



AMERICAN INTELLECTUAL PROPERTY LAW ASSOCIATION
241 18th Street, South, Suite 700, Arlington, VA 22202 Phone: 703.415.0780 – Fax: 703.415.0786 – www.aipla.org

May 15, 2009

Darren Greninger
National Institutes of Health
Office of Biotechnology Activities
6705 Rockledge Drive, Suite 700
Bethesda, MD 20892

Comments on Draft Report to the Secretary of Health and Human Services:
“Public Consultation Draft Report on Gene Patents and Licensing Practices
and Their Impact on Patient Access to Genetic Tests”
74(52) Federal Register 11730 (March 19, 2009)

Dear Mr. Greninger:

The American Intellectual Property Law Association (AIPLA) appreciates the opportunity to offer comments regarding the Draft Report on Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests (“Report”) proposed by the Secretary’s Advisory Committee on Genetics, Health, and Society (SACGHS).

AIPLA is a national bar association whose more than 16,000 members are primarily lawyers in private and corporate practice, in government service, and in the academic community. AIPLA represents a wide and diverse spectrum of individuals, companies, and institutions involved directly or indirectly in the practice of patent, trademark, copyright, and unfair competition law, as well as other fields of law affecting intellectual property. Our members represent both owners and users of intellectual property. AIPLA’s primary objectives are to aid in the improvement in laws relating to intellectual property and in their proper interpretation by the courts, and to provide legal education to the public and to its members on intellectual property issues.

Introduction

The Report results from an initial study by SACGHS of the effect of gene patents and patent licensing practices on patient and clinical access to genetic tests, specifically to patents claiming nucleic acid-related inventions associated with genetic tests that rely on analysis of nucleic acid molecules to determine human genotype for diagnostic, predictive, or other clinical purposes. The SACGHS study arose from suggestions that patents may be limiting the availability, cost, and/or quality of these tests. Of particular concern were the possibilities of chilling effects of patents on testing by diagnostic labs, fears of an inability to design around patents to create non-infringing alternative tests, and “hold-out” issues of blocking patents claiming only part of important testing technologies. Also of concern were potential quality control issues that might arise when an exclusive license to a single test lab might prevent verification of test results by unlicensed labs.

We appreciate that the Report acknowledges the tradeoff between the potential social costs incurred from patents relating to genetic testing and the incentives provided by patents to develop new genetic tests. We believe, however, that the Report grossly inflates those costs and fails to adequately value the incentives derived from patents. Notwithstanding the Report's admission of a lack of evidence that patents pose any problem with access to genetic testing, it nevertheless concludes that there are, or will be, problems and leaves it to commentators to prove otherwise. In fact, among the 8 case studies in the Report, in only one (Long QT Syndrome) did there appear to be any significant negative implications from patented technology. And even in that case, many of the negative results were unclear—the test cost data was ambiguous, the clinical data secrecy was only temporary, and the split IP issue has not blocked any tests.

The Report thus cites no convincing data that patents have had any negative impact on access to genetic tests. The report also fails to demonstrate that patents lack their usual motivating force for innovation and commercialization in the realm of genetic technologies. In fact, by our reading of the data, successful private patent licensing agreements have made genetic testing readily available when patents cover a test, and patents have not significantly impacted the costs of tests. Also, the large number of patented gene test-related patents arising from industrial research indicates that patents have indeed had their intended incentive effects in the biotechnology industry. Thus, at the very least, serious doubt as to the validity of the committee's asserted hypothesis has been provided by their own data.

AIPLA Member Commentary

We conducted a voluntary survey of the members of the Biotechnology and FDA Law Committees of the AIPLA regarding the Report, and we summarize their views here.

Unbalanced Analysis

Generally, the members of these committees did not believe that the Report provided a balanced analysis of the effects of patents on diagnostic genetic testing. In particular, the Report discounted the patent incentive to develop new tests and to invest in research with no apparent basis in spite of evidence that patents did encourage researchers. They questioned why the Report concludes that the inventions by Myriad and Mercator (p. 99) would have been discovered even absent patent incentive, when it provides no basis for this conclusion. The Report discounts that the patent incentive actually stimulated “races” in both cases as evidence of positive motivation inspired by patent availability. Even though patents provided motivation in these and the Johns Hopkins cases, the Report concludes that “it seems to [sic] reasonable to conclude that if patent protection for genetic tests did not exist, scientists likely would continue to pursue research into gene-disease associations with equal fervor....” (p. 99). This conclusion did not seem reasonable to many of our respondents due to lack of evidentiary support.

Committee members disagreed with the Report's implication that gene patents impede innovation and development of diagnostic tests—most asserted the opposite is true. It is difficult to quantify the incentive effects of a strong patent system. But the conclusions in the Report appear to be based much more on subjective opinion than objective analysis. One suggestion is to compare the biotechnology research and development efforts in countries with strong patent systems with those in countries lacking strong patent systems. Even to the extent patents do not

directly encourage research efforts, having a strong patent system provides a research industry infrastructure that promotes invention whether or not every particular innovation is patented. The SACGHS and the taskforce are composed primarily of academic and government members with few industry representatives, which likely accounts for the perceived one-sidedness of the Report.

Generally, the Report is flawed because it draws broad conclusions from too few case studies and inconclusive data. That the conclusions it draws consistently discount the benefits of patents despite evidence to the contrary, and emphasize potential but as yet unrealized pitfalls without substantial evidence gives the strong impression of bias.

No Evidence of Patents Having Any Systemic Negative Effects

Committee members believed that the Report did not provide any analysis showing that patents have any systemic negative effect on access to diagnostic testing. As the Report acknowledges, “SACGHS found little in the way of broad or consistent evidence that indicates either positive or negative effects of gene patents on patient access to diagnostic tests.” (p. 98). The Report further acknowledges that excessive pricing of patented diagnostics is not an issue because “multiple factors already constrain the price a sole provider of a genetic test may set.” (p. 103). Despite these conclusions, the Report conjures up future scenarios never yet realized that may someday have negative effects on patient access. It is premature to address any such imagined future effects. The industry has demonstrated the ability to successfully provide access at a reasonable cost—the system is not broken; it does not need fixing.

Patents do not negatively impact innovation. The only evidence presented to the contrary was that “Sole providers, such as Myriad, Athena Diagnostics, and PGx Health, also have failed to publicly assure would-be innovators that they will not consider innovations to be infringing.” (p. 105). A prospective guarantee of non-infringement without knowing what a future innovation would be demands too much of these intellectual property owners. Furthermore, it is apparent from the LQTS case study that the patent owners themselves continue to build upon their inventions.

In 1998, a theory commonly referred to as “the tragedy of the anticommons,” posited that intellectual property rights would restrict or otherwise adversely impact biomedical research. Ten years later, one of the authors of this theory, Rebecca Eisenberg, reported on the results of empirical testing of the theory. Ms. Eisenberg found that “the results suggest, overall, intellectual property has presented fewer impediments to research than policymakers may have projected on the basis of early salient controversies. Most scientists report no difficulties in attempting to acquire IP-protected technologies, and only a small percentage report significant delays in research or having to abandon a project because of IP issues.”¹ One empirical study which was quoted in the draft Report and was reported by the National Academy of Sciences² could not provide evidence that supports an “IP anticommons” (“it appears that access to

¹ R. S. Eisenberg, “Noncompliance, Nonenforcement, Nonproblem? Rethinking the Anticommons in Biomedical Research,” 45:4 *Houston L. Rev.* 1059 (2008).

² “Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation, and Public Health” National Academies of Science, Committee on Intellectual Property Rights in Genomic and Protein Related Inventions (2006) available at www.nap.edu.

patented inventions or information inputs into biomedical research rarely imposes a significant burden for biomedical researchers”).³ This NAS report further supports Ms. Eisenberg’s findings.

Nevertheless, the Report goes on to list a number of potential future harms that could occur “if the patent holder makes incomplete and ineffective changes to the test,” or “choose[s] not to innovate on his or her own test,” or “failing to provide notice that they will not enforce patents against research use or innovations made by others.” (p. 106). There is no evidence that any of these potential ill effects has materialized, nor does the Report indicate the likelihood that any ever would.

On page 58, the Report summarized an analysis by Huang and Murray by broadly stating that “gene patents decrease public genetic knowledge....” This is a grossly inaccurate distortion of the Huang and Murray analysis, which concluded that “follow-on genetic researchers forego about one in ten research projects ... through the causal negative impact of the gene patent grant.” The Report’s summary concludes that the genes subject to the gene patents would have been discovered even absent the patent incentive. The Report provides not even a scintilla of evidence supporting this unlikely conclusion, particularly for gene patents owned by the private sector, where patents are a primary research motivator.

Additionally, despite the lack of evidence of any negative impact of gene patents, the Report in several places explicitly or implicitly criticizes patents, either directly or through citation of literature. *E.g.*, 7:168-69 (mentioning “concern” that patents can be “too broad” with “overly broad claims”), 18:468 (characterizing as a mere “theory” the innovation effect of patents), 54:1400-01 (stating that “patents . . . have a significant negative effect on the ability of clinical laboratories to continue to perform already-developed genetic tests”), 56:1434 (referring to “problem” patents), 73:1890-91 (“[P]atents on the *BRCA* genes stifled further basic research.”), 106:2791 (patents can cause “a chilling effect on R&D”). Sometimes the Report even acknowledges the lack of evidence, *e.g.*, 73:1891-92, but then proceeds to make an amorphous, indefinite attack on patents nevertheless. *E.g.*, 73:1895-96 (stating that a patentee’s decision not to waive outright its ability to enforce its patent rights in the research context creates an “ambiguity” that “*may be a factor in stifling research to the extent that any research has been impeded*” (emphasis added)). This approach essentially treats patents as being guilty until proven innocent, which is quite curious given the long and successful record of patents as innovation motivators, which on occasion the Report does acknowledge. *E.g.*, 2:31-32 (“The role of patents in spurring innovation and investment in biomedical research is widely recognized and supported.”).

Patents Spur Innovation

Committee members noted that, even when based solely on the data in the report, the patent and patent licensing system appears to be self-correcting and favoring access, reasonable costs, and further development and innovation in genetic testing and related technology. The Report fails to give sufficient weight to the role of patents in innovation. Properly viewed, innovation has two components: (1) invention, and (2) commercialization and public distribution

³ *Id.*

of the invention. While patents effectively stimulate both components of innovation, it is the second component that would certainly suffer without the patent incentive. Commercialization requires economic incentive, which is often lacking absent exclusive patent rights. The Report fails to address the high probability that patents bring some genetic tests to the market that may not otherwise have been commercially available. Furthermore, the Report did not conduct a thorough survey of innovator companies to determine what effect a ban on gene patents would have on their current or planned R&D investments in genetic testing.

Patents to Genetic Discoveries Should Not Be Legislatively Weakened

Committee members were particularly concerned about some of the listed options related to statutory change. (pp. 122-123). Committee members agreed that both human and non-human genes are and should remain patentable subject matter. They almost universally disapproved of the Report's option of prohibiting patenting of genetic diagnostic tests (option B).

Likewise, the committee members disapproved of the option of withholding injunctive relief (option C). Such an option appears completely unnecessary after the Supreme Court's *eBay* decision, which will cause courts to refuse to grant injunctions when a patentee does not commercialize its patented genetic test and tries to prevent others from doing so as well.

While AIPLA supports legislation codifying an exemption from infringement under which uses of a claimed invention related to scientific, research or experimental inquiries are exempted from infringement,⁴ committee members also disagreed with the option exempting medical practitioners from liability for ordering, using, or performing diagnostic tests (option D). A much greater majority rejected the option of allowing related health care entities exemption from liability. The main concern is that such an option would greatly diminish the economic value of a patent, and thus reduce its innovation incentive.

Committee members disagreed that human health-related nucleic acid sequences should be limited to the utilities specified in the patent (option F1). Generally, a patent need not set forth all of the utilities for a particular invention. The Report does not demonstrate why this particular type of invention should be singled out for different treatment. The question of whether a particular claim covers a particular application should be determined on a case-by-case basis using well-established procedures for determining literal infringement and infringement under the doctrine of equivalents. Furthermore, the stringent written description and enablement requirements applied to biotechnology-related inventions likely already address any concern that option F1 was intended to address. Further, care must be taken not to adopt rules that discriminate against patent protection for specific technologies, which is prohibited under Article 27.1 of the TRIPS Agreement. Thus, the rules are in place. But, AIPLA acknowledges that for better implementation of those rules the USPTO requires sufficient funding in support of better training for patent examiners, which in turn will result in more robust examination.

Committee members also disagreed with prohibiting patents on processes using human health-related nucleic acid sequences for diagnostic purposes (option F2) and prohibiting patents on human health-related nucleic acid sequences (option F3). Such drastic changes may cause

⁴ AIPLA Past Action Manual, Board Resolution 230-06, March 17, 2005.

serious adverse impact on the drug and biotechnology industries. Absent any data supporting either the necessity or advisability of such patenting prohibitions, we strongly oppose any such measures.

No New Legislation is Necessary Given the Requirements of 35 U.S.C. §§ 101, 102, 103, and 112

Contrary to the strong undercurrent in the Report that gene patent legislation is needed, the existing statutes, as interpreted by the patent examiners and the courts, already provide the necessary checks and balances. Additional legislation is not needed. This observation is supported by recently decided cases such as *In re Bilski*, 545 F.3d 943 (Fed. Cir. 2008), *In re Kubin*, No. 2008-1184 (Fed. Cir. Apr. 3, 2009), *Ariad Pharmaceuticals, Inc. v. Eli Lilly and Co.*, No. 2008-1248 (Fed. Cir. Apr. 3, 2009), and *In re Gleave*, No. 2008-1453 (Fed. Cir. Mar. 26, 2005).

The 2008 decision in *Bilski* presented further guidance for interpreting the utility statute, 35 U.S.C. § 101. While *Bilski* addressed the patentability of business methods, it has implications for diagnostic, prognostic, and other medical determination step claims. Some of these medical methods include genes or probes in their claim language, and some do not. These method claims must meet the requirements of the machine-or-transformation test set forth in *Bilski*.⁵ Additionally, diagnostic method claims are currently under consideration by the Federal Circuit in at least *Prometheus v. Mayo*, Federal Circuit No. 2008-1403.

Turning to *In re Kubin* and *In re Gleave*, these cases directly addressed issues of patentability under the obviousness and novelty statutes, 35 U.S.C. §§ 103 and 102, respectively. The Federal Circuit on April 3, 2009 held that the prior art disclosing a monoclonal antibody that bound to the human protein, a murine homolog, and general molecular cloning techniques⁶ rendered the human homolog to the gene and its corresponding protein obvious even though none of the references disclosed the DNA or protein sequence for the human p38 (NAIL) protein.

In *In re Gleave*⁷, the Federal Circuit found bispecific antisense oligodeoxynucleotides both anticipated and obvious in view of the known nucleic acid sequence of the gene, and a teaching listing all the sense 15-mer oligonucleotides, together with a statement regarding the antisense sequence facilitating the oligonucleotides binding to the complement. The Court came to this conclusion, even though the reference did not disclose what the antisense compounds could bind to and inhibit.

Finally, 35 U.S.C. § 112, first paragraph, requires that the invention as claimed have sufficient written description to place the public in possession of all that is claimed and to enable one to practice the invention. Expressed Sequence Tags (ESTs) were determined to be not patentable for lack of utility (35 U.S.C. §101) and for failing to have sufficient description for their use (enablement). The fears that ESTs would prevent researchers from patenting complete genes never materialized due to existing statutory constraints.

⁵ *In re Bilski*, 545 F.3d 943, 954-956 (Fed. Cir. 2008).

⁶ Joseph Sambrook et al., *MOLECULAR CLONING: A LABORATORY MANUAL* 43-84 (2nd ed 1989).

⁷ *In re Gleave*, No. 08-1453 (Fed. Cir. Mar. 26, 2009).

As recently as April 3, 2009 in *Ariad Pharmaceuticals, Inc. v. Eli Lilly and Co.* (No. 08-1248), the Federal Circuit reiterated that the inventors were not entitled to claim all inhibitors of NF- κ B, because their specification failed to provide any examples of NF- κ B inhibitors, and thus did not place the public in possession of the invention *as claimed*. The specification only disclosed three classes of compounds (*i.e.*, specific inhibitors, dominantly interfering molecules, and decoy molecules), which the inventors asserted could inhibit NF- κ B; however no examples of NF- κ B inhibitors were provided. Thus, the Federal Circuit held the claims invalid as failing to provide a sufficient written description as required by § 112, first paragraph.⁸

In *University of Rochester v. G.D. Searle & Co.*, (358 F.2d 916 Fed. Cir. 2004), the Federal Circuit found that the University of Rochester patent failed to satisfy both the written description and enablement requirements of § 112, first paragraph. Here, the claims were directed to methods for selectively inhibiting PGHS-2 gene activity in a human by administering a non-steroidal compound that selectively inhibited the activity. Again in this instance, the specification failed to provide any examples of PGHS-2 inhibitors and failed to meet both the enablement and the written description requirements and accordingly, the claims were held invalid

These cases are representative of courts' interpretations of the patent statutes with regard to biotechnology and specifically, nucleic acid sequences. The patent statutes, especially 35 U.S.C. §§ 101, 102, 103, and 112, first paragraph, offer the requisite framework to promote innovation, while properly constraining the innovator from overreaching.

Conclusion

We believe that the SACGHS has undertaken an important and timely endeavor with this Report, which reflects an initial effort to study the effects of patenting and patent licensing on the development, availability, and costs of genetic testing. However, it is apparent that much more research should be conducted, particularly into what effects some of the more drastic legislative options would have to future development and commercialization of genetic tests before any further steps can be taken or any recommendations can be made. Until then, the anti-patent conclusions and implications of the Report should be revisited before it is finalized.

We appreciate the opportunity to provide comments on the draft Report and are available to assist the SACGHS in further developing it.

Sincerely,



Teresa Stanek Rea
President, AIPLA

⁸ Given that these decisions are recent, the parties may seek to appeal their decision to the U.S. Supreme Court, or have an *en banc* review of the decision by the Federal Circuit in *Kubin*, *Gleave*, and *Ariad*.