American College of Medical Genetics
Medical Genetics: Translating Genes Into Health™

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Steven Teutsch, MD, MPH
Chair, Secretary's Advisory Committee on Genetics, Health, and Society
National Institutes of Health
Office of Biotechnology Activities
6705 Rockledge Dr.
Suite 700
Bethesda, MD 20892

Dear Dr. Teutsch:

RE: **Public Consultation Draft report on Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests**

The American College of Medical Genetics (ACMG) is grateful for the opportunity to comment on the recent "SACGHS Public Consultation Draft Report on Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests" on which public comment is being sought. The mission of ACMG is to define and promote excellence in medical genetics practice and the integration of translational research into practice; promote and provide medical genetics education; increase access to medical genetics services and integrate genetics into patient care; and to advocate for and represent providers of medical genetics services and their patients. As such, our members have significant interest in how gene patenting influences patient access to genetic tests. ACMG has had a position since 1999 that genes are naturally occurring substances that are not patentable but that, if they are allowed to be patented, should be subject to fair and nonexclusive licensing agreements.

While the patent system is greatly valued for its goal of protecting intellectual property to encourage investments that promote good outcomes for the public, it is ACMG's view that issues of medical practice warrant special consideration. There are significant "practice of medicine" issues involved with genetic testing for which monopolies on a medical service should not be allowed. In high investment areas such as the development of therapeutics, patents are critical to the long and expensive process of bringing a product to the marketplace. However, genetic tests are typically are well- developed and being delivered BEFORE patent holders seek to control the

testing. Therefore, it is self-evident that gene patents are NOT required to stimulate the development of tests. In the current system, the patents have served only to generate profits for patent and exclusive license holders and to limit access to tests because of high costs.

In general terms, the ACMG appreciates the thorough review of the literature and the case studies to support the recommendations to be made by the SACGHS. However, there are premises made that should be considered when arriving at the Committee's final recommendations. A recent publication by CM Holman is referenced as providing data indicating that the limited evidence of gene patent litigation implies community acceptance. ACMG believes that this is not a true and complete assessment of the situation. It is important to realize that the costs of challenging a gene patent to the point when the merits of the case are decided is typically $1.5 million to $3 million. This fact is well known among those who provide genetic testing and for the great majority, particularly those in academic environments, the cost of litigation precludes their ability to consider a challenge against a well-resourced corporation. It is also important to realize that only a relatively small proportion of patents on genes are enforced. Nearly always, the genes are associated with rare genetic diseases for which there is little incentive to engage in enforcement. This conclusion is evidenced by the remarkably few genes that have been developed into products as testing kits and devices by the manufacturing sector. It is only when a particular gene test becomes useful to a large segment of the population, as occurs in carrier screening, that financial interests justify to the patent holder's their interests in enforcement against those perceived to be infringing their patent.

Pricing of tests is often used as evidence that the patents have had no direct impact on cost and, hence access. It is important to realize that billing of genetic tests is largely based on the general methodologies used rather than on the specific genes being tested, so there is no inherent reason to expect that tests held under patent but performed using similar methodologies will be significantly different in price. In this circumstance, comparison to costs in countries with payment systems that are better aligned with actual costs rather than historical reimbursement rates might be more informative.

Monopolies on Medical Procedures

The ACMG remains concerned that monopolies on genetic tests stifle competition for quality. Examples in the SACGHS report, such as that of the test for long QT syndrome (LQTS), highlight the reality of this concern. Competition for cost also remains a concern. While it may be possible to show that genetic tests done on a disease-by-disease basis aren't significantly different in cost, it is in the transition to multiplexed and high throughput low cost whole genome analysis that cost would be expected to become a significant issue.

Practice of Medicine Issues

There have been several instances in which patented genes have had significant impact on the practice of medicine.

- The SACGHS report highlights the withholding of medical information from the scientific and medical literature in the case of LQTS testing. This behavior had direct implications for patients seen during the period when such information was withheld from physicians.

- There have been situations in which the terms of licensing agreements with the patent holders have prescribed national medical practices. The volume limits placed on the laboratories that offered Canavan disease testing led laboratories to change from couple-based testing that provided results to both members of a couple being screened for carrier status to less thorough sequential screening in which the second parent was only tested if the first parent lacked one of the common mutations for which testing was available. This occurred despite the fact that the tested individual still had a residual risk of being a carrier that would go untested.

- Monopolies on gene tests preclude the ability of an individual to seek an independent confirmatory test or second opinion. For genes such as the *BRCA1* and *BRCA2* for which abnormal results can lead to patient deciding about life-altering interventions such as double mastectomies, the inability to seek an independent confirmation is treated quite differently than would be a similar decision based on, for example, results from imaging.

- The move to new technologies is being significantly impacted by gene patents. In the 1960s through the 1980s, chromosome analysis was among the most common of genetic tests. This provided whole genome analysis, but at very low resolution. Many genes were identified by virtue of gains or losses of parts of the human genome. In the subsequent years genetic testing shifted to tests on a gene-by-gene basis as directed by clinical presentations of patients. During this period genes were being identified individually and patented. We have now come full circle with whole genome analysis at very high resolution. Unfortunately, laboratories offering tests such array-comparative genomic hybridization are now asked to ignore parts of the human genome that are held under patent rights. It is absurd to consider that laboratories have been told by their own legal counsel that they can leave the markers in their tests of the whole genome but cannot tell a patient when a copy number variation of clinical significance is identified, whether or not found prior to the onset of disease-specific symptoms.

- Individuals with diseases such as hearing loss or LQTS for which multiple genes are involved are unable to obtain a single test to address their questions of genetic etiology. Fractionating clinical testing increases all of the risks related to specimen handling. The absurdity reaches new heights in the context of high-density whole genome analysis where an enormous number of genes and markers must be considered.

- Genes do not operate independently and clinically interpreting gene test results is not straightforward. For some genes, the first gene found may be held under one patent while the modifying genes that alter expression of the first gene or the severity of the disease may be held separately. Of particular concern are the genetic testing situations in which patients may not have one of the well understood genetic variations that provide information much like any laboratory test. When rare or unknown sequence variation is found and its clinical significance must be determined, we shift into a classical practice of medicine in which genetic and clinical information from multiple family members must be assessed and individualized decisions must be made by clinicians about the clinical implications for the patient and their family. Physicians placed in this situation are limited in their ability to practice independently if they cannot obtain comprehensive testing and do not have access to databases that document the pathogenetic significance of specific genetic variants.

- Genetic tests are commonly used for more than one indication. However, some tests held under monopolies by virtue of patent rights may not be offered for all indications. For instance diagnostic testing for spinocerebellar ataxia (SCA) is held under such a monopoly while prenatal testing for this disorder is not. Since diagnostic testing is run in much higher volume than is prenatal testing, laboratories that are restricted to only prenatal testing acquire much less day-to-day experience with the genes of interest. This is particularly problematic when critical decisions are being made on prenatal test samples.

- Genetic tests that are held under monopolies can limit access by virtue of the reimbursement systems accepted by the laboratory. Some will not bill state Medicaid for reimbursement, thereby requiring patients to pay the fees and subsequently seek their own reimbursement. Many can not do so.

Given the concerns we have expressed above, we remain opposed to gene patenting and the potential for monopolies of that health care service. Since we consider genes and their mutations to be naturally occurring substances whose maintenance in the population is driven by classical means of natural selection we do not think they are patentable. If ultimately held to be patentable, there are alternative compromises but none as comprehensive as would occur if genes were not patented in the first place.

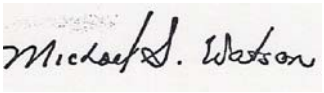
Under the Bayh-Dole Act, NIH retains the rights to “march-in” to require fair practices. However, this solution would be exercised on a gene by gene basis and, therefore, would be exceedingly inefficient.

Under the Ganske-Frist amendments that blocked physicians who infringe a patent in the course of the practice of medicine from being held subject to damages for such infringement, genetic testing was, in principle, exempted from this protection. Removal of this exemption would allow genetic testing to be considered under the practice of medicine in the same way that other medical procedures are considered.

Interestingly, one of the most common forms of genetic testing, newborn screening for treatable genetic diseases, is not subject to patent enforcement. Under the Florida Tuition Fund case, it was found that enforcement of a patent against a state offering screening under its public health mandates would violate the state's sovereignty. This finding applies to those providers and laboratories in the diagnostic community who are in states in which the state has business agreements to follow up the patients who have positive screens but not to those in states that essentially refer the patients into the private sector without such business agreements in place.

We appreciate the thorough assessment and the opportunity to comment on this SACGHS draft report.

Sincerely,



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