

KEI Response to Federal Register Notice, [Docket No.: PTO-P-2012-0003]
Request for Comments and Notice of Public Hearings on Genetic Diagnostic Testing

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I Introduction

Knowledge Ecology International (KEI) is a non-profit, non-governmental organization that searches for better outcomes and new solutions to the management of knowledge resources, particularly in the social justice context. Among other areas, KEI has expertise in access to the economic, legal and human rights aspects of innovation, and access to knowledge and medical technologies, including diagnostic testing.

There is extensive evidence that the practice of patenting and exclusive rights to use inventions involving human DNA and more generally patents on diagnostic testing present barriers to the development of and access to new medical technologies.

The granting of patents with the exclusive rights on human DNA and other aspects of diagnostics is typically justified as a necessary measure to promote investments in R&D.

In addition to other policy questions, such as the ratio of costs to the benefit of granting patents and exclusive rights in diagnostic patents, USPTO should address these two questions:

1. Are there better ways to reward investors in diagnostic inventions than the grant of patents, such as, for example, by creating prize funds that are resourced by third party insurance reimbursement systems?
2. For the many cases where products involve multiple patented inventions, should the United States amend its patent law to provide for compulsory licenses of dependent patents or follow-through inventions on diagnostics?

It is increasingly costly and indefensible for policy makers to act as if the systems of exclusive rights in patents is the only possible mechanism to stimulate private investments in R&D for medical technologies. Such a comparison only pits one systems of incentives against a regime of no incentives; it ignores possible alternatives or reforms that would do better in terms of promoting both innovation and access.

II. Innovation inducement prizes

We have collected links to research on innovation inducement prizes at <http://keionline.org/prizes>. Note that the World Health Organization (WHO) has called upon governments to experiment with prizes as a way of de-linking R&D costs from prices of products, and there is currently considerable interest in the use of prizes to stimulate investments in low cost diagnostics for Chagas disease, Tuberculous and fever.

III. Compulsory Licensing of Patents

Perhaps of greater relevance to the USPTO is the issue of compulsory licensing of patents on diagnostic technologies. There is in fact extensive experience with compulsory licensing for patents globally, including within the United States, and in both high income and developing countries. Outside of the United States, Roche has sought compulsory licensing on diagnostic patents held by Chiron in Germany for a test involving HIV/AIDS, and several countries in Europe and Canada considered compulsory licenses on the patents on the BRCA1 and BRCA2 patents.¹ During the controversy over the BRCA1 and BRCA2 patent on diagnostics, Belgium, France and Switzerland amended their patent laws to make it easier for the government to grant compulsory licenses on patents on diagnostic tests, and Canada threatened to grant compulsory under its patent law.

In the United States, the Department of Energy conducted march-in cases for the FISH patents related to the test for HER2+ breast cancer, which led to a license being granted to the plaintiff in the march-in case, and Abbott Laboratories obtained a compulsory license to an Innogenetics patent for a method of genotyping the hepatitis C virus, marketed in the form of diagnostic test kits.²

To the extent that patents are relied upon to reward private investments in R&D on diagnostic tests, the USPTO should evaluate whether or not the appropriate protection should be one of exclusive rights, or a system that relies more on compulsory licensing, including by implementing patent rights on diagnostics as part of a liability rule regime that awards rights to remuneration, rather than the exclusive rights to use an invention.

KEI suggests the USPTO consider in particular the following proposal for a liability rule. That anyone be allowed to use any patented invention to make and sell a medical diagnostic test or service, if the manufacturer of the diagnostic test or the provider of the patented testing service pays a royalty of [ten or another number] percent of its revenue into a fund that will be distributed to patent owners by the USPTO or its designee. Under such a system, the manufacturer would have the option of negotiating a royalty for a lesser amount than paying the statutory rate, to satisfy all patent claims. This would work in a way similar to the statutory license on the copyright in music compensations. Legally, such a system could be implemented under the flexibility provided in Article 44.2 of the TRIPS, as a limit on the remedies for

1 James Love, Recent examples of the use of compulsory licenses on patents, KEI Research Note 2007:2

2 Anne Mira Guha. U.S. Compulsory licensing of medical inventions as a limit on remedies under *eBay v MercExchange*. <http://keionline.org/node/862>

infringement of a patent.³

The benefits of the liability rule approach are that it would (1) eliminate the high transaction costs, including time and money, for negotiating patent licenses, (2) ensure open non-discriminatory access to new technologies, and (3) reduce the monopoly power of the patent owners. The last point is quite important for expanding access to diagnostic tests, and the USPTO would need to consider if the reduced monopoly power was a net benefit, given the public interest in inducing investments. In such a system, the USPTO could provide the possibility of a patent owner making a case to be exempt under from the liability rule, if the patent owner could provide evidence that such an exemption was necessary to induce sufficient investment in R&D in a new diagnostic test, and that the patent owner would otherwise protect the public interest, such as by pricing the invention at an affordable price, and accommodating follow-on innovations.

IV. Notes on the American Molecular Pathology v. Myriad Genetics litigation

The following comments are largely a summary of arguments that KEI has made in a January 13, 2012, amicus brief to the Supreme Court of the United States in the case, *Association for Molecular Pathology, et. al. v. Myriad Genetics, Inc., et. al.*, Docket No. 11-725.⁴

In *American Molecular Pathology v. Myriad Genetics*, patents were filed on two genes, known as the BRCA1 and BRCA2, associated with an individual's susceptibility to breast cancer. Women who have a mutation on one of these two genes are approximate 80 percent more likely to develop breast cancer during her lifetime. The genes were isolated and discovered through federal funding from the National Institute for Environmental Health Sciences, a subdivision of the National Institutes of Health, at the University of Utah. The University of Utah subsequently patented the BRCA1 and BRCA2 genes and exclusively licensed them to Myriad Genetics.

Myriad Genetics then developed a diagnostic test to identify mutations of the BRCA1 and BRCA2 genes. Although other researchers have either tried or expressed interest in developing their own tests, Myriad has sent cease-and-desist letters to prevent researchers from doing so and has also prevented clinics from providing second opinion testing. Exclusive rights over these genes has permitted Myriad to price their test at a monopoly price, which many patients cannot afford and a number of insurance companies do not cover because of the price.

In addition to the monopoly pricing over its diagnostic test, Myriad's diagnostic was found to have a high error rate. One study published in the Journal of National Cancer Institute reported that Myriad's test failed to find up to twenty percent of *known* BRCA1 mutations.⁵ Another study found that the test at times also failed to correctly identify the mutations it was intended to

3 This flexibility has been preserved in the ACTA, but is not included in the USTR proposals to the TPPA IPR chapter.

4 <http://keionline.org/node/1347>

5 Steve Benowitz, French Challenge to BRCA1 Patent Underlies European Discontent, 94 J.Nat'l Cancer Inst. 2, 80 (2002).

find, with a twelve percent error rate.⁶ Minority women fared even worse in this study as the error rate was higher for them than for women of Caucasian descent.

Patents and exclusive rights over human DNA harms patient access to affordable, quality testing

Using the *Myriad* case as an example, the negative effects of exclusive rights over human DNA and genes on patients and public health is evident. Patenting and exclusive licensing impacts the availability of genetic testing, both primary and secondary testing. In the *Myriad* example, some insurance companies do not cover *Myriad*'s BRCA testing because of the high price; half of all state Medicaid programs, for example, do not cover BRCA testing. The monopoly price of the comprehensive test, which can be more than \$4,000, is cost prohibitive for many women thus impacting their access to primary testing.

The failure to correctly find known mutations and significant error rate harms patients, particularly when they cannot receive a second opinion. Providing a test known to be flawed when better tests could be developed and administered is a disservice to the public health. Although *Myriad* now offers an additional test, known as BART testing, to find mutations not covered by their original test, this additional diagnostic might not have been realized without the research of other scientists. Greater research and development would help provide a greater understanding of targeted genes, thus improving testing and treatment for patients.

DNA patents and exclusive licensing harms future innovation

In addition to harming patients by not permitting second opinion testing, patents and exclusive rights prevent future research and development. In the case of the BRCA1/2 genes, the full extent of the function of the targeted DNA is still unknown. It is difficult to predict what other uses the BRCA1/2 genes could have, not just for identifying mutations associated with breast and ovarian cancer, but for other genetic diseases. Some studies have shown that the BRCA1/2 patents would broadly preempt a range of genetic tests, including those not directly related to BRCA1/2 research or breast or ovarian cancer.⁷

Exclusive rights over DNA effectively forecloses all uses of the DNA and such patents are notoriously difficult, if not impossible, to invent around.⁸ We note that the constitutional rationale of the patent system is to “promote the Progress of Science and useful Arts.” Inducement to invest and the promotion of future progress is an essential element to a functioning patent system. Thus, where a patent fails to serve the purported goal, as is the case where an exclusive right hinders rather than promotes progress, serious consideration must be given as to the wisdom of granting such rights.

6 Tom Walsh, et. al., Spectrum of Mutations in BRCA1, BRCA2, CHECK2, and TP53 in Families at High Risk of Breast Cancer, 295 JAMA 1369, 1386 (2006).

7 Thomas B. Kepler, et. al., *Metastatisizing patent claims on BRCA1*, Genomics, May 2010.

8 See Isabelle Huys, et. al., *Legal Uncertainty in the Area of Genetic Diagnostic Testing*, 27 Nature Biotechnology 903, 907 (2009) (noting that one of *Myriad*'s patent was a “blocking patent” that was “almost impossible to circumvent.”)

A report completed by the Department of Health and Human Services Advisory Committee on Genetics, Health, and Society concluded that DNA patents were not necessary to provide incentives for research or the development of clinical testing. Francis Collin noted that, “the supposed need to provide an incentive for companies to develop DNA diagnostics is unconvincing. Researchers and companies do not need additional incentives to commercialize genetic knowledge.”

Knowledge of the purpose of particular DNA, as well as the existence of mutations, are critical facts that are used to develop diagnostics and treatments. Patents over DNA, such as the BRCA1/2 patents dramatically restricts the ability of future researchers to use these discoveries in the interest of promoting public health. The BRCA1 and BRCA2 patents have not led to greater knowledge, but rather, has lead to a decrease in information concerning these genes. A163, A2672-74, A7271-73

For example a study on the effect of DNA patents on the disease haemochromatosis found that further development on the genetic disease dropped thirty percent when a patent was granted on the gene.⁹ Another study, conducted by one of the plaintiffs in the *Myriad* case, found that fifty-three percent of laboratory directors in the United States decided not to develop a new clinical test because of an existing patent or exclusive license, and sixty-seven percent believed that such exclusive rights over DNA decreased their ability to conduct research.¹⁰ DNA patents thus represent blocking patents that create patent thickets, thereby preventing further research and decreasing knowledge and information on the targeted DNA. Such patents may detrimentally affect the future of genomic testing and personalized medicine.

It should be noted that the Supreme Court of the United States recently issued a unanimous decision invalidating patents that related to Prometheus Laboratories’ diagnostic test that measured metabolites to determine appropriate treatment dosage for certain autoimmune diseases. The Court’s decision in *Mayo v. Prometheus Laboratories*, repeatedly stressed the “concern that patent law not inhibit further discovery by improperly tying up the future use of laws of nature.” The Court noted the danger of granting patents that will inhibit future innovation and impeding the flow of information.

Non-patent mechanisms to induce and reward research and development

Patents and exclusive licensing may not be the most appropriate mechanism to reward isolation and identification of DNA sequences. Numerous non-patent mechanism exist to induce investment and reward research and development. These mechanisms can provide a superior alternative to the current practice of patents and exclusive licensing over DNA.

Cash innovation inducement prizes, for example, may be a more appropriate mechanism to stimulate research in this area. Prizes can provide a more efficient alternative to promote innovation in this field because they would not create the barrier of a patent but still reward investment. As noted above, DNA patents represent basic information and such patents preempt

9 Matthew Herder, Patents & The Progress of Personalized Medicine: Biomarkers Research as Lens, 18 Ann. Health L. 187, 209-211(2009)

10 A2672-73

all other uses, thereby foreclosing research and development. Exclusive rights therefore represent an inefficient, burdensome and inappropriate reward, and other reward mechanisms should be considered to permit further innovation.

Additional alternative mechanisms, including the range of *sui generis* protections that exist in the United States to protect investments in research and development, may also be considered. Some alternate mechanisms are listed in the amicus brief of Knowledge Ecology International.¹¹

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Krista Cox, Knowledge Ecology International
March 26, 2012

11 Available at <http://keionline.org/node/1347>