Boston University
Journal of Science & Technology Law

Note

Loose-Fitting Genes:
The Inadequacies in Federal Regulation of Institutional Review Boards

Kerry Burke

Table of Contents

Loose-Fitting Genes: The Inadequacies in Federal Regulation of Institutional Review Boards†

Kerry Burke*

I. INTRODUCTION

1. Researchers are continually designing new devices to evaluate the genetic probability of disease in humans. Recently, scientists created several genetic tests[1] that detect mutations on the BRCA1 and BRCA2 genes.[2] These tests, marketed by OncorMed[3] and Myriad Genetics [4] ("Myriad"), evaluate a patient's genetic predisposition for breast and ovarian cancer. Genetic tests have promising potential for both society and for the biotechnology industry. The tests, however, also pose

---

* B.S., 1995, Clarkson University, J.D. (anticipated), 1998, Boston University School of Law.

1 A genetic test is "the analysis of human DNA, RNA, chromosomes, proteins or other gene products to detect disease related genotypes, mutations, phenotypes, or karyotypes for clinical purposes." TASK FORCE ON GENETIC TESTING OF THE NIH-DOE WORKING GROUP ON ETHICAL, LEGAL, AND SOCIAL IMPLICATIONS OF HUMAN GENOME RESEARCH, DRAFT INTERIM PRINCIPLES, *Introduction* (visited Jan. 7, 1997) <http://infonet.welch.jhu.edu/policy/genetics/intro.html> (emphasis omitted) [hereinafter DRAFT INTERIM PRINCIPLES, *Introduction*].

2 *See* National Cancer Institute and National Institutes of Health, *Cancer Facts: Breast Cancer and the BRCA1 Gene: Questions and Answers* (visited Jan. 7, 1997) <http://cancer.med.upenn.edu/pdq/600350.html> (explaining that BRCA1 is a gene located on chromosome 17 altered in families with genetic tendency for breast cancer). BRCA2 is a gene located on chromosome 13. *See* MYRIAD GENETIC LABORATORIES, INC., A REFERENCE FOR HEALTH CARE PROFESSIONALS 2 (1996) (on file with the *Boston University Journal of Science & Technology Law*) [hereinafter REFERENCE FOR PROFESSIONALS]. Women with a mutation in the gene also have an increased risk of developing breast cancer. *See id.*

3 OncorMed, Inc. applies genetic discoveries in the formulation of tests for the detection and management of cancer. For more information on OncorMed, see *OncorMed* (visited Apr. 4, 1997) <http://www.oncormed.com>.

4 Myriad Genetics, Inc. engages in the discovery and sequencing of genes related to diseases such as cancer to identify a predisposition to the development of the disease. For more information on Myriad Genetics, see *Myriad Genetics, Inc.* (visited Apr. 4, 1997) <http:/www.myriad.com/>.

unique problems that have resulted in less profit than expected for biotechnology companies.[5]

2. Most research institutions maintain at least one institutional review board ("IRB") to approve or reject research protocols involving human clinical subjects. Institutional review boards help to ensure that these scientific protocols protect the health and privacy of the participating human subjects. The federal government requires IRB approval of protocols in two situations: (1) when the institution is seeking FDA approval,[6] and (2) when an institution is seeking government research funds.[7] IRB review is not legally required for genetic testing protocols offered by a laboratory as an in-house service.[8] Irrespective of this distinction, most large institutions establish IRBs to review all complex genetic testing research.[9]

3. The current mechanism of regulating IRBs is inadequate. Federal regulations do not set salary limits or require institutions to disclose the amount of compensation paid to IRB members, and some IRB members *are* paid. In addition, the regulations provide no mechanism for resolving IRB conflicts of interest. Problems with IRBs are especially acute in the genetic testing industry because the tests have far-reaching physical and psychological implications.[10] IRB review of research protocols better ensures that patients make educated decisions about their

---

5 Originally, experts anticipated that the revenues from biotechnology-derived drugs alone would exceed $20 billion by the year 2000. *See* Dennis N. Longstreet, *Government and Industry: Meeting the Challenges of Biotechnology Together*, 47 FOOD DRUG COSM. L.J. 687 (1992). Sales from genetic tests, however, "have increased from only $13.3 million in 1989 to $122 million in 1995." *Gene Testing to Be Big Business*, APPLIED GENETICS NEWS, Dec. 1, 1996, *available in* 1996 WL 8541893. Further, analysts have reduced the projected sales estimates from Myriad Genetics's DNA tests "from 14,000 to 3,000 in fiscal 1997 and from 32,000 to 16,000 in fiscal 1998." Francis Bishopp, *Myriad Pulls Offering After Sales Projections Lowered*, BIOWORLD TODAY, Nov. 27, 1996, *available in* 1996 WL 13888773 (quoting Matthew Murray, Lehman Brothers analyst).

6 *See* 45 C.F.R. § 46.101 (1995).

7 *See* 21 C.F.R. § 50.1 (1996).

8 *See* TASK FORCE ON GENETIC TESTING OF THE NIH-DOE WORKING GROUP ON ETHICAL, LEGAL, AND SOCIAL IMPLICATIONS OF HUMAN GENOME RESEARCH, DRAFT INTERIM PRINCIPLES, *The Scientific Validation of Genetic Tests* (visited Jan. 7, 1997) <http://infonet.welch.jhu.edu/policy/genetics/i.html>, at Principle I-6 (noting that the Task Force requested a legal opinion from the FDA in regard to applying these regulations to an in-house service) [hereinafter DRAFT INTERIM PRINCIPLES, *Scientific Validation*].

9 *See* Harold Edgar & David J. Rothman, *The Institutional Review Board and Beyond: Future Challenges to the Ethics of Human Experimentation*, 73 MILBANK Q. 489, 490 (1995) (noting that, although not required to, most academic institutions pass all their research protocols through an IRB).

10 *See Advances in Genetic Research and Technologies: Challenges for Public Policy: Hearings Before the Senate Comm. on Labor and Human Resources*, 104th Cong. 86 (1996) (testimony of Dr. Garber, Dana Farber Cancer Institute) [hereinafter *Hearings I*].

future because an IRB will not approve a research protocol that lacks adequate informed consent provisions.[11] Informed consent provisions require the patient to voluntarily participate in the research study and to fully understand the experimental procedure, including the risks, benefits, possible alternatives, and the level of confidentiality of the research records.[12]

4. This note will discuss the BRCA1 and BRCA2 genetic tests marketed by OncorMed and Myriad, and will describe two inadequacies in the current federal regulatory framework of IRBs. Finally, the note suggests several ways to improve the regulation of IRBs before this framework is applied to genetic testing services.

II. BACKGROUND

A. *Genetic Testing*

5. Everyone has a genetic risk for some type of abnormality[13] because "[n]early all human conditions, except physical injury, are related to changes . . . in the structure and function of DNA."[14] Clinical laboratories can examine these genetic mutations through screening and susceptibility tests.[15] The general public can use a screening test to detect the presence of a particular ailment.[16] Only high-risk individuals can use susceptibility tests to evaluate their risk of developing a disease.[17] Susceptibility tests, like the BRCA1 and BRCA2 tests, are unique because they are performed on healthy people who do not manifest any symptoms of the tested ailment.[18] These tests explore the individual and familial risk of disease since there is a 50% chance that individuals testing positive will pass the mutation to their children.[19] Discovering one's genetic predisposition to a disease, such as

---

11 *See* 45 C.F.R. § 46.116 (1995); 21 C.F.R. § 50.20 (1996).

12 *See* 45 C.F.R. § 46.116(a); 21 C.F.R. § 50.20(a).

13 *See Hearing of the Tech. Subcomm. of the House Science Comm. on Genetic Testing*, 104th Cong. (1996) (statement of Dr. Francis Collins, Director, National Center for Human Genome Research), *available in* Lexis, News Library, Curnws File (explaining that we all carry between four and five misspelled genes, and another 20 or 30 more that have moderate alterations) [hereinafter *Hearings II*].

14 Francis S. Collins & Leslie Fink, *The Human Genome Project*, ALCOHOL HEALTH & RESEARCH WORLD, June 22, 1995, at 190.

15 *See Hearings I, supra* note 10, at 56 (statement of Patricia D. Murphy, Vice President, Genetic Services, OncorMed, Inc.).

16 *See id.*

17 *See id.*

18 *See id.*

19 *See* ONCORMED, INC., HEREDITARY BREAST CANCER: QUESTIONS AND ANSWERS FOR

breast cancer, is beneficial to a high-risk woman because this knowledge may encourage her to actively monitor and treat the disease.[20]

B. *The BRCA1 and BRCA2 Genetic Tests*

6. Breast cancer is a serious medical concern for many women. Approximately one in eight women develops breast cancer during her lifetime,[21] and five to ten percent of breast cancer is inherited.[22] An individual carrying a mutated, or altered BRCA1 or BRCA2 gene has an increased risk for developing breast or ovarian cancer.[23] Everyone possesses two copies of every gene in each cell, inheriting one from each parent.[24] Obtaining an altered BRCA1 or BRCA2 gene from either parent increases an individual's risk for developing breast and ovarian cancer because the cell lacks a "backup" gene if the normal copy of the gene mutates.[25] The increase in risk is not identical for each mutation.[26]

PHYSICIANS 3-4 (1996) (on file with the *Boston University Journal of Science & Technology Law*) [hereinafter ANSWERS FOR PHYSICIANS].

20 *See Hearings I, supra* note 10, at 56 (statement of Patricia D. Murphy, Vice President, Genetic Services, OncorMed, Inc.).

21 *See Breast Cancer Diagnostics: IVDP Focuses on Genetics*, GENESIS REP., Jan. 1, 1996, *available in* 1996 WL 9660615 (noting that approximately 183,400 new cases of breast cancer occur each year in the United States and predicting 845,000 cases by 2000).

22 *Industry News (Diagnostics): BRCA2 Mutation Analysis to Hereditary Cancer Testing Service Introduced*, CANCER WKLY. PLUS, Aug. 5, 1996, *available in* LEXIS, News Library, Curnws File. Researchers attribute 45% of these mutations to BRCA1 and 35% to BRCA2. *See id.* Approximately one in 200 women in the United States is a BRCA1 gene carrier. *See* Richard Saltus, *Breast Cancer Testing: Do You Want to Know?*, BOSTON GLOBE, Mar. 11, 1996, at 25. The BRCA1 gene is located on chromosome 17 and produces a protein that is thought to act as a tumor suppressor. *See* ANSWERS FOR PHYSICIANS, *supra* note 19, at 3; *Breast Cancer Diagnostics: IVDP Focuses on Genetics, supra* note 21. There are over 120 known BRCA1 gene mutations that elevate the risk of developing cancer. *See* REFERENCE FOR PROFESSIONALS, *supra* note 2, at 2. Scientists also think that the BRCA2 gene, found on chromosome 13, possesses tumor suppressing capabilities. *See* ANSWERS FOR PHYSICIANS, *supra* note 19, at 3.

23 Women possessing a BRCA1 or BRCA2 mutation will have an 85% chance of developing breast cancer. *See* Saltus, *supra* note 22, at 25. A BRCA1 gene carrier has a 50% greater risk of developing ovarian cancer. *See id.* Researchers have also connected the BRCA2 gene to ovarian cancer. *See OncorMed Offering BRCA2 Mutation Analysis*, BIOTECH. NEWSWATCH, Aug. 15, 1996, *available in* 1996 WL 8453653.

24 *See* REFERENCE FOR PROFESSIONALS, *supra* note 2, at 2.

25 *See id.*; Joseph D. Schulman & Harvey J. Stern, *Genetic Predisposition Testing for Cancer* (visited Jan. 7, 1997) <http://www.givf.com/cancer_journal1.html>.

26 *See* REFERENCE FOR PROFESSIONALS, *supra* note 2, at 2.

1. OncorMed's BRCA1 and BRCA2 Tests

7. OncorMed's and Myriad's tests examine the BRCA1 and BRCA2 genes for mutations.[27] OncorMed only offers the BRCA tests to high-risk patients.[28] The company requires physicians to follow an IRB approved protocol for both BRCA1 and BRCA2 testing so that all patients provide true informed consent.[29] The physicians can either use the protocol supplied by OncorMed or adhere to one developed by an IRB at their own institution.[30]

8. The protocols developed by OncorMed for the BRCA1 and the BRCA2 tests provide a means for physicians to assist in the consent process, both before and after the BRCA1 or BRCA2 evaluation.[31] Under the OncorMed protocol, pre-test counseling should incorporate a discussion of the individual's family history, an explanation of BRCA1 and BRCA2 genes, and a description of the BRCA1 and BRCA2 genetic tests.[32] The physician's explanation of the genetic tests should disclose the test's benefits and risks as well as the implications of a positive or negative result.[33] OncorMed's protocols also contain post-test counseling on

---

27 *See News from the AACR Conference: Biotech at the Cutting Edge of Technology and Controversy,* BIOWORLD TODAY, Apr. 25, 1996, *available in* 1996 WL 9518218 [hereinafter *News from the AACR Conference*]. "A gene is like a chapter in a book. The genetic analysis for BRCA1 and BRCA2 mutations is similar to proofreading every word in the chapter. A mutation can be a single misspelling in any spot." MYRIAD GENETIC LABORATORIES, INC., GENETIC ANALYSIS FOR RISK OF BREAST AND OVARIAN CANCER: IS IT RIGHT FOR YOU? 6 (1996) (on file with the *Boston University Journal of Science & TechnologyLaw*) [hereinafter GENETIC ANALYSIS FOR RISK].

28 The BRCA1 and BRCA2 tests are available to

> 1. persons with breast and/or ovarian cancer who have two or more first or second degree blood relatives . . . with either breast or ovarian cancer, 2. persons with breast and/or ovarian cancer who have one first- or second-degree blood relative . . . with either breast or ovarian cancer, 3. persons with breast cancer and/or ovarian cancer which developed at an early age . . . 4. persons with breast and/or ovarian cancer with multiple primary cancers or bilateral disease, 5. males with breast cancer diagnosed at any age, 6. relatives of persons with documented mutations in the BRCA1 or BRCA2 gene.

ANSWERS FOR PHYSICIANS, *supra* note 19, at 1.

29 *See* Telephone Interview with Joan Scott, M.S., C.G.C., Director, Genetic Services, OncorMed, Inc. (Jan. 14, 1997).

30 *See id.*; F-D-C Reports, THE GRAY SHEET, July 29, 1996, *available in* LEXIS, Health Library, Gray File.

31 *See* F-D-C Reports, *OncorMed BRCA1 Testing Service Commercialization Enters Second Phase Through New IRB Protocol*, THE BLUE SHEET, Jan. 17, 1996, *available in* LEXIS, Health Library, Blue File.

32 *See* ONCORMED, INC., PRE-TEST COUNSELING CHECKLIST FOR BRCA1 AND BRCA2 TESTING 1-4 (1996) (on file with the *Boston University Journal of Science & Technology Law*).

33 *See* Caryn Lerman et al., *BRCA1 Testing in Families with Hereditary Breast-Ovarian Cancer:*

surveillance and management options, including the types of preventative surgery available.[34]

9. OncorMed followed the regulations promulgated by the Food and Drug Administration ("FDA") and the National Institute of Health ("NIH") when it formed its IRB.[35] OncorMed was not required to follow FDA or NIH regulations because it marketed the genetic test as a service and did not obtain any government funding for its research.[36] Nevertheless, OncorMed established this review framework because the company recognized the necessity of IRB review for promoting informed consent.[37] In addition, Dr. Patricia Murphy, Vice President of OncorMed's Genetic Services, observed that operating without "caution, conservatism, and restraint" would negatively impact the future market for the new genetic testing industry.[38]

10. OncorMed's six-member IRB contains a variety of individuals, including a consumer advocate, several genetic counselors, a physician, a nurse, a social worker, and an attorney.[39] In addition, the IRB contains several ad hoc members who provide specialized knowledge to the IRB when needed.[40] No IRB member is affiliated with the company.[41]

2. Myriad Genetics's BRCA1 and BRCA2 Tests

11. Myriad's BRCA1 and BRCA2 tests are different from OncorMed's in that Myriad did not use an IRB to approve its research protocols.[42] The company supplies physicians with guidelines for evaluating appropriate candidates, pretest

---

A Prospective Study of Patient Decision Making and Outcomes, 275 JAMA 1885, 1891-92 (1996).

34 *See* ONCORMED, INC., POST-TEST COUNSELING CHECKLIST FOR BRCA1 AND BRCA2 TESTING (1996) (on file with the *Boston University Journal of Science & Technology Law*).

35 *See Hearings I, supra* note 10, at 63 (testimony of Patricia D. Murphy, Vice President, Genetic Services, OncorMed, Inc.); Telephone Interview with Joan Scott, *supra* note 29.

36 *See* 45 C.F.R. § 46 (1995); 21 C.F.R. § 50.1 (1996).

37 *See* Telephone Interview with Joan Scott, *supra* note 29.

38 *Hearings I*, *supra* note 10, at 63 (testimony of Patricia D. Murphy, Vice President, Genetic Services, OncorMed, Inc.).

39 *See id.*; Telephone Interview with Joan Scott, *supra* note 29.

40 *See* Telephone Interview with Joan Scott, *supra* note 29.

41 *See id.*

42 *See* Telephone Interview with Glenda Lowe, Client Services Manager, Myriad Genetics, Inc. (Nov. 7, 1996). FDA approval of Myriad's in-house genetic testing service was not required. *See id.*

checklists,[43] consent forms,[44] and informational materials for both physicians[45] and patients.[46] Myriad encourages physicians to suggest genetic counseling to patients so that they fully understand the repercussions of a negative or positive test result.[47] The company "hopes" physicians follow these guidelines but does not require it.[48]

C. *Institutional Review Boards*

12. Institutional review boards review human clinical testing research.[49] The IRB's primary focus is ethical concerns, such as risk minimization and informed consent.[50] These review boards are "agent[s] of [their] own institution, not a branch office of any regulatory agency."[51] An IRB derives its power from "the institution's legal authority to regulate any investigations it sponsors or funds."[52] Legally, an institution cannot override an IRB's decision to accept or refuse a research protocol.[53]

---

43 *See* MYRIAD GENETIC LABORATORIES, INC., PRETEST CHECKLIST FOR PHYSICIANS (1996) (on file with the *Boston University Journal of Science & Technology Law*).

44 *See* MYRIAD GENETICS LABORATORIES, INC., INFORMED CONSENT FOR GENETIC SUSCEPTIBILITY TESTING FOR BREAST AND OVARIAN CANCER (on file with the *Boston University Journal of Science & Technology Law*).

45 *See* MYRIAD GENETICS LABORATORIES, INC., PRACTITIONER'S GUIDE TO USING BRCA ANALYSIS (1996) (on file with the *Boston University Journal of Science & Technology Law*); MYRIAD GENETICS LABORATORIES, INC., GENETIC COUNSELING RESOURCE DIRECTORY (1996) (on file with the *Boston University Journal of Science & Technology Law*); REFERENCE FOR PROFESSIONALS, *supra* note 2.

46 *See* GENETIC ANALYSIS FOR RISK, *supra* note 27; MYRIAD GENETIC LABORATORIES, INC., BILLING POLICY (1996) (on file with the *Boston University Journal of Science & Technology Law*); MYRIAD GENETICS LABORATORIES, INC., UNDERSTANDING BRCA ANALYSIS (1996) (on file with the *Boston University Journal of Science & Technology Law*).

47 Telephone Interview with Glenda Lowe, *supra* note 42.

48 *Id.*

49 A quorum of IRB members evaluate research protocols during regularly scheduled meetings. *See* ROBERT J. LEVINE, ETHICS & REGULATION OF CLINICAL RESEARCH 326 (1986).

50 *See id.* The American Society of Clinical Oncology emphasizes the importance of consent because, "experimental conditions cannot be so rigorously controlled as those in the laboratory." F-D-C Reports, *NIAID Establishes Office of Clinical Research: NIH Clinical Center Developing Resource Guidelines*, THE BLUE SHEET, Feb. 7, 1994, *available in* LEXIS, Health Library, Blue File [hereinafter *NIAID Establishes Office*].

51 LEVINE, *supra* note 49, at 326.

52 John A. Robertson, *Ten Ways to Improve IRBs*, HASTINGS CENTER REP., Feb. 1979, at 29, 29.

53 *See* Edgar & Rothman, *supra* note 9, at 492.

13. IRBs are a decentralized form of federal regulation.[54] Local committee review is more advantageous than regional or national review because local peer review groups are more aware of the real conditions enveloping research in their institution.[55] In addition, decentralization enables IRBs to develop methods of research approval best suited to their institution while still following federal regulations.[56]

14. Clinical testing laboratories are regulated under the Clinical Laboratory Improvement Amendments ("CLIA").[57] IRB review of research is not required under the CLIA. The federal government only requires IRB review when the institution receives funding from the government[58] or if the institution seeks FDA approval.[59] Often, a laboratory developing a genetic testing service will not fall within one of these two categories and thus, will not seek IRB approval of its protocols. Indeed, a survey performed several years ago found that only 41% of the 54 biotechnology companies developing genetic tests had ever contacted an IRB or the FDA.[60] Further, only 29% of the biotechnology companies offering "home brews"[61] have approached a regulatory body.[62] Almost all of the laboratories performing complex genetic testing sought IRB approval of their research protocols to ensure proper informed consent and to reduce liability.[63] However, only two of these companies sought the FDA's assistance.[64]

---

54 *See* Robertson, *supra* note 52, at 29.

55 *See* Lucas Bergkamp, *American IRBs and the Dutch Research Ethics Committees: How They Compare*, IRB, Sept.-Oct. 1988, at 1, 5.

56 *See* LEVINE, *supra* note 49, at 326.

57 *See* 42 C.F.R. § 493.1 (1995).

58 *See* 45 C.F.R. § 46.101 (1995).

59 *See* 21 C.F.R. § 50.1 (1996).

60 *Scant Regulatory Oversight Found at Genetics Testing Facilities*, BIOTECH. NEWSWATCH, Nov. 6, 1995, *available in* 1996 WL 8453653.

61 "Home brews" are clinical tests performed in-house using the institution's own reagents. *See* Lisa Seachrist, *Testing Genes: Physicians Wrestle with the Information that Genetic Tests Provide*, 148 SCI. NEWS 394, 395 (1995).

62 *Scant Regulatory Oversight Found at Genetics Testing Facilities*, *supra* note 60.

63 *See* Dale L. Moore, *An IRB Member's Perspective on Access to Innovative Therapy*, 57 ALB. L. REV. 559, 564 (1994) ("[M]any IRBs do not distinguish between federally funded and privately funded research in applying their standards of evaluation and review."); Carole Kavanagh et al., *Multi-Institutional Review of a Genetic Counseling Study*, IRB, Apr. 1979, at 1, 3 ("Many institutions require [IRB] clearance for any research conducted within their purview . . . .").

64 *See Scant Regulatory Oversight Found at Genetics Testing Facilities, supra* note 60.

15. The Joint NIH-DOE Ethical, Legal, and Social Implications Working Group of the Human Genome Project Task Force on Genetic Testing (the "Task Force")[65] recently proposed that IRBs review all protocols pertaining to the clinical validation of genetic testing, including tests performed by in-house laboratories.[66] Legally, laboratories offering genetic testing services are not required to submit their genetic testing protocols to an IRB. Thus, an institution's IRB may never evaluate genetic testing protocols simply because it is not mandated by law.[67]

III. THE SPECIAL PROBLEMS WITH GENETIC TESTS

16. Genetic tests are unique and possess many problems that are not associated with other susceptibility tests. Several of these problems concern informed consent, risk assessment, clinical validity, and insurance discrimination.

A. *Informed Consent and Risk Assessment*

17. IRB review of genetic testing protocols is crucial to achieving informed consent. Most doctors lack the skills and training necessary either to interpret a complex genetic test or provide a patient with enough information to make an informed decision.[68] Today, there are just 800 physicians certified in medical genetics, and only 50% of United States medical schools provide educational opportunities in genetics.[69] It is not surprising then, that many physicians feel that they lack the ability to accurately use genetic tests as a diagnostic tool.[70] Without strong IRB approved protocols, clinical subjects will not receive the counseling they

---

65 The Task Force on Genetic Testing is a committee of 20 individuals responsible for evaluating and proposing recommendations for genetic testing in the United States. *See* The National Human Genome Research Institute, *Task Force on Genetic Testing* (visited Jan. 7, 1997) <http://www.nhgri.nih.gov/Policy_and_public affairs/Communications/Meeting_reports/task-force.html>.

66 *See* Proposed Recommendations of the Task Force on Genetic Testing; Notice of Meeting & Request for Comment, 62 Fed. Reg. 4539, 4540 (1997) [hereinafter Proposed Recommendations].

67 *See generally* BRENDA BARBER ET AL., RESEARCH IN HUMAN SUBJECTS 149 (1979) (reporting that only "[e]ighty five percent of the institutions responded that 'all clinical research' was now reviewed"). However, Myriad Genetics does not use an IRB to approve it genetic testing research. *See* Telephone Interview with Glenda Lowe, *supra* note 42.

68 *See* Proposed Recommendations, *supra* note 66, at 4540, 4545. In addition, there is an inadequate number of genetic counselors to satisfy the predicted magnitude of genetic testing. *See id.* at 4540.

69 *See* Lisa Seachrist, *supra* note 61, at 394. Indeed, medical genetics was acknowledged as a medical field only 14 years ago. *See id.*

70 "But the second you tell a patient, 'Your risk is increased, 'they say, 'How much?' If you don't have the answer for them, you haven't done them much good." *Id.* at 395. (quoting Dr. Watson).

need to make informed decisions.[71] Mistaken evaluation of test results can be devastating for research subjects, both economically and psychologically. Thus, an IRB approved protocol detailing the requisite elements of informed consent is critical so that a patient will be aware of the consequences associated with the genetic test.

18. Informed consent prior to testing is essential in genetic testing for cancer because "with cancer, there is a cure or death, but nothing in between."[72] A positive test result is not conclusive evidence that the patient will develop breast cancer[73] because the environment and other genes also influence cancer development.[74] Thus, knowledge of a genetic predisposition places the patient in "purgatory."[75] The uncertainty of the cancer diagnosis and the lack of a cure makes it essential that patients are able to interpret the results and reach informed decisions about surveillance options.

19. An IRB-approved protocol also ensures that other effects of being a BRCA1 or BRCA2 carrier are addressed. An individual testing positive for a BRCA mutation may experience a wide range of emotions, including guilt, if she passes the gene on to her children, anger, and fear.[76] In addition, the positive test result may strain family relations since the knowledge of a genetic predisposition will affect other family members.[77] For instance, relatives could learn that a child was adopted and, therefore, was not at risk for developing a BRCA1 or BRCA2 mutation.[78] Hence, a strong, nonaffiliated IRB must examine genetic testing protocols to better ensure that the patient is aware of the actual meaning of testing positive for an incurable disease.

---

71 *See id.*

72 *Pediatrics: UF Named Phase I Trial Center for Pediatric Cancer Drugs*, CANCER WKLY. PLUS, Aug. 12, 1996, *available in* 1996 WL 11463624 (quoting Dr. Paulette Mehta).

73 For example, a genetic test may determine that a patient has an 80% likelihood of developing the disease by the time they are 50 years of age. *See Hearings on Technological Advances in Genetic Testing: Implications for the Future Before the Subcomm. for Tech. of House Comm. on Science*, 104th Cong. (1996) [hereinafter *Hearings III*] (prepared testimony of Dr. Alan Goldhammer, Director of Technical Affairs, Biotechnology Industry Organization), *available in* LEXIS, News Library, Curnws File. No one knows if the patient is in the 80% risk group or in the 20% risk group "or why." *Id.*

74 Joan Stephenson, *Questions on Genetic Testing Services*, 274 JAMA 1661, 1661 (1995). Indeed, there is a 15% likelihood that all mutation carriers will never develop cancer. *See* Saltus, *supra* note 22, at 26.

75 Saltus, *supra* note 22, at 25.

76 *See* ANSWERS FOR PHYSICIANS, *supra* note 19, at 7.

77 *See id.*

78 *See id.*

20. Furthermore, a negative result on a genetic test provides no greater certainty than a positive one.[79] Negatively tested individuals do not have a zero risk for developing cancer; rather, they have the same risk as the general population.[80] In addition, a negatively tested individual could still acquire hereditary cancer if the test missed a mutation or if the individual possessed a mutation that the test was incapable of identifying.[81] This negative result may act as a "false reassurance," causing a woman to forego preventative measures, such as mammograms or self breast-examinations.[82] Finally, the psychological effects of a negative result may be profound as an individual may feel guilty that they did not inherit the mutation while another family member did.[83]

21. Informed consent is crucial and genuinely impacts a patient's decision to have the genetic test performed. One study revealed that just 47 of the 279 relatives of women BRCA1 carriers surveyed desired the same predisposition testing for themselves.[84] Most women were afraid the testing would negatively impact their insurance coverage and their lives.[85]

B. *Clinical Validity*

22. Currently, there are no regulations to guarantee that a genetic test is clinically valid.[86] It is "technically difficult" to interpret the results from a genetic

---

79 *See* DRAFT INTERIM PRINCIPLES, *Scientific Validation*, *supra* note 8, at Principle I-7. For example, "[t]he risk of breast cancer in a women whose sister with breast cancer has an inherited BRAC1 susceptibility mutation drops from about 85% to 12% if the women's test result is negative . . . ."

80 *See* ANSWERS FOR PHYSICIANS, *supra* note 19, at 8.

81 *See id.* at 7.

82 DRAFT INTERIM PRINCIPLES, *Scientific Validation*, *supra* note 8, at Principle I-7.

83 *See* GENETIC ANALYSIS FOR RISK, *supra* note 27, at 10.

84 *See Hearings II*, *supra* note 13 (testimony of Rep. Louise Slaughter). Similar circumstances occurred in a genetic test for the Huntington disease gene. *See* Lerman et al., *supra* note 33, at 1885. After patients were informed about the test's implications, less than 15% of the people who expressed an interest in the testing elected to have it done. *See id.*

85 *See Hearings II*, *supra* note 13 (testimony of Rep. Louise Slaughter).

86 *See* Proposed Recommendations, *supra* note 66, at 4545. *See also* DRAFT INTERIM PRINCIPLES, *Scientific Validation*, *supra* note 8, at Principle I-8 ("Current regulations do not establish an endpoint for clinical validation studies in clinical laboratories.").

test,[87] and the frequency of false-negative results is unknown.[88] Furthermore, a lab technician usually cannot perform another, alternative test to verify the genetic test's results.[89] It is essential that a physician inform genetic testing candidates of these uncertainties so that an individual can give informed consent and assess the test results accurately. Both of these goals can best be achieved through an IRB approved protocol.

C. *Insurance Coverage*

23. Discovering a genetic predisposition may negatively impact insurance coverage, and informed consent is critical to ensure that test subjects are aware of this risk. The BRCA1 and BRCA2 tests are expensive,[90] but many women will pay the expenses themselves to prevent their insurance companies from having access to the results.[91] Typically, an individual's participation in a research study is confidential. Doctors may inadvertently note this participation in a patient's medical record while authorizing or interpreting the test's results. Such notation may alert the patient's insurance company that the individual participated in a research study and is now aware of her genetic predisposition for a disease.[92]

24. Moreover, awareness of an increased personal or familial risk of disease can be an impediment when seeking new insurance.[93] Many insurance providers refuse to cover individuals "whose probability of disease exceeds three times the

---

87 National Cancer Institute & National Institutes of Health, *supra* note 2.

88 *See id.*

89 *See* DRAFT INTERIM PRINCIPLES, *Introduction, supra* note 1 ("only the appearance of the disease itself confirms the prediction.").

90 Myriad charges $2,400 for performing both the BRCA1 and the BRCA2 gene test. *See* MYRIAD GENETIC LABORATORIES, INC., BILLING POLICY, *supra* note 46. OncorMed offers combined Stage I and Stage II BRCA1 and BRCA2 testing for $1,300. ONCORMED, INC., HEREDITARY BREAST CANCER: QUESTIONS AND ANSWERS FOR PATIENTS 3 (1996) (on file with the *Boston University Journal of Science & Technology Law*).

91 *See* Nancy E. Kass, *Participation in Pedigree Studies and the Risk of Impeded Access to Health Insurance*, IRB, Sept.-Oct. 1993, at 7, 8.

92 *See id.* For example, in one case, a doctor, after a "casual conversation" with the patient, noted in the patient's medical record that the patient was a participant in an HIV research study. *See id.* The insurer refused to consider the patient's application, stating that "the applicant might have access to information about himself that they did not have, which was not fair, and which might be leading him to seek insurance." *Id.* The patient was effectively forced to learn of his HIV status, "which he had deliberately chosen not to learn." *Id.*

93 *See id.* at 9.

average for their age and sex."[94] If denied, the patient's name and the reason for refusal are sent to the Medical Information Bureau, a national database for insurance providers.[95] This ensures that the risky individual will not obtain insurance in the future by misrepresenting their condition.[96] A genetic predisposition may increase the risk of disease to the extent that a person becomes uninsurable. Positive test results may also restrict job mobility because a new employer's insurance policy may deny coverage based on the patient's elevated risk.[97] Finally, there may be insurance repercussions for the genetically tested individual's offspring, who are also potential carriers of the gene.[98]

25. The Health Insurance Portability and Accountability Act prohibits the denial of health insurance coverage to individuals based on their genetic information.[99] The Act is an important first step in remedying the problem of insurance denial, but the scope of the Act is still uncertain. The Act explicitly refers only to health insurance; thus it may not protect genetically predisposed individuals against other types of insurance discrimination. Hence, an IRB approved protocol explaining these risks is still necessary to ensure that tested patients are aware of potential insurance problems.

IV. THE CURRENT FEDERAL REGULATORY SCHEME

26. Genetic testing and the rest of the biotechnology industry are not regulated extensively by the federal government. Both the FDA and the NIH established baseline requirements for IRBs. The regulations were flexibly designed so that IRBs could create procedures to meet their institutions' specific demands.[100] The FDA and NIH, however, only regulate genetic testing performed by clinical laboratories in specific circumstances.[101] Further, clinical laboratories offering

---

94 *Id.* at 8.

95 *See id.*

96 *See id.*

97 *See id.* at 9.

98 *See* Saltus, *supra* note 22, at 25 ("Each offspring of a gene carrier has a 50-50 chance of inheriting the gene.").

99 Health Insurance Portability & Accountability Act of 1996, Pub. L. No. 104-191, § 702(a)(1)(F), 110 Stat. 1936, 1945 (to be codified at 29 U.S.C. § 1182(a)(1)(F)).

100 *See* Ada Sue Selwitz & Sherry A. Marts, *The Institutional Review Board: Local Policies and Procedures*, 47 FOOD DRUG COSM. L.J. 695, 695 (1992).

101 These agencies only regulate genetic testing when the clinical laboratory is seeking either FDA approval or federal research funds. *See* 45 C.F.R. § 46.101 (1995); 21 C.F.R. § 50.1 (1996).

genetic testing services only need to comply with the Clinical Laboratory Improvement Amendments of 1988, which contain no provisions requiring IRB review of research protocols.[102] Genetic testing is a unique diagnostic tool that requires greater regulatory oversight to address the special problems explained previously.[103] Therefore, the federal government should promulgate comprehensive requirements for all types of genetic testing, that include IRB review of all research protocols.

A. *The Clinical Laboratory Improvement Amendments of 1988*

27. The Health Care Financing Administration ("HCFA") enforces the Clinical Laboratory Improvement Amendments ("CLIA") to ensure that all laboratories maintain a minimum level of quality in their testing.[104] All clinical laboratories must follow the CLIA.[105] The CLIA describes the requirements for laboratory certification and inspection, including the methods for obtaining certificates of compliance, registration, and accreditation.[106] To obtain certification, a laboratory must comply with certain broadly-defined requirements.[107] The CLIA also establishes requirements for clinical labs performing high-level tests, but fails to list specific regulations for complex genetic testing.[108]

28. The HCFA regulatory scheme is an insufficient framework for addressing the unique concerns inherent in genetic testing. The Task Force criticized the CLIA for requiring laboratories to demonstrate the "analytical validity" of tests but not the "clinical validity or utility."[109] Further, the Task Force suggested an alternative government framework that requires all laboratories to clinically validate their genetic tests.[110]

---

102 42 U.S.C. § 263a (1991).

103 *See supra* notes 68-99 and accompanying text.

104 *See* 42 U.S.C. § 263a.

105 *See id.*

106 42 C.F.R. § 493 (1995).

107 42 C.F.R. § 493.56.

108 *See* 42 C.F.R. § 493; Proposed Recommendations, *supra* note 66, at 4545. (The "CLIA has no standards specific for genetic tests except for cytogenetics"); Stephenson, *supra* note 74, at 1662 (stating that the CLIA does not have specific requirements for DNA-based genetic testing).

109 DRAFT INTERIM PRINCIPLES, *Scientific Validation, supra* note 8, at Principle I-7. *See generally* Proposed Recommendations, supra note 66, at 4545 ("Many tests currently on the market have not been systematically validated nor subject to external review.").

110 *See* DRAFT INTERIM PRINCIPLES, *Scientific Validation, supra* note 8, at Principle I-7.

B. *FDA Regulation of Medical Devices*

29. IRB approval is mandatory for all clinical testing subject to the FDA's jurisdiction, including genetic testing kits.[111] The FDA's jurisdiction over laboratories not offering their tests for sale, but performing in-house genetic testing, is questionable.[112]

30. The FDA regulates commercially marketed genetic testing kits as medical devices under the Medical Device Amendments ("MDA").[113] The FDA should have the authority to regulate in-house genetic tests since the MDA's definition of a device also encompasses these tests offered by laboratories. According to the Food, Drug, and Cosmetic Act ("FDCA"), a device is "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part or accessory, which is . . . *intended for use in diagnosis of disease or other conditions*."[114] Clinical laboratories use genetic tests to determine if an individual has a genetic predisposition for a particular disease. Thus, the tests serve the diagnostic function described in the FDA's definition of a device.

31. Furthermore, there are three categories of medical devices.[115] A device's classification indicates the minimum amount of FDA oversight required to guarantee the safety and effectiveness of that device.[116] Class I devices require "general controls," and Class II devices require "special controls."[117] Class III devices pose a "potential[ly] unreasonable risk"[118] to the public because of the lack of

---

111 *See* Stephenson, *supra* note 74, at 1662; DRAFT INTERIM PRINCIPLES, *Scientific Validation, supra* note 8, at Principle I-6.

112 *See* Stephenson, *supra* note 74, at 1662.

113 21 U.S.C. § 360 (1994 & Supp. V 1996); *see generally Hearings I, supra* note 10, at 57 (testimony of Patricia D. Murphy, Vice President, Genetic Services, OncorMed, Inc.) (arguing that although FDA regulates genetic test kits as medical devices, the CDC and HCFA are more appropriate regulatory agencies).

114 21 U.S.C. § 321(h) (1994 & Supp. V 1996) (emphasis added). A modern day hospital uses over 5,000 medical devices, and the designation encompasses apparati such as artificial joints and tongue depressors. *See* Mary Kay Ryan, *Researching Involving Medical Devices, in* HUMAN SUBJECTS RESEARCH: A HANDBOOK FOR INSTITUTIONAL REVIEW BOARDS 107 (Robert A. Greenwald et al. eds., 1982) [hereinafter HUMAN SUBJECTS RESEARCH].

115 *See* 21 U.S.C. § 360c (1994 & Supp. V 1996).

116 *See* Center for Devices and Radiological Health, *Information on Premarket Approval Applications* (last modified Nov. 20, 1996) <http://www.fda.gov/cdrh/pmapage.html>.

117 21 U.S.C. § 360c.

118 *Id.*

knowledge about the devices' safety.[119] Today, all new devices are classified as Class III.[120] The FDA requires premarket approval for all Class III devices unless the device is "substantially equivalent" to another Class III device that is already approved.[121] One aspect of this premarket approval process involves IRB review of the clinical protocol.[122]

32. An institution could request an investigational device exemption ("IDE") to the FDA's classification system for experimental genetic testing devices.[123] IDEs would be useful for the BRCA tests because there are no other tests that can independently validate these tests' results.[124] All researchers applying for this exemption cannot begin the research until both an IRB and the FDA have approved their protocols.[125] The IRB reviews the research plan, specifically, the informed consent provisions, for "adequacy to justify the commencement of such testing."[126] Obtaining IRB approval of the IDE enables the laboratory to gather data about the genetic test's safety and validity while ensuring that patients are well informed of the genetic test's inherent risks and benefits.

C. *NIH and FDA Regulation of Institutional Review Boards*

33. The Office of Protection of Research Risks ("OPR") administers the NIH's regulations for human clinical testing.[127] These regulations apply "to all research involving human subjects conducted, supported or otherwise subject to regulation by any federal department or agency."[128] The NIH regulations for human clinical

---

119 21 U.S.C. § 360e(a); Center for Devices and Radiological Health, *Information on Premarket Approval Applications, supra* note 116.

120 *See* 21 U.S.C. § 360c(f). This is true unless the device falls within one of the MDA's statutory exceptions or was marketed commercially before May 28, 1976. *See id.*

121 21 U.S.C. § 360e(b)(1)(B); *see* 21 C.F.R. § 812.20 (1996).

122 *See* 21 C.F.R. § 812.20(b)(6)(ii).

123 *See* 21 U.S.C. § 360j(g).

124 *See* DRAFT INTERIM PRINCIPLES, *Scientific Validation, supra* note 8, at Principle I-6.

125 *See* 21 U.S.C. § 360j(g)(3)(A); 21 C.F.R. § 812.42; 21 C.F.R. § 812.62.

126 21 U.S.C. § 360j(g)(3)(A)(D).

127 *See* Stuart L. Nightingale, *The Food and Drug Administration's Role in the Protection of Human Subjects*, IRB, Jan.-Feb. 1983, at 6, 7. Only four people, however, work full-time for the OPR. *See* Joseph Palca, *Institutional Review Boards: A Net too Thin*, HASTINGS CENTER REP., May 1996, at 4. The "OPR can hardly be expected to keep a close watch on the thousands of experiments involving humans." *Id.*

128 45 C.F.R. § 46.101(a) (1995). Research is defined as "a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable

testing are nearly identical to the FDA regulations.[129] This "industry friendly" approach eliminates the need for two different types of IRBs at each institution, one to review all FDA research and another to follow the NIH's regulations.[130] The FDA's regulations apply to all devices, foods, drugs, and biological and medical products researched and sold commercially.[131]

34. Both the NIH and the FDA regulations establish membership requirements for every IRB.[132] According to these requirements, each IRB must contain at least five members of diverse backgrounds,[133] for example, varied in gender and vocation.[134] An IRB cannot have fewer than one scientific and one nonscientific member,[135] and no IRB member can be affiliated with the institution.[136] A member cannot participate in the review of a research project when they have a "conflicting interest,"[137] although the regulations do not define what constitutes a conflicting interest. The NIH and FDA regulations also do not limit IRB salaries or provide any reporting mechanism for the institution to disclose their remuneration of IRB members.

35. An IRB can only approve a research proposal that satisfies all of the requirements contained in the NIH and FDA regulations.[138] An acceptable protocol must include evidence that the "risks to the subjects are minimized"[139] and are "reasonable" when compared to the "anticipated benefits."[140] Researchers must obtain informed consent from each human subject prior to clinical testing.[141] The

---

knowledge." 45 C.F.R. § 46.102(d).

129 *See News from the Federal Front: So You Want to Develop Gene Therapy Products?* BIOVENTURE VIEW, Aug. 1995, *available in* LEXIS, News File, Curnws Library.

130 *Id.*

131 *See* 21 C.F.R. § 50.1 (1996).

132 *See* 45 C.F.R. § 46.107 (1995); 21 C.F.R. § 56.107 (1996).

133 *See* 45 C.F.R. § 46.107(a); 21 C.F.R. § 56.107(a).

134 *See* 45 C.F.R. § 46.107(b); 21 C.F.R. § 56.107(b).

135 *See* 45 C.F.R. § 46.107(c); 21 C.F.R. § 56.107(c).

136 Nor may any relative of an IRB member be affiliated with the institution. *See* 45 C.F.R. § 46.107(d); 21 C.F.R. § 56.107(d).

137 45 C.F.R. § 46.107(e); 21 C.F.R. § 56.107(e).

138 *See* 45 C.F.R. § 46.111; 21 C.F.R. § 56.111.

139 45 C.F.R. § 46.111(a)(1); 21 C.F.R. § 56.111(a)(1).

140 45 C.F.R. § 46.111(a)(2); 21 C.F.R. § 56.111(a)(2).

141 *See* 45 C.F.R. § 46.111(4); 21 C.F.R. § 56.111(4).

IRB must also confirm that the research protocol contains provisions that safeguard against invasions of the research subject's privacy.[142]

36. An IRB has the legal authority to suspend or halt a scientist's research that is not proceeding according to the IRB approved protocol.[143] The institution can always subject the IRB approved protocol to additional review procedures, but cannot begin research that an IRB has rejected.[144]

V. PROBLEMS WITH THE CURRENT FEDERAL REGULATION

37. The federal government should subject all genetic testing protocols to IRB review to promote risk minimization and informed consent. Federal regulation of IRBs is, in some respects, too general. The IRB regulations fail to address several problems, including, the payment of IRB members by institutions and the conflicts of interest among IRB members. Thus, the federal government should modify the current regulatory framework to account for these problems before applying it to genetic testing.

A. *IRB Reimbursement*

38. The current rules governing IRBs do not prevent or limit an institution from paying its IRB members.[145] In the past, most research was performed at academic institutions.[146] These institutions did not compensate IRB members, who were mostly faculty and administrators that considered their IRB service a component of their overall academic responsibilities.[147]

39. As the amount of research performed in privately owned, corporate laboratories increases, the number of IRBs demanding fees for their services have also increased.[148] Institutional sponsors negotiate and pay fees directly to IRB

---

142 *See* 45 C.F.R. § 46.111(7); 21 C.F.R. § 56.111(7).

143 *See* 45 C.F.R. § 46.113; 21 C.F.R. § 56.113.

144 *See* 45 C.F.R. § 46.112; 21 C.F.R. § 56.112.

145 *See* Richard C. Thompson, *Protecting 'Human Guinea Pigs,' in* BIOTECHNOLOGY: NEW DEVELOPMENTS IN FEDERAL POLICIES AND REGULATIONS 121, 159 (PLI Patents, Copyrights, Trademarks, & Literary Property Course Handbook Series No. G4-3819, 1988).

146 *See* Edgar & Rothman, *supra* note 9, at 500.

147 *See* Mary Kay Ryan, *IRB Procedures, in* HUMAN SUBJECTS RESEARCH, *supra* note 114, at 75.

148 *See* David M. Cocchetto, *Practical Considerations in Direct Interactions Between Sponsors and Institutional Review Boards*, 49 FOOD DRUG COSM. L.J. 77, 83 (1994).

members.[149] Generally, an institution will pay a consulting fee and reimburse IRB members for travel and expenses, such as parking.[150] Paying substantial fees or salaries to IRB members creates an implied obligation on the part of these members to approve testing that is financially advantageous for the institution whether or not it is beneficial to human subjects. IRBs that are not affiliated with the institution, but are hired to review research, essentially "serve at [the institution's] leisure."[151] Furthermore, there is no regulatory framework requiring institutions to disclose the compensation they pay to IRB members.

B. *Conflicts of Interest*

40. IRB members' personal activities may influence their bias in approving or rejecting research proposals.[152] A conflict of interest arises in a "situation where regard for one duty leads to the disregard for another."[153] It is "a clash between a public interest and a private, pecuniary interest."[154] A conflict of interest is different from scientific misconduct, fraud, or plagiarism.[155] There is great potential for conflicts of interests for IRB members because many are researchers themselves and may be more interested in new scientific discoveries than protecting human research subjects.[156]

---

149 *See id.* at 84.

150 *See* Mary Kay Ryan, *IRB Procedures, in* HUMAN SUBJECTS RESEARCH, *supra* note 114, at 75; Cocchetto, *supra* note 148, at 83.

151 F-D-C Reports, *Institutional Review Boards Suffer from Conflict of Interest, Witness Charge at Wyden Hearing*, THE BLUE SHEET, May 25, 1994, *available in* LEXIS, Health Library, Blue File (quoting Arthur Caplan) [hereinafter *Wyden Hearing*]. "[I]t's a situation where you've got the fox guarding the chicken coop . . . ." *Id.*

152 *See* Tabitha M. Powledge, *The FDA's New Sheriff,* HASTINGS CENTER REP., Jan.-Feb. 1992, at 5, 5, *available in* LEXIS, News Library, Curnws File.

153 United States v. Miller, 463 F.2d 600, 602 (1st Cir. 1972).

154 Thomas L. Kurt, *FDA Issues Concerning Conflicts of Interest*, IRB, Sept.-Oct. 1990, at 6. "[W]hat might look like a mutually beneficial working relationship for the researcher, might appear as [a] conflict of interest to the public." *Id.* "Although a member may ultimately decide an issue unfavorably to the outside interests with whom he is associated, he is unlikely to do so without considering the effect such a decision will have on his relationship with those interests." Kenneth John Shaffer, *Improving California's Safe Drinking Water and Toxic Enforcement Act Scientific Advisory Panel Through Regulatory Reform*, 77 CAL. L. REV. 1211, 1239 (1989).

155 *See* Kurt, *supra* note 154, at 6.

156 An anonymous survey of university biomedical faculty members revealed that 11.1 to 31.1% have conflicts of interest. *See* Marshal Eliot*, When Commerce And Academe Collide,* 248 SCIENCE 152, 152.

41. Moreover, current federal regulations do not guarantee that a research subjects' interests will supersede an organization's interests.[157] In *Ten Ways to Improve IRBs*, John Robertson observed that the structure of IRB review "unduly favors" the researcher.[158] It is the researcher and not the research subject who explains the proposal to an IRB and lobbies for its approval.[159] No IRB member needs to be exclusively responsible for articulating the interests of the human subjects, and therefore, these interests may seem "less compelling" than the scientist's "need to meet a grant deadline or begin recruiting subjects."[160] The quality of the IRB review at each institution is contingent upon the conscience and commitment of its members,[161] and at times, this dedication may not be enough to outweigh the members' own powerful conflicts of interest.

1. Pecuniary Interests

42. An institution may have difficulty locating individuals who possess scientific expertise but no pecuniary or personal conflict of interest.[162] For instance, the FDA recently faulted an IRB for having the "appearance of a conflict of interest" when the FDA discovered that the IRB chairperson also was the head of the Joint Clinic Voluntary Research Fund, an organization that sponsored the research approved by the IRB.[163] Many researchers participate in their employer's retirement funds or purchase stock in the company for which they are performing research.[164] An IRB member with a pecuniary or other personal conflict of interest could be more inclined to renounce the protection of research subjects for the "bottom line."[165]

---

157 *See* Edgar & Rothman, *supra* note 9, at 493; Robertson, *supra* note 52, at 31 ("There is an implicit structural bias in favor of investigators.").

158 Robertson, *supra* note 52, at 30.

159 *See id.*

160 *Id.* at 30-31.

161 *See* Edgar & Rothman, *supra* note 9, at 497.

162 *See* Shaffer, *supra* note 154, at 1239 ("nearly every qualified scientific expert maintains some continuing relationship with private industry or with public interest groups, either as an investor, employee, consultant, or recipient of private research funds").

163 *FDA Checks Excimer Lasers, MDRs, IRB Conflict of Interest*, WARNING LETTER BULL., Apr. 22, 1996, *available in* 1996 WL 8733585.

164 *See* David S. Shimm & Roy G. Spence, Jr., *Conflict of Interest and Informed Consent in Industry-Sponsored Clinical Trials*, 12 J. LEGAL MED. 477, 507 (1991); *see, e.g.*, William Booth, *Conflict of Interest Eyed at Harvard*, 242 SCIENCE 1497, 1497 (discussing a Harvard researcher who published a study on a product marketed by SpectraPharm, a company in which he was a principal stockholder).

165 George J. Annas, *Questing for Grails: Duplicity, Betrayal and Self-Deception in Post Modern*

43. In addition, many institutions rely on the results of their clinical research for revenue,[166] and a successful clinical trial is often critical to achieving large profits.[167] An institution may exert pressure on IRB members so they can reap these rewards.[168] Many companies, in an effort to "buy [IRB] acquiescence," will give "gifts" to researchers.[169] Most researchers probably would be unwilling to forego these financial rewards to serve on an IRB, especially in light of the cost of "travel, possible training, and time" the individual must dedicate to the meetings.[170] These circumstances make it difficult, if not impossible, to locate a capable, objective, non-affiliated reviewer.

44. Conflict of interest problems are further exacerbated by the reduced amount of governmental funding available for research.[171] Since the 1970s, the NIH has been forced to dramatically reduce the amount of money available for research, even though the cost of scientific study has continued to increase.[172] The shortage of government funding has caused many medical school faculty members to turn to industry to fund their research.[173] This increases the possibility that even the most esteemed IRB members will possess a conflict of interest.

Medical Research, 12 J. CONTEMP. HEALTH L. & POL'Y 297, 317 (1996).

166 *See* Edgar & Rothman, *supra* note 9, at 503 (Now, there is a "entrepreneurial character [to] biomedical science").

167 *See* Annas, *supra* note 165, at 317 ("Medicine . . . is currently faced with a new dominate ideology--the ideology of the marketplace, which puts profit making . . . as its highest priority").

168 *See* F-D-C Reports, *National IRB for Review of Xenotransplantion Research is Needed, Pittsburgh's Arnold Suggests*, THE BLUE SHEET, June 28, 1995, *available in* LEXIS, Health Library, Blue File.

169 Shimm & Spence, *supra* note 164, at 510.

170 F-D-C Reports, *Cooperative Group Members Should Form Core of Data/Safety Monitoring Boards-NCI Task Force*, THE BLUE SHEET, Aug. 3, 1994, *available in* LEXIS, Health Library, Blue File.

171 *See generally* Ethel S. Siris, *In Search of Funding: The Clinical Investigator and the Drug Company*, IRB, Nov.-Dec. 1983, at 1 ("Industry has begun to examine its role as a supplier of capital to universities . . . .").

172 *See id.* Private agencies cannot support all of the new research ventures, and the pharmaceutical industry has filled the funding void. *See id.* "The primary goal of the pharmaceutical industry is to fulfill its corporate obligations to its stockholders and to be profitable." *Id.* at 2. This often conflicts with the central goal of federal research, namely, "sponsorship to support the progress of science [and] to benefit the public." *Id.*

173 *See id.* Many medical schools expect their faculty members to "bring in a substantial portion of their salaries" and, therefore, will not pay their wages using university funds. *Id.* Thus, researchers must find grant money or some other source of private income to supplement their salary. *See id.*

2. Personal Interests

45. IRB members employed by an institution have an interest in approving new genetic testing protocols to enhance the institution's reputation as a "genetic powerhouse."[174] This reputation will increase the prestige of the IRB members' own research if it is conducted at the same institution. It will also benefit IRB members who possess a financial interest in the company. Thus, an IRB member with this type of conflict of interest may have incentive to approve a novel, challenging research protocol without fully considering the risks and benefits to the human clinical subjects.

46. Moreover, IRB members are often on the faculty or are employees of the institution financing the IRB's activities.[175] These affiliated IRB members may approve research protocols so as not to adversely affect their fellow colleagues' well being.[176] Today, there is a congenial atmosphere in the field of biomedical research.[177] IRB members who are cordial with the researcher seeking approval may consider the scientist's proposal in the framework of a "good researcher doing good research."[178] Psychologically, IRB members cannot fathom that a respected peer would conduct "bad" research,[179] and so the protocol is presumed acceptable simply because it was offered to the IRB for approval.[180] Thus, IRB members may not hold their peers to standards high enough to protect human subjects.[181] In addition to facing disappointed colleagues on a daily basis, there is also incentive for researchers affiliated with an institution to set a lower threshold for research approval because their own research will ultimately be held to the same standard.[182]

---

174 Rick Weiss, *It May Be Over for Biotech Oversight Panel*, WASH. POST, May 29, 1996, at A17.

175 *See* Jay Katz, *Human Experimentation and Human Rights*, 38 ST. LOUIS L.J. 7, 40-41 (1993).

176 *See id.* In fact, there has been evidence of "IRB shopping," where researchers submit their proposals to the IRB board they think will approve it. *See Wyden Hearing, supra* note 151.

177 Kathleen A. Nolan, *Student Members: 'Informed Outsiders' on IRBs,* IRB, Oct. 1980, at 1, 2.

178 *Id.*

179 *Id.* at 2-3.

180 *See id.* at 3.

181 *See* Katz, *supra* note 175, at 44; Palca, *supra* note 127, at 4 (stating "collegial ties among IRB members and researchers whose work they were asked to review could hamper an IRB member's ability to critically evaluate protocols").

182 *See* Palca, *supra* note 127, at 4.

VI. PROPOSED SOLUTION

47. The federal government should take several steps to remedy the lack of regulation in clinical genetic testing. First, the FDA should create an advisory committee to devise uniform standards for IRBs. This committee should make IRB review mandatory for genetic testing protocols.[183] Specific regulations addressing salary and conflict of interest issues would facilitate the informed consent process that is the "cornerstone" of any clinical testing program.[184] These regulations must be flexible enough to allow institutions to develop their own protocols for review of research that is not federally-funded.[185] The new regulations must also achieve a reasonable balance between society's interests in scientific advancement, and safe and effective products for the public use.[186]

A. *The FDA Advisory Committee*

48. Currently, only professional societies have established guidelines that an IRB can use to appraise a genetic testing protocol.[187] Voluntary guidelines are an ineffective way to regulate the genetic testing industry for two reasons. First, voluntary guidelines are problematic because genetic testing companies, such as Myriad Genetics,[188] do not seek IRB review of protocols. Second, these guidelines are also troublesome because companies are not required to adhere to them. Indeed, a survey of laboratories revealed that approximately one-half of the laboratories "will test patients directly - without a referral from a doctor or counseling about the

---

183 *See* Proposed Recommendations, *supra* note 66, at 4540.

184 F-D-C Reports, *IoM Panel Recommends HHS Create National Advisory Committee on Genetic Testing*, THE BLUE SHEET, Nov. 10, 1993, *available in* LEXIS, Health Library, Blue File [hereinafter *National Advisory Committee*].

185 *See* G. Harry Stopp, Jr., *The Internal IRB Structure: Models in Academic Settings,* IRB, Nov.-Dec. 1985, at 9.

186 *See* Longstreet, *supra* note 5, at 693.

187 *See* OncorMed, Inc., *Comparison of the Statement of the American Society of Clinical Oncology: Genetic Testing for Cancer Susceptibility to OncorMed's Institutional Review Board Approved Protocols for BRCA1 and HNPC Testing* (last modified June 23, 1996) <http://www.oncormed.com/asco.html>; *see also* F-D-C Reports, *NCI Cancer Genetics Network to Implement Research Protocols to Evaluate New Cancer Genetic Tests*, THE BLUE SHEET, Apr. 17, 1996, *available in* LEXIS, Health Library, Blue File. The guidelines suggest topics to address in pre- and post-test counseling, including the "accurac[ies] in the various methods of testing . . . the risks of developing cancer[] . . . the appropriate medical management . . . the counseling and educational needs of people considering testing [and] the impact of genetic testing and counseling on quality-of-life and medical decision-making." *Id.*

188 *See* Telephone Interview with Glenda Lowe, *supra* note 42.

implications of the test."[189] A federal regulatory mechanism mandating IRB review would better ensure that all genetic tests are conducted on informed, consenting human subjects.

1. Committee Framework and Responsibilities

49. A national advisory committee, responsible for structuring federal regulations for IRBs, and extending these regulations to genetic testing, is an important first step in alleviating the problems with genetic tests. The committee, composed of experts possessing technical and social expertise in clinical testing, could be under the FDA's jurisdiction. The Task Force on Genetic Testing could provide a framework for the proposed advisory committee. The committee should also contain several lay members who are interested in or have had experience with clinical testing.[190] Lay members are an important addition because this committee will be designing regulations to better ensure informed consent from all research subjects, who are typically lay people. In addition, a working group could assist the advisory committee in collecting and distributing information to the IRBs.[191] The working group could also accumulate information and assess the effectiveness of new clinical tests.[192]

50. This advisory committee could create a uniform set of regulations based on voluntary professional society guidelines to require test subjects to be advised of the risks in genetic testing protocols. Uniform requirements would decrease the burden on IRBs and help eradicate "IRB shopping."[193] In addition, this committee could provide "policy advice and oversight" to Congress on clinical testing issues.[194]

51. Advisory committee oversight would not frustrate the purposes and benefits of local institutional review. The local character of IRB review is advantageous because IRB members possess knowledge about the research activities in their institution.[195] The basic regulatory framework of IRBs would remain the same. The proposed advisory committee's purpose is not to micro-manage the individual IRBs; however, the committee would alleviate the inconsistencies in IRB review by establishing uniform guidelines for specific problem

---

189 Seachrist, *supra* note 61, at 395.

190 For example, the committee could include several individuals who had participated in a genetic test examining their predisposition to a particular disease.

191 *See National Advisory Committee, supra* note 184 (citing the IoM panel).

192 *See id.*

193 *See Wyden Hearing, supra* note 151.

194 *National Advisory Committee, supra* note 184.

195 *See* Bergkamp, *supra* note 55, at 5.

areas in the current regulations.[196] The committee may recommend that the FDA and NIH regulations continue to mirror each other to reduce the burden on industry resulting from two different systems of IRB review. The committee could also examine issues, such as the long-term consequences of genetic testing, that an IRB is not allowed to consider when evaluating research protocols.[197]

52. Industry often views government regulation as a "grim specter standing between the company and the marketplace"[198] and therefore, may oppose any effort to increase IRB oversight. First, industry representatives may complain that new regulations will impede IRB efficiency,[199] cause delays, and increase the costs of research. Industry representatives may express concerns that IRBs will lose their credibility if they are regulated too tightly[200] and that over-regulation will increase the cost of research to the extent that companies are forced to choose between not offering tests or performing tests outside of the United States.[201] Experts may also argue that genetic testing is just another biomedical test and, therefore, does not require any additional regulation.[202]

53. These allegations are unfounded because the proposed advisory committee regulations will not impede the IRB review process.[203] The unique physical and psychological problems in genetic testing vastly outweigh the perceived detriments of heightened regulation. In addition, the new regulations will not destroy the basic localized nature of IRB review. The main focus of the committee would be on standardizing and clarifying current regulations. Thus, the new regulations may actually facilitate the review process because IRBs will now have a

---

196 *See* Carol Levine & Arthur L. Caplan, *Beyond Localism: A Proposal for a National Research Review Board*, IRB, Mar.-Apr. 1986, at 7, 9 (This "should not be seen as a threat to the integrity and importance of local review, but an essential supplement to it.").

197 *See id.*

198 *News from the Federal Front: So You Want to Develop Gene Therapy Products?*, *supra* note 129.

199 *See* John A. Robertson, *The Law of Institutional Review Boards*, 26 UCLA L. REV. 484, 544 (1979).

200 *See* Jesse A. Goldner, *An Overview of Legal Controls on Human Experimentation and the Regulatory Implications of Taking Professor Katz Seriously*, 38 ST. LOUIS L.J. 63, 132 (1993).

201 *See Hearing of Subcomm. on Reforming the Food and Drug Administration of the House Comm. on Commerce and Environment,* 104th Cong. (1996) (testimony of John K. Clarke, National Venture Capital Association), *available in* 1996 WL 5508897.

202 *See Hearings III, supra* note 73 (prepared testimony of Dr. Alan Goldhammer).

203 It is important to note that IRBs were considered an impracticable burden on the rights of clinical investigators when first implemented. *See* Emily Miller, *International Trends in Ethical Review of Medical Research*, IRB, Oct. 1981, at 9, 10. Now, most investigators and commentators acknowledge the benefits of IRB review for both researchers and their subjects. *See id.*

specific set of regulations to follow when reviewing a protocol. These regulations, containing disclosure and lay membership requirements, will enhance the protection of human subjects, the main objective of IRB review.

2. Jurisdiction Under the FDA

54. Recently, the Task Force sought a legal opinion from the FDA as to whether the agency has jurisdiction over genetic testing services.[204] The agency stated that it possesses the authority to regulate genetic testing services because genetic tests fall within the FDA's statutory definition of a device.[205] The courts in both *United States v. Bacto-Unidisk*[206] and *United States v. Undetermined Number of Unlabeled Cases*[207] stated that an expansive reading of the definitions in the FDCA was "consistent with the Act's overriding purpose [of protecting] the public health, and . . . ensur[ing] that . . . products marketed serve the public with 'efficacy' and 'safety.'"[208] In *Unlabeled Cases*, the court held that the specimen collection containers used by the clinical laboratory for their in-house HIV testing were Class II devices.[209] The court stated that these containers served a diagnostic purpose and, therefore, could be regulated under the FDCA.[210] Genetic testing services could also fall within a broad construction of the FDCA's definition of a device because these laboratory tests also assist in detecting disease.[211] Thus, a court following *Unlabeled Cases* and *Bacto-Unidisk* could hold that the FDA has jurisdiction over genetic tests offered by an in-house testing laboratory.

55. Furthermore, the proposed FDA advisory committee would not frustrate the purposes of the CLIA. In *Unlabeled Cases*, the defendants argued that the CLIA

---

204 *See* DRAFT INTERIM PRINCIPLES, *Scientific Validation, supra* note 8, at Principle I-6.

205 *See* Proposed Recommendations, *supra* note 66, at 4544.

206 United States v. Bacto-Unidisk, 785 U.S. 784, 798 (1968) (stating that "Congress fully intended that the Act's coverage be as broad as its literal language indicates--and equally clearly, broader than any strict medical definition might otherwise allow.").

207 United States v. Undetermined Number of Unlabeled Cases, 21 F.3d 1026 (1994).

208 *Bacto-Unidisk*, 785 U.S. at 798.

209 *Undetermined Number of Unlabeled Cases*, 21 F.3d at 1027. The court, however, declined to decide whether the FDA had jurisdiction over the laboratory's testing protocols. *See id.* at 1029 n.1.

210 *Id.* at 1028. "A diagnosis is the 'art or act of identifying a disease from its signs and symptoms' or alternatively 'an investigation or analysis of the cause or nature of a condition, situation, or problem.'" *Id.* (quoting WEBSTER'S THIRD NEW INTERNATIONAL DICTIONARY 622 (1981)).

211 21 U.S.C. § 312(h) (1994 & Supp. V 1996).

preempted the FDA's jurisdiction over the defendant's collection media.[212] The Court of Appeals declined to address this issue.[213] The lower court, however, rejected this argument and held that the FDA's regulation of specimen containers was compatible with the purposes of the CLIA.[214] Hence, a court may likely hold that the activities of an advisory committee under the FDA would not preempt the CLIA.

56. Furthermore, the Task Force on Genetic Testing designed a specific process for validating genetic tests without regard for their consistency with the CLIA.[215] The CLIA applies to all laboratories conducting genetic tests on human specimens,[216] but the CLIA's testing requirements are more general than the Task Force's recommendations. For the most part then, the Task Force recommendations can be read in conjunction with the CLIA. Similarly, any advisory committee recommendations promulgated by the FDA could also be designed in a manner consistent with the provisions of the CLIA.

B. *Disclosure Requirements*

57. Today, there are no disclosure requirements for IRB salaries or for potential IRB conflicts of interest. The proposed national committee could establish regulations pertaining to these matters. These new requirements would enhance an IRB's ability to impartially evaluate research protocols and would also lend credence to IRB activities within the community.

1. Salary Disclosure

58. The national advisory committee should establish regulations limiting the amount of money that an institution can pay an IRB member for their services. This salary cap would allow institutions to reimburse IRB members for their direct expenses, such as transportation and parking.[217] This cap would include all money

---

212 *Undetermined Number of Unlabeled Cases*, 21 F.3d at 1029 n.1.

213 *See id.*

214 *See* Clinical Reference Lab., Inc. v. Sullivan, 791 F. Supp. 1499, 1509 (D. Kan. 1992), *aff'd in part, rev'd in part by* United States v. Undetermined Number of Unlabeled Cases, 21 F.3d 1026 (1994).

215 *See* DRAFT INTERIM PRINCIPLES, *Scientific Validation, supra* note 8, at Principle I-8.

216 42 C.F.R. § 493.1 (1995).

217 *Cf.* LEVINE, *supra* note 49, at 330. Levine describes the IRB system at Yale University. *See id.* According to Levine, only non affiliated members of Yale's IRB receive payment. *Id.* These members are compensated in accordance with the NIH guidelines for payment for service on an advisory committee, with the exception that the individuals are not paid for preparation time or personal expenses. *Id.*

paid directly or indirectly to IRB members, including gifts. Forcing every institution to submit an annual disclosure statement to the federal advisory committee and publishing this salary list in the Federal Register may ensure that institutions are more mindful of obeying this requirement. Salary disclosure regulations would promote more objective IRB review of research protocols because the members of the IRB will feel less indebted to the institution if they are not paid for their service on the committees.

2. Disclosure of Conflicts of Interest

59. In addition, the advisory committee could establish a mechanism for IRB members to disclose any financial conflicts of interest. The committee could remedy the conflict of interest problem by providing a clear definition of a conflict of interest in the regulations governing human clinical testing.[218] The committee could model the explanation of this term after the Department of Health and Human Services ("HHS") financial disclosure guidelines for investigators.[219] These rules require that each institution establish a written conflict of interest policy which forces all investigators performing government-sponsored research to disclose all "significant financial interests."[220] A "significant financial interest" includes salary and remuneration for services, such as consulting; "equity interests," such as stocks; and "intellectual property rights."[221] The institution must review these financial

---

218 Currently, this term is undefined in the regulations. *See* 21 C.F.R. § 56.107(e) (1996).

219 An investigator is defined as "the principal investigator and any other person who is responsible for the design, conduct, or reporting of research funded by PHS [Public Health Service], or proposed for such funding." 42 C.F.R. § 50.603 (1995). The spouse and dependent children are included in this definition. *See id.*

220 *Id*.

221 *Id*. Significant financial interests do not include:

> (1) Salary, royalties, or other renumeration for the applicant institution; (2) Any ownership interests in the institution, if the institution is an applicant under the SBIR program; (3) Income from seminars, lectures, or teaching engagements sponsored by nonprofit entities; (4) Income from service on advisory committees or review panels for public or nonprofit entities; (5) An equity interest that when aggregated for the Investigator and the Investigator's spouse and children, meets both of the following tests: Does not exceed $10,000 in value . . . and does not represent more than a five percent ownership interest in any single entity; (6) Salary, royalties, or other payments that when aggregated for the Investigator, the Investigator's spouse and dependent children over the next 12 months, are not expected to exceed $10,000.

Id. (emphasis added). Furthermore, the committee could review these financial interest guidelines every two years and adjust them to account for inflation.

statements, which are updated at least annually by the investigators.[222] HHS suggests several approaches for an institution to alleviate an actual or potential conflict of interest.[223] These include "public disclosure . . . monitoring of research by independent reviewers . . . disqualification from [research] participation . . . or severance of relationships that create actual or potential conflicts."[224]

60. The HHS regulations would provide an adequate basis for the committee's definition of a conflicting interest. Creating regulations similar to those established by HHS will eliminate the need for investigators, who also serve as IRB members, to participate in two separate conflict of interest inquiries. These reporting requirements would ensure that impartial IRB members review all research without imposing a large administrative burden on IRB members.

C. *Mechanisms for Increasing Lay Membership*

61. The FDA committee should also recommend modifying current federal regulations and increasing the number of lay members on IRBs. A 1978 study revealed that lay members comprised 30% of IRBs.[225] A nonscientist member has several important functions on an IRB, including providing a community perspective for the IRB, ensuring that informed consent statements are clear and understandable, functioning as an advocate for research subjects, and reviewing conflicts of interest.[226] Adding lay members to IRBs may reduce IRB bias because most lay people lack the conflicts of interests common in the scientific community today.[227] In addition, it may be easier for lay members to establish consistent standards of review for research protocols since they are not submitting any research of their own for IRB approval.[228]

62. The proposed advisory committee should consider increasing the number of lay people to represent the views of the community at large.[229] Most nonscientist

---

222 *See* 42 C.F.R. § 50.604(c)(2).

223 *See* 42 C.F.R. § 50.605.

224 *Id*.

225 *See* Joan P. Porter, *What Are the Ideal Characteristics of Unaffiliated Nonscientists IRB Members?*, IRB, May-June 1986, at 1, 1.

226 *See* Joan P. Porter, *How Unaffiliated/Nonscientist Members of Institutional Review Boards See Their Roles*, IRB, Nov.-Dec. 1987, at 1, 4 (1987) [hereinafter Porter, *Roles*].

227 *See* Robertson, *supra* note 52, at 30 ("The presence of one or two 'community representatives' has not been enough to offset professional dominance . . . expanding the role of nonscientists and the public may blunt the worst excesses of professional bias.").

228 *See* Porter, *Roles, supra* note 226, at 2.

229 Currently, the FDA and NIH regulations require that IRBs have at least one nonscientific

IRB members would probably not be considered ordinary lay members by their communities.[230] A survey of 200 IRBs in 1984 revealed that "approximately 32 percent [of the nonscientist IRB members] held doctoral degrees, 40 percent masters degrees, 23 percent baccalaureate degrees, and about four percent, associate degrees."[231] Most of these degrees were in liberal arts, theology, or law.[232] The advisory committee could bolster true lay membership by modeling the United States IRB system after the Danish system. In addition, the advisory committee could also increase lay membership by advocating medical student participation on IRBs.

1. The Danish System

63. One possible model for increasing lay membership is the Danish system of ethical review boards, or RECs.[233] The Danish government requires all RECs to contain a majority of lay members.[234] Unlike the United States IRBs, the nonscientific members in Denmark are "lay people in the full sense of the word" and lack any technical, moral, or legal expertise.[235] REC members are compensated like any other member of an official organization in Denmark.[236] In addition, one professional and one lay member of each REC serve on a national committee called the Central Research Ethical Committee ("CREC").[237] The CREC is responsible for promulgating uniform guidelines for all RECs.[238]

64. In addition, the CREC is similar to the proposed FDA committee because the FDA advisory committee would also be responsible for creating uniform guidelines for IRBs. The FDA committee might need to be structured differently than the CREC because the volume of IRBs in the United States would make it

---

member and at least one nonaffiliated member. *See* 45 C.F.R. § 46.104(c) (1995); 21 C.F.R. § 56 (1996).

230 *See* Porter, *Roles, supra* note 226, at 2.

231 *Id.*

232 *See id.*

233 *See* Søren Holm, *How Many Lay Members Can You Have in Your IRB?--An Overview of the Danish System*, IRB, Nov.-Dec. 1992, at 8, 8 (1992).

234 *See id.* at 9. The RECs have one more lay member than professional member. *See id.*

235 *Id.* at 8.

236 *See id.* at 9.

237 *See id.* at 8-9.

238 *See id.* at 9.

impossible for every IRB to send two members to a national committee.[239] In Denmark, there were only 15 major research institutions in 1986.[240] There were 63 established RECs and plans to create 40 more.[241] There were 550 major research institutions in the Unites States in 1988, each containing at least one IRB.[242] There was at least one IRB at 2,000 smaller American institutions, but some of these institutions contained more than 10 IRBs.[243] Now, the NIH receives data from approximately 4,000 IRBs,[244] while the FDA supervises approximately 1,100 IRBs.[245] Thus, even if every IRB sent only one representative to a national committee, the committee would be too large to coordinate.

65. Increasing lay membership may be an effective method of eliminating bias on IRBs. Scientists may question the value of an IRB dominated by lay members who they feel lack the technical expertise necessary to interpret research protocols.[246] An institution could alleviate this problem by making consultants available to provide an IRB with technical assistance.[247] Indeed, OncorMed's IRB has several ad hoc members who provide information about a particular type of research and serve on an as-needed basis.[248] Consultants would provide lay members with enough technical knowledge to interpret a research protocol and still enable them to bring the community perspective to the IRB.

66. Moreover, the most important attribute of an IRB member is not their technical proficiency.[249] An IRB functions to examine both the risks and benefits of the research and to promote informed consent. Informed consent may be based on a reasonable person standard.[250] Thus, it is logical to have an IRB comprised of lay

---

239 *See* Bergkamp, *supra* note 55, at 2.

240 *See id.*

241 *See id.*

242 *See id.*

243 *See id.*

244 Telephone Interview with Tom Puglisi, Office of Protection of Research Risks, NIH (Apr. 9, 1997).

245 Telephone Interview with Glen Drew, Office of Health Affairs, FDA (Apr. 9, 1997).

246 *See* LEVINE, *supra* note 49, at 331.

247 *See* Robertson, *supra* note 52, at 30.

248 Telephone Interview with Joan Scott, *supra* note 29.

249 *See* Susan M. Goold, *Allocating Health Care: Cost-Utility Analysis, Informed Democratic Decision Making or the Veil of Ignorance?,* 21 J. HEALTH POL. POL'Y & L. 69, 93 (1996).

250 *See, e.g.*, Canterbury v. Spence, 464 F.2d 772, 787 (D.C. Cir. 1972) (stating that a medical practioner must alert patients to all risks that a "reasonable person" would consider significant).

members who have the same understanding of the research process as a human clinical subject would. An IRB containing these types of individuals guarantees that the benefits of the experiment do not outweigh the risks to the human subjects and that patients truly understood the consent process. Thus, lay members serve as a "link between the technical clinical world and the ordinary outside world."[251]

67. The advisory committee could decide that the domination of Danish RECs by lay members would not be the most conducive way of approving research in the United States. Nevertheless, any increase in lay membership would help to counterbalance the bias of scientific investigators on an IRB. Thus, the national committee could still follow the Danish system and increase the number of lay members on IRBs without requiring an absolute majority of lay members on any IRB.[252]

2. Medical Students

68. Furthermore, the advisory committee could suggest that IRBs increase their lay membership by adding medical, nursing, and public health students to IRBs.[253] Medical students act as a "midpoint on two continua," since the students possess the technical knowledge necessary to make an informed risk assessment but do not depend on research for their livelihood.[254]

69. The dual role of a student as a technically proficient layperson may enhance the review process for several reasons. For instance, students, in their "role [as] constant questioner[s] and learner[s]," may facilitate more intense questioning of a research protocol.[255] Lay members may also feel more comfortable asking medical students questions since the students are still able to identify with nonscientific members' unfamiliarity with medical procedures.[256] Many students participate in experiments as research subjects while at medical school.[257] These research experiences provide the student with a different and valuable perspective.

---

251 Charles E. Hollerman, *Membership of Institutional Ethics Committees,* PHYSICIAN EXECUTIVE, May 1991, *available in* LEXIS, News Library, Curnws File.

252 *See* Bradford H. Gray, *Changing Federal Requirements of IRBs Part II: Social Research & the Proposed DHEW Regulations,* IRB, Jan. 1990, at 1, 5 (1980). "[B]etween one third and two thirds of IRB members should be scientists. This would presumably result in an increase in nonscientific representation." *Id.*

253 *See* Robertson, *supra* note 52, at 30.

254 Nolan, *supra* note 177, at 2.

255 *Id.*

256 *See id.* at 4.

257 *See* Talcott Parsons, *Research with Human Subjects and the "Professional Complex," in* EXPERIMENTATION WITH HUMAN SUBJECTS 116, 117 (Paul A. Freund ed., 1970).

Further, medical students' uncertainties about their own skill may cause them to be "hyper aware of a procedure's risks" and focus on a proposal's errors.[258]

70. It is important to note that as most medical students progress through their education, they gradually become more of a part of the medical community and less of a "true outsider."[259] Indeed, a biomedical researcher admitted that he was more inclined to be biased against an investigator and to associate himself with research subjects when he first began medical school.[260] As the researcher progressed through his training, however, his outlook began to change "from being prejudiced against the researcher to being prejudiced in his favor."[261] Thus, an IRB may only want to accept students in their first few years of graduate school to ensure that these students function as technically competent lay members.

71. Student IRB members will only be valuable in an institution's review process if the other IRB members are comfortable with medical students offering their opinions and asking questions.[262] Students have been successfully integrated into one of Yale's IRBs, called the Human Investigation Committee ("HEC").[263] There are 26 individuals on the HEC, and four HEC members are students from the medical school and the school of public health.[264] Although the HEC contains many distinguished members with numerous advanced degrees,[265] any question from an IRB member is "treated with respect."[266] In addition, it is not uncommon for a mixture of scientists, students, and other committee members to endorse the same side of an ethical issue.[267] The acceptance of student members' questions and opinions by Yale's HEC illustrates that a medical student's unique perspective can be successfully integrated into the IRB setting.

72. Furthermore, adding highly qualified students to IRBs is a cost-effective manner of increasing lay participation. Generally, students are not compensated for

---

258 Nolan, *supra* note 177, at 3.

259 *See id.* at 4.

260 *See* BARBER ET AL., *supra* note 67, at 142-43.

261 *Id.* at 143. "Now he understands better the importance of good medical research, even at times, when there is no potential benefit for the subjects themselves . . . if important research is to get done and he is to publish, 'salesmanship' is necessary." *Id.*

262 *See* Nolan, *supra* note 177, at 4.

263 *See* LEVINE, *supra* note 49, at 328-30.

264 *See id.* at 330.

265 *See id.*

266 *Id.* at 332.

267 *Id.* at 331.

their IRB service.[268] Student competition for IRB positions, however, can be intense because many students view IRB membership as a great honor.[269] Therefore, it is easy for IRBs to obtain proficient student members at virtually no cost to them. Hence, supplementing IRBs with qualified students is a financially efficient method of increasing lay participation on IRBs.

73. The addition of students to IRBs can also promote responsible research in the future.[270] Many students will conduct research at some point in their careers, and student IRB members will have the benefit of observing the protocol review process before actually participating in it. The IRB setting affords these future researchers the opportunity to interact with other individuals who are committed to conducting ethical research.[271] The IRB review process also reinforces the importance of consent provisions to students at an early stage in their research careers. Thus, the knowledge gained during IRB service will be beneficial for both the student and their research subjects if the individual elects to conduct research in the future.

VII. CONCLUSION

74. Both OncorMed and Myriad Genetics have established responsible testing procedures for their BRCA1 and BRCA2 genetic tests. Without mandated IRB review of genetic testing protocols, however, there is no guarantee that the next institution that designs a genetic test will be as careful. Mandating IRB approved protocols for genetic tests is necessary to avoid the potential physical and psychological repercussions of uninformed consent in human clinical subjects.

75. A committee under the FDA's jurisdiction could address the lack of regulation of genetic testing services and design regulations that contain disclosure requirements for IRBs. This committee should also explore the possibility of increasing lay membership on IRBs to counterbalance the bias of scientific members, perhaps by following a system similar to the one established in Denmark. The committee could encourage the addition of beginning medical students on IRBs to facilitate this process. Implementing more specific regulations will not overburden the research community or chill future research efforts. Rather, the proposed modifications would ensure that scientific progress is not accomplished at the expense of human clinical subjects.

---

268 "We found that differences of opinion among committee members are virtually never determined by profession, discipline, or presumed constituency." *Id.* at 330.

269 *See id.*

270 *See* Nolan, *supra* note 177, at 4.

271 *See id.*