PGD to eliminate embryos carrying an inherited BRCA gene mutation was born. For some rare diseases, embryo selection seems to be significantly more cost effective than long term expensive therapy. Over the next decades, medico-economic arguments could influence health authorities to adopt an elective, rather than curative, approach to control health care expenditures.

A new phenomenon is occurring with regards to PGD. There has been a small number of cases in which deaf couples have used IVF and PGD to select embryos with the same genetic traits that they themselves have in order to share a common lifestyle with their offspring. Since 2007, the Human Fertilization and Embryology Act 1990 has been under revision by the U.K. House of Parliament to update the regulation of embryo research and assisted reproduction. The revisions state that it should become illegal to perform PGD and choose to keep an embryo that has a “serious medical condition” when there is the choice of other embryos without such conditions. In addition to this, it may become illegal for an adult with genes for a “serious medical condition” to donate eggs or sperm for use in IVF when there are other available donors without genetic defects. The description that accompanies the bill includes genetically-induced deafness as one example of a “serious medical condition.” If passed, the legislation would make it illegal for parents using PGD to implant embryos with “deafness” genes if “non-deaf” embryos are available. The bill would also make it illegal for a deaf adult to donate gametes for IVF, even to close relatives.

This pending regulation revives the debate over normative reproduction and

151. See id.
152. See, e.g., TROY DUSTER, BACKDOOR TO EUGENICS 53-54 (2d ed. 2003); Ralph Snyderman & Jason Langheier, Prospective Health Care: The Second Transformation of Medicine, 7 GENOME BIOLOGY 104 (2006).
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the dissemination of genetic traits to future generations. With powerful tools such as genetic tests, should public health authorities continue to invest in treating individuals after birth rather than selecting them before birth?

C. Wrongful Births and Health Economics

Gaucher’s disease illustrates the economic implications of using genetic testing in order to minimize health care expenditure through reducing the incidence of catastrophic diseases. This rare genetic disorder is characterized by a lysosomal deficit, which causes a dysfunction of the spleen, liver, lungs, and skeleton.156 The treatment for Gaucher’s disease, which has been commercialized by Genzyme Diagnostics, is an intravenous enzyme replacement therapy that costs on average $200,000 per year per patient.157 Genzyme has also commercialized a genetic test that costs around $800 to detect the embryo’s predisposition to this disease. From a utilitarian approach, the cost disparity between prevention and treatment is considerable for health insurers and public health authorities. For families affected by the disease, the cost of treatment alone could justify the systematic diffusion and reimbursement of the genetic test to couples with predispositions.158 In order to maintain the principle of guaranteeing equal access to health care, treatment reimbursement could be given to those rare cases that the test did not detect (false negatives).

In other cases, false negative tests could lead to wrongful birth litigations. This was illustrated in 2000 with the Perruche case in France. During her pregnancy in 1982, Mrs. Perruche showed symptoms of rubella and was therefore prescribed a diagnostic test. Test results were falsely negative, she did not therefore voluntarily interrupt her pregnancy and she gave birth to a child who developed Gregg’s syndrome, or congenital rubella syndrome, which caused the child to have mental and neurological disabilities. She sued her obstetrician for not having been given the possibility to abort and won the trial. She received damages from the obstetrician’s insurance company (Le Sou Médical - Mutuelle d’Assurances du Corps de Santé Français, MACSF), and subsequently filed a new claim for damages for her disabled son. Although the obstetrician did not cause the disability, he was simply unable to diagnose the rubella that caused it. The French final court of appeal condemned him and the medical laboratory which had performed the test to pay damages of €120,000 ($180,000) to the Perruche family. This judgment sparked a legal controversy and a national

156. Gregory A. Grabowski, Gaucher Disease: Lessons from a Decade of Therapy, 144 J. PEDIATRICS (SUPPLEMENT 1) 15, 15-16 (2004).
debate: can handicapped persons file suit against and obtain damages from their parents and obstetricians for letting them be born with a disability?\textsuperscript{159} The Perruche jurisprudence was an affirmative answer to this question.\textsuperscript{160}

In 2002, the French parliament passed a law, known as the "Loi Kouchner," overruling this jurisprudence highlighting that the prejudice caused to a child born handicapped cannot be repaired, unless the liability for the handicap is attributable to the physician.\textsuperscript{161} The law states that in case of non-detection of a fetal disorder, only the parents can claim damages. Within a year following the Perruche case verdict, MACSF monthly premiums for obstetricians increased five-fold (€457 to €2000; $684 to $3000).\textsuperscript{162} After the law was enforced in 2002, these premiums dropped significantly but nevertheless remained three times higher than prior to the case. In 2005, annual premiums were €10,000 ($15,000) for gynecologists and €15,000 ($22,750) for obstetricians.\textsuperscript{163}

The risk of wrongful birth damages is setting new standards for obstetricians and their insurance companies, paving the way for widespread adoption of genetic testing for embryo selection.\textsuperscript{164} Referring to the Perruche case, one obstetrician confessed that "when in doubt, it is more prudent to discard any suspicious embryo in order to avoid litigation."\textsuperscript{165} In this context, precautionary eugenics would appear to find legal and economic justification, thus reframing the scope and scale of the "baby business."\textsuperscript{166}

\textit{D. Stakeholders' Converging Interests}

Typically limited to sterile couples, IVF is now offered to fertile couples.\textsuperscript{167} Egg freezing techniques by companies such as Extend Fertility\textsuperscript{168} are offering fertile women a chance to take control of their biological clock and, thereby, take

\begin{itemize}
  \item \textsuperscript{159} DANIELLE MOYSE \& NICOLE DIEDERICH, \textit{L’IMPACT DE L’ ‘ARRÊT PERRUCHE’ SUR LES ÉCHOGRAPISTES ET LES GYNOÉCOLOGUES OBSTÉTRICIENS} 7 (2005), http://www.snude.org/public/2_la_vie_syndicale/7_les_dossiers/pdf/Impact_Perruche2.pdf
  \item \textsuperscript{160} See id. at 8.
  \item \textsuperscript{162} GRÉGORY KATZ-BÉNICHOU, \textit{LE CHIFFRE DE LA VIE} 239 (2002).
  \item \textsuperscript{163} See MOYSE \& DIEDERICH, supra note 159, at 34.
  \item \textsuperscript{164} Cf. Roger D. Klein \& Maurice J. Mahoney, \textit{Medical Legal Issues in Prenatal Diagnosis}, 34 CLINICS PERINATOLOGY 287, 290-95 (2007) (discussing the wrongful birth lawsuits and prenatal testing).
  \item \textsuperscript{165} Israël Nisand, \textit{La naissance sous condition}, 3 \textit{LA LETTRE DE L’ESPACE ÉTHIQUE DE L’AP-HP} 18 (2001) (quotation in text translated by author).
  \item \textsuperscript{166} DEBORA L. SPAR, \textit{THE BABY BUSINESS: HOW MONEY, SCIENCE, AND POLITICS DRIVE THE COMMERCE OF CONCEPTION} 99 (2006).
  \item \textsuperscript{167} See Grégory Katz-Bénichou, \textit{Le tamisage des naissances}, \textit{Cités}, Issue 4, 2006, at 83, 92.
  \item \textsuperscript{168} Extend Fertility, http://www.extendfertility.com (last visited Nov. 11, 2009).
\end{itemize}
advantage of IVF cycles to perform embryo genotyping and birth screening.\textsuperscript{169} The spreading use of preimplantation genetic selection results widely from converging interests among different stakeholders:

1) IVF clinics are willing to offer a wider range of services to couples, including birth screening;

2) Healthcare providers and malpractice insurers are attempting to reduce medico-legal risks and minimize compensation claims in cases of a wrongful birth;

3) Genetic test manufacturers and retailers are seeking to increase their sales;

4) Parents are keen to pay for new diagnostic technologies in order to optimize their child’s genetic heritage; and

5) Health authorities are willing to invest in primary prevention to control health expenditures.

The converging interests of these stakeholders may accelerate the adoption of genetic testing for birth screening. Preventative medicine is entering a new era in which the concept of prevention is itself being redefined. Until the end of the twentieth century, primary prevention focused on avoiding the appearance of a disease through control of environmental factors or patient behavior. In the twenty-first century, genetic tests may transform primary prevention to include avoiding the birth of a diseased person altogether.

\textbf{E. Genetic Testing Applied to Semen Donors}

Overarching these ethical concerns are pragmatic considerations applied to artificial reproductive technologies and the genetic selection of sperm donors. For example, a technique known as Intra Cytoplasmic Sperm Injection (ICSI) is used to circumvent male infertility. In most cases of male infertility, the sperm cell is fertile per se, however, it cannot break the female egg membrane due to a genetic mutation inactivating the sperm tail. The ICSI process consists in collecting such a genetically deficient sperm cell, and injecting it mechanically with a micropipette into the female egg. On the one hand, this technique allows infertile males to procreate; on the other hand, it transmits the infertility mutations to the next male generation.\textsuperscript{170} Medical scientists have since


recognized that this attempt to eliminate a genetic defect could, in fact, contribute to its dissemination.\textsuperscript{171}

Hence, why not test upstream the genetic profile of the sperm donor, rather than use downstream complex and expensive techniques such as ICSI at each generation?\textsuperscript{172} Is it not more cost effective to clear the entire germ line of this genetic mutation once and for all? In other words, why not adopt germinal decontamination through genetic donor screening?\textsuperscript{173}

The business model of sperm banks today echoes, to some extent, the Nobel Prize sperm bank created in 1980 by Robert Graham in collaboration with and in memory of the biologist Hermann Muller.\textsuperscript{174} Set up in California, this bank, known as “The Repository for Germinal Choice,” accepted sperm donations only from Nobel laureates and high IQ individuals.\textsuperscript{175} The bank was closed in 1999.\textsuperscript{176} Since then, sperm banks, such as the California Sperm Bank, Cryobiology, Xytex and California Cryobank, have developed a thriving and competitive market.\textsuperscript{177} Fairfax Cryobank, a subsidiary of the American firm Genetics and IVF Institute, commercializes sperm and eggs with a genetic profile presented as being from “high quality donors.”\textsuperscript{178} Pricing for IVF vials varies according to donor profiles: the standard offer, or “family solution,” costs $175; the “Fairfax” label costs $235; and the “Fairfax doctorate” costs $305.\textsuperscript{179} The “doctorate” label indicates that the sperm donor holds a Ph.D., a degree considered to be a sign of high intellectual ability. Assuming that intelligence is genetically inherited,\textsuperscript{180} the message to parents is evident: for an additional $130, parents can offer their offspring a superior IQ. Why not pay the high price then, if a Ph.D. is encoded in the sperm’s DNA?

\textsuperscript{171} See David C. Page, Sherman Silber & Laura G. Brown, Men with Infertility Caused by AZFc Deletion Can Produce Sons by Intracytoplasmic Sperm Injection, But Are Likely To Transmit the Deletion and Infertility, 14 Hum. Reprod. 1722, 1725 (1999).

\textsuperscript{172} Grégory Bénichou, Comment transformer l’humain en sable, in VERS LA FIN DE L’HOMME, 127, 135 (Christian Hervé & Jacques J. Rozenberg eds., 2006).

\textsuperscript{173} Cf. Silber & Repping, supra note 170, at 225 (discussing how couples must decide for themselves if the likely transmission of infertility is worth the benefit of ICSI treatment).


\textsuperscript{175} See id. at 4.

\textsuperscript{176} See id. at xviii.

\textsuperscript{177} See id. at 173.


\textsuperscript{180} RICHARD J. HERRNSTEIN & CHARLES MURRAY, THE BELL CURVE: INTELLIGENCE AND CLASS STRUCTURE IN AMERICAN LIFE 1, 11-13 (1994).
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In its 2009 brochure, Fairfax Cryobank claims that “fewer than 3% actually are accepted as semen donors for Fairfax Cryobank.”\textsuperscript{181} Donors are selected following screening processes involving a health questionnaire; physical examination; medical, genetic, and infectious disease testing; a semen quality evaluation; and several interviews with staff.\textsuperscript{182} Presented as a biological elite, these genetically screened donors are asked to provide their medical history as well as pictures of themselves as children in order to give prospective parents an idea of their future child’s physical appearance.\textsuperscript{183} Customers may also browse among donor physical traits to select height, weight, skin, eye and hair colors, as well as personality traits.\textsuperscript{184} The sperm bank business is creating a shift in the way genetic tests are utilized. Originally applied to embryo selection in order to prevent the transmission of medical conditions, genetic tests are now also used to elect and transmit genetic traits to future generations.

For $2995, parents undergoing IVF can also select their child’s gender through MicroSort, a sperm sorting tool commercialized by the IVF Institute.\textsuperscript{185} The technique consists of separating sperm cells carrying the Y and X chromosomes based on their molecular weight.\textsuperscript{186} The MicroSort technique appears to be a commercial success in Asia, especially in China where parents must comply with the one child policy. Boys are favored over girls because they can obtain higher earning jobs. Already, demographic studies anticipate that by the end of the twenty-first century, a fifth of the Chinese male population will not be able to find a wife.\textsuperscript{187} What will be the result of the widespread use of genetic testing for gender selection?

In India, Dr. Anoop Gupta, medical director of the IVF and Fertility Clinic in New Delhi, reported that hundreds of couples undergoing IVF cycles would be prepared to use the MicroSort test.\textsuperscript{188} In India, girls are considered to be an economic burden to their family as they need a dowry to get married. Rather than resorting to euthanasia of newborn girls, parents are willing to invest in the MicroSort technique to maximize their chances of having boys. Although the semen sorting process might reduce euthanasia practices in some countries, it

\textsuperscript{182} See id. at 2-5.
\textsuperscript{183} See id. at 6-7.
\textsuperscript{184} Fairfax Cryobank, supra note 179.
\textsuperscript{185} MicroSort, http://www.microsort.net (last visited Nov. 11, 2009).
will probably not prevent sex discrimination at birth but, on the contrary, may contribute to IVF popularity among fertile couples because of the opportunity to select gender.

The principles behind semen sorting are not limited to screening sperm for gender selection; ongoing research attempts to apply similar techniques to women’s gametes to screen for competent oocytes. Genetic testing appears to be a useful tool for the discovery of new genes and to provide information on oocyte quality. This technology is helping to improve the selection of healthy eggs and embryos that will result in good pregnancy rates. Applied to sperm or oocytes, semen selection might, in the future, improve or even replace embryo selection. On the one hand, germinal screening may sidestep ethical controversies related to the moral status of human embryos and their destruction; on the other hand, it might fuel the debate over normative reproduction and private eugenics.

F. Regulation of Gender Selection and Prenatal Screening

Present throughout the history of mankind, gender selection is met with renewed enthusiasm thanks to the development of powerful genetic tests. Traditional methods, such as sweet or salty diets before and during pregnancy have often been used by parents in the hope that it will influence the outcome of the child’s gender. These techniques were successful, but only in fifty percent of cases! Nowadays, genetic technologies such as MicroSort offer parents a ninety-three percent chance of having a girl. However, the current debate over these tests is less about their reliability, but more about the social and ethical implications of sex discrimination. Although many countries have established guidelines for gender selection based on medical reasons, this practice seems more difficult to regulate for non-medical reasons. Indeed, on what basis should

regulators interfere with parents’ choices, as long as gender selection is often proposed to sterile and fertile couples in the IVF package in addition to PGD?

In the Oviedo Convention on Human Rights and Biomedicine, the Council of Europe states that “[t]he use of techniques of medically assisted procreation shall not be allowed for the purpose of choosing a future child’s sex, except where serious hereditary sex-related disease is to be avoided.”197 Despite the Convention, private companies nevertheless operate in European countries, such as Belgium, to offer parents sperm sorting technologies for gender selection.198 In the United Kingdom, clinics offering PGD can only operate under a HFEA license.199 Furthermore, PGD can only be performed for gender selection in order to select embryos that do not carry a serious, inherited, sex-linked disorder.200 However, because sperm sorting does not systematically involve storage of sperm, it does not come under the HFEA jurisdiction. This legal loophole allows private, non-licensed clinics to perform sex selection for non-medical purposes.201

In the United States, sperm sorting is proposed in almost every state, and is often associated with prenatal genetic testing procedures. Signature Genomic Laboratories is a private firm in Washington that charges parents $1850 to use its “Signature PrenatalChip” to test for various genetic disorders.202 By 2008, physicians had sent the company DNA samples of fetuses from 380 women in order to have them analyzed for the presence of over seventy genetic disorders, including mental retardation, physical malformation, and health and behavioral problems.203 A federally funded study to evaluate prenatal genetic screening has been conducted in 4000 pregnancies.204 Until now distinctive approaches, prenatal testing and neonatal screening are bound to converge in a fully integrated preventative approach. Why then should parents and obstetricians wait until birth to diagnose genetic disorders that could have been detected at an embryonic stage through genomic profiling?205

197. See Council of Europe, supra note 97, at 5.
200. See id. at 219; Human Fertilisation & Embryology Auth., supra note 196, at 7.
201. See Kanellopoulou, supra note 199, at 219.
203. See id. at 80-81.
205. See President’s Council on Bioethics, supra note 202, at 80.

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The President’s Council on Bioethics 2008 report on newborn screening206 reaffirms the essential validity and relevance of the Wilson-Jungner screening criteria adopted by the World Health Organization in 1968.207 Among these criteria, “[t]he condition sought should be an important health problem” and “[t]here should be an accepted treatment for patients with recognized disease.”208 The President’s Council on Bioethics also rejects “any simple application of the technological imperative, i.e., the view that screening for a disorder is justified by the mere fact that it is detectable . . . even if the disorder is poorly understood and has no established treatment.”209

In the midst of this complex and evolving regulatory framework, genomic tools could lead health systems from a curative approach to a predictive and preventative model. Health care practitioners – particularly obstetricians and oncologists – may soon find themselves at the leading edge of the application of assisted reproductive technologies for families affected by genetic disorders such as cancer.210 Indeed, physicians might be increasingly mindful of informing the patient and/or family members regarding hereditary cancer risks. They might also more frequently be subject to liability for wrongful birth, resulting from their perceived failure to inform their patients of the possible application of reproductive technologies.211 These trends raise central challenges for policymakers, particularly due to the difference of pace between the fast online commercialization of genetic tests and the lengthy adoption of regulatory procedures meant to frame their distribution.

IV. EVOLUTION OF REGULATORY PROCEDURES FOR THE COMMERCIALIZATION OF GENETIC TESTS

A. U.S. National Regulation

Reports on the regulatory framework for genetic tests highlight a pressing need for tougher regulation and clearer guidelines212 to assess test sensitivity,

206. See id.
207. Id.; see J.M.G. WILSON & G. JUNGNER, PRINCIPLES AND PRACTICE OF SCREENING FOR DISEASE (1968).
208. PRESIDENT’S COUNCIL ON BIOETHICS, supra note 202, at 22.
209. See id. at 106.

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specificity, and reliability.213 Within the U.S. Department of Health and Human Services, agencies that oversee genetic testing are diffuse. They include the Centers for Medicare and Medicaid Services, the Food and Drug Administration (FDA), the Centers for Disease Control, and the Office of Human Research Protections. These different regulatory bodies are working towards defining and setting quality standards for genetic testing, including implementing the Clinical Laboratory Improvement Amendments (CLIA) of 1988, which aim to “strengthen federal oversight of clinical laboratories to assure that the test results are accurate and reliable.”214

Early in their history in the United States, the speed with which diagnostic genetics tests developed resulted in limited oversight. Regulation depended largely on whether a laboratory used its own reagents or a manufacturer’s test kit to perform genetic tests. The first regulations came about in 1998 with the analyte-specific reagent rule that allowed only physicians and certified laboratories access to reagents to ensure their quality and safety.215 In order to circumvent regulatory constraints and access the market more rapidly, some test manufacturers began to produce “home-brew” tests to evade accreditation procedures.216 “Home-brews” are genetic tests developed in-house by certified laboratories with approved reagents, rather than by non-accredited corporations, and they are marketed to consumers or other companies. The FDA, according to the analyte-specific reagent rule, regulates only the reagents that compose the home-brew test, but does not regulate how reagents are assembled to produce the test.217 Additionally, CLIA does not require laboratories to demonstrate the clinical validity of their home-brews. Furthermore, CLIA prohibits the Centers for Medicare and Medicaid Services from giving either prospective review or pre- or post-market approval of new tests.218 Test kits, on the other hand, are regulated by the FDA as in vitro diagnostic devices. Out of the 1100 genetic tests commercially available on the market in 2006, less than a dozen were subject to FDA oversight.219

213. “Genetic tests have varying degrees of sensitivity (does the test find the allele(s) it was designed to find or does it produce ‘false negatives’?), specificity (does the test register only the allele(s) it was designed to find, or does it produce ‘false positives’?), and reliability (will the same test produce the same results at different times and in different laboratories?).” Goven, supra note 88, at 5.

214. JAVITT & HUDSON, supra note 212, at 7 (citing H.R. REP. NO. 100-899 (1988)).


218. JAVITT & HUDSON, supra note 212, at 10.

219. AUDREY HUANG, GENETICS & PUB’Y CTR., WHO REGULATES GENETIC TESTS?
Companies also attempt to evade CLIA and FDA regulations through a variety of other means. Some testing laboratories present test results to their customers as “data” and not “diagnoses” in order to prevent any litigation on test reliability. Others sell their tests on the Internet in order to bypass physicians’ prescriptions, reach customers directly, and widen their market.

**Definitions**

- **A market approved genetic test** is validated in the United States by the FDA’s Pre-Market Notification (PMN or 510k). In the EU, a market approved genetic test must comply with the directive on In Vitro Diagnostic Medical Devices (Directive 98/79/EC or IVD Directive). Introduced in 2003, this directive is implemented by health authorities in each EU member state. Approved medical devices must bear the CE mark.

- **Test kits** are ready-to-use genetic tests assembled by a laboratory and sold to another laboratory, distributor, or customer.

- **A home-brew test** is developed in-house by laboratories and marketed as a clinical laboratory service. Neither the FDA nor the European Union oversees home brew tests. However, home brew test ingredients - or analyte specific reagents (ASRs) - are regulated in the United States by the FDA, under the Clinical Laboratory Improvement Amendments (CLIA), and by the IVD Directive in the EU.

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221. See Sarah E. Gollust, Benjamin S. Wilfond & Sara Chandros Hull, Direct-to-Consumer Sales of Genetic Services on the Internet, 5 GENETICS MED. 332, 336 (2003); Gollust et al., supra note 42, at 1762.


226. U.S. Food and Drug Administration, Clinical Laboratory Improvement Amendments (CLIA), available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/...
In 2000, the Secretary's advisory committee on genetic testing recommended that the FDA oversee all genetic tests, but the FDA decided not to exercise its authority.228 Industry involved in the field of genetic testing feared that regulation would stifle innovation and lead to high costs.229 In this patchy regulatory framework, could the FDA risk being held accountable for not protecting the population from potentially inaccurate medical tools?230

However in 2007, the FDA took a stance on overseeing genetic tests by issuing a draft guidance for industry, clinical laboratories, and FDA staff on the use of In Vitro Diagnostic Multivariate Index Assays (IVDMIAs),231 a type of laboratory-developed test, based on gene expression analysis of a large number of genes,232 produced by companies such as Clinical Data, CombiMatrix, Dako and Monogram. Nevertheless, these recommendations are not legally binding for test manufacturers and users as stated by the FDA itself: "FDA’s guidance documents . . . do not establish legally enforceable responsibilities. Instead, guidances describe the Agency’s current thinking on a topic and should be viewed only as recommendations . . . The use of the word should in Agency guidances means that something is suggested or recommended, but not required."233

In response to the FDA’s minimal oversight, biotech firm Genentech filed a petition with the FDA in December 2008. The firm requested that the FDA oversee and regulate all in vitro diagnostic tests according to the same standards, regardless of their end use.234 In line with this position, the Dutch firm Agenda
was the first genetic test manufacturer to have voluntarily submitted a test to the FDA for distribution in the United States. On the other hand, the test manufacturer Clinical Data firmly opposed the suggested regulatory enforcement. The company argued that its tests, such as the PgxPredict used in treatment response, demonstrated clinical value and any additional regulation would only impede innovation. Such a position could, however, imply that any manufacturer of non FDA-cleared genetic tests would be free to make claims of superiority regardless of scientific and clinical evidence. This lack of oversight might also be a concern for physicians who would not have access to clinical data to evaluate the medical implications of new molecular diagnostic tools.

In 2007, the FDA’s IVDMIA guidelines highlighted the importance of adopting formal regulation. Following Genentech’s petition, the FDA announced in December 2008 that it would “explore ways” to collaborate with the Centers for Medicare and Medicaid Services in order to coordinate their roles regarding genetic diagnostic products. This decision is all the more pressing as the lack of an adapted legal framework could eventually become detrimental to patient safety and create an uneven marketplace for test manufacturers.

B. State Regulation

Although U.S. national regulation apparently remains stagnant, some states have taken action in response to consumer complaints about the cost and accuracy of genetic tests. In June 2008, the California Department of Public Health issued letters to thirteen laboratories, including 23andMe, Navigenics, and deCode Genetics, to cease and desist performing genetic testing for California residents until the laboratories meet the requirements specified in state law. A few months before, the New York Department of Public Health sent letters to thirty-one genetic testing companies requiring them to obtain licenses in order to solicit DNA specimens from the state’s residents. Similarly, the California letters stated that “genetic test companies must obtain state licenses as clinical laboratories.”


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In order to be granted a California clinical laboratory license, these firms must provide satisfactory validation documentation to verify the test performance specifications of all genetic tests. These companies are under the jurisdiction of the California Business & Professions Code which prohibits offering a clinical laboratory test directly to the consumer without a physician’s order.

Despite regulations by certain states, the strategic location of genomic scanning facilities and online marketing services has allowed manufacturers to cross borders and bypass local laws. For instance, companies such as Navigenics and 23andMe claim they do not need a local state license since their testing platforms are located outside California and operate under a different state license. Moreover, these companies would be able to sell their tests online to residents in over a dozen states such as Alaska, Kansas, or Texas where no law prohibits individuals from ordering a genetic test. On top of this, online customers are recruited globally and ship their tissue samples from abroad, further weakening state regulation.

C. European Regulation

There are disparities among European countries concerning the classification of and access to genetic tests. Some European country regulatory bodies consider analytic validity, how accurately the test identifies the gene or marker, as sufficient to commercialize a test. Others believe that the test’s clinical validity, the accuracy with which the test predicts or diagnoses a disease, is a more pressing concern. The U.K. Genetic Testing Network has developed a “Gene Dossier” in order to evaluate genetic tests and assess which tests should be used by the National Health System. In France, the health product authority (AFSSAPS) requires genetic test manufacturers to conform to essential

C1.
239. CAL. BUS. & PROF. CODE § 1265 (West 2003).
240. See id. § 1288.
241. See Hogarth et al., supra note 3, at 171.
243. OECD, GENETIC TESTING, supra note 7, at 12.
requirements concerning technical quality. Clinical validity and utility of a genetic test are considered to be only marginal criteria for access to the market. A market approval procedure, similar to that applied to drugs, is expected to be implemented for genetic tests in France. In an attempt to harmonize regulation in the European Union, Germany’s genetic tests indication criteria are regarded as the basis of future guidelines to be endorsed by the European Society of Human Genetics and to be adopted throughout Europe.

The European Union’s In Vitro Diagnostic (IVD) Directive, adopted in 2000, seeks to harmonize national legislation among EU member states in order to improve an individual’s level of health protection. Although the directive provides a framework for the regulation of IVD product approval, it does not regulate the methods used by manufacturers to achieve the CE-mark required to commercialize a test developed in-house by laboratories, known as laboratory developed tests (LDTs).

Moreover, in the EU, most genetic tests are classified as “low risk,” which means that they are not independently evaluated before reaching the market. For example, in the U.K., if a company sells its tests as kits to a laboratory, then these tests are subject to the IVD Directive. On the other hand, if a test is developed by a company and performed in its own laboratory, it is classified as a LDT. The regulatory status of such tests is ambiguous, because some European countries consider them to be medical devices, while others do not. Therefore, not all European countries are obliged to regulate LDTs under the IVD Directive. Companies such as 23andMe commercialize LDTs in the European Union but perform the tests in laboratories outside the European Union. These tests do not come under the IVD Directive. Nevertheless, in an attempt to tighten regulation on the use of genetic tests, the U.K. government’s advisory body, the

247. CODE DE LA SANTÉ PUBLIQUE art. L.5221 (Dalloz 2008).
251. The CE mark is mandatory for products placed in the European Economic Area. This marking certifies that a product has met European Union consumer safety, health and environmental requirements.
254. See THE REGULATORY FRAMEWORK FOR GENOMIC TESTS, supra note 244.
Human Genetics Commission, has called for a new system of regulation, particularly for non-medical “lifestyle” genetic tests. Lifestyle genetic tests are typically over-the-counter diagnostic kits that claim to identify a person’s chances of developing conditions such as obesity, heart disease or even osteoporosis. Depending on test results, health-conscious consumers will adapt their lifestyle to reduce the risk of onset of an illness.\textsuperscript{255} In Germany, a new law was passed in 2009 to significantly limit the use of direct-to-consumer genetic tests, such as paternity tests.\textsuperscript{256}

These persistent disparities in European regulation of genetic tests are cause for concern. This situation offers the public little confidence that regulatory bodies are capable of adequately controlling this developing market.\textsuperscript{257} In response, the Global Harmonization Task Force, which includes the European Union, the United States, Canada, Australia, and Japan, is actively following the developments in IVD regulation in order to achieve greater uniformity between national medical device regulatory systems.\textsuperscript{258} In the EU, the enforcement of the Directive 2007/47/EC, which will become mandatory in March 2010, will contribute to harmonizing the classification and use of medical devices.\textsuperscript{259}

On an international scale, in response to this lack of clear premarket approval for genetic tests, both the FDA and the European Medicines Agency (EMEA) issued guidance on Voluntary Genomic Data Submissions in 2006. This initiative is a concerted effort to regulate the outcome of genetic testing and to bridge technologies in an attempt to fill the regulatory gaps associated with genetic tests.\textsuperscript{260} However, because submissions are voluntary, data are not consistently collected and regulatory agencies are still a long way from overseeing the entire genetic testing value chain.

**CONCLUSION**

The growing availability of genetic tests has a number of implications for public health. In this paper, we have analyzed four interconnected issues: (i) patient access to online genetic services and its impact on medical practices; (ii) the disclosure of genetic information to health insurers and the risk of


\textsuperscript{257} Jane Kaye, \textit{The Regulation of Direct-to-Consumer Genetic Tests}, 17(R2) HUM. MOLECULAR GENETICS R180, R180 (2008).


\textsuperscript{260} Michael S. Orr et al., \textit{The Experience with Voluntary Genomic Data Submissions at the FDA and a Vision for the Future of the Voluntary Data Submission Program}, 81 CLINICAL PHARMACOLOGY & THERAPEUTICS 294, 294 (2007).
discrimination; (iii) the expansion of genetic testing for embryo selection and the risk of liberal eugenics; and (iv) the adoption of adequate regulation to ensure quality standards for test commercialization.

Access to online genetic services has, on the one hand, empowered patients to become more proactive in the management of their health. On the other hand, these services often bypass physicians’ prescriptions and expertise to interpret genetic information. Dilemmas arise from this shift in the patient-physician relationship. If genetic transparency provides a chance for prevention, does lack of disclosure from one family member hinder adequate treatment for another? Although there is no consensus on this debate, fundamentally, the underlying ethical dilemma that policymakers face is assessing whether the harm due to failure of disclosure outweighs the harm that may be caused by disclosure.

The tension between confidentiality and transparency is also related to health insurance. Indeed, the fear of genetic discrimination dissuades some patients from using genetic tests, thus depriving themselves of appropriate treatment. In order to avoid genetic information impinging on public freedom, most European countries adopted the Oviedo Convention in 1997 and, more recently, the U.S. Congress passed the Genetic Information Nondiscrimination Act in 2008. Both statutes seek to protect individuals from genetic discrimination by insurance companies. However, in some cases outlined in these laws, insurers and employers might still find roundabout ways of discriminating on the basis of genetic information. Furthermore, refusing to take a genetic test could be interpreted by the insurer as a refusal of transparency, exposing the patient to medical risks and the insurer to excess health costs. Although preserved, the right to not disclose genetic information is facing growing economic pressure.

Risks of genetic discrimination do not affect adults alone; they also concern human embryos. The convergence of reproductive technologies (IVF) and predictive technologies (PGD) revives the debate over normative reproduction and the dissemination of genetic traits to future generations. The risk of wrongful birth damages is setting new standards for obstetricians and their insurance companies, paving the way for the widespread adoption of genetic testing for embryo selection. With powerful tools such as genetic tests, should public health continue to invest in treating individuals after birth rather than selecting them before birth? The converging interests of parents, IVF clinics, test manufacturers, health care professionals, and health authorities may further accelerate the adoption of genetic testing for birth screening, with medico-economic justifications.

Beyond ethical challenges related to liberal eugenics, policymakers are confronted with other regulatory issues, in particular the adoption of quality standards for test commercialization. National and international regulation of test approvals and services has developed erratically, creating gaps on a local scale. Both the United States and the EU are striving to harmonize their procedures for
test commercialization in order to guarantee the quality, validity, and utility of diagnostic tools. This issue is becoming all the more pressing due to the growing frequency of genetic services operating beyond borders, at the crossroads of different legal and health care systems. Furthermore, the digitization of genetic information and the dematerialization of medical data reinforce the need for international harmonization. However, regulation alone cannot cope with all the present challenges. The education of health care professionals as gatekeepers is undoubtedly central in order for patients and society to reap the medical benefits of this promising genetic era.
Evolution of diseases for which genetic testing is available
(Source: GeneTests, February 2009)

### IMPLICATIONS OF GENETIC TESTING

#### FIGURE 2^262^-

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<td>• Alport’s Syndrome</td>
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262. See Human Fertilisation & Embryology Authority, supra note 149.

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*These conditions are licensed by the HFEA on a case-by-case basis, for specific patients.

**These conditions have also been licensed for use in cases involving HLA tissue typing. HLA tissue typing tests are licensed on a case-by-case basis, for specific patients.