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PhRMA

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VIA EMAIL: genetest@uspto.gov

Office of Chief Economist
United States Patent and Trademark Office
Mail Stop External Affairs
P.O. Box 1450
Alexandria, VA 22313-1450

Attention: Saurabh Vishnubhakat, Attorney Advisor, Office of Chief Economist

Dear Mr. Vishnubhakat,

I am writing on behalf of the Pharmaceutical Research and Manufacturers of America ("PhRMA") to convey the views of PhRMA's members in response to the "Request for Comments and Notice of Public Hearings on Genetic Diagnostic Testing," 77 Fed. Reg. 3748 [Docket No. PTO-P-2012-0003]. PhRMA's members are leading pharmaceutical research and biotechnology companies devoted to researching and developing new medicines to allow patients to live longer, healthier and more productive lives. PhRMA's members lead the way in finding cures and new treatments as well as in developing critically important improvements in existing therapies. Patent protection is an important incentive to promote the innovative research necessary for such advances and to make available to society the benefits of that research.

The enclosed comments include views of PhRMA's members on the subject matter discussed in the notice. PhRMA's members appreciate the PTO seeking comments in the area, and would welcome further dialogue with the PTO on the issue.

Please feel free to contact me if you have any questions.

Sincerely,

David E. Korn

Enclosure

Comments of the Pharmaceutical Research and Manufacturers of America in Response to the Request for Comments and Notice of Public Hearings on Genetic Diagnostic Testing

The Pharmaceutical Research and Manufacturers of America (PhRMA) files these comments in response to the United States Patent and Trademark Office's (PTO's) above-referenced notice. PhRMA represents the country's leading pharmaceutical research and biotechnology companies, which are devoted to inventing medicines that allow patients to live longer, healthier, and more productive lives. PhRMA companies are leading the way in the search for new cures. PhRMA members alone invested an estimated $49.4 billion in 2010 in discovering and developing new medicines.

The America Invents Act requires the PTO to prepare and submit to Congress a study and recommendations regarding independent second opinion genetic diagnostic testing where patents and exclusive licenses cover primary genetic diagnostic tests. Congress specifically mandated that the PTO examine: (1) the impact that the current lack of independent second opinion testing has had on the ability to provide the highest level of medical care to patients and recipients of genetic diagnostic testing and on inhibiting innovation to existing testing and diagnoses; (2) the effect that providing independent second opinion genetic testing would have on the existing patent and license holders of an exclusive genetic test; (3) the impact that current exclusive licensing and patents on genetic testing activity has on the practice of medicine; and (4) the role that cost and insurance coverage have on access to and provision of genetic diagnostic tests. The PTO has requested general comments on independent second opinion genetic diagnostic testing and its relationship to medical care and medical practice, the rights of innovators, and medical costs and insurance coverage, as well as input on fourteen specific questions provided in the above-referenced notice.

PhRMA members are increasingly engaged in personalized medicine research. Up to half of our member company pipelines involve personalized medicines, not only for cancer treatment but also in other therapeutic areas, including cardiovascular diseases, central nervous system conditions, immunology, virology, and metabolic and respiratory therapies. We offer the comments below from the perspective of research-based biopharmaceutical companies engaged in the development of new drugs and biologics that may be used in conjunction with diagnostic tests in the context of personalized medicine or that may be developed concurrently with diagnostic tests. Some of our members that develop or co-develop genetic diagnostic tests may be commenting separately from that perspective.

Comments

To foster continued economic growth and deliver the new breakthroughs that are needed to address the most complex and costly diseases and lower health care costs, PhRMA members rely on public policies, including an intellectual property regime that encourages and protects innovation. Given the importance of strong intellectual property rights to continued innovation in medicine, PhRMA provides the following comments.

Rather than responding to any of the specific questions proposed by PTO in its Federal Register notice, we address below four issues that we believe the PTO should take into account as it explores independent second opinion genetic testing and prepares its recommendations to Congress. These are: *first*, the importance of fostering the development of personalized medicine; *second*, the paramount need for robust protection of intellectual property in order to ensure continued innovation in personalized medicine; *third*, the need for the PTO to examine coverage and reimbursement issues as part of its work in this space; and *fourth*, the need for PTO to consider the nature, purpose, and appropriate role of independent second opinion genetic testing before making any recommendations.

First, we urge the PTO to begin by recognizing the importance of fostering the development of personalized medicine.

Broadly speaking, personalized medicine is the tailoring of medical treatment to the individual characteristics of each patient.[1] Often, personalized medicine involves the use of genetic and genomic information to predict an individual's disease susceptibility, disease course, and response to treatment.[2] Personalized medicine can entail use of this information to increase the likelihood of improved health outcomes through targeted therapies; reduce the probability of adverse events from therapies; monitor therapy response; improve therapy dosing; prevent and predict disease; and intervene earlier in the course of a disease.[3] Personalized medicines not only improve health outcomes for individual patients, but also have the potential to resolve inefficiencies in the health care system, such as trial-and-error dosing, unnecessary hospitalizations (e.g., due to adverse drug reactions), late diagnoses, and reactive treatments.[4]

The research-based biopharmaceutical industry is very actively engaged in personalized medicine research. A recent survey by the Tufts Center for the Study of Drug Development found, for example, that 94 percent of the biopharmaceutical companies it surveyed were investing in personalized medicine research.[5] Moreover, 100 percent indicated they were using biomarkers in the discovery stage to learn more about promising compounds.[6] The research-based biopharmaceutical industry is increasingly focused on a branch of personalized medicine called "pharmacogenomics," generally understood as the "study of variations of DNA and RNA characteristics as related to drug response."[7] Pharmacogenomic-guided therapy usually involves

[1] President's Council of Advisors on Science and Technology, *Priorities for Personalized Medicine* (September 2008) at 1, *available at* http://www.whitehouse.gov/files/documents/ostp/PCAST/pcast_report_v2.pdf.
[2] Duke Medicine & US News & World Report, *Personalized Medicine* (March 20, 2012), *at* http://health.usnews.com/health-conditions/cancer/personalized-medicine.
[3] *Id.*
[4] Personalized Medicine Coalition, *The Case for Personalized Medicine* (3d ed) at 4, *available at* http://www.personalizedmedicinecoalition.org/sites/default/files/files/Case_for_PM_3rd_edition.pdf.
[5] Tufts Center for the Study of Drug Development. Personalized Medicine is Playing a Growing Role in Development Pipelines. Impact Report no. 12 (Nov. /Dec 2010):6.
[6] *Id.*
[7] FDA, Guidance: E15 Definitions for Genomic Biomarkers, Pharmacogenomics, Pharmacogenetics, Genomic Data and Sample Coding Categories 3 (Apr. 2008).

use of a diagnostic test to test a patient for a particular genomic feature, followed by treatment with a drug, device, or biologic based on the test result.

Pharmaceutical companies contribute to the development of diagnostic testing in several ways. In the very early stages of drug development, pharmaceutical companies invest in the development of assays to better understand the mechanism of action of lead compounds and therefore the patient populations most likely to benefit. As part of the development process, these tests may be used or further improved during clinical trials to better understand opportunities for personalized medicine applications of new medicines. Companies incorporate genetic diagnostic tests into study protocols for clinical trials of drugs and biological products. The data collected from these clinical studies are used to support validation of the laboratory tests, which may be incorporated into applications to FDA for marketing clearance or approval of the diagnostic test or in-vitro diagnostic product. Pharmaceutical companies also may co-develop the tests that will be used with their new drugs, or partner with diagnostic device companies and clinical laboratories to develop tests or tailor tests for personalized medicine use.

Society has a profound interest in the continued development of personalized medicines as the scientific potential for making progress against some of the most complex and costly diseases and conditions has never been greater. We urge the PTO to keep the promise of personalized medicine in mind when exploring the role of independent second opinion genetic testing and when developing its recommendations for Congress.

Second, we ask that PTO keep in mind the importance of fostering continued medical innovation particularly in personalized medicine through appropriate intellectual property protections.

PhRMA members face significant challenges in their development of new medical treatments. The process of taking a promising compound from initial discovery stages through early stage research, clinical testing, and marketing authorization is risky, expensive, and time consuming. Recent estimates place the average cost at over $1 billion for a new medicine and suggest the process can take 10 to 15 years.[8] Only 1 out of up to 10,000 potentially promising compounds result in an FDA approved medicine.[9]

Adequate protection of the intellectual property generated during this process is critical for fostering the substantial investments needed. Patents in particular have proven essential to allow industry to realize the benefits of their significant investments. Patents not only help stimulate the early-stage discovery and development of new medical treatments, but also

[8] Joseph A. DiMasi and Henry G. Grabowski. *The Cost of Biopharmaceutical R&D: Is Biotech Different?*, 28 MANAGERIAL & DECISION ECON. 467-79, 470 (2007); *Drug Discovery and Development: Understanding the R&D Process*, INNOVATION.ORG (PhRMA, Washington, DC), Feb. 2007, at 1-2.

[9] Pharmaceutical Research and Manufacturers of America, Pharmaceutical Industry Profile 2011 (Washington, DC: PhRMA, April 2011) at 12, *available at* http://www.phrma.org/sites/default/files/159/phrma_profile_2011_final.pdf.

safeguard a company's ability to carry out the lengthy and costly clinical trials that are essential to ensure that those treatments are safe and effective.[10]

Personalized medicine research and development, although very promising, may present even more challenges, costs, and risks than traditional biopharmaceutical research and development. The Tufts study report notes, for example, that personalized medicine research requires additional investment in technologies associated with target validation, early toxicology markers, and micro-sequencing. Companies also need to invest capital in the development of protocols to efficiently validate biomarkers and to conduct clinical trials for personalized medicines. In some cases, companies are co-developing pharmaceutical products with companion diagnostics, which leads to additional challenges. These challenges stem from the need to coordinate research and development efforts and secure regulatory approval for an integrated therapeutic approach involving the pharmaceutical product and companion diagnostic.

To the extent that the PTO's questions consider innovation incentives surrounding primary genetic testing, it is important to use intellectual property rights to stimulate and reward the development of innovative new primary tests. Patents provide time limited exclusivity rights over subject matter that passes into the public domain upon patent expiration. Thus, it would be unwise to disincentivize innovation of primary tests in the short term because there will be less to pass into the public domain in the longer term.

In view of the critical role of intellectual property protection in incentivizing the continued development of personalized medicines, PhRMA requests that the PTO's recommendations to Congress will support the robust protection of all forms of intellectual property relevant in this space. The absence of robust patent protection could have profoundly adverse implications for personalized medicine, to the detriment of innovation and the public health. We are concerned that recommendations relating to remedies that are akin to a compulsory license could also have profound implications for innovation and the public health. We are also concerned that any weakening of patent protection could discourage the use of patents as companies' primary means of protection, which would remove the benefit that accrues to society from disclosure of the invention — specifically, the stimulation of additional research and discovery by third parties.

Third, we suggest that the PTO examine coverage and reimbursement issues.

Health insurance is important to ensuring patient access to the full range of health care services, including prescription medicines and new technologies such as genetic diagnostic testing. AdvaMed and the Personalized Medicine Coalition as well as others have cited the need

[10] *See* Claude Barfield and John Calfee. *Biotechnology and the Patent System: Balancing Innovation and Property Rights*, AEI PRESS, at 1-2 (2007). ("Without patent protection, potential investors would see little prospect of profits sufficient to recoup their investments and offset the accompanying financial risk."); Edwin Mansfield, *Patents and Innovation: An Empirical Study*, 32 MGMT. SCI. 2, at 174-75, T.1 (Feb. 1986) at 173-181 (estimating that without patent protection, 65 percent of pharmaceutical products would never have been brought to market, while the average across all other industries was a mere 8%); *see generally* Henry Grabowski, *Patents, Innovation and Access to New Pharmaceuticals*, 5 J. OF INT'L ECONOMIC L. 849 (2002).

to ensure that the processes related to coverage, tracking (coding), and payment support continued innovation and access to new medical technologies. [11] We therefore urge the PTO to examine coverage and reimbursement policies related to genetic diagnostic testing. We suggest that PTO review the findings and recommendations of a recent report from Boston Healthcare Associates, which concluded that the current reimbursement system for personalized medicine diagnostics may impede patient access to genetic diagnostic tests.[12] Boston Healthcare Associates noted, in particular, "the way tests are coded and the evidence currently needed to obtain coverage," which fail to recognize "the clinical utility or economic value of these tests, or the realities of the niche markets they serve."[13]

Fourth, we recommend that the PTO consider the purpose and appropriate role of independent second opinion genetic testing before making its recommendations.

PhRMA also believes that PTO should fully understand the many types of genetic testing available and the role that genetic testing — and second opinions — play (and do not play) in medical care before issuing its reports and recommendations under the America Invents Act. PhRMA does not have access to data on genetic testing and any issues that independent second opinion testing may or may not address. The PTO should specifically identify the issues that second opinion testing is intended to resolve based upon reliable data, rather than anecdotal reports. Any recommendations that the PTO makes regarding independent second opinion testing should likewise be data driven.

In PhRMA's view, a report on independent second opinion genetic testing should be informed by the larger medical care landscape in which second opinion genetic tests are performed. For example, even where only one genetic test has been developed and is available, it might be possible to obtain a "second opinion" on the interpretation of the test results from a qualified physician, geneticist or genetic counselor, or other healthcare professional. Where the tests themselves are highly reliable already, a retest may be sufficient to provide the statistical reassurance if that is the desired endpoint. Genetic tests might also be intended for use in conjunction with other test data and clinical information, rather than the sole basis for medical decision making.

[11] *See, for e.g.,* Advanced Medical Technology Association, Medicare & Reimbursement (March 20, 2012), *at* http://www.advamed.org/MemberPortal/Issues/Medicare/. *See also* Personalized Medicine Coalition, *Public and Private Reimbursement* (March 20, 2012), *at* http://www.personalizedmedicinecoalition.org/policy/topics/public-and-private-sector-reimbursement.

[12] David Parker, Issue Brief: The Adverse Impact of the U.S. Reimbursement System on the Development and Adoption of Personalized Medicine Diagnostics, Boston Healthcare Associates (Dec. 2010), *available at* http://www.bostonhealthcare.com/objects/pdfs/reimbursementissuebrief.pdf.

[13] Press Release, Personalized Medicine Coalition Workgroup Issue Brief Highlights Need for Updates to Diagnostics Reimbursement System (Dec. 7, 2010) (quoting author of issue brief), *available at* http://www.personalizedmedicinecoalition.org/communications/press-releases/2010_12_7.

PTO should also recognize that "genetic testing" covers a wide range of different kinds of tests. Diagnostic tests may be ordered for a number of reasons including the following:

- To establish diagnosis of a disease or condition.
- To provide a patient's genetic profile to help identify subpopulations of patients that may benefit from a particular treatment or who may be more susceptible to a particular type of adverse event.
- To provide prognostic information in patients with established disease.
- To monitor the effectiveness of a particular treatment.
- To confirm that a patient is free from a disease or condition.

The various uses of genetic diagnostic testing can raise a range of different issues with respect to the value and effectiveness of independent second opinion genetic testing.

Conclusion

We are pleased that PTO is reaching out to a range of stakeholders to inform public policy in this important area. We believe that personalized medicine — which is grounded in part in the availability of accurate, sensitive, and specific genetic testing — holds the key to improved medical care and reduced costs to our healthcare system. We urge the PTO to consider in its recommendations the need to continue to foster the R&D investment to take full advantage of the scientific promise offered by personalized medicine.

We would be pleased to provide further assistance to the PTO as it develops its report and recommendations.