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NOTE: EXCLUSIVE LICENSING OF DNA DIAGNOSTICS: IS THERE A NEGATIVE EFFECT ON QUANTITY AND QUALITY OF HEALTHCARE DELIVERY THAT COMPELS NIH RULEMAKING?

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I. INTRODUCTION

The National Institutes of Health (NIH) recently published for comment a draft regulation entitled "Best Practices for the Licensing of Genomic Inventions."[1] The NIH believes that "[a]necdotal and empirical data is beginning to reveal a pattern of exclusive licensing practices for genomic technologies . . . that could have detrimental effects on . . . the quantity and quality of healthcare products and services."[2] The NIH recommends granting exclusive licenses when "necessary to encourage research and development by private partners" and non-exclusive licenses "whenever possible."[3] In contrast, a spokesperson for the United States Patent and Trademark Office (PTO) states unequivocally that there is no "evidence that the patenting of gene-related inventions is impeding progress."[4]

This comment surveys the costs of deoxyribonucleic acid (DNA) diagnostic tests and argues in favor of non-exclusive licensing as a means to provide broad access to affordable DNA diagnostic testing. Part II provides background information on genetic testing, patenting genes as applied to genetic testing, the Bayh-Dole Act, and technology transfer.[5] In addition, Part II summarizes academic commentary regarding the implications of exclusive licensing for biotechnology.[6] Scholars propose a number of solutions, including expanding the experimental use exception.[7]

1. Best Practices for the Licensing of Genomic Inventions, 69 Fed. Reg. 67747 (proposed Nov. 19, 2004) [hereinafter Licensing Genomic Inventions].
2. *Id.*
3. *Id.* at 67748.
4. Lee Drutman, *It's in the Genes: Patent Barriers to Genetic Research*, 25 MULTINATIONAL MONITOR 17 (July 1, 2004).
5. *See infra* Part II.
6. *Id.*
7. *Id.*

Part III details proposed rulemaking for DNA diagnostics.[8] Part IV reviews anecdotal examples of genetic testing for breast cancer, hereditary hemochromatosis, and Canavan Disease.[9] These genetic testing examples include survey evidence from clinical laboratorians.[10] The survey and anecdotal evidence indicates that patents may increase prices and reduce access to genetic testing. This note contends that, although only a partial solution, Licensing Genomic Inventions addresses genetic tests developed with NIH funding.[11] This comment also discusses improvements to the draft language.[12] Part V concludes that exclusive licensing increases the prices of and decreases access to diagnostic genetic tests.[13] Licensing Genomic Inventions means to address the patent system's undesirable effects on the delivery of public health.

II. BACKGROUND

A. *Genetic Testing*

An all-inclusive definition of genetic testing is the "analysis of human DNA, RNA [ribonucleic acid], chromosomes, proteins, and certain metabolites in order to detect heritable disease-related genotypes, mutations, phenotypes, or karyotypes for clinical purposes."[14] Genetic testing can provide clinical benefits as well as diagnostic information to aid in difficult clinical decision-making.[15] Most genetic testing involves rare diseases, but the scope is expanding to include genetic risk assessment for common diseases such as cancer and cardiovascular disease.[16] With some genetic tests, however, "[t]he identification of risk does not necessarily lead to treatment options."[17]

8. *See infra* Part III.
9. *See infra* Part IV.
10. *Id.*
11. *Id.*
12. *Id.*
13. *See infra* Part V.
14. Wylie Burke, *Genetic Testing*, 347 NEW ENG. J. MED. 1867, 1867 (2002) (citation ommited).
15. *Id.*
16. *Id.*
17. *Id.* at 1868. With Huntington's disease, which currently has no treatment, it is possible to associate the severity and onset of the disease with the length of repeated non-coding regions within the gene. *See id.* The individual choice to undergo testing is thus potentially psychologically harmful. *Id.* at 1867-70. In the

DNA diagnostic tests encompass a subset of genetic testing. DNA diagnostic tests recently came to the forefront of genetic testing because of the DNA sequence information that emanated from the Human Genome Project, the availability of inexpensive molecular genetic technologies (such as polymerase chain reaction (PCR)), and the existence of a genetic component in nearly every disease.[18] One can obtain genetic testing information through a variety of molecular analyses.[19]

Currently, there are clinical tests for more than 790 diseases.[20] New genetic associations between molecular markers and diseases are published monthly; these new genetic associations make tests available for an increased number of diseases.[21] Mass screening has begun for cystic fibrosis while screening for a variety of other diseases has been discussed.[22] In addition, biological, methodological, ethical, and social complexities involved in genetic testing affect genetic tests for disease associations.[23] Concerns persist regarding the possible effect genetic testing has on obtaining insurance coverage.[24]

United Kingdom, only about twenty percent of those at risk for Huntington's disease undergo the test. *Id.* at 1870.

18. Wayne Grody, *Molecular Genetic Risk Screening*, 54 ANN. REV. MED. 473, 474 (2003).

19. Molecular biological techniques used in genetic testing include: DNA sequencing, Restriction Fragment Length Polymorphism (RFLP) analysis (also termed Southern blot hybridization), RNA expression analysis, PCR amplification, fluorescent in situ hybridization, and cytogenetic analysis. Peter Kopp & J. Larry Jameson, TRANSMISSION OF HUMAN DISEASE in PRINCIPLES OF MOLECULAR MEDICINE 50 (J.L. Jameson ed., 1998).

20. University of Washington-Seattle, *GeneTests: Medical Genetics Information Resource Database Online (1995-2005)*, *at* http://www.genetests.org (last visited Feb. 11, 2005) [hereinafter *GeneTests*].

21. There are currently 1637 clinical disorders for which a genetic mutation is known. Online Mendelian Inheritance in Man, *at* http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM (last visited Jan. 11, 2005).

22. Grody, *supra* note 18, at 473. Diseases for which mass screening has been discussed include hereditary hemochromatosis, thrombophilias, familial cancer predisposition, and pharmacogenetic risk factors. *Id.*

23. *See id.* at 475-76.

24. According to the National Library of Medicine, "[i]n many cases, health insurance plans will cover the costs of genetic testing when it is recommended by a person's doctor. . . . [But different] health insurance providers have different policies about which tests are covered. . . . [In addition, individuals] may choose not to use their insurance to pay for testing because the results of a genetic test can affect a person's health insurance coverage." *Will Health Insurance Cover the Costs of Genetic Testing?*, U.S. National Library of Medicine, *at* http://ghr.nlm.nih.gov/info=genetictesting/show/insurance_coverage (last

A large number of laboratories and clinics perform genetic tests.[25] Currently, genetic testing is accomplished with "home-brew" tests performed in-house by the manufacturer and marketer, and thus the tests fall outside the Food and Drug Administration's (FDA's) review.[26] With demand for genetic tests expected to grow, manufacturers propose diversified FDA regulation in this area of the medical laboratory.[27]

B. Patenting Genes

In a landmark patent decision, the Supreme Court granted patent protection to living organisms as long as the organisms remain "human-made" and not "products of nature."[28] Dr. Ananda Chakrabarty "constructed" a microorganism containing a number of different plasmids that allowed it to digest hydrocarbons.[29] In reaching its decision, the Supreme Court invoked the language from the 1952 Patent Act, which states that "anything under the sun that is made by man" is patentable.[30] This watershed decision ultimately resulted in the development of the biotechnology industry by providing patent protection for biological inventions.[31]

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visited Feb. 11, 2005).

25. *See* Kopp & Jameson, *supra* note 19. A voluntary listing of laboratories indicates that 575 laboratories and 1078 clinics perform genetic testing services. *GeneTests*, *supra* note 20.

26. *See* Michael J. Malinowski & Robin J.R. Blatt, *Commercialization of Genetic Testing Services: The FDA, Market Forces, and Biological Tarot Cards*, 71 TUL. L. REV. 1211, 1211, 1229-32 (1997) (concluding "that the present regulatory system is inadequate and places a dangerous amount of reliance on primary care physicians").

27. *See* Elizabeth Mansfield, *Genetic Testing and Personalized Medicine: An FDA View*, 1 PRECLINICA 155 (2003). Laboratory tests, regulated under the Clinical Laboratory Improvements Amendments of 1988 (CLIA), involve emphasis on analytical test performance and quality control. Steven Gutman & David W. Feigel Jr., *The Status of ASR Regulations* (May 2004), *available at* http://www.devicelink.com /ivdt/archive/04/05/007.html. In 1997, the FDA began regulating components of in-house tests and analyzing specific reagents (ASRs). *See id.* ASRs include nucleic acid sequences and similar reagents intended for use in a diagnostic application for identification of a substance in biological specimens. *Id.* Manufacturers propose a new regulatory category termed in vitro analytical tests (IVAT) for which analytical utility is established but clinical utility has not yet been proven. *Id.*

28. Diamond v. Chakrabarty, 447 U.S. 303, 313 (1980).

29. *Id.* at 305.

30. *Id.* at 309 (citations omitted).

31. DAVID B. RESNIK, OWNING THE GENOME: A MORAL ANALYSIS OF DNA PATENTING 67 (2004).

Recently, United States courts have upheld the patenting of genes from mammals and plants.[32]

In 1982, the United States Patent Office issued the first gene patent to the Regents of the University of California for work carried out on the construction of a plasmid contained in a bacterium and expression of genes for chorionic somatomammotropin.[33] Two years later, one of the first patent claims for diagnostic detection of a disease gene was for the Restriction Fragment Length Polymorphism (RFLP) test for Huntington's disease.[34] Thus, courts uphold gene patents in diagnostic use claims.

An invention in a United States patent application must satisfy the utility requirement.[35] The invention must contain a specific, substantial, and credible utility.[36] As a result, the utility requirement precludes patenting inventions such as the use of a DNA sequence as landfill.[37] It is also possible to satisfy the utility requirement by showing a readily apparent and well-established utility.[38]

Recently, the first gene patent was issued to a patient advocacy group.[39] The four co-inventors from Hawaii assigned their rights to

32. *See* J.E.M. Ag Supply, Inc. v. Pioneer Hi-Bred Int'l, Inc., 534 U.S. 124 (2001) (affirming right to patent plant material); U.S. Patent No. 4,736,866 (issued Apr. 12, 1988) (issuing patent for non-naturally occurring genetically altered oncomouse).

33. U.S. Patent No. 4,363,877 (issued Dec. 14, 1982) (claiming "6. A recombinant DNA transfer vector comprising codons for human growth hormone"). Chorionic somatomammotropin is commonly known as the "human growth" hormone. *Id.*

34. U.S. Patent No. 4,666,828 (issued May 19, 1987) (claiming "1. A method for detecting the presence in a subject of the gene for Huntington's Disease which comprises: analyzing the human chromosome 4 of said subject for a DNA polymorphism linked to Huntington's Disease. 2. The method of claim 1 wherein said polymorphism is a restriction fragment length polymorphism (RFLP)."). The patent was filed on August 15, 1984. *Id.*

35. 35 U.S.C. §§ 101, 112, (1952).

36. Utility Examination Guidelines, 66 Fed. Reg. 1092, 1097-98 (proposed Jan. 15, 2001) (internal regulation to be used by U.S. PTO personnel in their review of patent applications for compliance with the "utility" requirement of 35 U.S.C. § 101).

37. *Id.*

38. *Id.*

39. Press Release, PXE International, U.S. Patent Office Issues First Gene Patent to Patient Advocacy Group: Co-Inventors Include Non-Scientist "Mom" (Aug. 24, 2004), *at* http://www.pxe.org/patent.html; Methods for diagnosing *Pseudoxanthoma elasticum*, U.S. Patent No. 6,780,587 (issued Aug. 24, 2004) (claiming "a method for screening a patient for the presence of the PXE mutation

the University of Hawaii, which assigned its rights to the patient advocacy group.[40] Assignment of patent rights to advocacy groups may have important implications for future disease gene diagnostic patenting and test development. This could direct licensing income obtained from genetic testing to further research and development in addition to treatment for a specific genetic disease.

C. Patenting Genes in Europe and Canada

In Europe, patents are awarded upon successful demonstration of novelty, utility, and an inventive step.[41] Additionally, patents must satisfy a moral requirement.[42] The oncomouse patent was not as broad when issued in Europe, because it applied only to mice and not all rodents.[43] In contrast, Canada refuses to allow the oncomouse patent to issue because it rebuffs the idea that life forms are patentable.[44]

In the future, the Biotechnology Patents Directive "98/44" will control European gene patents.[45] Under the Directive, Article 5 allows the patenting of genes identical to those in the human body

. . .").

40. *See* Press Release, PXE International, *supra* note 39.

41. Convention on the Grant of European Patents (Oct. 5, 1973), Art. 52, a*vailable at* http://www.european-patent-office.org/legal/epc/e/ar52.html#A52.

42. *Id.* at Art. 53 (stating "European patents shall not be granted in respect of: (a) inventions the publication or exploitation of which would be contrary to 'ordre public' or morality, provided that the exploitation shall not be deemed to be so contrary merely because it is prohibited by law or regulation in some or all of the Contracting States; (b) plant or animal varieties or essentially biological processes for the production of plants or animals; this provision does not apply to microbiological processes or the products thereof.").

43. "*EPO Oncomouse ruling*," News in Brief, 22 NATURE BIOTECHNOLOGY 937 (2004).

44. Harvard Coll. v. Can. Comm'r of Patents, [2002] 4 S.C.R. 45 (holding that a higher life form is not patentable under the Canadian Patent Act because it is not a "manufacture" or "composition of matter" within the meaning of "invention").

45. Council Directive 98/44/EC, Art. 5, 1998 O.J. (L 213) 13, 18 (stating that "1. The human body, at the various stages of its formation and development, and the simple discovery of one of its elements, including the sequence or partial sequence of a gene, cannot constitute patentable inventions. 2. An element isolated from the human body or otherwise produced by means of a technical process, including the sequence or partial sequence of a gene, may constitute a patentable invention, even if the structure of that element is identical to that of a natural element. 3. The industrial application of a sequence or a partial sequence of a gene must be disclosed in the patent application."), *available at* http://europa.eu.int/eur-lex/pri/en/oj/dat/1998/l_213/l21319980730en00130021.pdf (last visited Oct. 19, 2004).

as long as the patent application discloses an "industrial application."[46]

Although Switzerland is not a member of the European Union (EU), it is working on draft guidelines to put Swiss patent law in line with 98/44.[47] While the EU directive is silent on the scope of protection, the proposed Swiss patent guidelines restrict a patent on a gene sequence to a specific, credible, and non-speculative function.[48] By limiting patent protection to the specific utility claimed, the Swiss Patent Office believes the limitation will stimulate specific gene research exploration for additional utilities.[49]

Between 2001 and 2003, Myriad Genetics received four European patents for testing susceptibility to breast cancer and ovarian cancer.[50] These patents were challenged by the Institut Curie (Paris, France), and the BRCA2 gene test (EP 785216) was overturned by the European Patent Office (EPO) in February 2004.[51] In addition, the EPO revoked one of the BRCA1 gene tests (EP 699754) in May 2004.[52] The EPO found the BRCA1 patent inadequately inventive under the provisions of European patent law.[53] In contrast, Cancer Research UK received a patent on BRCA2 in Europe and will make BRCA2 screening widely available

46. *Id.*

47. Jane Burgermeister, *Swiss Patent Proposal Prompts Criticism*, 22 NATURE BIOTECHNOLOGY 1323, 1323 (2004).

48. *Id.* "Art. 8c (new) If the discovery relates to a non-synthetically developed sequence or partial sequence the coverage is limited to the concrete functions described in its patent. Art. 49 The patent application must contain: f. in the case of a nucleotide sequence or partial sequence or partial sequence of a gene, a concrete description of its function." Bundesgesetz über die Erfindungspatente (proposed alteration of the June 1954 Patent Act), *available at* http://www.ige.ch/D/jurinfo/documents/j10013d.pdf (last visited Feb. 11, 2004).

49. Burgermeister, *supra* note 47, at 1323.

50. European Patent No. 699754 (issued Jan. 10, 2001); European Patent No. 705903 (issued May 23, 2001); European Patent No. 705902 (issued Nov. 28, 2001) (describing BRCA1-related inventions); European Patent No. 785216 (issued Jan. 8, 2003) (describing BRCA2-related invention).

51. Graeme O'Neill, *How Myriad's GCAT got out of the bag*, AUSTRALIAN BIOTECHNOLOGY NEWS, Jun. 21, 2004, at 1, *available at* http://esvc001057.wic005u.server-web.com/archives/1/220/447/How%20Myriads%20GCAT%20got%20out% 20of%20the%20bag%2024062004.pdf.

52. Press Release, European Patent Office, Myriad/Breast Cancer Patent Revoked After Public Hearing (May 18, 2004), *available at* http://www.european-patent-office.org/news/pressrel/2004_05_18_e.htm.

53. Andrew Pollack, *European Patent on U.S. Gene Test is Revoked*, INTL. HERALD TRI., May 20, 2004, at 16, *available at* 2004 WL 77528899, at *1.

across Europe.[54]

There is a belief in Europe that gene patents will have a negative influence on providing healthcare.[55] It is feared that the BRCA1 gene patents will create a precedent.[56] Due to the large number of patent applications on genes filed over the last few years, there are concerns that monopoly rights to genes and genetic testing will undermine reimbursement systems and negatively influence European healthcare.[57]

D. The Bayh-Dole Act

The policy and objective of the Bayh-Dole Act[58] (Act) is "to promote the utilization of inventions arising from federally supported research or development" and "to promote the commercialization and public availability of inventions made in the United States."[59] The Act sponsors believed that university ownership of patent rights would allow the grant of exclusive licenses to private firms.[60] The sponsors thought university ownership was necessary for the development of commercial products from government-sponsored research discoveries.[61]

The Act permits universities to "retain title to any subject invention"[62] and subjects universities to "a requirement that the contractor share royalties with the inventor."[63] The Act specifies that any remaining royalties "shall be used by the contractor for

54. Press Release, Cancer Research UK, Charities to Make Breast Cancer (BRCA2) Gene Freely Available Across Europe (Feb. 11, 2004), *at* http://www.cancerresearchuk.org/news/pressreleases/breastcancergene_11feb04?version=1.

55. Swiss Society of Medical Genetics, BCRA1 Patent, *at* http://www.ssgm.ch/sections/News/brca1testing.htm (last visited Aug. 31. 2004).

56. Press Release, Curie Institut, European-Wide Opposition Against the Breast Cancer Patents (Sept. 26, 2002), *at* http://www.curie.fr/upload/presse/europeanoppmyriad _sept02_gb.pdf.

57. *Id.*

58. Bayh-Dole Act, Pub. L. No. 96-517, § 6(a), 94 Stat. 3015, 3019 (1980) (codified as amended at 35 U.S.C. §§ 200-12 (1994)).

59. 35 U.S.C. § 200 (1952).

60. Arti K. Rai & Rebecca S. Eisenberg, *The Public Domain: Bayh-Dole Reform and the Progress of Biomedicine*, 66 LAW & CONTEMP. PROBS. 289, 290 (2003).

61. *Id.*

62. 35 U.S.C. § 202(a) (2004) (stating that "[e]ach nonprofit organization or small business firm may, within a reasonable time after disclosure as required by paragraph (c)(1) of this section, elect to retain title to any subject invention.").

63. *Id.* § 202(c)(7)(B).

scientific research, development, and education."[64] While rights were originally granted to nonprofit organizations and small companies, President Reagan extended these rights to large corporations.[65] The Act also prescribes "march-in rights" to allow the federal agency responsible for funding the invention to require "the contractor . . . to grant a nonexclusive, partially exclusive, or exclusive license in any field of use to a responsible applicant" if certain conditions are not met.[66] Exercise of march-in rights may be necessary in the following situations:

- if "effective steps" have not been taken "to achieve practical application of the subject invention;"
- to "alleviate health or safety needs;"
- "to meet requirements for public use specified by federal regulations;" or
- if the subject invention is not manufactured substantially in the United States.[67]

In a few publicly known cases, NIH commented on the exercise of march-in rights and then refused to exert them. In the first case, CellPro petitioned NIH to enforce its march-in rights to four federally funded Johns Hopkins University (JHU) patents that JHU had licensed to Baxter Health Care Corporation.[68] CellPro wanted NIH to intervene to alleviate alleged health or safety needs because the infringement of CellPro's patents on those of Baxter Healthcare precluded further sale of a stem cell separation device.[69] NIH stated that both companies failed to present evidence that cell separation devices improve stem cell engraftment, disease free survival, or overall survival.[70] Thus, NIH declined to intervene and

64. *Id.* § 202(c)(7)(E)(i).

65. Exec. Order No. 12,591, 52 Fed. Reg. 13,414 (Apr. 10, 1987), *as amended by* Exec. Order No. 12,618, 52 Fed. Reg. 48,661 (Dec. 22, 1987) (allowing executive departments to enter into cooperative research projects with the private sector, and providing ownership of title to patents resulting from research to the contractors in exchange for royalty-free use by the government).

66. 35 U.S.C. § 203 (2004).

67. *Id.* §§ 203(a)(1)-(4) to 204 (2004).

68. *See* Barbara M. McGarey & Annette C. Levey, *Patents, Products, and Public Health: An Analysis of the CellPro March-In Petition*, 14 BERKELEY TECH. L.J. 1095 (1999).

69. Harold Varmus, M.D., National Institutes of Health, Office of the Director, Determination in the Case of Petition of CellPro, Inc., (Aug. 1, 1997), *available at* http://www.nih.gov/news/pr/aug97/nihb-01.htm.

70. *Id.*

exercise march-in rights either for health or safety reasons[71] or for inability to "achieve practical application of the subject invention in such field of use."[72]

NIH more recently declined to exercise march-in rights in a case where the price quadrupled for Abbott Laboratories' (Abbott) Norvir® (ritonavir), a drug used to treat patients with HIV/AIDS.[73] NIH had funded preclinical research for about $3.5 million and Abbott had invested over three hundred million dollars to continue developing the drug in an effort to bring it to market.[74] Following a public hearing on May 25, 2004, NIH found that Abbott sufficiently showed the practical application of the subject invention under 35 U.S.C. § 203(a) because of the "manufacture, practice and operation of ritonavir and the drug's availability and use by the public."[75] The complainants presented no evidence at the hearing to show that march-in rights could alleviate any health or safety needs not reasonably satisfied by Abbott.[76] NIH agreed with public testimony that the exercise of march-in rights was not an appropriate way to address drug prices, but instead suggested that Congress should address the issue.[77] NIH maintained that the Federal Trade Commission (FTC) is the appropriate agency to address any question of anticompetitive behavior by Abbott.[78]

E. Experimental Use Exemption

Statutory and common law components define the experimental use defense in the United States.[79] The Hatch-Waxman Act[80] created a statutory experimental use defense and gave proprietary pharmaceutical manufacturers a patent extension

71. *Id.*; *see also* 35 U.S.C. § 203 (a)(2) (2004).

72. Varmus, *supra* note 69; *see also* 35 U.S.C. § 203 (a)(1) (2004).

73. Elias A. Zerhouni, M.D., National Institute of Health, Office of the Director, In the Case of Norvir® Manufactured by Abbott Laboratories, Inc., (July 29, 2004), *available at* http://ott.od.nih.gov/Reports/March-In-Norvir.pdf.

74. Bonnie Joy Sedlak, *National Institutes of Health Decides Not to March in: Exploring the Decision Reached in the Case of Abbott's Norvir*, 24 GENETIC ENGINEERING NEWS 1, 18 (2004).

75. *Id.*

76. *Id.*

77. *Id.*

78. *Id.*

79. *See* Rochelle Dreyfuss, *Protecting the Public Domain of Science: Has the Time for an Experimental Use Defense Arrived?*, 46 ARIZ. L. REV. 457, 459 (2004).

80. Hatch-Waxman Act, Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified as amended at 21 U.S.C. § 355 and 35 U.S.C. § 271(e)).

to cover delays in testing obligations.[81] This statutory use defense was "solely for uses reasonably related to the development and submission of information under a federal law which regulates the manufacture, use, or sale of drugs. . . ."[82]

Two recent cases highlight what remains of the experimental use defense. The *Madey v. Duke University* decision essentially eliminated the common law experimental use defense for universities.[83] Duke University was using patented laser technology in its teaching and research laboratory.[84] In that case, the court concluded "the experimental use defense persists albeit in [a] very narrow form. . . ."[85] The court followed reasoning in *Embrex*, where the court interpreted the experimental use defense narrowly and limited its scope to actions performed "for amusement, to satisfy idle curiosity, or for strictly philosophical inquiry."[86] *Madey's* holding may mean that most university research will fail to fall within the research exception.[87]

Integra Lifesciences I v. Merck KGaA highlights how narrowly courts interpret the statutory defense.[88] In *Integra*, the defendants used a peptide, employed originally in wound healing, in experiments to identify the best drug for halting tumor growth.[89] The court found the new use of halting tumor growth fell short of benefiting from the statutory experimental use defense because the "statutory language strictly limits the exemption 'solely' to uses with a reasonable relationship to FDA procedures."[90]

The doctrine exempting experimental use from infringement has considerably more breadth in Europe and Japan than in the United States.[91] Various European states define the experimental

81. Dreyfuss, *supra* note 79, at 459.

82. 35 U.S.C.A. § 271(e)(1) (West 2004).

83. Madey v. Duke Univ., 307 F.3d 1351 (Fed. Cir. 2002), *cert. denied*, 539 U.S. 958 (2003).

84. *Id.* at 1352.

85. *Id.* at 1361.

86. Embrex, Inc. v. Service Eng'g Corp., 216 F.3d 1343, 1349 (Fed. Cir. 2000) (citations omitted).

87. Dreyfuss, *supra* note 79, at 461.

88. Integra Lifesciences I, Ltd. v. Merck KGaA, 331 F.3d 860 (Fed. Cir. 2003).

89. *Id.* at 863. "The Scripps-Merck experiments did not supply information for submission to the United States Food and Drug Administration (FDA), but instead identified the best drug candidate to subject to future clinical testing under the FDA processes." *Id.* at 865.

90. *Id.* at 866.

91. Janice M. Mueller, *No "Dilettante Affair": Rethinking the Experimental Use Exception to Patent Infringement for Biomedical Research Tools*, 76 WASH. L. REV. 1, 37-38

use exception in their patent law.[92] Under German law, the patentee's rights do "not extend to acts performed for experimental purposes relating to the subject-matter of the patented invention."[93] "French law provides that 'acts accomplished for personal or domestic purposes or for the purpose of testing the object of the patented invention shall not be considered as affecting the patentee's rights.'"[94] Japanese law provides that "'the effects of the patent right shall not extend to the working of the patent right for the purposes of experiment or research.'"[95]

F. Exclusive Versus Non-exclusive Licensing

Anecdotal evidence suggests that exclusive licensing of DNA diagnostics hinders innovation, reduces quality, sidesteps regulatory approval, and increases costs.[96] Patented diagnostics do not allow the study of a gene in local laboratories if all the samples must be shipped off to a reference laboratory.[97] A broad-based preliminary survey showed that non-profit organizations licensed DNA inventions exclusively at more than twice the rate of companies.[98]

Additional survey evidence indicates that in the previous three years, nearly twenty percent of life science faculty have delayed publication of research results by at least six months to pursue a patent application.[99] In addition, the most productive laboratories

(2001).

92. *See id.* at 39.

93. *Id.* at 38 (citations omitted).

94. *Id.* n.187 (citations omitted).

95. *Id.* at 39 (citations omitted).

96. Shanshan Zhang, *High Tech Law Institute Publications: Proposing Resolutions to the Insufficient Gene Patent System*, 20 SANTA CLARA COMPUTER & HIGH TECH. L.J. 1139, 1158-59 (2004).

97. O'Neill, *supra* note 51.

98. Michelle R. Henry et al., *A Pilot Survey on the Licensing of DNA Inventions*, 31 J.L. MED. & ETHICS 442, 444 (2003).

99. David Blumenthal et al., *Withholding Research Results in Academic Life Science: Evidence from a National Survey of Faculty*, 277 JAMA 1224 (1997). The 3394 faculty members in the fifty universities receiving the most NIH funding in 1993 were asked whether they had "delayed publication of their research results for more than [six] months" and whether they had "refused to share research results with other university scientists in the last three years." *Id.* "A total of 410 respondents (19.8%) reported that publication of their research results had been delayed by more than [six] months at least once in the last [three] years to allow for patent application, to protect their scientific lead, to slow the dissemination of

maintained the most pronounced delays.[100] In another series of interviews with clinical laboratories, responses indicated patented tests stopped laboratories from performing some diagnostic genetic tests.[101]

Companies and non-profit institutions differ in their strategy and breadth of patent coverage and the extent to which exclusive licenses are used. Generally, non-profits grant more licenses that are exclusive.[102] There is also a concern that raising the cost of access to diagnostic technologies through patents may be retarding the pace of biomedical discovery.[103] Industry and researchers argue over how valid the data is that supports these contentions.[104] Royalties on diagnostic tests account for two to ten percent of the test cost and in the absence of commercial tests, individual hospitals would be responsible for test development costs.[105]

G. Criticisms of Bayh-Dole Act Relative to DNA Diagnostics

Two critics argue that Bayh-Dole went too far in making results of publicly funded research in the health arena patentable at the expense of benefits to the general public. Rai and Eisenberg contend that the Bayh-Dole Act should be "reformed" to give funding agencies greater discretion to determine when to require that publicly funded research discoveries be dedicated to the public domain.[106]

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undesired results, to allow time to negotiate a patent, or to resolve disputes over the ownership of intellectual property. Also, 181 respondents (8.9%) reported refusing to share research results with other university scientists in the last [three] years." *Id.*

100. *Id.*

101. Mildred K. Cho et al., *Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services*, 5 J. MOLECULAR DIAGNOSTICS 3 (2003).

102. *See* Henry, *supra* note 98, at 447. A 1999 survey indicated that sixteen percent of licenses granted by NIH were exclusive while fifty percent of licenses granted by universities were exclusive. *Id.* Furthermore, companies reported granting an average of twenty-seven percent exclusive licenses for all licenses granted while for non-profits the average was sixty-eight percent. *Id.* at 444.

103. John P. Walsh et al., *Working Through the Patent Problem*, 299 SCIENCE 1021 (2003).

104. *See* Henry, *supra* note 98 (arguing that patents have a negative impact on the cost and availability of genetic testing); Ken Chahine, *Industry Opposes Genomic Legislation*, 20 NATURE BIOTECHNOLOGY 419 (2002) (arguing that in the long term the lack of patent protection for diagnostic tests would have a negative impact on biotech funding).

105. *See* Chahine, *supra* note 104.

106. Arti K. Rai & Rebecca S. Eisenberg, *Bayh-Dole Reform and the Progress of*

1. The Tragedy of the Anticommons

The tragedy of the commons theory was originally proposed to explain the overuse of resources owned in common with no incentive for conservation.[107] The theory predicts that privatization of public resources would increase resource utilization effectiveness.[108] The anticommons effect unexpectedly results from encouraging privatization, whereas a proliferation of patents on upstream inventions discourages the development of downstream inventions.[109] Some experts argue this could stifle important medical inventions.[110] Heller and Eisenberg famously posited the "tragedy of the anticommons" to suggest that scarce resources are underutilized because too many owners can block each other.[111]

These blocking patents also referred to as a "patent thicket," consist of overlapping intellectual property rights that a company must attempt to navigate through in order to commercialize a new technology.[112] With too many patents, a company may not develop a new product because of the fear of infringement. When a single firm did not control the components of the production of brass, copper, and zinc, the price of brass was higher and this illustrates the problem of complementary monopolies.[113] In addition, the profits of the producers were shown to be lower.[114] This is similar to the current problem in many industries with a large number of upstream patent holders possibly preventing the development of new technology.

2. Responses to the Anticommons Argument

The anticommons hypothesis has generated a powerful paradigm in which one can examine the effects of patenting on innovation and use of technology in the biotechnology field.

Biomedicine, 66 LAW & CONTEMP. PROBS. 289, 291 (2003).

107. Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCIENCE 698 (1998).

108. *Id.*

109. *Id.*

110. *Id.*

111. *Id.*

112. CARL SHAPIRO, *Navigating the Patent Thicket: Cross-Licenses, Patent Pools, and Standard-Setting*, INNOVATION POLICY & THE ECONOMY 119, 123 (Adam Jaffe et al. eds., 2001), *available at* http://faculty.haas.berkeley.edu/shapiro/thicket.pdf.

113. *Id.* at 124-25.

114. *Id.* at 125.

There have been a number of academic comments published regarding the anticommons theory. A sample of the representative arguments is presented below.

a. No Anticommons Problem

Some commentators have concluded that there is no anticommons problem. Professor Merges notes that in some cases, commercial firms have been injecting information into the public domain.[115] As an example, biotechnology firms invested millions of dollars in public domain gene sequence databases to prevent the hold-up of their research by patents issued on short gene sequences.[116] The issuance of these first patents on single nucleotide polymorphisms (SNPs) led ten pharmaceutical companies to establish the SNP Consortium in 1999.[117] The original goal of the SNP Consortium was to place 300,000 SNPs throughout the human genome in the public domain.[118] The final release of the SNP Consortium placed 1.25-million SNPs in the public domain.[119] Professor Merges believes that policy makers should examine these private sector responses before implementing major changes in response to an anticommons situation.[120]

Professor Kieff disagrees with the possible negative effects of the anticommons theory and believes that patents on inputs do not decrease production of outputs.[121] There is a large incentive for biotechnology patentees to license technology as a means of reducing the risk of commercialization.[122] This incentive makes sense for "Big Pharma," where the cost of commercializing a new drug may average $800 million and fifteen years.[123] Once a

115. Robert P. Merges, *A New Dynamism in the Public Domain*, 71 U. CHI. L. REV. 183, 190 (2004).

116. *Id.* at 183.

117. *Id.* at 190.

118. *Id.*

119. The SNP Consortium Ltd., SNP Data Release Notes, *available at* http://snp.cshl.org/about/2001_TSC_project_overview.shtml (last visited Jan. 20, 2005). The tenth release, in September 2001, of the SNP Consortium database contained 1,255,326 SNPs anchored to the human genome. *Id.*

120. Merges, *supra* note 115, at 190.

121. F. Scott Kieff, *Property Rights and Property Rules for Commercializing Inventions*, 85 MINN. L. REV. 697, 720 (2000).

122. *Id.* at 726.

123. Joseph S. DiMasi et al., *The Price of Innovation: New Estimate of Drug Development Costs*, 22 J. HEALTH ECON. 151 (2003). Depending on the drug

company develops a technology, the company likely licenses the technology to hedge risk in areas ancillary to the business.[124]

Professor Walsh and collaborators found that restricted access to upstream technology "has not been especially problematic" in impeding innovation in biomedical research.[125] These commentators concluded that the possibility exists where access to upstream technologies is impeded and this requires ongoing scrutiny.[126] More specifically, survey respondents reported that negotiations over rights to intellectual property from many owners seldom result in a project's cancellation.[127] The total royalty payments for multiple input technologies in a drug development program range from one to five percent of sales, and are somewhat higher for exclusive licenses.[128] The cost of purchasing patented reagents was found to be two to four times higher than making in-house versions of the same reagents.[129]

b. Anticommons Problem

Conversely, other authors believe that there is an anticommons problem and have proposed various solutions. Professor Mueller suggests that it is possible to resolve the anticommons problem. Mueller suggests expanding the experimental use doctrine so that researchers may use patented research tools for follow-on research without automatic disqualification from the experimental use doctrine.[130] Professor Mueller argues that a researcher who does not hold the patent to a

industry's accounting, the industry's $800 million figure may be an overestimate. Half of the $800 million involves "opportunity costs" with the money if invested in equities. Removal of built-in profits would make the research and development costs $108 million ninety-three percent of the time and $400 million seven percent of the time. The $800 million estimate also fails to include taxpayer subsidies through deductions and credits. Donald W. Light & Joel Lexchin, *Will Lower Drug Prices Jeopardize Drug Research?*, Physicians for a National Health Program, *available at* http://www.pnhp.org/news/2004/february/will _lower_drug_pric.php (last visited Jan. 20, 2005).

124. *See* Kieff, *supra* note 121, at 726.

125. JOHN P. WALSH ET AL., *Effects of Research Tool Patents and Licensing on Biomedical Innovation*, *in* PATENTS IN THE KNOWLEDGE-BASED ECONOMY 285, 331 (Wesley M. Cohen & Stephen A. Merrill eds., 2003).

126. *Id.*

127. *Id.* at 298.

128. *Id.* at 300.

129. *Id.*

130. *See* Mueller, *supra* note 91, at 9 (suggesting this approach where there are high transaction costs required for using patented research tools).

research tool should be allowed the use of the tool, but any products developed as a result would be subject to a "reach-through" royalty.[131] NIH does not favor reach-through royalties because they can inhibit downstream research.[132] Others have suggested that it would be wise to implement an experimental use exception, especially for researchers undertaking pre-competitive research.[133]

Professor Leibovitz intones that non-exclusive patents would "alleviate monopolistic power while accommodating the practical peculiarities of different situations."[134] He proposes a system that does not grant exclusive property rights to inventors.[135] These non-exclusive rights would protect an inventor against "free-riding competitors" but would not protect against "competitors who independently develop the same technology."[136] Implementation of non-exclusive patents would "reduce the possibility of anticompetitive behavior in the commercialization of technologies."[137] The difficulty in implementing this proposal centers on determining in which cases such misappropriation had occurred and where monopolistic power could be invoked.[138]

Professor Gitter suggests that Congress should create a compulsory licensing scheme for patents on human DNA sequence and codify the experimental use exception.[139] A compulsory

131. *Id.* at 55.

132. Principles and Guidelines for Recipients of NIH Research Grants and Contracts on Obtaining and Disseminating Biomedical Research Resources, 64 Fed. Reg. 72,090, 72,091 (Dec. 23, 1999) (final notice)

> Royalties on the sale of a final product that does not embody the tool, or other reach-through rights directed to a final product that does not embody the tool, discourage use of tools and are not appropriate in these circumstances. Royalties on the sale of final products are more appropriate to situations where a for-profit entity seeks to commercialize the tool, *e.g.*, by developing a marketable product or service, or incorporating the tool into a marketable product or service.

Id.

133. Sandy Thomas, *Reply to "Impact of Patenting on R&D and Commerce*," 21 NATURE BIOTECHNOLOGY 730 (2003); *see also* David C. Hoffman, Note, *A Modest Proposal: Toward Improved Access to Biotechnology Research Tools by Implementing a Broad Experimental Use Exception*, 89 CORNELL L. REV. 993 (2004).

134. John S. Leibovitz, *Inventing a Nonexclusive Patent System*, 111 YALE L.J. 2251, 2265 (2002).

135. *Id.* at 2268.

136. *Id.*

137. *Id.* at 2270.

138. *Id.* at 2268.

139. Donna M. Gitter, *International Conflicts over Patenting Human DNA Sequences*

licensing scheme would permit further use of the research, and allocate royalties for inventors based on the invention's commercial value while allowing researchers access to DNA sequence data at a fair price.[140] The approach would also allow scientists in public and nonprofit institutions to conduct non-commercially oriented research free of charge.[141] Such an approach would work to harmonize United States and European Union patent law.[142]

One commentator has proposed amending the Physician Immunity Statute to allow patient access to diagnostic testing of any gene, whether patented or not.[143] In 2002, there was a proposal for similar legislation that would have allowed the use of human genetic information for research and diagnostic purposes without the threat of patent infringement.[144] Congress did not pass this legislation.[145]

Ethicist Williams-Jones notes that "intellectual property protection affects the costs and, therefore, the availability of health care services . . . ."[146] Some commentators' note that whatever portions of public funds are expended on health care, it is impossible to cover all beneficial services.[147] The increased cost of patented genetic tests makes it more difficult to justify providing such testing services to the public.[148]

The costs of using patented PCR tests and DNA sequencing

in the United States and the European Union: An Argument for Compulsory Licensing and a Fair-Use Exemption, 76 N.Y.U. L. REV. 1623, 1679 (2001).

140. *Id.*

141. *Id.*

142. *Id.*

143. Gregory P. Lekovic, *Genetic Diagnosis and Intellectual Property Rights: A Proposal to Amend "The Physician Immunity Statute,"* 4 YALE J. HEALTH POL'Y L. & ETHICS 275, 296 (2004). The author proposed amending 35 U.S.C. § 287 (c)(2)(A)(iii) to include the words "other than for purposes of diagnosis" thus including genetic testing in "medical activity" that is not subject to patent infringement. *Id.*

144. Washington Business Information, *Legislation to Exempt Genes Used for Diagnostic Purposes*, DEVICE & DIAGNOSTIC LETTER, March 15, 2002, *available at* 2002 WL 8415113.

145. The bills were sent to Committee and no further action was taken. Legislative Updates, Office of Legislative Policy & Analysis, *available at* http://olpa.od.nih.gov/legislation/107/pendinglegislation/9gene.asp (last visited Feb. 18, 2005).

146. Bryn Williams-Jones & Michael M. Burgess, *Social Contract Theory and Just Decision Making: Lessons from Genetic Testing for the BRCA Mutations*, 14 KENNEDY INST. ETHICS J. 115 (2004).

147. *Id.* at 118.

148. *Id.* at 132.

are paid by diagnostics laboratories because the cost of laboratory instruments and reagents include the cost of licenses. In addition, commercial testing laboratories pay a fee for each PCR test that they perform.[149] The patent on PCR encourages laboratories to develop alternative technology in order to avoid the cost of PCR.[150]

H. The Future of Genetic Testing

Pharmacogenomics is the study of the effect of genetic variation on drug response.[151] The regulation of diagnostic genetic tests will become increasingly important as pharmacogenomic uses increase.[152] Diagnostic tests, including genetic tests, can determine if a specific individual has the appropriate genetic makeup to respond to treatment with a specific therapeutic.[153] Pharmacogenomics, utilizing genetic tests, have been used to optimize patient treatment with therapeutics. The first example of this personalized medicine was an HIV test that involved genotyping the virus in order to determine which drugs would be most effective against a particular virus.[154]

The treatment of certain breast cancers with Herceptin demonstrates another example of a successful pharmacogenomic approach.[155] A diagnostic test utilizing either histochemical or cellular hybridization methods can determine the status of the human epidermal growth factor receptor 2 (HER 2) gene.[156] About twenty-five percent of breast cancers contain an overabundance of either the HER2 gene or too many HER2 receptors.[157] Herceptin is a monoclonal antibody that binds specifically to HER2 receptors.

149. Telephone Interview with Matt Bower, Certified Genetic Counselor, Fairview University Medical Center (Oct. 22, 2004).

150. *Id.*

151. The term pharmacogenomics is often used interchangeably with pharmacogenetics. Cambridge Healthtech Inst., Pharmacogenomic Glossary, *available at* http://www.genomicglossaries.com/content/pharmacogenomics.asp (last visited Oct. 26, 2004).

152. Kathryn R. Phillips et al., *Genetic Testing and Pharmacogenomics: Issues for Determining the Impact to Healthcare Delivery and Costs*, 10 AM. J. MANAGED CARE 425, 429 (2004).

153. *Id.* at 426.

154. HIV serological diagnosis was the first example of testing to match a patient with a treatment, here based on the serotype of the virus.

155. Genentech, Inc., *How Herceptin Works*, *available at* http://www.herceptin.com/herceptin/patient/f_works/works.htm (last visited Oct. 1, 2004).

156. *Id.*

157. *Id.*

When combined with chemotherapy, Herceptin has been shown to have a high probability of responding in women of the appropriate genotype.[158]

The expansion of new market systems will only increase with the move to pharmacogenomics.[159] A noted biotechnology industry analyst has predicted that genetic testing will become increasingly routine.[160] Healthcare will move toward more "predictive, preventative care with [increased] pre-symptomatic [diagnostics] and [therapeutic prescriptions]."[161] This increased demand for predictive genetic testing will require affordability for individual tests as multiple genetic tests will likely be run simultaneously.

III. PROPOSED RULEMAKING: NON-EXCLUSIVE LICENSING OF GENOMIC INVENTIONS

In response to perceived inequities in the quantity and quality of healthcare services that are dependent upon genomic technologies, NIH introduced draft guidelines for the non-exclusive licensing of genomic inventions, including "nucleic acid-based diagnostics, potential gene therapy applications, and the development of new DNA and RNA-based therapeutics."[162] Genomic inventions covered in the NIH draft guidelines include: "materials such as cDNAs; expressed sequence tags (ESTs); haplotypes; antisense molecules; small interfering RNAs (siRNAs); full-length genes and their expression products; as well as methods and instrumentation for the sequencing of genomes, quantification of nucleic acid molecules, detection of single nucleotide polymorphisms (SNPs), and genetic modifications."[163]

The Draft Best Practices suggests a tripartite plan. The first

158. *Id.*

159. Nina Flanagan, *Tailored Medicine no Longer Science Fiction*, 24 GENETIC ENGINEERING NEWS 30 (Sept. 30, 2004).

160. G. Stephen Burrill, *State of the Biotechnology Industry . . . Circa 2004* (Oct. 11, 2004), *available at* http://www.burrillandco.com/pdfs/Laguna-Laguna.pdf.

161. *Id.*

162. E-mail from Jack Spiegel, Senior Advisor for Technology Transfer Operations, Office of Technology Transfer, National Institutes of Health, to Edward Weck, student, William Mitchell College of Law (July 1, 2004, 10:08 EST) (containing attachments draft Licensing Genomic Inventions and Jack Spriegel, Address before the Association of University Technology Managers on Draft Best Practices (Mar. 4-6, 2004)) [hereinafter Spriegel Address] (on file with author); David Malakoff, *NIH Roils Academe with Advice on Licensing DNA Patents*, 303 SCI. 1757 (2004).

163. Licensing Genomic Inventions, *supra* note 1, at 67747.

prong seeks "patent protection on genomic inventions [that require] significant further research and development by the private sector . . . to bring the invention to practical and commercial application."[164] The second prong incorporates non-exclusive licensing "whenever possible [especially for] broad enabling technologies and research uses. . . ."[165] The third prong exclusively licenses technology when "necessary to encourage research and development by private partners. . . ."[166] Under the third prong, it will be important to control the scope of the invention by limiting "indications, fields of use, and territories . . . to be commensurate with the abilities and commitment of licensees to bring the technology to market expeditiously."[167] To ensure expeditious development, the Draft Best Practices recommend utilizing milestones, benchmarks, and performance-based royalty payments; monitoring and enforcing performance; and sublicensing.[168] It will also be important to address public health benefits by: (1) seeking to protect research uses, (2) seeking fair return on public investment, (3) recognizing public health goals, and (4) enhancing public access and availability.[169]

IV. ANALYSIS

A. *Genetic Testing Introduction*

NIH bases the need for rule making on "[a]necdotal and empirical data" that "reveal[s] a pattern of exclusive licensing."[170] In addition, there is a need to "balance[] the expansion of knowledge and direct public health benefit with the commercial needs of private interests."[171]

Examples of genetic tests previously developed and implemented in clinical laboratories are discussed below. A comparison of the tests describes the disease, the genetic defect, the type of test, source of funds for test development, and testing cost. The examples described below include the exclusive licensing

164. *Id.*
165. *Id.* at 67748.
166. *Id.*
167. *Id.*
168. *Id.*
169. *Id.*
170. Spiegel Address, *supra* note 162.
171. *Licensing Genomic Inventions*, *supra* note 1, at 67747.

of BRCA1 and BRCA2 by Myriad Genetics, Canavan Disease test development, and hereditary hemochromatosis testing.[172] These examples are compared with non-exclusive licenses for Cystic Fibrosis and Huntington Disease testing. Finally, there is the recent example of the PXE disease gene patent that is issued to an individual followed by licensing to a patient advocacy group.[173]

1. Breast/Ovarian Cancer Testing with BRCA1/BRCA2

Mutations in both BRCA1 and BRCA2 result in a predisposition to breast cancer, ovarian cancer, prostate cancer (BRCA1), as well as other cancers (BRCA2).[174] The risk of developing cancers associated with these genes is unknown and appears to be "variable even within families of similar ethnic background with the same mutation."[175] Of women diagnosed with breast cancer each year, "only 5 to 10% are likely to have [a genetic predisposition] associated with increased risk of developing the disease."[176] Depending on the specific mutation and family history, the "cumulative lifetime risk is 40 to 85% for breast cancer, and 16 to 40% for ovarian cancer. . . ."[177] "But even [with these] very accurate testing methods, only 20 to 25% of patients with a strong family history... will have a positive BRCA mutation. . . ."[178] This means that for "75 to 80% of breast cancer patients, the heritable component of their [disease] remains unknown."[179] In addition to the genetic factors, "social and environmental factors" may affect the development of breast cancer.[180]

172. *See* discussion *infra* Parts IV.A.1-9.

173. *See* Press Release PXE International, *supra* note 39.

174. Nancie Petrucell et al., *BRCA1 and BRCA2 Hereditary Breast/Ovarian Cancer*, (last revision Sept. 3, 2004), GENEREVIEWS, *available at* http://www.genetests.org/servlet/access?db=geneclinics&site=gt&id=8888891&key=m41BLW6o3jUNg&gry=&fcn=y&fw=Di2T&filename=/profiles/brca1/index.html.

175. *Id.*

176. Williams-Jones & Burgess, *supra* note 146, at 123.

177. *Id.*

178. *Id.*

179. *Id.* There is some genetic association of Chek2, BRCA2, ESR1, CYP1B1, COMT, PGR, BRCA1, VEGF, TGFB, CYP17, HSD17B1, patched, sulfotransferase 1A1, HER2 codon 655, NAT2, VDR, XRCC2, TP53, EBAG9, ADRB2, MnSOD, HER-2/neu, CYP19, AR, PR, IGFBP7, GSTP1, RB1, cerbB2, estrogen receptor, cHaras1, and Lmyc genes with breast cancer. Genetic Association Database, National Institute on Aging, *available at* http://geneticassociationdb.nih.gov (last visited Oct. 20, 2004) (searching on "breast cancer" results in a list of genes associated with the disease).

180. *See* Williams-Jones & Burgess, *supra* note 146, at 124.

Myriad Genetics (Myriad) controls the testing for BRCA1 and BRCA2, and retains exclusive licenses for the use of the genes in diagnostic testing.[181] Myriad initially charged $2,400 for both the BRCA1 and BRCA2 tests and currently charges a list price of $2,975.[182] The cost of these tests is high because they require sequencing 35,000 base pairs of DNA.[183] The company negotiated a deal with the National Cancer Institute in 2002 and, as a result, reduced licensing fees to $1,200 for combined BRCA1 and BRCA2 testing, $600 for BRCA1 alone, and $750 for BRCA2 alone.[184]

Myriad noted in its annual report that its profit margin from the diagnostics testing business is sixty-eight percent.[185] For the fiscal year ending June 30, 2004, Myriad's estimated cost of testing is $944.[186] Estimates of the cost of contract sequencing a gene alone, without the cost of oligonucleotide synthesis, is between $945 and $1,050.[187] Myriad estimates that it spent $2 million to develop the genetic tests for BRCA1 and BRCA2. In 2004, Myriad reported a net loss of $40.6 million[188] due to its research

181. *See* Kimberly Blanton, *Corporate Takeover Exploiting the US Patent System: A Single Company Has Gained Control over Genetic Research and Testing for Breast Cancer, and Scientists, Doctors, and Patients Have to Play by Its Rules*, BOSTON GLOBE, Feb. 24, 2002, at 10, *available at* 2002 WL 4113872; MATTHEW RIMMER, *Myriad Genetics: Patent Law and Genetic Testing*, 25 EUR. INTELL. PROP. REV. 20 (2003).

182. David B. Resnik, *Are DNA Patents Bad for Medicine?*, 65 HEALTH POLICY 181, 186 (2002). BRACAnalysis® analysis for hereditary breast and ovarian cancer involves sequencing the genes in both directions for a total of approximately 35,000 bp, costs $2,975, and is covered by all major health maintenance organizations. Myriad Genetics, Inc., SEC Annual Report (Form 10-K) for fiscal year ending June 30, 2004, [hereinafter Myriad 10-K] *at* http://www.edgar-online.com/bin/cobrand/?doc=A-8999230001047469-04-028434&nav=1&form type=10%2DK.

183. Telephone Interview with Bill Rusconi, Vice President of Marketing, Myriad Genetics (September 24, 2004).

184. Resnik, *supra* note 182, at 186.

185. *See* Myriad 10-K, *supra* note 182.

186. *Id.* Profit margins have steadily increased for fiscal years ending June 30: in 2001 profits were 56.68% of sales; in 2002 profits were 60.1% of sales; in 2003 profits were 63.81% of sales; and in 2004 profits were 68.24% of sales. *Id.* Based on profit margins for 2004, the cost alone of running tests would be $619 for MLH1 and MSH2 (hereditary nonpolypopsis colorectal cancer syndrome) and $535 for APC (familial adenomatous polyposis). Services and Price List, Myriad Genetics Laboratories, Inc., (effective as of 02/15/04). The ratio of tests done for BRCA1 and BRCA2 to those done for MLH1 and MSH2 is between five and ten to one. Rusconi, *supra* note 183.

187. E-mail from David Gingrich, DNA Sequencing, Colorado State University, to Edward Weck, student, William Mitchell College of Law (Sept. 27, 2004, 14:27:22 CST) (on file with author).

188. *See* Myriad 10-K, *supra* note 182, at 4.

expenditures in developing therapeutics, including Flurizan, its lead therapeutic candidate for the treatment of Alzheimer's disease.[189]

2. Canavan Disease

The Greenbergs had two children who both developed Canavan disease.[190] The Greenbergs decided to lead an effort to identify the gene for the disease so that their children's struggle with the disease would not be in vain.[191] They worked with Dr. Reuben Matalon, a physician working at the University of Illinois Hospital in Chicago.[192] The Greenbergs helped Dr. Matalon obtain tissue samples from other children suffering from Canavan disease and their parents.[193] The Greenbergs also raised donations and grants.[194] The Miami Children's Hospital (MCH) hired Dr. Matalon to establish a center for research on genetic diseases.[195] In 1993, Dr. Matalon isolated the Canavan gene and MCH applied for a patent on the gene.[196] Dr. Matalon assigned all of his rights to the gene in his contract to MCH.[197] MCH charges $12.50 per test to laboratories that perform the test.[198] The Greenbergs sued MCH and lost.[199] Genzyme currently provides Canavan testing for $225.[200]

3. Hereditary Hemochromatosis

Hereditary hemochromatosis is a common autosomal recessive disease with as many as 80 to 85% of the cases caused by the two most common alleles of the HFE gene (C282Y and H63D).[201]

189. *See id.* at 3 (providing that Flurizan recently completed phase I of human clinical trials).
190. *See* Resnik, *supra* note 182, at 185.
191. *Id.*
192. *Id.*
193. *Id.*
194. *Id.*
195. *Id.*
196. *Id.*; U.S. Patent No. 5,679,635 (issued Oct. 21, 1997). Canavan disease was shown to be a mutation in the aspartoacylase gene resulting in accumulation of N-acetylaspartic acid in the brain. *Id.*
197. Resnik, *supra* note 182, at 185.
198. *Id.*
199. *Id. See generally* Greenberg v. Miami Children's Hosp. Res. Inst., Inc., 208 F. Supp. 2d 918 (N.D. Ill. 2002).
200. Telephone Interview with Customer Service, Genzyme Genetics (Oct. 26, 2004) [hereinafter Genzyme Interview].
201. Jon F. Merz et al., *Diagnostic Testing Fails the Test*, 415 NATURE 577, 577

Testing for hemochromatosis requires a PCR amplification step. Bio-Rad Laboratories (Bio-Rad) currently holds the rights to hemochromatosis testing and either requires purchase of reagents from Bio-Rad or a license to perform the test in the laboratory.[202] Bio-Rad charges $84 for the chemicals required for the test.[203] Bio-Rad charges royalties up to $20 per test.[204] One clinical laboratory charges $163 for the hemochromatosis test.[205] A survey of clinical laboratories testing for hereditary hemochromatosis showed that limiting testing to the patented test discouraged the development of better or less-expensive tests.[206] Bio-Rad, however, has entered into an exclusive licensing agreement with Nanogen for use of the hemochromatosis test on a proprietary nanochip system.[207] The patents on these alleles expire during 2015 and 2016.[208]

A quick survey of the European Patent Office databases shows that there are a number of new patent applications for hemochromatosis testing.[209] Some applications are by other research groups and others are follow-on inventions from the

(Feb. 7, 2002).

202. *Id.* at 578.

203. Reagents for twenty-four tests cost $2016. Product no. 406-1262, mDx Hereditary Hemochromatosis ASR, Bio-Rad Laboratories, *available at* http://www.biorad.com (last visited Jan. 11, 2005).

204. *See* Merz, *supra* note 201, at 579.

205. CompGene Fees, *at* http://www.compgene.com/fees.htm (last visited Jan. 11, 2005) [hereinafter CompGene Fees].

206. *See supra* note 203 and accompanying text.

207. *Bio-Rad Enters Licensing Deal With Nanogen*, East Bay Business Times, *available at* http://www.bizjournals.com/eastbay/stories/2002/06/24/daily27.html (last visited Jan. 11, 2005) (quoting John Goetz, vice president of Bio-Rad's clinical diagnostics group, as saying "The demand for molecular-based tests used to detect genetic disorders continues to increase, and we believe the agreement with Nanogen will help accelerate that trend by providing laboratories a greater variety of licensed hemochromatosis testing options.").

208. U.S. Patent No. 5,705,343 (issued Jan. 6, 1998); U.S. Patent No. 5,712,098 (issued Jan. 27, 1998); U.S. Patent No. 5,753,438 (issued May 19, 1998).

209. U.S. Patent Application No. 2,004,101,868 (published May 27, 2004). Entitled "Analysis method for hemochromatosis mutation," the abstract posits that it is "possible to combine three concepts each known separately in prior art from different sources: allele specific PCR, mutagenically separated PCR, and amplicon identification by specific dissociation curves." *Id.* In addition this method was claimed to be "significantly more straightforward and economic" than those is the prior art. *Id.* U.S. Patent Application No. 2,004,086,862 (published May 6, 2004) (entitled "Method and probes for the genetic diagnosis of hemochromatosis," and claiming methods and probes for hybridizing with nucleic acids with HFE mutations in a biological sample); U.S. Patent Application No. 2,003,148,972 (published Aug. 7, 2003) (entitled "Hereditary hemochromatosis gene" and consists of a follow-on invention from original inventors).

group that patented the original sequence. This shows that innovation has not been completely stifled by the patenting of the gene.

4. Huntington's Disease

The test for Huntington's Disease (HD) requires a determination of the number of CAG repeats in the 5' coding sequence.[210] The CAG repeat is expanded in individuals with Huntington's Disease.[211] The assay is a Southern blot and approximately 85 to 93% of individuals with HD can be correctly diagnosed.[212] Currently, no treatment for the disease exists. Quotes for the cost of Huntington's Disease testing are between $190 and $200 per test.[213]

5. Cystic Fibrosis

Cystic fibrosis is the most common disease in humans but there is currently no simple test available for genetic testing because a large number of different genetic mutations can result in the disease.[214] Because of this genetic complexity, the American College of Medical Genetics recommended a panel of twenty-five common alleles for testing.[215] The gene was patented and licensed non-exclusively for $2 per test.[216] Cystic fibrosis testing with this panel costs between $150 and $300.[217]

210. Brendan Haigh, *Huntington Disease*, GENEREVIEWS, *at* http://www.genetests. org (last modified May 25, 2004).

211. *Id.*

212. *Id.*

213. Genzyme Interview, *supra* note 200; CompGene Fees, *supra* note 205.

214. Cystic fibrosis is caused by mutations in the gene encoding the cystic fibrosis transmembrane conductance regulator (CFTR). Gregory P. Lekovic, *Genetic Diagnosis and Intellectual Property Rights: A Proposal to Amend The Physician Immunity Statute*, 4 YALE J. HEALTH POL'Y & ETHICS 275, 276 n.6 (2004).

215. Moskowitz et al., *CFTR-Related Disorders*, GENEREVIEWS, *at* http://www.genetests.org/ (last modified Aug. 24, 2004).

216. U.S. Patent No. 5,776,677 (issued July 7, 1998); Peter Gorner, *Parents Suing over Patenting of Genetic Test They Say the Researchers They Assisted are Trying to Profit from a Test for a Rare Disease*, CHI. TRIB., Nov. 19, 2000, at 1, *available at* 2000 WL 3735425.

217. CompGene Fees, *supra* note 205; Genzyme Interview, *supra* note 200; Telephone Interview with Chrissi Coolbaugh, Client Services, Ambry Genetics (Oct. 26, 2004) (noting that Ambry Genetics charges $200 for three selected mutations, or for sequencing the entire gene, $450 for patients and $495 for institutions).

6. Alzheimer's disease

Alzheimer's Disease remains the most common cause of dementia in North America and Europe.[218] There is currently no curative treatment.[219] There is a significant association of the disease with the Apolipoprotein E (ApoE) gene.[220] Duke University, with NIH funding, developed the test for ApoE alterations and Athena Diagnostics holds the exclusive license.[221] Testing for the ApoE gene from Athena Diagnostics costs between $295 and $450.[222]

7. Familial Colon Cancer

Hereditary Non-Polyposis Colon Cancer (HNPCC) is associated with mutations in four genes in the mismatch repair pathway.[223] Mutations in two of these genes, MLH1 and MSH2, account for approximately ninety percent of detected mutations in families with HNPCC.[224] Myriad tests for two of the four genes involved in (HNPCC), MLH1 and MSH2. The cost is $1,950[225] and requires approximately sixty-seven percent of the sequencing required for the BRCA1 and BRCA1 sequences.[226] Ambry Genetics, a competitor of Myriad, sequences the same two genes for an institutional cost of $1,395 and a patient cost of $1,295.[227]

218. Thomas D. Bird, *Alzheimer Disease Overview*, GENEREVIEWS, (last revision on Dec. 22, 2004), *available at* http://www.genetests.org/.

219. *Id.*

220. *Id.*

221. U.S. Patent No. 5,508,167 (issued Apr. 16, 1996).

222. The lower charge is for billing facilities and the higher charge is for billing commercial insurance. Telephone Interview with Customer Service, Athena Diagnostics (Oct. 26, 2004) [hereinafter Athena].

223. Wendy Kohlmann & Stephen B. Gruber, *Hereditary Non-Polyposis Colon Cancer*, GENEREVIEWS (Feb. 5, 2004), *available at* http://www.genetests.org/.

224. *Id.*

225. Comprehensive COLARIS® analysis for familial colorectal cancer by sequencing MLH1 and MSH2 (about two-thirds as many bases as BRCA1 and BRCA2) is $1950 and is covered by all major health maintenance organizations. *See* Myriad 10-K, *supra* note 182.

226. *See* Rusconi, *supra* note 183.

227. E-mail from Chrissi Coolbaugh, Client Services, Ambry Genetics, to Edward Weck, student, William Mitchell College of Law (Oct. 29, 2004, 14:33:03 CST) (on file with author). Sequence of either MLH1 or MSH2 costs $700 for the patient and $750 for an institution. *Id.*

8. Duchenne's Muscular Dystrophy

Molecular genetic testing of the Duchenne Muscular Dystrophy (DMD) gene is available clinically and can establish the disease diagnosis without a muscle biopsy in the majority of DMD cases and Becker Muscular Dystrophy.[228] The cost of testing ranges from $425 to $695.[229]

9. Spinocerebellar Ataxias

There are a number of genes, which affect spinocerebellar ataxias (SCA).[230] The University of Minnesota, with NIH funding, developed the SCA-1 genetic test, and Athena Diagnostics holds the patent and exclusive license.[231] The cost for the SCA-1 test, and other SCA tests individually, is $395 to $550.[232]

B. Positions of Professional Associations on Genetic Testing

The Council on Governmental Regulations (Council) is an association of research universities that has been involved in the development of financial and administrative aspects of federally funded research since 1948.[233] The Council complained about the process involved in adjusting the licensing practices.[234] The Council believes this is an example of NIH amending its granting regulations and requirements with little, if any, formal process.[235] The Council is unsure if data supports NIH assumptions.[236]

The executive board of the Academy of Clinical Laboratory Physicians and Scientists' (ACLPS)[237] approved its resolution

228. Bruce R. Korf et al., *Dystrophinopathies*, GENEREVIEWS (Oct. 1, 2004), *at* http://www.genetests.org.

229. *See* Athena, *supra* note 222.

230. There are tests for Spinocerebellar Ataxia Type 1, 2, 3, 6, 7, 8, 10, 12, 14 and 17. *See GeneTests*, *supra* note 20.

231. U.S. Patent No. 5,741,645 (issued Apr. 21, 1998).

232. *See* Athena, *supra* note 222.

233. Council on Governmental Relations, *Agenda: Meeting at the Council of Governmental Relations* 10-14, *available at* http://206.151.87.67/docs/AgendaJune 04.doc (last visited Jan. 21, 2005).

234. *Id.*

235. *Id.*

236. *Id.*

237. Academy of Clinical Laboratory Physicians and Scientists, *ACLPS Resolution: Exclusive Licenses for Diagnostic Tests Approved by the ACLPS Executive Council* (June 3, 1999), *available at* http://depts.washington.edu/lmaclps/license.htm.

regarding exclusive licenses for diagnostic tests. The resolution recommends:

> Physicians and scientists should oppose patent licensing agreements that inappropriately limit clinical care, medical training, and medical research; Government and non-profit institutions that hold patents controlling in vitro diagnostic testing services should not issue exclusive licenses for these patents unless there is a clear and compelling need for exclusivity in order to make the technology available to the public. Such cases are expected to be extremely rare; when patent holders choose to require royalty-bearing licenses for use of their technology for in vitro diagnostic testing, such licenses should be nonexclusive and available to any qualified, CLIA-certified laboratory on an equal basis. Financial terms for such licenses should be reasonable; license agreements should be free of any terms that dictate specific methods of testing, methods of reporting results, or clinical uses of the test.[238]

The American College of Medical Genetics (ACMG) also issued a position statement on genetic testing:

> The decision of the Patent and Trademark Office (PTO) to permit the patenting of naturally occurring genes and disease-causing mutations has produced numerous difficulties... Enforcement has been effected in one or more of these ways: monopolistic licensing that limits a given genetic test to a single laboratory, royalty-based licensing agreements with exorbitant up-front fees and per-test fees, and licensing agreements that seek proportions of reimbursement from testing services. These limit the accessibility of competitively priced genetic testing services and hinder test-specific development of national programs for quality assurance. They also limit the number of knowledgeable individuals who can assist physicians, laboratory geneticists and counselors in the diagnosis, management and care of at-risk patients. Further, restricting the availability of gene testing has long-term implications beyond patient care. It affects the training of the next generation of medical and laboratory geneticists, physicians, and scientists in the area enveloped by the patent or license. It also retards the

238. *Id.*

> usually very rapid improvement of a test that occurs through the addition of new mutations or the use of new techniques by numerous laboratories that have accumulated samples from affected individuals over many years. Therefore, it is the ACMG's position that: Genes and their mutations are naturally occurring substances that should not be patented. Patents on genes with clinical implications must be very broadly licensed. Licensing agreements should not limit access through excessive royalties and other unreasonable terms.[239]

C. Is This New Rulemaking Justified?

Genetic testing requires balancing a variety of interests. The rights of the patient, the patent holder, the government funding agency, the doctor and the insurance company all need to be considered.[240] Protection of these interests requires "patient choice, neutral genetic counseling, physician involvement, and regulation of process and information management."[241]

If health care providers can be convinced that the predictive savings from diagnostic tests offset the cost of testing, they will be willing to reimburse the costs of testing.[242] However, if an individual is not part of an insurance pool, e.g., lacks insurance through employment, then genetic discrimination may become a possibility.[243] This possibility varies from state to state. One commentator noted that genetic "counselors 'routinely advise' clients not to pursue health insurance reimbursement because of the 'potential risk in obtaining future health and life insurance.'"[244]

There is empirical evidence of negative effects for exclusive licensing. This note's brief survey of commercialized genetic tests shows that the monopoly right granted by patent exclusive

239. American College of Medical Genetics, *Position Statement of Gene Patents and Accessibility of Gene Testing*, (Aug. 2, 1999), *available at* http://genetics.faseb.org/genetics/acmg/pol-34.htm.

240. *See* Allen C. Nunnally, *Commercialized Genetic Testing: The Role of Corporate Biotechnology in the New Genetic Age*, 8 B.U.J. SCI. TECH. L. 306 (2002) (reviewing "the prominent problems that underlie commercialized genetic testing" and offering recommendations for commercialized diagnostic genetic testing).

241. *Id.* at 337.

242. *See* Chahine, *supra* note 104, at 419.

243. *See* Jennifer S. Geetter, *Coding for Change: The Power of the Human Genome to Transform the American Health Insurance System,* 28 AM. J.L. & MED. 1, 44-56 (2002) (analyzing, in part, the health insurance industry and the states regulation of it).

244. *Id.* at 51.

licensing results in increased costs to licensees.[245] Although it is very difficult to make head-to-head comparisons of genetic tests for different diseases, as each genetic defect is unique and the concomitant tests differ in complexity, the evidence indicates that exclusive licenses increase the cost of testing two to three-fold.[246] Some laboratories have discontinued using specific tests.[247] In other markets outside the United States, the increased prices have had a documented effect on the delivery of health care.[248] The evidence is strongest for a decline in breast cancer testing (BRCA1 and BRCA2) in Canada and the European Union.[249]

A large number of independent laboratories carry out genetic tests. Most of the tests utilize routine molecular biological techniques and reagents that should be easily transferable from a scientific publication. Some university laboratories have the time and inclination to develop laboratory tests from published recipes. Conversely, not all laboratories will want to develop their own tests and will instead find satisfaction by purchasing reagents (ASRs) from commercial research test developers. The commercial production of reagents would increase both quality and price, but these price increases would not match those associated with patented tests.

For example, reagent costs are probably higher for genetic tests with a requirement for synthetic oligonucleotides. Non-exclusive licensing might switch development to reagent companies instead of to companies that are providing genetic testing services. Laboratories could establish consortia for purchasing specialized reagents.

245. *See supra* Part IV.

246. *Id.*

247. *See supra* Part II.F.

248. *See* Williams-Jones & Burgess, *supra* note 146, at 119-20, 125. The patenting of the BRCA genes led to a tripling of prices in Canada. *See* Bryn Williams-Jones, *History of a Gene Patent: Tracing the Development and Application of Commercial BRCA Testing* 10 HEALTH L.J. 123, 142 (2002) (describing the patenting by Myriad Genetics of the genes BRCA1 and BRCA2, which are associated with hereditary breast and ovarian cancer). From July 2001 to February 2003, in-house BRCA testing was halted at the Hereditary Cancer Agency at the British Columbia Cancer Agency in Vancouver, British Columbia. *Id.* The Institut Curie in Paris, France argues that the Myriad BRCA testing misses 10 to 20% of mutations jeopardizing the quality and usefulness of the information. *Id.* at 139. Complying with patent requirements would result in an estimated additional cost of thirty-six-million francs ($4.8 million) to hospital budgets. *Id.*

249. *See* Bryn Williams-Jones, *History of a Gene Patent: Tracing the Development and Application of Commerical BRCA Testing*, 10 Health L.J. 123 (2002).

It will be important under the new draft guidelines to distinguish the non-exclusive and exclusive licensing categories created by the "when possible" and "when necessary" language.[250] The first consideration would be the number of interested potential licensees for a specific genetic test. If there were only one potential licensee, the use of milestones and benchmarks would ensure the development of the technology.[251] This would also ensure licensing of the genetic test. The second consideration would be the number of individuals affected by the disease. The Orphan Drug Act defines a "rare disease or condition" for development of drugs as "any disease or condition which . . . affects less than 200,000 persons in the United States . . . ."[252] This number, or another appropriate number of affected individuals, could be used to determine the genetic test for which exclusive licensing would be necessary. The third consideration might include the complexity of the test for the disease, because the cost of testing relates directly to the number of mutations causing the disease. When establishing criteria for exclusive licensing, a proposed regulation must require that newly developed genetic tests not be frequently monopoly-priced.

A broad definition of "research use" is imperative under the proposed rulemaking. This broad definition becomes especially important with genetic diseases because the initial observations of allele prevalence may vary following analysis of different ethnic subpopulations. Ongoing research with the genetic tools is essential to improve genetic testing for a particular disease.

V. CONCLUSION

The non-exclusive licensing of genetic tests, as recommended in NIH's new rulemaking, is necessary to allow potentially affected individuals broad access to genetic testing.[253] It is also necessary to strike a balance between encouraging further development of genetic tests with federal funding, patent protection for university research, and development of that technology into viable commercial products and broad access to health care.[254]

250. *See supra* Part III.
251. Licensing Genomic Inventions, *supra* note 1, at 67748.
252. 21 U.S.C.A. § 360ee (b)(2) (West 2001).
253. *See supra* Part III.
254. *Id.*

Patenting of genes for genetic testing has different standards in the United States and Europe.[255] The United States' standard for patenting DNA sequences requires a specific and substantial utility, and the United States grants more patents with broader coverage than the European standards allow.[256] Europeans have expressed great concern that increasing patent coverage for genetic testing will negatively influence healthcare access and costs.[257]

The enactment of the Bayh-Dole Act more than twenty years ago has been a boon for university technology transfer departments and an additional source of income for universities.[258] Patents and licenses on biological inventions were incentives that furthered the development of the biotechnology industry.[259] Concurrently, the reduction in breadth of the experimental use exception has reduced academic experimentation that could be undertaken to support further development and understanding of population effects of genetic tests.[260]

Survey evidence from various laboratories indicates that patenting of diagnostic tests reduces the amount of experimentation at local laboratories. It has been suggested that the anticommons effect on upstream inventions has stifled downstream inventions.[261] Academic positions have been proffered on both sides of the anticommons divide.[262] For those who see an anticommons problem, solutions include compulsory licensing, non-exclusive patents, and expanded access to diagnostic testing.[263] As the number of pharmacogenetic tests expands in the future, assuring access to genetic testing will become increasingly important.

Each disease diagnostic is unique. It is not possible to compare the average price of an exclusively licensed test to a non-exclusively licensed test.[264] The cost of a genetic test is determined by the complexity, variety and number of genetic variants, and the

255. *See supra* Part II.B-C.
256. *Id.*
257. *See* Bryn Williams-Jones, *History of a Gene Patent: Tracing the Development and Application of Commerical BRCA Testing*, 10 Health L.J. 123 (2002).
258. *See supra* Part II.D.
259. *Id.*
260. *See supra* Part II.E.
261. *See supra* Part II.G.
262. *Id.*
263. *Id.*
264. *See supra* Part IV.

complexity of the technique involved (DNA sequencing or other allelism tests).[265] The more complex tests have higher costs as well as attendant monopoly costs associated with patent rights.[266] Using the BRCA test as an example, the cost of providing the test in a dedicated laboratory is one-third of the market list price.[267] These increased costs can make it necessary to reduce overall testing in order to pay for testing for selected individuals.[268] A number of professional associations have spoken out against the patenting of genes for diagnostic tests or for the use of non-exclusive licensing provisions.[269]

The non-exclusive licensing of DNA diagnostics is necessary to ensure that genetic tests are widely available at reasonable costs. The policy of federally funding research to promote basic discoveries must be balanced with mechanisms for rapidly developing those technologies at reasonable costs that then support laboratory implementation within a suitable time frame.

265. *Id.*
266. *Id.*
267. *Id.*
268. *Id.*
269. *Id.*