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The Honorable David J. Kappos  
Under Secretary of Commerce for Intellectual Property and  
Director of the United States Patent and Trademark Office

Saurabh Vishnubhakat  
Attorney Advisor  
Officer of the Chief Economist  
United States Patent and Trademark Office  
Mail Stop EXTERNAL AFFAIRS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
genetest@uspto.gov

**Joint Comments of Roche Molecular Systems, Inc., Ventana Medical Systems, Inc.,  
Roche Diagnostics Operations, Inc., Roche Diagnostics Corporation, Hoffmann-La  
Roche Inc., and Abbott Laboratories, Inc. on Genetic Testing**

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## **INTRODUCTION AND SUMMARY**

Section 27 of the Leahy-Smith America Invents Act, Pub. L. No. 112-29, 125 Stat. 284 (2011) (“AIA”) charges the Director of the United States Patent and Trademark Office (“USPTO”) with providing Congress a study regarding “independent, confirming genetic diagnostic test activity where gene patents and exclusive licensing for primary genetic diagnostic tests exist.” The study must include examination of the four topics listed in Section 27, but is not limited to those topics. *See* AIA, § 27(b). The USPTO, in turn, issued a Request for Comments and Notice of Public Hearings on Genetic Diagnostic Testing, 77 Fed. Reg. 3748 (Jan. 25, 2012), that invited comments on fourteen questions posed by the USPTO and on other issues believed to be relevant to the scope of the study.

Roche Molecular Systems, Inc., Ventana Medical Systems, Inc., Roche Diagnostics Operations, Inc., Roche Diagnostics Corporation, and Hoffmann-La Roche Inc. (collectively “Roche”) and Abbott Laboratories, Inc. (“Abbott”) appreciate this opportunity to comment on the issues raised in Section 27 and the USPTO’s notice. These comments do not attempt to address every question posed by the USPTO or every issue that might inform the USPTO’s thinking as it prepares its report. They do, however, address the following issues, which cut across the field of the USPTO’s request for comments: the nature of genetic testing and its role in modern personalized medicine; the role of patents in attracting funding for research and development, and in spurring innovation in the field of genetic testing; the effect of patents on the availability of primary and “second opinion” genetic testing; and the ways in which government can improve patient care by fostering better, more accurate genetic testing.

I. Genetic testing is ushering in a new era of patient treatment—personalized medicine. Traditional medicine uses a trial-and-error approach both in diagnosing illnesses and in identifying the best treatments for particular patients. Personalized medicine, by contrast, uses genetic testing to diagnose illnesses earlier and more accurately than ever before. Through “companion diagnostics,” moreover, personalized medicine utilizes genetic testing to identify from the outset which treatments will benefit a patient, preventing the needless suffering and wasteful spending that results when patients try drug regimens that do not work for them. The federal government has recognized the promise of personalized medicine and made fostering its development a priority health care issue.

Genetic tests are performed for numerous reasons—from carrier testing to predictive testing to therapeutic monitoring. Genetic testing also implicates many different types of patented technologies—from diagnostic assays to instruments used in testing to reagents. It is thus crucial that the USPTO’s recommendations to Congress address ambiguities in the terms “genetic diagnostic test” and “patents on genetic testing activity” so as to avoid unintended consequences that would flow from sweeping in tests and technologies unrelated to the particular issues that Congress raised in Section 27.

II. Several of the USPTO’s questions touch upon the relationship between patents and the availability of genetic testing. The short answer to many of those questions is that, without the incentives provided by patents, many of the genetic tests that currently exist

would never have been developed or made commercially accessible in the first place. Developing genetic tests is expensive, time-consuming, and risky. It is costly to identify associations between a biomarker and a disease or drug response and to develop commercially viable tests and techniques, and even more costly to validate the utility and safety of a test through clinical trials. For every successful test, many more end in failure.

Regulators, industry participants, and commentators have all observed that patent protections are essential to creating the incentives for the investment necessary not only to research and develop a genetic test, but to validate it and bring it to market. The period of exclusivity a patent affords is crucial to ensuring that innovators can recoup not only the costs of research, development, and commercialization of successful products, but also the costs of the many efforts that do not succeed.

But patents do not merely reward patentees for their innovations. They also foster innovation by others. Patent disclosures create an expanded knowledge base on which others may build, whether by improving a patented innovation—making it faster, cheaper, more accurate, etc.—or transforming a scientific breakthrough into an actual, marketable product or service. Patents, coupled with competitive pressures, also provide an incentive for others to “design around” the patent by developing new, non-infringing tests for the same condition. The result is a proliferation of different tests for the same condition, giving doctors and patients more options than the simple repetition of an existing test. Finally, patents also promote innovation by permitting more extensive collaboration between different entities, allowing patentees to partner with entities that may have expertise they lack (for example, in marketing and distribution) without fear of having their innovation stolen.

III. Claims that patents limit research and patient access are not substantiated. Although some have voiced concern that patents may impede upstream research, empirical studies have proved those fears to be unfounded. Players in the field of genetic testing, like Roche and Abbott, have a significant interest in the free flow of information and technologies for research purposes and are rationally reluctant to enforce their patents against researchers. Similarly, there is no evidence of patient access problems with respect to primary genetic testing.

With regard to “second opinions,” it is important to recognize that the term “second opinion” can refer to several different actions. It could involve re-running a particular genetic test, running a different test for the same condition, or having a second doctor advise on the proper course of treatment in light of the results of a single, initial test. There is scant evidence that there are significant problems with patient access to second opinions in any of those contexts. To the contrary, because genetic tests are typically broadly sold or licensed, in most instances it will be possible to have a second laboratory re-run a test to confirm the results of the primary test. Because patents create strong incentives to develop competing tests, moreover, it will also typically be possible to run a second *type* of test for the same condition to compare it to the results of the first test. Then, of course, there is the traditional form of a *medical* second opinion, which may, in practice, be what patients most often desire—having another doctor review the results of the genetic test and provide another

perspective on the meaning of the test for the patient's prognosis and the appropriate course of treatment. Patents have no bearing at all on that most common form of "second opinion." To the extent there are barriers to any of the forms of second-opinion testing, moreover, they are not caused by patents, but by limitations on insurance reimbursement for second-opinion testing and physician doubts about the value of running the same test twice.

IV. The USPTO should not recommend any changes to patent law, but if it does, it should proceed with extreme caution. In addition to choosing its terms carefully, the USPTO should focus exclusively on those instances in which a single laboratory is the sole provider of a patented test. It should guard against abuse by making clear that confirmatory testing refers solely to re-running the *same* testing protocol a second time. It should limit any proposed changes to situations in which there is evidence that having a second provider run a confirmatory test would produce a materially more accurate result than if the original provider were to re-run the test. And it should give serious consideration to the practical effect that any weakening of patent protection on confirmatory tests would have on the ability to enforce patents against primary-test infringers.

V. It is also important to recognize the negative impact that certain second-opinion testing can have on patient outcomes, including harm from delayed treatment and expense to the patient. The best way to ensure that patients have accurate information and can make informed decisions is to ensure that diagnostic testing is accurate when first performed. Patent protection encourages companies to invest the substantial resources needed for clinical validation and Food and Drug Administration ("FDA") approval. Other providers, however, may choose to meet only the requirements of the Clinical Laboratory Improvement Amendments ("CLIA"), which are far less stringent. An unintended consequence of weakening patent protection in the name of providing patients with a second opinion is that it could discourage providers from investing in rigorous validation techniques and instead encourage the proliferation of laboratories with less rigorous controls, thereby diminishing the reliability of test results and depriving patients of the certainty they deserve.

One further point deserves mention. On March 20, 2012, the Supreme Court issued its decision in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, No. 10-1150, 566 U.S. \_\_\_, 2012 WL 912952 (Mar. 20, 2012). *Mayo Collaborative Services* ruled that, while new and inventive applications of natural laws can be patented, the underlying law of nature (and certain non-inventive methods that "monopolize the law of nature itself") cannot. The full impact of that decision on the law of patent eligibility under 35 U.S.C. § 101, and on diagnostic patents in particular, has yet to be determined. As these comments show, it is far from clear that the patent system ever posed a significant impediment to appropriate second-opinion testing. But even if patents had the potential to impede second-opinion genetic testing before *Mayo Collaborative Services*, the situation is now in flux. It would be premature for Congress to make further changes in the patent law without determining whether the concerns that animated Section 27 of the AIA remain operative following *Mayo Collaborative Services*.

## **DISCUSSION**

### **I. Background, Terminology, And Scope Of Comments**

#### **A. Roche And Abbott**

Roche Molecular Systems, Inc., Ventana Medical Systems, Inc., Roche Diagnostics Operations, Inc., Roche Diagnostics Corporation, and Hoffmann-La Roche Inc. are affiliates of F. Hoffmann-La Roche Ltd., the world's largest biopharmaceutical company. Close cooperation within Roche's pharmaceutical and diagnostic divisions enables it to tailor treatments to specific patient subpopulations based on the latest scientific understanding of biology and disease at the molecular level. Roche develops and manufactures a wide array of innovative diagnostic products used in the diagnosis, prognosis, and treatment of cancer and infectious diseases. Some of Roche's diagnostic tests utilize the company's Nobel Prize-winning polymerase chain reaction ("PCR") technology to detect the genetic material (DNA or RNA) in cancerous cells and in infecting pathogens such as HIV or hepatitis. Because DNA- and RNA-based tests are capable of identifying and characterizing disease earlier and more specifically than tests based on the body's immune response, patients can be treated and monitored with great precision. Roche's tissue-based diagnostic tests enable the detection of genetic biomarkers that facilitate the ability of health care providers to prognose or even predict patient outcomes for various cancer therapeutic regimens. Roche has a broad line of oncology, virology, microbiology, and blood screening tests, which are used by researchers, physicians, patients, hospitals, laboratories, and blood banks around the world.

Abbott Laboratories, Inc. is a diverse, global health care company with scientific expertise and products that address the full range of health care needs—from disease prevention and diagnosis to treatment and cure. For more than 120 years, Abbott has been a pioneer in developing innovative solutions that improve health and the practice of health care. Among other things, Abbott develops and markets tests that can detect subtle but key changes in patients' genes and chromosomes. These award-winning technologies permit earlier detection and diagnosis of diseases, assist in the selection of therapies that are more likely to prove effective, and improve the monitoring of disease progression. Abbott offers more than 350 products related to molecular diagnostics for infectious disease, oncology, genetics, and automation, including breakthrough DNA probe technologies critical to the diagnosis and treatment of lung, breast, and bladder cancer.

The questions posed in Section 27 of the AIA and the USPTO's notice are of great significance to Roche and Abbott. Both companies invest substantial resources in the research and development of genetic testing products and related technologies to improve treatment and decrease the costs of therapy for those suffering from often fatal diseases. Both also license or purchase rights to patented diagnostic technologies owned by others. Roche

and Abbott thus have a uniquely balanced perspective on the issues being addressed in the USPTO's study.<sup>1</sup>

## **B. Gene-Based Diagnosis And Treatment Are Ushering In An Era Of Personalized Medicine**

In response to the USPTO's request, this section provides background on the impact of genetic testing on "the practice of medicine, the quality of care that patients receive, and medical costs." 77 Fed. Reg. at 3748. The health sciences are on the verge of a new era of personalized medicine that promises dramatic improvements in how we diagnose and treat disease. Genetic testing is critical to realizing that promise. Physicians, clinicians, and researchers have long recognized that people with the same disease often respond very differently to the same treatment. Yet, traditional medicine relies on a trial-and-error approach to the problem and can be slow to diagnose disease or to identify at-risk patients who will benefit from early intervention. For some conditions, less than half of patients respond positively to prescription medications; for the remainder, the drug is either ineffective or toxic. Spear et al., *Clinical Application of Pharmacogenetics*, 7 Trends Molecular Med. 201, 201-202 (2001); see also Phillips et al., *Potential Role of Pharmacogenomics in Reducing Adverse Drug Reactions: A Systematic Review*, 286 J. Am. Med. Ass'n 2270, 2270 (2001) (adverse drug reactions are among the leading causes of death in the United States (citing Lazarou et al., *Incidence of Adverse Drug Reactions in Hospitalized Patients: A Meta-Analysis of Prospective Studies*, 279 J. Am. Med. Ass'n 1200 (1998))). As a result, scarce resources are wasted on the purchase of medicines that either do no good or actually harm the patient. Worse still, effective treatments are not implemented unless and until they are identified through a wasteful and potentially painful trial-and-error process.

Genetic testing offers a potential solution to these problems. It is estimated that genetic tests for more than 2,000 diseases are now clinically available. See Centers for Disease Control and Prevention, *Genomic Testing*, <http://www.cdc.gov/genomics/gtesting>. These tests can be used to diagnose disease or risk for disease before the first symptoms appear, permitting earlier and more effective intervention. They can also indicate which treatments will work most effectively and which can be safely disregarded as ineffectual or potentially harmful. Genetic testing thus has the potential to decrease the incidence of adverse drug reactions dramatically, while lowering the cost of care. See Personalized Medicine Coalition, *The Case for Personalized Medicine* 4-7 (3d ed. 2011), available at [http://www.personalizedmedicinecoalition.org/sites/default/files/files/Case\\_for\\_PM\\_3rd\\_edition.pdf](http://www.personalizedmedicinecoalition.org/sites/default/files/files/Case_for_PM_3rd_edition.pdf) ("*The Case for Personalized Medicine*").

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<sup>1</sup> The scope of patentable subject matter under 35 U.S.C. § 101 is beyond the scope of these comments and the USPTO's report. These comments therefore do not address the effect of *Mayo Collaborative Services*, other than to note that Congress should wait until the full impact of that decision becomes clear before considering any changes to the patent law.

As leaders in this field, Roche and Abbott have developed tests and associated treatments that promise to save lives, prevent needless suffering, and save billions of health care dollars. Roche, for example, has designed a microarray device called the AmpliChip® CYP450, which provides comprehensive detection of gene variations—including deletions and duplications—for the CYP2D6 and CYP2C19 genes. The AmpliChip® test assists physicians in determining the best therapeutic strategy and treatment dose for an estimated 25% of all prescription drugs, including many common antipsychotics and antidepressants. Abbott’s Urovysion Bladder Cancer test identifies genetic aberrations in urine specimens from persons with hematuria (blood in urine), allowing the early detection of bladder cancer before any morphological changes manifest, which can dramatically increase survival rates. Other biopharmaceutical companies have developed other diagnostic tests that permit more accurate prognoses for other conditions. Genomic Health, Inc., for example, markets the OncoType DX®, which predicts the likelihood of breast cancer recurrence and patient survival within 10 years of diagnosis. *See, e.g.,* Hornberger et al., *Economic Analysis of Targeting Chemotherapy Using a 21-Gene RT-PCR Assay in Lymph-Node-Negative, Estrogen-Receptor-Positive, Early-Stage Breast Cancer*, 11 *Am. J. Managed Care* 313 (2005).

The promise of this area is also reflected in new AIDS detection and monitoring techniques. For example, Abbott’s new fourth-generation Architect® HIV Ag/Ab Combo detects infections 7 to 20 days earlier than prior HIV antibody tests. It was the first FDA-approved test for the diagnosis of HIV-1 and -2 infections in pregnant women and children under two. Early detection of AIDS is obviously critical not merely to its treatment, but also to preventing its spread. Roche’s cobas® AmpliPrep/cobas® TaqMan® HIV-1 Test v.2.0, in turn, determines the quantity of HIV-1 RNA in human plasma to help assess patient prognosis and to monitor the effects of anti-retroviral therapy.

Roche and Abbott are also leaders in the development of “companion diagnostics,” a special class of tests used to identify the patients most likely to benefit from a particular drug. *See FDA, Draft Guidance for Industry and Food and Drug Administration Staff—In Vitro Companion Diagnostic Devices* 6-7 (July 14, 2011), available at <http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM262327.pdf> (“FDA, *Draft Guidance*”) (defining companion diagnostic as a “diagnostic device that provides information that is essential for the safe and effective use of a corresponding therapeutic product”). Roche recently received FDA approval to commercialize its cobas® 4800 BRAF V600 Mutation Test, a test that identifies patients who would benefit from Roche’s drug Zelboraf®, which is indicated for the treatment of certain types of inoperable or metastatic melanoma.<sup>2</sup> The FDA has also recently approved a new molecular diagnostic

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<sup>2</sup> Zelboraf® and its companion diagnostic were cited by the FDA as a “great example of how companion diagnostics can be developed and used to ensure patients are exposed to highly effective, more personalized therapies in a safe manner.” FDA, Press Release, *FDA Approves Zelboraf and Companion Diagnostic Test for Late-Stage Skin Cancer* (Aug. 17, 2011), available at <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm268241.htm>.

test—Abbott’s Vysis ALK Break Apart FISH Probe—for detecting rearrangements of the anaplastic lymphoma kinase (ALK) gene in non-small-cell lung cancer. That test identifies a genetic variation (the ALK fusion gene) that indicates a high likelihood that a patient will respond positively to Pfizer’s XALKORI® (crizotinib) therapy. These breakthroughs in the advancement of companion diagnostics permit cancer treatments that are custom-tailored to patients’ unique genetic profiles. By excluding patients who would not benefit from a particular treatment, the companion diagnostics developed by Roche, Abbott, and others in the industry also save health care dollars and prevent needless suffering.<sup>3</sup>

This type of personalized medicine has become a priority health care issue at the highest levels of government. Following a wide-ranging review of the field, the President’s Council of Advisors on Science and Technology concluded that “personalized medicine warrants significant public and private sector action to facilitate the development and introduction into clinical practice of this promising class of new medical products.” President’s Council of Advisors on Science and Technology, *Priorities for Personalized Medicine* 1 (Sept. 2008), available at [http://www.whitehouse.gov/files/documents/ostp/PCAST/pcast\\_report\\_v2.pdf](http://www.whitehouse.gov/files/documents/ostp/PCAST/pcast_report_v2.pdf) (“*Priorities for Personalized Medicine*”). The current Director of the National Institutes of Health (“NIH”) has observed that “personalized medicine remains one of the most compelling opportunities we have to improve the odds of staying healthy.” Collins, *Personalized Medicine: A New Approach to Staying Well*, Boston Globe, July 17, 2005, at E12.

Congress and the Executive Branch have begun laying the foundation for investment in research and infrastructure necessary to support a rapid expansion in personalized medicine over the coming decades. In 2006, the Department of Health & Human Services (“HHS”) launched the “Personalized Health Care Initiative” for the purpose of coordinating “activities in HHS agencies that could help accelerate a personalized health care future.” HHS, *Personalized Health Care: Pioneers, Partnerships, Progress* 13 (Nov. 2008), available at [http://www.hhs.gov/myhealthcare/news/phc\\_2008\\_report.pdf](http://www.hhs.gov/myhealthcare/news/phc_2008_report.pdf) (“HHS, *Personalized Health Care*”). And FDA has made it a priority to “stimulate innovation in clinical evaluations and personalized medicine to improve product development and patient outcomes.” FDA, *Advancing Regulatory Science at FDA: A Strategic Plan* 10-13 (Aug. 2011), available at <http://www.fda.gov/downloads/ScienceResearch/SpecialTopics/RegulatoryScience/UCM268225.pdf>. In 2010, NIH and FDA announced “a new collaboration on regulatory and translational science to accelerate the translation of research into medical products and therapies ... to help make personalized medicine a reality.” Hamburg & Collins, *The Path to Personalized Medicine*, 363 New Eng. J. Med. 301, 304 (2010). Also in 2010, Congress enacted legislation that calls for improvements in health care services through comparisons of the effectiveness of various treatments in patient subpopulations. See Patient Protection and Affordable Care Act, Pub. L. No. 111-

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<sup>3</sup> Other examples of life-saving companion and molecular diagnostics abound. A more comprehensive list may be found in *The Case for Personalized Medicine* at 18.

148, §§ 3011, 3013, 3113, 6301, 124 Stat. 119, 378-379, 381-382, 422, 727-728 (2010).<sup>4</sup> Such initiatives are intended to set the stage for further research and development activities that will increase the number of diseases and treatments for which commercial genetic tests are available. *See* Garber & Tunis, *Does Comparative-Effectiveness Research Threaten Personalized Medicine?*, 360 *New Eng. J. Med.* 1925, 1925 (2009).

### C. Genetic Testing Comes In Many Forms And Is Done For Many Purposes

Although Section 27 of the AIA refers to “genetic diagnostic tests,” it does not define the term. Genetic testing comes in multiple forms and is performed for a variety of purposes. The USPTO should take care to define the terms it is using in its report and to distinguish among the various forms of genetic testing to ensure that its recommendations do not sweep too broadly or have other unintended consequences. To assist in that effort, this section provides a list and brief description of various common categories of genetic testing related to the practice of medicine. The list is not intended to be exhaustive, but rather to provide the USPTO with a sense of the variety in this field and the need to take care in selecting its terms.

The following are common types of genetic tests used in medicine and the situations in which they are performed:

1. **Carrier Testing.** Carrier testing identifies individuals or couples who carry a gene mutation that may cause a genetic disorder in their offspring, such as Tay-Sachs disease or Canavan disease.
2. **Prenatal and Preimplantation Testing.** Prenatal testing screens for genetic abnormalities in fetuses, such as cystic fibrosis or Down Syndrome. Testing can also be conducted on embryos before implantation.
3. **Newborn Screening.** Newborn screening detects various conditions with a genetic component, including phenylketonuria and congenital hypothyroidism.
4. **Presymptomatic Testing.** Presymptomatic testing determines whether an asymptomatic individual is likely to develop a genetic disorder, such as Huntington’s disease, later in life. Such testing is commonly performed where a patient has a family history of the condition.
5. **Symptomatic Testing.** In contrast to presymptomatic testing, symptomatic testing determines whether a symptomatic individual has a known and detectable genetic disorder, identification of which could assist in diagnosis and treatment.

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<sup>4</sup> Genetic testing and personalized medicine were also the subject of earlier congressional efforts at health care reform. *See, e.g.*, Genomics and Personalized Medicine Act of 2007, S. 976, 110th Cong. (2007); Genomics and Personalized Medicine Act of 2008, H.R. 6498, 110th Cong. (2008).

**6. Genomic-Risk Testing.** Genomic-risk testing identifies genetic traits that are associated with a heightened risk of developing a particular disorder with multiple causes, such as cancer or diabetes.

**7. Predictive Testing.** Although the term is sometimes used loosely, in the context of FDA approval or clearance, predictive testing generally identifies patients likely to respond or not respond to a particular therapeutic. Predictive companion diagnostic assays reviewed by the FDA are generally validated in Phase III clinical trials, or via retrospective analysis of clinical trial data.

**8. Pharmacogenetic Testing.** Pharmacogenetic tests, also a form of companion diagnostics, help identify genotypic variations in patients and enable the selection of patients most likely to benefit from a particular drug. Examples of such tests include Roche's cobas® 4800 BRAF V600 Mutation Test and Abbott's Vysis ALK Break Apart FISH Probe. *See pp. 6-7, supra.*

**9. Qualitative Diagnostic Testing.** Qualitative diagnostic testing involves the detection and identification of viral or bacterial nucleic acids (DNA or RNA) to diagnose or rule out a suspected disease or disorder, such as *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, Hepatitis C, or HIV.

**10. Therapeutic Monitoring.** Therapeutic monitoring uses genetic techniques to monitor the severity and progression (or regression) of a disease to assist with treatment decisions or monitor the efficacy of treatment. For example, Roche's cobas® Amplicor CMV Monitor Test measures changes in the level of cytomegalovirus to aid in assessing viral response to antiviral treatment.

**11. Donor Screening.** Genetic testing is used to reduce the risk that infection will be transferred through donated blood, organs, and tissue. Such tests may reveal information about the donor's health status, but are not conducted for the purpose of diagnosis. Indeed, the package inserts for FDA-approved donor screening products often say that they are not intended to be used as diagnostics. *See, e.g.,* Package Insert, cobas® TaqScreen West Nile Virus Test 6 (Apr. 3, 2008), *available at* <http://www.fda.gov/downloads/BiologicsBloodVaccines/BloodBloodProducts/ApprovedProducts/LicensedProductsBLAs/BloodDonorScreening/InfectiousDisease/UCM091938.pdf> ("This test is not intended for use as an aid in diagnosis.").

Genetic testing can also fall into more than one category depending on its purpose. For example, Roche's cobas® AmpliPrep/cobas® TaqMan® HCV Quantitative Test v.2.0 can be used both *qualitatively* to detect the presence of Hepatitis C and therefore diagnose the condition and *therapeutically* in conjunction with clinical and laboratory markers of infection to predict the probability of sustained virologic response early during a course of antiviral therapy and to assess viral response to antiviral treatment.

The variety of genetic tests currently available demonstrates the need for caution in defining the term “genetic diagnostic test.” At a minimum, the USPTO’s definition of “genetic diagnostic test” should exclude therapeutic monitoring and donor screening, because the primary purpose of such testing is not to diagnose a patient’s condition, but rather to assist in the management of that condition or the prevention of infection.

Further, there is no indication that Congress intended the term “genetic diagnostic test” to extend beyond the testing of *human* genetic material to include, for instance, a pathogen’s genetic material. In the debate on the manager’s amendment that added Section 27 to the AIA, Representative Wasserman Schultz referred specifically to “the actual *human* gene being tested.” 157 Cong. Rec. H4433 (daily ed. June 22, 2011) (emphasis added). Similarly, in discussing a precursor provision during the House Judiciary Committee’s markup of the AIA, Representative Wasserman Schultz again referred to the “*human* gene being tested.” *Markup of H.R. 1249, the America Invents Act Before the H. Comm. on the Judiciary*, 112th Cong. 189 (Apr. 14, 2011), available at <http://judiciary.house.gov/hearings/pdf/04142011MarkupTranscript.pdf> (emphasis added). All of the examples in the legislative history also related to the testing of human genes, and there was no discussion of tests that detect the presence of pathogens based on their genetic signature.

Previous studies and legislation have also focused exclusively on human genetic material. *See, e.g.*, Secretary’s Advisory Comm. on Genetics, Health, & Society, HHS, *U.S. System of Oversight of Genetic Testing: A Response to the Charge of the Secretary of Health and Human Services* 53 (2008), available at [http://oba.od.nih.gov/oba/SACGHS/reports/SACGHS\\_oversight\\_report.pdf](http://oba.od.nih.gov/oba/SACGHS/reports/SACGHS_oversight_report.pdf) (“SACGHS, *Oversight of Genetic Testing*”) (defining genetic/genomic testing as “an analysis of human chromosomes, deoxyribonucleic acid (DNA), ribonucleic acid (RNA), genes, and/or gene products (e.g., enzymes and other types of proteins) that is primarily used to detect heritable or somatic mutations, genotypes, or phenotypes related to disease and health”); Genetic Information Nondiscrimination Act of 2008, Pub. L. No. 110-233, § 101(d)(7), 122 Stat. 881, 885 (2008) (“The term ‘genetic test’ means an analysis of human DNA, RNA, chromosomes, proteins, or metabolites, that detects genotypes, mutations, or chromosomal changes.”).

For all these reasons, the USPTO should note the potential ambiguity in the term “genetic diagnostic test” and focus its report on testing of *human* DNA, RNA, chromosomes, proteins, or metabolites that detects genotypes, mutations, or chromosomal changes, for the primary purpose of diagnosing a specific disorder caused by a genetic defect or a genetic predisposition to a particular disease. It should specifically exclude from its analysis tests that are directed to non-human genetic material and proteins; tests that do not diagnose a patient’s condition but rather assist in its management; and donor screening.

#### **D. Genetic Testing Implicates Many Different Types Of Patented Technologies**

Section 27 of the AIA also fails to define the term “patents on genetic testing activity.” That term is also ambiguous and should be carefully defined to avoid unintended consequences.

A single genetic test may implicate a variety of different types of patents, including those directed to the following:

1. **Isolated Nucleic Acids.** Some patents claim compositions of matter consisting of isolated nucleic acids, often those having a mutation associated with a particular disease. As information about the human genome has proliferated, it has become increasingly difficult to claim isolated nucleic acids corresponding to human genes, and many early patents in this area will expire in the near future.
2. **Primer/Probe Combinations.** Some patents claim a defined set of synthetic oligonucleotide primers and/or probes having a specific nucleotide sequence. Such patents may cover the combination of the primers and probes or methods of utilizing the primers and probes for a given purpose.
3. **Diagnostic Assays.** Some patents are directed to specific assays used in genetic testing. For example, they may claim a kit for performing the assay or a method for performing the assay.
4. **Diagnostic Techniques.** Some patents claim techniques that may be used in a variety of genetic tests. Examples of such techniques include polymerase chain reaction, microarray and sequencing techniques that allow for the processing and interpretation of a large amount of genetic data in a single experiment, and techniques to purify nucleic acids.
5. **Instruments.** Some patents cover instruments used in genetic testing, such as instruments for sample preparation or real-time amplification and detection of RNA or DNA.
6. **Reagents/Consumables.** Some patents cover particular materials used in genetic testing, such as enzymes and buffers.

There is no indication in the legislative history of the AIA that Congress intended to reach all patents that relate in any way to genetic testing. For example, the precursor amendment to Section 27 defined “confirming diagnostic test activity” to exclude “(i) the use of a patented machine or manufacture in violation of such patent, or (ii) the practice of a process in violation of a biotechnology patent.” Amend. 21, *Markup of H.R. 1249, the America Invents Act Before the H. Comm. on the Judiciary* (Apr. 14, 2011), available at <http://judiciary.house.gov/hearings/pdf/Wasserman%20Schultz%2021%20Amdt%20TEXT.pdf>. More generally, no lawmaker expressed concern about the effect of patents on research

tools, such as patents on diagnostic techniques, instruments, and reagents/consumables that can be used in a variety of genetic tests.

The USPTO should therefore limit its report and recommendations to those isolated nucleic acid, primer/probe, or diagnostic assay patents that claim a particular test for a particular genetic marker. In addition, the USPTO should make clear in any patent-related findings or recommendations precisely what types of patents are at issue.

### **E. Scope Of Roche's And Abbott's Comments**

As discussed, the USPTO should interpret the terms “genetic diagnostic test” and “patents on genetic testing activity” in a way that focuses on the specific issues that prompted the passage of Section 27 of the AIA. Because the terms are ambiguous, however, the comments that follow occasionally mention other genetic tests and patent claims in the interest of providing additional context that may assist the USPTO.

## **II. Patent Protections Are Critical To Creating Incentives For The Development Of New Genetic Testing Procedures**

Congress has asked the USPTO to address the “impact” that genetic testing activity has on the practice of medicine. AIA, § 27(b)(3). In turn, the USPTO has asked about the effect of patents on “the availability of primary genetic diagnostic testing” and “second opinion diagnostic tests.” *See* 77 Fed. Reg. at 3749. The short answer to these questions is that patents often are the reason that testing becomes available at all. Too often, public debate in this area has been reduced to the claim that, once an invention has been discovered and the manner of its operation disclosed to the world, the public would be better off if the invention were not patented and instead free for all to use. The difficulty with that line of thinking is that it ignores the critical antecedent question: Would that invention exist if patent protection were not available? In the area of diagnostics, and personalized molecular diagnostics in particular, the answer is frequently “no.”

Patents are critical for multiple reasons. First, establishing the necessary correlations between a biomarker and disease, creating reliable tests, making those tests commercially viable, and proving their safety and efficacy to the satisfaction of regulators is enormously expensive, time consuming, and fraught with risk. Absent the potential financial rewards that patents offer, there would be insufficient incentives to make the enormous investments that are required to turn paper theories into commercially viable products that improve the health and quality of life of the public. Patents also promote the availability of genetic testing by ensuring that innovations and the means of reproducing them are fully shared with the public. Those disclosures spur further innovation as learning builds on learning. Finally, patents encourage the development of a diverse range of competing tests. They ensure that would-be competitors do not simply copy a patented technology, but instead work to develop a non-infringing alternative—an alternative that may turn out to be superior (in particular attributes, in certain circumstances, or overall) to prior technologies. Weakening patent incentives in

the name of increasing patient access thus runs the serious risk that patients in the future may not have anything to access.<sup>5</sup>

**A. The Development And Commercialization Of A Genetic Test Requires Substantial Investments**

Developing genetic tests, like other areas of biotechnology, is an expensive, time-consuming, and risky venture. In 2011, publicly-traded companies invested more than \$22 billion in biotechnology-related research and development. Ernst & Young, *Beyond Borders: Global Biotechnology Report 37* (2011), available at [http://www.ey.com/Publication/vwLUAssets/Beyond\\_borders\\_global\\_biotechnology\\_report\\_2011/\\$FILE/Beyond\\_borders\\_global\\_biotechnology\\_report\\_2011.pdf](http://www.ey.com/Publication/vwLUAssets/Beyond_borders_global_biotechnology_report_2011/$FILE/Beyond_borders_global_biotechnology_report_2011.pdf). In 2009, biopharmaceutical companies spent over \$5 billion in research and development activities directed towards biomarkers and companion diagnostics alone. Staples et al., *The Role of the Academic Medical Center in Advancing Personalized Health Care*, in HHS, *Personalized Health Care* 85-86 (“Advancing Personalized Health Care”).<sup>6</sup> For every successful product, many more are abandoned, often after substantial investments that cannot be recouped. Grabowski, *Follow-On Biologics*, 7 *Nature Reviews Drug Discovery* 479, 481 (2008) (only 30% of biological therapeutics that make it as far as human trials succeed); see generally Graham et al., *High Technology Entrepreneurs and the Patent System: Results of the 2008 Berkeley Patent Survey*, 24 *Berkeley Tech. L.J.* 1258, 1288, 1290 (2009) (finding that patents are considered important to innovation in the biotechnology and medical device sectors). Investments in this area can be justified only if the returns on successful products are sufficient to cover the costs of developing not merely those products but also the many more that end in failure.

The research and development activities needed to make advances in genetic testing are costly. To make a molecular biomarker such as a genetic sequence clinically useful, the first task is to find associations between the biomarker and a disease or drug response. “Such studies usually require thousands of participants and the collection and preservation of a large number of biological specimens and genetic material, and as such can go well beyond the resources of a single company or laboratory.” See Personalized Medicine Coalition, *The Case for Personalized Medicine* 9 (2d ed. 2009). A company must then design a test for measuring, or method of using, the biomarker that is accurate, reproduceable, and robust.

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<sup>5</sup> Further, it is well known that market exclusivity through patent protection creates strong incentives for advertising efforts that educate patients and health professionals who are interested in purchasing the end product. As with pharmaceuticals and medical devices generally, the incentive to inform the public about patented diagnostic products creates a social benefit by improving access and creating awareness among at-risk individuals. Cook-Deegan & Heaney, *Gene Patents and Licensing: Case Studies Prepared for the Secretary’s Advisory Committee on Genetics, Health, and Society*, 12 *Genetics Med.* S1, S32 (2012); see also *Sorrell v. IMS Health Inc.*, 131 S. Ct. 2653, 2670 (2011) (describing the “benign and, many would say, beneficial speech of pharmaceutical marketing”).

<sup>6</sup> Roche and Abbott spend more than \$1 billion annually on developing diagnostic products and systems.

Clinical trials may then be required to demonstrate and validate the clinical utility of the product or method. Many such trials are equivalent to pharmaceutical trials in both design and scope, and sometimes involve following patients for years to determine long-term safety and efficacy. *See generally Advancing Personalized Health Care* 83. Bringing a single diagnostic product to market typically requires tens of millions of dollars and can cost well over \$100 million under certain circumstances, an investment coupled with several years of research and clinical studies involving hundreds of patients. *See, e.g., id.* at 84-85.

Even with the existing promise of patent protection, and setting aside the potential impact of the *Mayo Collaborative Services* decision, finding the private capital needed to fund the clinical research required to discover and validate a broader array of biomarkers is one of the greatest challenges facing the genetic testing industry. *See Advancing Personalized Health Care* 83. Diagnostic products generally offer a very low rate of return on investment, particularly in light of the staggering amounts required for their development. *Id.* at 83-85; *see generally* Kling, *Diagnosis or Drug? Will Pharmaceutical Companies or Diagnostics Manufacturers Earn More from Personalized Medicine?*, 8 *EMBO Rep.* 903 (2007). Absent the potential rewards of patent protection, the incentive to invest in this area would virtually evaporate.

Regulatory burdens—although often necessary—further increase costs and lower incentives. The FDA, for example, is increasingly requiring that diagnostic products that go through the premarket approval process satisfy the same clinical and premarket criteria as those usually reserved for pharmaceuticals and medical devices. *See* FDA, *Draft Guidance* 8-10; Press Release, FDA, *FDA To Host Public Meeting on Oversight of Laboratory-Developed Tests* (June 16, 2010), available at <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm215766.htm>.<sup>7</sup> Moreover, the vast majority of health care dollars are paid not by individual consumers, but by insurance companies, which often demand validating data before approving a test for reimbursement. *See* National Center for Health Statistics, *Health, United States, 2010: With Special Feature on Death and Dying* 7 (2011), available at <http://www.cdc.gov/nchs/data/abus/abus10.pdf> (“In 2008, 35% of personal health care expenditures were paid by private health insurance, consumers paid 14% out of pocket, and 47% were paid by public funds,” primarily “Medicare and Medicaid expenditures.”). These demands of regulators and insurance providers for clinical evidence demonstrating safety and effectiveness increase costs and deter private investment. *See* Human Genetics Comm’n, *Intellectual Property and DNA Diagnostics: A Report of a Seminar on the Impact of DNA Patents on Diagnostic Innovation* 5-6 (Oct. 2010), available at <http://www.instituto-roche.es/web/pdf/2011/humangenteicscommision.pdf> (“*Intellectual Property and DNA Diagnostics*”).

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<sup>7</sup> As discussed below, there is an important distinction between *in vitro* diagnostics such as those made by Roche and Abbott, which receive premarket approval or clearance from the FDA, and laboratory-developed tests that are not reviewed by the FDA. *See* pp. 36-37, *infra*.

On top of that, there are the costs associated with innovations that either fail in development, fail to make it to market, or fail to succeed in the market. *See* p. 13, *supra*. As in other areas of biotechnology and pharmaceutical development, there is simply no guarantee *ex ante* that investments in research and development will be recouped through a commercially viable product. *See, e.g., Intellectual Property and DNA Diagnostics* 5-6; *Advancing Personalized Health Care* 85. The reward for a successful technology thus must be sufficient to cover not only the costs of that technology, but also the costs of many unsuccessful efforts that are the inevitable companions and predecessors of each successful one.

### **B. Patents On Diagnostic Tests Are Necessary To Promote Innovation And Clinical Research**

In light of the costs and high risk of failure, patents are critical to providing investors and innovators the realistic possibility of a reasonable financial return on those diagnostic products that actually make it to market—and preventing others from simply free-riding on their discoveries and funding. In a 2008 report on the subject, the President’s Council of Advisors on Science and Technology concluded:

The ability to obtain strong intellectual property protection through patents has been, and will continue to be, essential for pharmaceutical and biotechnology companies to make the large, high-risk R&D investments required to develop novel medical products, including genomics-based molecular diagnostics.

*Priorities for Personalized Medicine* 21.<sup>8</sup>

Indeed, regulators, industry participants, and commentators have all recognized that patent protections are vital to creating proper incentives for clinical research in the area of genetic testing and personalized medicine. *See* Nat’l Research Council, *Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation, and Public Health* 20 (Merrill & Mazza eds., 2006) (“Nat’l Research Council, *Reaping the Benefits*”) (“[I]ntellectual property protection is essential to ... enable firms to garner the sustained investments needed for diagnostic and drug development and testing[.]”); Secretary’s Advisory Comm. on Genetics, Health, & Soc’y, HHS, *Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests* 23 (2010), available at [http://oba.od.nih.gov/oba/sacghs/reports/SACGHS\\_patents\\_report\\_2010.pdf](http://oba.od.nih.gov/oba/sacghs/reports/SACGHS_patents_report_2010.pdf) (“SACGHS, *Gene Patents*”) (“Both the case studies and literature reveal that when researchers or companies sought private funds to initiate or advance their genetic research, investors were willing to provide funding because of the prospect of patents being granted as a result of the research.”); Toneguzzo, *Impact of Gene Patents on the Development of Molecular Diagnostics*, 5 Expert

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<sup>8</sup> In March 2000, investors mistakenly interpreted statements by President Clinton and British Prime Minister Blair as announcing their intention to narrow patent protection for gene-based innovations. Although the statements were later clarified, leading American biotechnology companies lost \$50 billion in aggregate shareholder value over the following two weeks. Davies, *Cracking the Genome* 205-207 (2001).

Op. Med. Diag. 273, 275 (2011) (“For validation of molecular diagnostics, patents are critical to incentivize the significant investment required for these activities.”); Paci et al., *Impact of DNA Patents on Pharmacogenomics Research and Development: Economic and Policy Issues*, 71 Drug Dev. Res. 485, 490 (2010) (patent protections “can stimulate private investments in an underexploited field with great potential for innovation and public health”); Sung, *Alarming Challenges Facing Medical Technology Innovation*, 6 J. Bus. & Tech. L. 35, 55-56 (2011) (“Tinkering with patent eligibility ... may bring unforeseeable consequences, including the unfortunate chilling of future innovation.”).<sup>9</sup>

For their part, Roche and Abbott filed about 350 priority patent applications in 2010 in an effort to protect their diagnostics research and development, while also timely sharing their scientific advances with the public. Roche and Abbott firmly believe that patenting their advancements is critical to their ability to continue their investments and forward planning in the diagnostic arena. Patents, moreover, are particularly important to small companies and start-ups because they rely on regular infusions of capital from investors, who often insist on the availability of patent protection as a precondition to funding ongoing research and development efforts. See, e.g., Biotechnology Industry Organization, *Guide to Biotechnology* 77 (2008), available at <http://www.bio.org/sites/default/files/BiotechGuide2008.pdf>; Barfield & Calfee, *Biotechnology and the Patent System* 27 (2007); Grabowski et al., *The Market for Follow-On Biologics: How Will It Evolve?*, 25 Health Aff. 1291, 1299 (2006).<sup>10</sup>

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<sup>9</sup> Some commentators argue that patents are not necessary because the costs of researching, developing, and commercializing diagnostic tests are lower than those in the biopharmaceutical industry generally. See, e.g., Robertson, *The Role of DNA Patents in Genetic Test Innovation and Access*, 9 Nw. J. Tech. & Intell. Prop. 377, 389-394 (2011); SACGHS, *Gene Patents* 30-35. Those costs are nevertheless substantial, and they rise even higher when the FDA and insurance providers subject diagnostic tests to the same level of scrutiny as pharmaceuticals and medical devices. See p. 14, *supra*.

<sup>10</sup> The authors of the SACGHS report state that “the role of patents in stimulating genetic research . . . appears to be limited to stimulating *private* funding that is supplemental to the significant Federal Government funding in this area,” suggesting that this somehow lessens the importance of patent protection. SACGHS, *Gene Patents* 26 (emphasis added). But government investment in genetic research in no way diminishes the need to stimulate private funding. Countless major scientific breakthroughs have resulted from private funding. In any event, it has been remarked that “[a] dollar’s worth of [federally funded] academic invention or discovery requires upwards of \$10,000 of private capital to bring [it] to market.” *Innovation’s Golden Goose*, *The Economist*, Dec. 14, 2002. Without the billions of dollars spent annually by the private sector on research, development, and clinical trials, the vast majority of scientific discoveries made by publicly-funded entities would not have been translated into actual diagnostic products brought to market for patient treatment. Indeed, that is the premise of the Bayh-Dole Act. See p. 18 n.12, *infra*. The lesson to take away from the SACGHS report is not that patents are unnecessary, but rather that the critical role the private sector plays in this field depends upon strong patent protections. See SACGHS, *Gene Patents* 23.

**C. Patents Spur “Spirals Of Innovation” And Design-Arounds That Result In Further Advances In Genetic Testing And More Options For Doctors And Patients**

Patents do not merely reward the patentee for its innovation. They also spur innovation by competitors. They publicize new scientific breakthroughs, enabling further breakthroughs by others. They provide a strong incentive for the development of competing technologies that increase treatment options for doctors and patients. And they facilitate cooperation by permitting companies to work collaboratively without risking the loss of their rights.

**1. Patents increase innovation by encouraging full disclosure of advances**

A patent represents “a carefully crafted bargain” in which the patentee is granted “an exclusive monopoly for a limited period of time” in exchange for “the public disclosure” of a new invention. *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 63 (1998). That disclosure must describe the advance in detail and provide enough information to enable others to practice it themselves. 35 U.S.C. § 112. It must also “set forth the best mode contemplated by the inventor of carrying out his invention.” *Id.*<sup>11</sup>

That bargained-for disclosure of the patented invention accelerates innovation. It does not merely publicize the invention itself, allowing for its immediate use by the whole public on the patent’s expiration. It also allows other inventors to build on the work of those who have gone before them. *See Scott Paper Co. v. Marcalus Mfg. Co.*, 326 U.S. 249, 255 (1945). In that sense, patent disclosures allow everyone to stand on the shoulders of giants (as well as lesser innovators). The USPTO reports that as a result of the American Inventor Protection Act of 1999, Pub. L. No. 106-113, 113 Stat. 1501, 1501A-552, “roughly 90 percent of all pending patent applications are published at eighteen months.” FTC, *To Promote Innovation: The Proper Balance of Competition and Patent Law and Policy*, ch. 1, at 26 (Oct. 2003), available at <http://www.ftc.gov/os/2003/10/innovationrpt.pdf> (discussing testimony of USPTO personnel). Companies utilize that expanded knowledge base to develop further advances that build on the patented technique. *See Toneguzzo*, 5 Expert Op. Med. Diag. at 275 (“the evidence shows that patents do not inhibit research leading to new discoveries and, in fact, may in some cases stimulate it through the disclosure of innovations”).

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<sup>11</sup> Under the AIA, failure to fulfill the “best mode” requirement of 35 U.S.C. § 282(a)(3) is no longer a basis for challenging the patent’s validity in infringement proceedings. *See* AIA, § 15. But it remains a requirement for the USPTO’s issuance of a patent; as a result, it does not affect the patent examination practices set forth in the USPTO’s Manual of Patent Examining Procedures § 2165. Thus, even in a post-AIA world, a patent applicant remains under an obligation to disclose the best mode of practicing an invention in order to obtain a patent thereon.

The requirements that patents contain a detailed description of the invention, enable others to practice the invention, and set forth the best mode of implementing it, make patents particularly powerful tools for the advancement of knowledge. Those seeking to understand the invention do not need to re-invent a hidden or omitted step or detail. Nor do those who seek to understand the optimal implementation of the invention need to waste time and effort reverse-engineering the product or trying to cobble it together using disparate, incomplete sources of public information, such as academic articles.

The development of tests for cystic fibrosis, a genetic disorder that afflicts approximately 30,000 Americans, exemplifies the effect patents have in spurring innovation by expanding the available knowledge base. A case study commissioned for the SACGHS report on gene patents explains that the University of Michigan, Johns Hopkins, and the Hospital for Sick Children in Toronto, Canada all hold patents covering probes relating to and methods of detecting mutations of the *CFTR* gene, which causes cystic fibrosis. Chandrasekharan et al., *Impact of Gene Patents and Licensing Practices on Access to Testing for Cystic Fibrosis 1-2* (2009) (“*Cystic Fibrosis Study*”) (SACGHS, *Gene Patents*, app. A, pt. C). Those entities grant non-exclusive licenses for use of their patents, a practice that has enabled other entities in turn to use those discoveries as a foundation for developing a multitude of diagnostic kits for cystic fibrosis. Using that licensed intellectual property, Luminex has created and received FDA approval for its xTag cystic fibrosis diagnostic kit, which tests for 39 mutations and 4 variants of the *CFTR* gene. *Id.* at 8. Ambrey Genetics’s CF Amplified test purports to sequence the full *CFTR* gene and surrounding critical introns. *Id.* And the study identified several other manufacturers “preparing FDA approved diagnostic kits to compete in the CF testing and screening markets,” including Nanogen and Third Wave (subsequently acquired by Hologic). *Id.* None of those tests would have been possible absent the patented discoveries licensed to the companies by the University of Michigan, Johns Hopkins, and HSC. The study thus correctly concluded that the “patenting and licensing decisions” made with regard to the *CFTR* gene and its mutations “allow for significant research without unduly hindering patient access or commercial markets. These practices also preserve strong patent protection and the accompanying investment incentives for possible therapeutic discoveries arising from the same DNA patents.” *Id.* at 21.<sup>12</sup>

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<sup>12</sup> The notion that private industry will build on the patented research of publicly-funded institutions like universities is one of the major premises underlying the Bayh-Dole Act, 35 U.S.C. §§ 200, *et seq.* The “polic[ies] and objective[s]” of the Act include “us[ing] the patent system to promote the utilization of inventions arising from federally supported research or development” by, among other things, “promot[ing] the commercialization and public availability of inventions.” 35 U.S.C. § 200. The Act is born of the recognition that while much federally-funded university research is “fundamental ... to technological advance” and may be patented by those institutions,

[u]niversities ... generally do not have the means of production necessary to take the results of research and generate marketable products. Such activities are carried out by industry. Thus, the emphasis in the Bayh-Dole Act on the promotion of cooperative efforts between academia and the business

Absent patent protection, some companies might opt to maintain their discoveries as trade secrets. For example, an innovator that discovered a novel correlation between a biomarker and certain health outcomes and developed a test based on that discovery might choose to maintain the details of its discovery and test as a trade secret, rather than risk having other companies copy it and undercut the innovator because those companies do not have the same research and development costs to recoup. Indeed, the number of instances in which only a single provider is available to perform a test could increase if companies feel that they must fall back on trade secret protection and tight control of the testing process instead of patenting and widely licensing their inventions.

## **2. Patents encourage competitors to develop non-infringing alternatives that may improve upon the original invention**

Sometimes patents serve less as a foundation that others build on and more as a catalyst for developing new—and potentially more accurate, cheaper, and faster—ways of achieving the same result. Because the patent prevents competitors from simply copying the innovator’s invention, competitors have a strong incentive to develop non-infringing alternatives. The result is a diversity of options for the medical community and patients alike.

No less than in other areas, the success of a patented innovation can demonstrate that there is a market for a test for a particular genetic condition, creating pressures for competitors to develop new ways of testing for that condition by “designing around” the original patent. That incentive to “‘design around’ a competitor’s products, even when they are patented,” has long been recognized as one of the “benefit[s] of [our] patent system.” *State Indus., Inc. v. A.O. Smith Corp.*, 751 F.2d 1226, 1236 (Fed. Cir. 1985); *see also Slimfold Mfg.Co. v. Kinkead Indus., Inc.*, 932 F.2d 1453, 1457 (Fed. Cir. 1991) (“Designing around patents is, in fact, one of the ways in which the patent system works to the advantage of the public in promoting progress in the useful arts, its constitutional purpose.”). The design-around process—“keeping track of a competitor’s products and designing new and possibly better or cheaper functional equivalents”—thus “bring[s] a steady flow of innovations to the marketplace” and is the very “stuff of which competition is made.” *A.O. Smith Corp.*, 751 F.2d at 1235-1236. Absent the period of exclusivity provided by patents, competitors often would not bother developing those alternatives; it would be cheaper and faster simply to copy any innovator, riding on its coattails.

The need to compete without infringing thus provides a strong incentive for the development of new, alternative, and often improved ways of testing for the same condition.

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community. By providing universities with intellectual property ownership with which to pursue and structure collaborative ventures, the legislation encourages the two sectors to work together to generate new goods, processes, and services for the marketplace.

Schacht, Cong. Research Serv., RL32076, *The Bayh-Dole Act: Selected Issues in Patent Policy and the Commercializing of Technology* 4-5 (2007).

Those pressures are no stranger to competitors like Abbott and Roche. For example, in 1998, Abbott obtained FDA premarket approval for the PathVysion HER-2 DNA probe kit, the first diagnostic test used to identify those patients who, due to a genetic anomaly, exhibit over-expression of a protein (“HER-2”) associated with certain particularly aggressive cancers. More importantly, it also predicts whether the patient will have a dramatic response to treatment with Herceptin®, a drug produced by Genentech. Thus, Abbott’s HER-2 companion diagnostic not only identifies patients who will respond to Herceptin®, it also helps identify patients who will not. Abbott patented the PathVysion assay.

Abbott’s patent, however, did not prevent others from developing alternative ways of testing for HER-2 over-expression. Roche’s subsidiary Ventana has developed, and the FDA has approved, a new tissue-based genetic test for the measurement of HER-2 in breast tumor tissue—the INFORM HER-2 Dual ISH DNA Probe Cocktail—that uses standard light microscopy to detect two color chromogenic labeling of targets. Thus, while both Abbott’s and Roche’s HER-2 tests are ISH (*in situ* hybridization) assays, they nevertheless provide different methods for performing the HER-2 test. And other, different types of tests have been developed as well. For example, Dako’s HercepTest and Ventana’s Pathway assays test for HER-2 over-expression using immunohistochemistry rather than ISH. The HER-2 story is a clear instance in which “designing around extant patents” has “creat[ed] viable substitutes and advances, resulting in competition among patented technologies. The public clearly benefits from such activity.” Nard, *A Theory of Claim Interpretation*, 14 Harv. J.L. & Tech. 1, 40-41 (2000).

Testing for human papilloma virus (“HPV”), although not the type of human genetic testing covered by Section 27 of the AIA, provides another example of approaching the same problem from multiple angles. HPV is a sexually-transmitted disease that causes cervical cancer. The CDC estimates that approximately 20 million Americans are currently infected with HPV. Nearly 12,000 U.S. women are diagnosed with cervical cancer each year, and HPV is suspected to be responsible for a large number of these cases. Following the characterization of HPV type 52, Digene (now owned by Qiagen) obtained a patent on a HPV 52 hybridization probe. *See* U.S. Patent 5,643,715. But Third Wave Technologies (now owned by Hologic) was able to design around the patent and produce its own test. *See Digene Corp. v. Third Wave Techs., Inc.*, 323 Fed. App’x 902 (Fed. Cir. 2009). Meanwhile, Roche conducted a study of more than 47,000 women in the United States and, in 2011, secured FDA approval for its own innovative approach. Roche’s test substantially improves on previous assays because it individually identifies HPV 16 and 18, the two highest-risk HPV types responsible for more than 70 percent of cervical cancer cases, while concurrently detecting twelve other high-risk types (including HPV 52) in a pooled result. Taking a different tack, mtm laboratories AG (now Roche mtm laboratories AG) developed and patented anti-p16 antibody-based tests for detecting cervical cancer in cytological and histological samples. Thus, against a backdrop of patent protection, competition and creativity have given patients multiple testing options and improved the screening of women at risk for cervical cancer.

The above examples, moreover, are just that—examples. Similar tales could be told with regard to the development of countless other genetic tests. In short, patents do not stifle innovation in the field of genetic testing. To the contrary, they disseminate discoveries and spur competition in ways that advance the state of medical knowledge and increase treatment options.

### **3. Patents facilitate cooperation and licensing among potential competitors**

It has long been recognized that protecting intellectual property can enhance rather than impede the dissemination and availability of important new technologies. *See, e.g.,* Heald, *A Transaction Costs Theory of Patent Law*, 66 Ohio St. L.J. 473, 489 (2005) (patents “enable[ ] a potential transferor to share an information asset without fear of misappropriation while assembling the complex team necessary to commercialize a new product”). For example, the first semi-synthetic penicillins like ampicillin—critical to overcoming staphylococci resistant to biological penicillins—owed both their development and their availability to strong patent protection. *See* Taylor & Silbertson, *The Economic Impact of the Patent System* 258-259 (1973). It is well accepted that the British inventors there would not have invested in the groundbreaking research that led to their invention absent the incentives created by the patent system. *Id.* at 259. More important for present purposes, the patent system was also responsible for their rapid public availability. Lacking experience in large-scale pharmaceuticals manufacturing, the original British inventor partnered with a more experienced American pharmaceutical company to develop manufacturing techniques, exchanging information and licenses. *Id.* at 258. “[H]ad effective sole patent protection been unavailable in the U.S.A.,” however, “it would have been extremely difficult to persuade [the American manufacturing expert] to divulge its manufacturing know-how” in return for distribution rights, delaying or even imperiling the life-saving antibiotic’s global distribution. *Id.* at 259.

The Wisconsin Alumni Research Foundation (“WARF”) provides a contemporary example of patents facilitating cooperation among different entities to transform discoveries into products that benefit society. WARF has developed a program to license its patents broadly on a non-exclusive basis. WARF, *Licensing Process*, <http://www.warf.org/industry/index.jsp?cid=1>. It thus seeks out partnerships with any company that

- “sees the likely commercial benefit to itself of one of WARF’s technologies developed at the [University of Wisconsin]-Madison”;
- “has the capability to develop early-stage technology (typical of university research) and is willing to make a reasonable effort to commercialize it”;
- “is able to demonstrate its serious intent by paying a reasonable licensing fee and reimbursing patent costs associated with the technology”; and

- “is willing to share some of the benefits of the commercial use of the technology with WARF and the UW-Madison through payment of a reasonable royalty on product sales.”

*Id.* WARF “shares in the development risk by requiring a reasonable license fee and a royalty that is received only after a product or process is being sold or otherwise used.” *Id.* WARF’s broad licensing practices generate significant revenue—over \$54 million in 2008 alone. *Licensing Revenue 2008*, OnWisconsin Magazine, <http://onwisconsin.uw alumni.com/departments/licensing-revenue-2008>. But WARF benefits in other ways as well, attracting “additional ‘margin of excellence’ research funding to the UW-Madison,” and knowing that “the inventions of the UW-Madison faculty” will be put “to work for the maximum benefit of society.” WARF, *Licensing Process*, <http://www.warf.org/industry/index.jsp?cid=1>.

WARF’s patents covering primate and human embryonic stem cell lines exemplify those benefits. Through its subsidiary, Wicell Research Institute, WARF licenses its stem cells broadly—fulfilling over 900 stem cell licenses since 1999—and has shipped stem cells to more than 500 researchers around the world. WARF News, *United States Patent And Trademark Office Upholds Key WARF Stem Cell Patent* (Feb. 28, 2008), [http://www.warf.org/news/news.jsp?news\\_id=224](http://www.warf.org/news/news.jsp?news_id=224). Those licenses have allowed pharmaceutical companies, research entities, and universities to rely on stem cell technology to devise new ranges of therapies that would otherwise be inaccessible to the public.

WARF’s non-exclusive licensing practices have also spawned numerous start-up companies that use their ideas to commercialize UW-Madison’s patents. Examples of start-ups using UW-Madison patents to further the field of genetic research include LifeGen Technologies LLC (acquired by Nu Skin Enterprises Inc.), Mirus Bio LLC (acquired by Roche), Nimblegen Inc. (also acquired by Roche), and Third Wave Technologies (acquired by Hologic). WARF, *Warf Startups*, <http://www.warf.org/startups/index.jsp?cid=44>.

Likewise in the area of genetic molecular diagnostics, patent protection allows Abbott and Roche to partner with other innovators—and other innovators to partner with them—to bring life-saving technologies more quickly to market. Patent protection allows innovators to share their technology with potential partners, who may be able to help develop, refine, commercialize, and distribute it—secure in the knowledge that it cannot be stolen. And potential partners can point to patent protection to encourage less-experienced companies with promising technologies to seek necessary assistance without risking the loss of their intellectual property.

For example, Roche’s subsidiary Ventana recently entered into a collaboration agreement with Pfizer, Inc. and a license agreement with Cell Signaling Technology (“CST”) to develop a companion diagnostic test that will identify ALK gene rearrangements in non-small cell lung cancer patients through the measurement of an associated protein. *See* Ventana, Media Release, *Ventana to Collaborate with Pfizer and CST on Companion Diagnostic to Identify Lung Cancer Patients with ALK Gene Rearrangements* (Jan. 10, 2012),

available at <http://www.ventana.com/site/page?view=press-release-january10-2012>.<sup>13</sup> The test will be based on CST's D5F3 antibody and Ventana's Optiview DAB detection, for performance on Ventana automated platforms. Absent patent protection to safeguard each company's contributions, this cross-company cooperation might not have been possible.

### **III. Patent Claims Directed To Genetic Tests Do Not Limit Scientific Research Or Patient Access**

As discussed in the preceding section, any analysis of patents' impact on the availability of primary and secondary genetic testing must consider the critical role that patents play in making those tests available in the first place. Further, as discussed in this section, claims that patents impede research or limit patient access to primary and secondary testing are greatly exaggerated.

#### **A. Patents On Diagnostic Tests Do Not Pose An Obstacle To Scientific Research**

Some have argued that patents are impediments rather than catalysts to the development and availability of genetic testing because patent protection prevents scientific research. In particular, some have speculated that patents stymie basic research by withdrawing certain innovations from the scientific "commons" available for all to use. See Caulfield et al., *Evidence and Anecdotes: An Analysis of Human Gene Patenting Controversies*, 24 *Nature Biotech.* 1091 (2006). The long-standing "conventional view," however, is precisely to the contrary: Biomedical research "is more likely to be impeded by lack of access to privately held research inputs such as materials, data and know-how than by patents." Chandrasekharan et al., *Proprietary Science, Open Science and the Role of Patent Disclosure: The Case of Zinc-Finger Proteins*, 27 *Nature Biotech.* 140, 140 (2009).

In fact, "empirical research suggests that the fears of widespread anticommons effects that block the use of upstream discoveries have largely not materialized." Caulfield et al., 24 *Nature Biotech.* at 1093; see also Adelman & DeAngelis, *Patent Metrics: The Mismeasure of Innovation in the Biotech Patent Debate*, 85 *Tex. L. Rev.* 1677, 1681 (2007) ("The existing empirical studies find few clear signs that the patenting of biotechnology inventions is adversely affecting biomedical innovation."); Paci et al., 71 *Drug Dev. Res.* at 485 ("recent evidence on genetic testing suggests that many of the issues might have been overestimated or overemphasized"). The Federal Trade Commission ("FTC") likewise noted that "concern previously centered on the belief that biotechnology patent protection was too strong" and "would actually obstruct commercialization of new products, thereby hindering follow-on

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<sup>13</sup> This approach to detecting ALK gene rearrangements differs from the one taken by Abbott's Vysis ALK Break Apart FISH Probe, and thus provides additional evidence that the incentive to design around, rather than merely copy, a competitor's test can increase the number of alternatives available to patients.

innovation. This problem has yet to materialize.” FTC, *Emerging Health Care Issues: Follow-on Biologic Drug Competition* 32 (2009) (footnote omitted).<sup>14</sup>

Thus, while the SACGHS report voices concern that patent issues *theoretically* could restrict genetic research and development, it conceded that, in reality, the “empirical research suggest[s] that research is not hampered” by patents. SACGHS, *Gene Patents* 88. Indeed, the case studies on which the SACGHS report purports to base its recommendations repeatedly conclude that patents have *not* inhibited follow-on research:

- “Concerns regarding inhibition of research due to the *HFE* gene patents do not seem to be supported. Substantial basic research, including identification of genes and mutations associated with other types of hemochromatosis has continued. Similarly, research on improved methods for detection of *HFE* mutations has also progressed.” Chandrasekharan et al., *Impact of Patents on Access to Genetic Testing for Hereditary Hemochromatosis* 3 (2009) (“*Hemochromatosis Study*”) (SACGHS, *Gene Patents*, app. A, pt. E).
- “We have not found any evidence that CF gene patents impeded subsequent basic or clinical research.” *Cystic Fibrosis Study* 20.
- “There is no evidence that patents have had any positive or negative impact on hearing loss genetics research.” Chandrasekharan & Fiffer, *Impact of Patents and Licensing Practices on Access to Genetic Testing for Hearing Loss* 4 (2009) (“*Hearing Loss Study*”) (SACGHS, *Gene Patents*, app. A, pt. D).
- “[W]e have no evidence that the virtual LQTS monopoly from 2003-2008 has had any stifling effect on research....” Angrist et al., *Impact of Patents and Licensing Practices on Access to Genetic Testing for Long QT Syndrome* 24 (2009) (“*LQTS Study*”) (SACGHS, *Gene Patents*, app. A, pt. F).
- “[No] evidence of a chilling effect in the basic science arena for either FAP or HNPCC.” Cook-Deegan et al., *Impact of Patents and Licensing on Access to Genetic Testing for Inherited Susceptibility to Cancer: Comparing Breast and Ovarian Cancers to Colon Cancer* 27 (2009) (“*Breast, Ovarian, and Colon Cancers Study*”) (SACGHS, *Gene Patents*, app. A, pt. A).

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<sup>14</sup> A 2005 survey of scientists involved in biomedical research found that “patenting does not seem to limit research activity significantly, particularly among those doing basic research.” Walsh et al., *Patents, Material Transfers and Access to Research Inputs in Biomedical Research* 3 (Sept. 20, 2005) (“Walsh, *Patents & Access*”); see also Walsh et al., *View From the Bench*, 309 *Science* 2002 (2005). An earlier study found that patents “rarely precluded the pursuit of worthwhile projects.” Walsh et al., *Working Through the Patent Problem*, 299 *Science* 1021, 1021 (2003) (“Walsh, *Working Through the Patent Problem*”). When requested, licenses were often available at minimal or no cost. Walsh, *Patents & Access* 17. “Thus, not only are barriers or delays rare, but costs of access for research purposes are negligible.” *Id.*

- “[N]ot f[inding] patents to be a significant impediment to research on [Alzheimer’s Disease.]” Skeehan et al., *Impact of Patents and Licensing Practices on Access To Genetic Testing for Alzheimer’s Disease* 14 (2009) (“Alzheimer’s Study”) (SACGHS, *Gene Patents*, app. A, pt. B).
- “It is clear that the Tay-Sachs gene patent did not stifle research as it was never enforced. ... [T]hrough the Canavan patent could in theory have impeded research until 2003, it does not anymore.” Colaianni et al., *Impact of Patents and Licensing Practices on Access to Genetic Testing and Carrier Screening for Tay-Sachs and Canavan Disease* 14 (2009) (“Tay-Sachs and Canavan Study”) (SACGHS, *Gene Patents*, app. A, pt. H).

In addition, Australia recently studied the very patent and licensing practices by Myriad Genetics concerning BRCA1 and 2 that prompted Section 27 of the AIA, *see* p. 27, *infra*, and concluded that “patents over human genes and biological materials have not hindered research, particularly medical research, in Australia.” Austl. Legal and Constitutional Affairs Legislation Comm., *Report on Patent Amendment (Human Genes and Biological Materials) Bill 62* (2010), available at [http://www.aph.gov.au/Parliamentary\\_Business/Committees/Senate\\_Committees?url=legcon\\_ctte/patent\\_amendment/report/report.pdf](http://www.aph.gov.au/Parliamentary_Business/Committees/Senate_Committees?url=legcon_ctte/patent_amendment/report/report.pdf). To the contrary, the report found, “patents have encouraged and contributed to research and development activities” because “[p]atents allow researchers to attract investment to pursue the development of new inventions and allow companies to mitigate the risk associated with developing costly new products.” *Id.*

One of the reasons that patents have not inhibited follow-on research is that patent holders in the biopharmaceutical industry are generally loath to threaten enforcement against the scientific and medical communities. Pressman et al., *The Licensing of DNA Patents by Large U.S. Academic Institutions: An Empirical Survey*, 24 *Nature Biotech.* 31, 37 (2006); Mossinghoff, *Remedies Under Patents on Medical and Surgical Procedures*, 78 *J. Pat. & Trademark Off. Soc’y* 789, 796-797 (1996). “Rational forbearance” from patent enforcement against non-commercial and/or non-competitive uses of patented technologies has become an industry norm that plays “a significant role in ensuring the broad use of many genomic technologies.” Fore Jr. et al., *The Effects Of Business Practices, Licensing, and Intellectual Property on Development and Dissemination of the Polymerase Chain Reaction: Case Study*, 1 *J. Biomed. Discovery & Collaboration* 7, 16 (2006); *see also* Nat’l Research Council, *Reaping the Benefits* 121-122. Patent holders, moreover, are reluctant to upset the norm of open access in the research and medical communities for fear of losing reciprocal privileges to materials and information. *See* Walsh, *Working Through the Patent Problem* 1021. Experimental and clinical uses are likely to benefit patent holders by increasing the value of patented technologies. Putative infringers in the academic and medical communities are, therefore, often viewed as prospective partners in the development of the technology. *Id.*; Pressman, 24 *Nature Biotech.* at 37.

Consistent with those observations, Roche has a long-standing policy of licensing its patented diagnostic technologies at little or no cost for research purposes. Fore et al., 1 J. Biomed. Discovery & Collaboration at 10 (noting that Roche’s stance with respect to non-commercial use of diagnostic patents was “in line with the traditional corporate practice of ‘rational forbearance’”). Abbott similarly cooperates with researchers and innovators to support their important work.

Far from having incentives to impede research and medical uses of patented diagnostic technologies, the biopharmaceutical industry has strong incentives to continue the dissemination of patented diagnostic tools and methods. There is no reason to believe that the effect of diagnostic patents in the future will be any different from their effect in the past: encouraging investment in personalized medicine and other breakthrough techniques for the benefit of patients and health care generally without posing any significant burden on research.

### **B. Patents Do Not Impede Patient Access To Genetic Tests In General**

Even apart from the role that patents play in encouraging the creation of new tests, empirical research confirms that patents themselves do not restrict patient access to genetic testing. The SACGHS report identified no evidence of significant patient-access problems caused by patents (as opposed to insurance coverage)—even where patents are exclusively licensed. See pp. 32-33, *infra*. And it further noted that “the case studies generally found that for patented tests that were broadly licensed”—the most common industry practice, and the one followed by Roche and Abbott, see pp. 28-29, *infra*—“there was *no evidence* of patient access problems.” SACGHS, *Gene Patents* 42 (emphasis added). For example, the SACGHS-commissioned study on cystic fibrosis found “no evidence that patents have significantly hindered access to genetic tests.” *Cystic Fibrosis Study 2*. Another study found that “[p]atents do not appear to have significantly impeded patient or clinical access for hearing loss genetic testing.” *Hearing Loss Study 26*. And the study on genetic testing for hemachromatosis found that “testing is widely available from multiple sources,” and that there is “little evidence bearing on the impact of patents on consumer utilization.” *Hemachromatosis Study 4, 5*.

To the extent there were any systemic problems with patient access to genetic testing as a result of patents—and Roche and Abbott are aware of none—those issues would best be resolved through market-driven approaches, such as patent pools and patent clearinghouses, rather than limitations on patent rights in genetic tests. Such collaborative licensing arrangements have succeeded in alleviating perceived barriers to entry and access in other industries. See Verbeure et al., *Patent Pools and Diagnostic Testing*, 24 Trends in Biotech. 115, 117-118 (2006); Ebersole et al., *Patent Pools as a Solution to the Licensing Problems of Diagnostic Genetics*, 17 Intell. Prop. & Tech. L.J. 1, 8 (2005). Stakeholders in the personalized medicine industry should be permitted to explore these options free from outside interference, which creates uncertainty and may actually hinder the development of market-based solutions. See Toneguzzo, 5 Expert Op. Med. Diag. at 275.

### C. Patents Do Not Impede Patients From Obtaining Independent Second Opinions With Regard To Genetic Tests

For similar reasons, patent protection and industry licensing practices do not impede—and in fact generally promote—the “independent second opinion genetic diagnostic testing” the USPTO is tasked with evaluating in these proceedings. *See* AIA, § 27(b)(1)-(2); 77 Fed. Reg. at 3748. Although the first question that Congress has posed to the USPTO presupposes that there is a “current lack of independent second opinion testing,” the evidence does not bear this out, and certainly does not demonstrate any widespread problem attributable to patent protection.

The apparent impetus for Section 27 was the BRCA diagnostic test marketed by Myriad Genetics. *See* 157 Cong. Rec. H4433 (daily ed. June 22, 2011). That test detects mutations in the BRCA1 and BRCA2 genes that indicate dramatically increased risk of breast and ovarian cancer. A Member of Congress noted that the Myriad test was the only “test on the market for this mutation,” and Myriad “also ha[s] an exclusive license for limited laboratories to administer the test.” *Id.* In that situation, the Representative expressed concern there was “no way” for patients testing positive “to get a truly independent second opinion” before making potentially life-altering decisions regarding their course of treatment. *Id.*

The Myriad BRCA situation, however, is an outlier, not a symptom of a more pervasive problem with patient access to independent second opinions. It is far from clear that even the Myriad example had an adverse effect on public health. Nor is there any reason to believe that weakening patent protections is the way to remedy any problem. Indeed, were it not for the incentives provided by patents, there might never have been a BRCA test to run in the first place. *See* pp. 17-23, *supra*. Moreover, for the reasons given above, *see* pp. 19-21, *supra*, and as explained in greater detail below, *see* pp. 29-31, *infra*, patent protection on the whole creates greater incentives for the development of competing tests and thus greater opportunities for *meaningful* second opinion testing under a diversity of techniques, as opposed to simply re-running the same exact test another time in a different lab.

Thus, at the outset, it is important to clarify the nature of the concern being addressed. Section 27 appears to conceive of a “second opinion” as entailing having a second laboratory re-run the same exact genetic test that another laboratory has already performed. In the context of genetic testing, however, a “second opinion” can take several different forms: apart from re-running the same particular genetic test, it could refer to running a different test for the same condition, or having a second doctor advise on the proper course of treatment in light of the results of a single, initial test. There is scant evidence that there are widespread problems with patient access to second opinions in any of those contexts, or that any limitations on patient access are the result of strong patent protections.

## 1. Accurate genetic tests rarely need to be run a second time

Whether to re-run a specific genetic test is at its core a medical decision left to the discretion of the treating physician. In general, however, re-running a test would be necessary only if there were reason to doubt the results of the first test. Where the test itself is known to be highly accurate, such “do-overs” rarely prove necessary. And, where the test itself is reliable, intellectual property rights would never preclude the physician from ordering a second test from the *same* laboratory to see if it reaches a different result. Instead, as discussed in more detail below, problems arise only if one lacks confidence in the test or the lab performing it. Because of that, the government’s focus should be on ensuring that all genetic tests are subjected to appropriate scrutiny before reaching the market so that they are more likely to yield the right result the first time, rendering it unnecessary to re-run the same test. *See pp. 35-37, infra*. If patent rights are weakened, that will only lessen the incentives that companies have to invest in clinical trials and other costly procedures to ensure that the tests they market are as accurate as possible.

## 2. Most genetic tests are broadly sold or licensed, and thus it is rare that a second laboratory cannot re-run a particular genetic test

Assuming there is a reason to have a second laboratory re-run a genetic test as a double-check on the first laboratory’s results, patent rights in the test typically pose no impediment to doing so. Any limits on the availability of Myriad’s BRCA test, for example, resulted not from the fact that it is patented, but from the fact that Myriad allows only its own laboratories to manufacture and administer certain BRCA1 and BRCA2 diagnostic tests in the U.S.—effectively providing them with an exclusive license with respect to the BRCA patents.<sup>15</sup> Myriad’s exclusive-licensing practices, however, are the rare exception rather than the rule. The far more common practice in the field of genetic testing is widespread selling of test kits or licensing of patents, which allows multiple providers to run the same test.

The standard industry practice of selling or licensing tests broadly to multiple competent providers reflects basic economics. As the SACGHS report explains, having “multiple providers” of a licensed test “leads to competition” among the *licensees* and thus “increases the size of the *patent holder’s* market.” SACGHS, *Gene Patents* 18 (emphasis added). To the extent patent holders hope to capture surplus value, that is achieved by encouraging competition among providers; restricting that competition transfers surplus from the patentee to the provider. Thus, most patentees broadly sell or license their tests because it is generally not in their financial interest to restrict the availability of their tests through exclusive licensing. The “large risks of commercialization in the biotechnology industry also provide a particularly strong incentive for patentees in this industry to license broadly as a

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<sup>15</sup> 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 Magazine, Feb. 24, 2002, at 10.

method for reducing risk.” Kieff, *Property Rights and Property Rules for Commercializing Inventions*, 85 Minn. L. Rev. 697, 726 (2000).

Consequently, when physicians determine that a second laboratory should re-run a test, there is usually no shortage of laboratories able to perform the service. The SACGHS report found, “[f]or example,” that “more than 50 private and public entities offer testing for cystic fibrosis (CF) ... in the United States under a nonexclusive license.” SACGHS, *Gene Patents 2*. It also found “more than 50 academic and commercial laboratories” offering genetic testing for Huntington’s disease. *Id.* The case studies commissioned for the SACGHS report likewise found broad licensing and multiple test providers to be the rule for the genetic tests they considered. *See, e.g., Tay-Sachs and Canavan Study 8* (finding “37 U.S. laboratories providing Canavan testing, and 34 for Tay-Sachs testing”); *Hearing Loss Study 6* (“A large number of providers offer these tests with a wide price range.”); *Hemochromatosis Study 4* (HFE “testing is widely available from multiple sources”); *Breast, Ovarian, and Colon Cancers Study 17* (at least 9 providers performing test for Lynch Syndrome; at least 7 providers performing test for FAP). And indeed, one need only consult the NIH’s Genetic Testing Registry (<http://www.ncbi.nlm.nih.gov/gtr>) to see that for the vast majority of conditions for which a genetic test exists, there are usually multiple test providers.

For their part, Abbott and Roche currently market hundreds of genetic diagnostic-related products. Those products are the results of decades of research and billions of dollars in investment, and are protected by hundreds of U.S. patents. But those patents do not restrict the options of patients using Abbott or Roche genetic tests. Indeed, both Abbott and Roche typically sell test kits they have developed or license their genetic patents on a non-exclusive basis, so multiple providers are able to utilize those innovations.

Abbott and Roche simply are not aware of any actual evidence that there is a widespread problem with patents and exclusive licenses restricting the ability of doctors to obtain confirmation of the results of a particular genetic test from a second, independent laboratory. There is certainly no proof that the problem is sufficient to warrant making major changes in the rights of patent holders.<sup>16</sup>

### **3. Patents promote the creation of alternative tests that may benefit patients more than simply re-running the same test**

In the long term, moreover, patients are better served through a diversity of testing procedures—not by having a large number of labs performing the same tests with the same potential shortcomings. After all, if there are doubts about the results of a particular test, the patient likely would be better off if a different *type* of test for the same genetic condition is available. There are typically no impediments to such a “second opinion” test being performed—at least none attributable to intellectual property rights—even if the first test were one of the few subject to an exclusive license.

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<sup>16</sup> This is particular the case given that, as noted in the Introduction, the full impact of the Supreme Court’s recent *Mayo Collaborative Services* decision has yet to be determined.

As discussed above, patents help promote the diversity of test options. One company's exclusive rights to a patented test, combined with competitive pressures, creates incentives for other companies to develop alternative tests for the same condition. *See pp. 19-21, supra.* For example, if a patient diagnosed with cystic fibrosis under Luminex's xTag kit wants a second opinion, she may seek to have Ambrey Genetics's CF Amplified test run to see if it confirms the diagnosis. Likewise, if the HercepTest indicates that a patient has an over-expression of the HER-2 protein, she could seek a "second opinion" by running any of the PathVysion HER-2 DNA probe test, the Pathway test, or the INFORM HER-2 Dual ISH DNA Probe Cocktail.

Consulting the NIH's Genetic Test Registry again confirms that multiple *types* of genetic tests are frequently available for a single condition, allowing for "second opinion" tests using different methods. For example, the Genetic Test Registry shows:

- In testing for Alzheimer Disease Type 1, doctors may choose from FISH-Interphase tests, FISH-Metaphase tests, sequence analysis of the entire coding region, deletion/duplication analysis, or sequence analysis of select exons.
- In testing for Autism Spectrum Disorder, doctors may choose from FISH-Interphase tests, FISH-Metaphase tests, sequence analysis of the entire coding region, or deletion/duplication analysis.
- In testing for Down Syndrome Critical Region, doctors may choose from FISH-Interphase tests, FISH-Metaphase tests, or deletion/duplication analysis.
- In testing for Huntington's disease, doctors may choose from targeted mutation analysis or linkage analysis.
- In testing for prostate cancer, doctors may choose from deletion/duplication analysis, sequence analysis of select exons, or sequence analysis of the entire coding region.

The Myriad BRCA test represents the perfect storm of a genetic test that was exclusively licensed *and* for which there may have been no viable alternative test. It is thus an extreme outlier, as patients usually will have multiple options for obtaining a "second opinion" genetic test.

Any such "perfect storm," moreover, will always be of limited duration. That is not merely because the patent exclusivity period itself is for only a limited time, but also because competitors will inevitably enter the market with alternative solutions. Indeed, as one of the SACGHS case studies has noted, for breast, ovarian, and colon cancer, "there are more genetic tests for cancer in the pipeline than are currently available." *Breast, Ovarian, and Colon Cancers Study* 30. Indeed, the FDA has approved "an investigational device exemption study for a breast cancer risk test developed by InterGenetics called Oncovue®." *Id.* InterGenetics bills Oncovue® as "the first genetic-based, breast cancer risk test that

incorporates both individualized genetic-based [single nucleotide polymorphisms] and personal history measures to arrive at an estimate of a woman’s breast cancer risk.” InterGenetics, *What is Oncovue®?*, <http://www.intergenetics.com/cms/technologyandproducts/whatisoncovue>. InterGenetics claims that its “ultimate goal” is for Oncovue® “to be the first FDA cleared product for the identification of breast cancer in women, and paving the way for other genetic research companies who come behind us.” *Id.* As the SACGHS case study concluded, the Oncovue® example is a “reminder that patent protection never guarantees permanent protection from competition.” *Breast, Ovarian, and Colon Cancers Study* 30.

**4. “Confirmatory testing”—as opposed to “second opinions” about the appropriate course of treatment based on an already conducted test—is rare**

Finally, even if one were to assume that, on rare occasions, licensing practices might restrict the available laboratories for “confirmatory testing”—i.e., re-running the same genetic test in the short term—it is far from clear that such “confirmatory testing” is often needed or desired. While Roche and Abbott leave the practice of medicine to the physicians, we know of no basis for the assertion that the “second opinion” patients most often seek is “confirmatory testing.” To the contrary, there is every reason to believe that what patients most often desire when faced with a life-altering decision is a second opinion from another *doctor* as to the proper course of treatment in light of the results of an otherwise reliable genetic test.

Indeed, the Biotechnology Industry Organization has already provided testimony to that effect:

The clinical practitioners with whom we spoke told us that it is rare for a patient to ask for a repeat of an advanced molecular diagnostic test, just like it is rare that patients would ask for a repeat of an MRI scan or x-ray. What patients ordinarily mean when they ask for a second opinion is a second medical opinion, a confirmation of the physician’s treatment recommendation, and the like.

Testimony of Hans Sauer, Deputy General Counsel for Intellectual Property, Biotechnology Industry Organization, *USPTO Public Hearing on Genetic Diagnostic Testing* (Feb. 16, 2012), <http://www.bio.org/sites/default/files/Genetic%20Testing%20Testimony.pdf>.

Patent rights do not prevent a patient from having a second doctor look at the results of a genetic test and offer independent advice on the appropriate course of treatment. That form of a second opinion is available to patients even if in some rare cases an exclusive license means that only certain laboratories can run or re-run the particular diagnostic test (and no other tests for the condition are available).

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Given the foregoing, there appears to be little evidence of problems with “second opinion” molecular genetic testing resulting from patents or exclusive licensing. It is far from clear that physicians or patients, in all but the rarest cases, truly need or desire a second *test*. Far more frequently, the patient seeks a true second “opinion”—a recommendation from a second physician on the appropriate course of treatment in light of the results of a single reliable test. Even assuming that demand for multiple *tests* exists, it is far from clear that running the test in the same (already-licensed) laboratory would be objectionable. And even if it were, exclusive licensing of tests to particular laboratories is a relative rarity. The almost universal practice of responsible (and economically rational) industry participants is to license their innovations broadly, maximizing availability and their own returns.

For similar reasons, the conclusions and recommendations of the SACGHS report cannot be invoked as plausible evidence of a meaningful problem. *See, e.g., SACGHS, Gene Patents* 89-100. The underlying facts—i.e., the actual case studies commissioned for the report and the findings that resulted—do not support the proffered assertions. For example, SACGHS recommends a blanket statutory “exemption from liability for infringement of patent claims on genes for anyone making, using, ordering, offering for sale, or selling a test developed under the patent for patient care purposes” to prevent patent rights from limiting patient access to genetic testing. *Id.* at 97. Yet the report is devoid of actual evidence demonstrating that patents in any way restrict patient access to existing genetic tests, much less evidence demonstrating an impact on public health that would support such an unprecedented and sweeping exemption.

For example, the SACGHS report states that, in some instances, “patents associated with genetic tests *and exclusive licensing* practices have limited *clinical* access to genetic tests,” reducing the number of laboratories available to perform a test. SACGHS, *Gene Patents* 39-42 (emphasis added). But even in those very limited cases in which laboratories have been granted an exclusive license, the underlying studies provided no evidence to support the claim that *patient* access was limited. As the report itself recognizes, it “is important to note” that even “limitations in *clinical* access do not necessarily limit *patient* access.” *Id.* at 42 (emphasis added). The report identifies only *one potential* example of exclusively-licensed patents restricting patient access—LQTS testing. There, based on evidence that was “acknowledg[ed]” to be “incomplete,” *id.*, a study concluded that “access problems *may* have occurred ... during an 18-month period due to patent enforcement,” “*if* there were patients seeking the test at that time,” but “[w]hether there were such patients is not documented,” *id.* at 44 (emphases added). Thus, the one example the SACGHS report could muster—“incomplete” evidence showing patients “*may*” have had access problems “*if*” any patients existed at all—does not establish that exclusive licensing of patents actually has restricted patient access, much less caused a significant problem or any actual health effects. Rather, the only evidence of patient access being limited concerned situations where an exclusive licensee “does not accept a particular insurance.” *Id.* at 42. But that is a problem with insurance coverage, not intellectual property rights. *See* p. 34, *infra*.

In any event, as discussed above, broad selling of kits and licensing of patents, rather than exclusive licensing, is the norm in the genetic testing arena. *See* pp. 28-29, *supra*. And the SACGHS report concedes that “the case studies generally found that for patented tests that were broadly licensed there was *no evidence* of patient access problems.” SACGHS, *Gene Patents* 42 (emphasis added). The SACGHS report thus suggests a radical change to patent law in the name of increasing patient access to genetic testing despite conceding there is no problem whatsoever when patentees follow the almost universal practice of selling or licensing broadly, and no meaningful evidence of any problems, much less health impacts, even in the rare instances where patentees do not.

Similarly, the SACGHS report elsewhere asserts that “U.S. law ... threatens medical progress,” SACGHS, *Gene Patents* 90, and recommends adoption of a statutory “exemption from patent infringement liability for those who use patent-protected genes in the pursuit of research,” *id.* at 95. But that statement and recommendation is contradicted by the report’s concession that the “empirical research suggest[s] that research *is not hampered* by the absence of a research defense.” *Id.* at 88 (emphasis added); *see also* pp. 24-25, *supra*. Again, the PTO should not recommend that Congress eviscerate the rights of patent holders in the name of remedying “problems” that concededly do not exist.

The SACGHS report is riddled with similarly sweeping conclusions that lack support in the evidence or that rest on an incomplete assessment of the issue. For example, the SACGHS report warns that “patent claims to genes and associations” are problematic because they “often claim (or come close to claiming) fundamental principles of nature.” SACGHS, *Gene Patents* 90. It has long been settled, however, that “laws of nature” and “natural phenomena” are not patentable, *Diamond v. Diehr*, 450 U.S. 175, 185 (1981), a point the Supreme Court recently reiterated in *Mayo Collaborative Services*. The SACGHS report states that “inventing around” patents “to create a genetic test is very difficult if not impossible.” SACGHS, *Gene Patents* 90. But that is belied by the numerous examples of design-arounds discussed by Roche and Abbott at pp. 19-20, *supra*, and by the example in one of the SACGHS case studies, which observes that InterGenetics is designing its breast-cancer test Oncovue® around Myriad’s BRCA patents. *Breast, Ovarian, and Colon Cancers Study* 30. The SACGHS report declares that “patents do not appear to be necessary to stimulate research and genetic test development.” SACGHS, *Gene Patents* 90. But that statement relates only to research performed (often at the federal government’s expense) by academics and non-profit medical institutions. *Id.* The SACGHS report concedes that “the role of patents in stimulating genetic research” is substantial when it comes to “stimulating *private* funding.” *Id.* at 16 (emphasis added); *see id.* at 23 (“Both the case studies and literature reveal that when researchers or companies sought private funds to initiate or advance their genetic research, investors were willing to provide funding because of the prospect of patents being granted as a result of the research.”). In sum, while the studies commissioned by the SACGHS report often contain valuable empirical research, the conclusions and recommendations of the SACGHS report simply do not match the underlying evidence.

#### **D. Insurance Coverage Is The Greatest Limitation On The Availability Of Genetic Testing**

There is thus scant evidence that patents, even those that are exclusively licensed, are broadly preventing patient access to genetic testing, whether in the first instance or with regard to confirmatory tests. Rather, the key barriers to the widespread adoption of genetic testing appear to be limits on and difficulty in obtaining insurance coverage for such tests. Toneguzzo, 5 Expert Op. Med. Diag. at 275. Although Roche and Abbott will leave it to others to discuss in more detail the “role that cost and insurance coverage have on access to and provision of genetic diagnostic tests,” *see* AIA, § 27(b)(4), we note that “multiple studies” have concluded that “when payment is out-of-pocket, price has a strong and direct impact on testing utilization, and thus affects patient access,” *Breast, Ovarian, and Colon Cancers Study* 38. The studies have found that “[a]ccess is thus linked tightly to coverage and reimbursement policies” and that such factors “*are far more important than any direct patent effects.*” *Id.* (emphasis added); *see also* *LQTS Study* 42 (“coverage decisions by insurers and health plans, and the level of reimbursement payments are arguably larger and more pervasive problems for clinical access to genetic testing than patent status”); *Alzheimer’s Study* 16 (“patents are irrelevant because the service is not covered as medically necessary”). Thus, in looking to increase the availability of genetic testing, Congress should look to ways of increasing insurance coverage for innovative genetic tests, rather than tampering with the patent rights that provide the incentives for the development of those tests in the first place.

#### **IV. The USPTO Should Not Recommend Any Changes To Patent Law, But If It Does, It Should Exercise Extreme Caution**

For the reasons discussed above, the USPTO’s report to Congress should not recommend any changes to patent law. To the extent the USPTO were to make any such recommendation, however, the USPTO should proceed with extreme caution and focus as narrowly as possible on the precise problem, if any, to be remedied—cognizant of the risk that changes to long-settled rules often produce unintended consequences.

*First*, it is important that the USPTO choose its terms carefully. As discussed, the USPTO should limit its analysis to the testing of *human* genetic material for the primary purpose of diagnosing a specific disorder caused by a genetic defect or a genetic predisposition to a particular disease. *See* p. 10, *supra*. The USPTO likewise should focus only on patents that claim compositions of matter or methods that have no substantial purpose other than to diagnose the specific genetic defect to which they are directed. *See* pp. 11-12, *supra*.

*Second*, the USPTO should focus exclusively on those instances in which a single laboratory is the sole provider of a patented test. The USPTO should not recommend any changes to patent protection on tests made available to more than one provider, such as where a patent owner offers to sell test kits or license its technology to more than one lab, because there can be, by definition, no patent barrier to confirmatory testing in that circumstance.

*Third*, any proposal should make clear that confirmatory (“second opinion”) testing refers solely to re-running the *same* testing protocol a second time. Any definition that included running a different test would create strong incentives for abuse. Under no circumstance, for example, should a person who initially elects a low-cost, low-sensitivity test be allowed to later order a “confirmatory” high-sensitivity test in contravention of licensing rights or patent protection. The same goes for running a non-FDA approved test followed by one that has been approved or cleared by the FDA, for running a test that detects only a limited number of mutations followed by a more comprehensive test, or for any other differences that might encourage people to game the system.

*Fourth*, the USPTO should limit any proposed changes to situations in which there is evidence that having a second provider run a confirmatory test would produce a materially more accurate result than if the original provider were to re-run the test. For tests approved or cleared by the FDA, that is unlikely ever to be the case.

*Fifth*, the USPTO should give serious consideration to the practical effect that any weakening of patent protection on confirmatory tests would have on the ability to enforce patents against primary-test infringers. Given the confidentiality of patient medical records, it could be very difficult for a patent owner to determine whether providers were abusing the system by providing primary testing in the guise of confirmatory testing. Further, unlicensed manufacturers might try to avoid liability for contributory infringement by labeling their kits “for second-opinion testing only.”

All of these complications—and others that assuredly exist but have not yet been anticipated—counsel against recommending any changes to the patent system or, at a minimum, in favor of exercising considerable caution. Fortunately, as described in the next section, there is a far better and more targeted way to address any concerns behind the calls for more confirmatory testing—one that helps all patients while respecting patents and the incentive to innovate.

## **V. The Best Way To Help Patients Make Informed Decisions Is To Ensure That All Genetic Tests Are Accurate And Clinically Valid When First Administered**

Proponents of second-opinion genetic testing generally argue that such testing is necessary to ensure that patients can make informed medical decisions on the basis of accurate information. But such testing can have unintended consequences. If a patient were to receive a falsely reassuring test result the second time around, the patient might forgo treatment entirely or, in the case of predictive testing, stop taking preventative steps or screening measures. *See SACGHS, Oversight of Genetic Testing* 131. Patients who delay treatment while waiting for a second test result may also lose the benefits of early detection and intervention. For example, patients suffering from metastatic melanoma typically live a year or less absent effective treatment. Retesting, which takes up to a month, wastes time that such patients can ill afford to lose. Other testing procedures may carry inherent risks, such as the risk of miscarriage associated with amniocentesis. *See CDC, Chorionic Villus Sampling and Amniocentesis: Recommendations for Prenatal Counseling* 2 (1995).

Additional testing also increases the costs of medical care and, as a practical matter, may be available only to those who can afford to pay out of pocket.

The better way to achieve the objectives of second-opinion testing is to ensure that all genetic tests are accurate and clinically valid the *first* time around and that providers are not making false or exaggerated claims about their tests. While this goal would require reconsidering the regulation of laboratories, it would be far less disruptive than changing the patent system and would directly target the root of the perceived problem without eroding the incentive to create new and better diagnostics.

Currently, the oversight of genetic tests offered in the United States varies markedly depending on who prepares the test and how it will be used. In vitro diagnostics (“IVDs”) that are sold to multiple laboratories, typically in the form of kits, are regulated as medical devices and, depending on their risk classification, must obtain premarket approval or clearance from the FDA under the Federal Food, Drug, and Cosmetic Act (“FDCA”). *See* FDCA, § 210(h) (codified as amended at 21 U.S.C. § 321(h)) (defining “device”). The FDA cannot provide premarket approval for an IVD unless the manufacturer demonstrates the test’s safety and effectiveness and the FDA determines that the proposed label is not false or misleading. *See* FDCA, § 515(d) (codified as amended at 21 U.S.C. § 360e(d)). In practice, this means that the manufacturer must establish the test’s analytical validity—i.e., its accuracy in measuring the property or characteristic that it is intended to measure. *See Public Meeting on Oversight of Laboratory Developed Tests Before the FDA* 52 (July 19, 2010) (statement of Katherine Serrano, Office of In Vitro Diagnostic Device Evaluation and Safety, Center for Devices and Radiological Health, FDA), *available at* <http://www.fda.gov/downloads/MedicalDevices/NewsEvents/WorkshopsConferences/UCM226203.pdf> (“*LDT Meeting*”). The FDA also requires evidence of a test’s clinical validity—i.e., its accuracy in diagnosing or predicting risk for a health condition—where it has not already been established. *Id.* The preparation of this data can require extensive clinical trials approaching the length and complexity of those required for pharmaceuticals. *See* pp. 13-14, *supra*. For example, Roche’s cobas® 4800 BRAF V600 Mutation Test was clinically validated through phase II and III clinical trials on more than 2,300 metastatic melanoma patients. IVDs also remain subject to good manufacturing practices and adverse event reporting requirements.

By contrast, laboratory-developed tests (“LDTs”)—tests created by laboratories for in-house use—are subject to far less regulation. The FDA has authority to exercise more oversight over LDTs, but it has traditionally declined to do so. *See LDT Meeting* 15 (statement of Dr. Courtney Harper, Director of Division of Chemistry and Toxicology Devices, Center for Devices and Radiological Health, FDA). LDTs have instead been regulated indirectly by the Centers for Medicare & Medicaid Services under the provisions of the Clinical Laboratory Improvement Amendments of 1988, 100 Pub. L. No. 578, 102 Stat. 2903 (“CLIA”). CLIA requires that labs register, receive accreditation, and implement certain quality assurance standards. But “CLIA takes a process-oriented approach that focuses on factors such as credentials of laboratory personnel and laboratory testing procedures rather than on data-driven regulatory clearance or approval for specific LDTs

before they can enter clinical use.” SACGHS, *Oversight of Genetic Testing* 30; see also *LDT Meeting* 32 (statement of Dr. Harper) (“[T]he focus of CLIA is actually on the quality of the laboratory performing the test, but not on the tests themselves.”).

CLIA thus permits laboratories to determine for themselves whether their LDTs are analytically valid, subject to only indirect oversight that evaluates the laboratory’s operations as a whole. CLIA does not require that laboratories establish the clinical validity of LDTs. See *LDT Meeting* 33 (statement of Dr. Harper). As the FDA put it, “nobody is looking to see whether ... the laboratory did a good job of demonstrating that their novel biomarker actually correlates with the disease they are claiming.” *Id.* at 34-35.<sup>17</sup> Most LDTs, moreover, are not subject to postmarket review or adverse event reporting requirements. See *id.* at 34-35.

As a result of this regulatory divide, the same test that would be subject to premarket approval or clearance by the FDA before being marketed as an IVD can be offered by a CLIA-compliant laboratory with far less rigorous oversight. The FDA has noted that “a lot of groups see lab developed testing as a way to get new tests on the market with ... a lower bar, and ... at an earlier stage than they might be, should they need to have scrutiny of the clinical data behind those tests.” *LDT Meeting* 29 (statement of Dr. Harper). It is therefore no surprise that LDTs, which began largely as specialty tests for underserved markets, have expanded rapidly into parts of the market traditionally reserved for IVDs. See Genentech, Inc., *Citizen Petition on the Regulation of In Vitro Diagnostic Tests* 6-7 (2008), available at <http://www.aab.org/images/aab/pdf/Genentech%20FDA%20Petition.pdf>; *LDT Meeting* 28-29 (statement of Dr. Harper); *id.* at 68 (statement of Dr. Elizabeth Mansfield, Director for Personalized Medicine, Office of In Vitro Diagnostic Device Evaluation and Safety, Center for Devices and Radiological Health, FDA). “Most genetic tests in use today are LDTs and have not been reviewed by FDA.” SACGHS, *Oversight of Genetic Testing* 39. This includes the BRCA1 and BRCA2 tests offered by Myriad Genetics. *Id.* (“no BRCA test has been approved by FDA”).

Therefore, to the extent Congress wants to ensure that patients can make informed medical decisions on the basis of accurate information, it should take account of the differences between IVDs and LDTs and encourage the use and development of the former whenever possible. That means maintaining strong patent protections, without which there is little incentive for companies to go through the often arduous process of seeking the FDA approval required for IVDs. It also means encouraging regulators to streamline the approval process for IVDs, particularly with regard to the companion diagnostic products that are essential to fulfilling the promise of personalized medicine. And finally, it means educating patients about the benefits of using IVDs over LDTs—not radically altering the patent system.

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<sup>17</sup> Under 42 C.F.R. § 493.1445(e)(3)(i), laboratory directors are supposed to ensure that “[t]he test methodologies selected have the capability of providing the quality of results required for patient care.” This regulation implicitly requires some assessment of clinical purpose by the laboratory director, but “CMS does not assess laboratory performance in clinical validity or utility.” SACGHS, *Oversight of Genetic Testing* 94 (2000).

**CONCLUSION**

Patents help patients by encouraging groundbreaking innovations that promise to revolutionize the practice of medicine. Indeed, without patents, many genetic tests would not be available in the first place. There is no significant evidence that patents harm research or patient health. Nor is there any evidence of widespread interference with “second-opinion” testing attributable to patents. And there is certainly nothing that supports radically altering patent rights.

If the USPTO were to make any recommendations regarding patent rights, it should proceed with extreme caution by carefully defining its terms, focusing exclusively on sole providers, limiting the definition of confirmatory testing, requiring evidence that confirmatory testing by a second lab would produce a materially more accurate result, and considering the practical effect that any weakening of patent protection would have on the ability to enforce patents against primary-test infringers. Even then, there is a serious risk of unintended consequences. The better approach by far to address the concerns behind second-opinion testing would be to ensure that all genetic tests are accurate and clinically valid the *first* time around and that providers are not making false or exaggerated claims.

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Sonali S. Srivastava  
Senior Counsel  
Abbott Laboratories  
100 Abbott Park Road  
Abbott Park, IL 60064

Rachel A. Polster  
Senior Counsel  
Abbott Laboratories  
1300 E. Touhy Avenue  
Des Plaines, IL 60018

Respectfully submitted,

Kevin A. Marks  
Vice President & General Counsel  
Roche Molecular Systems, Inc.  
4300 Hacienda Drive  
Pleasanton, CA 94588

Ventana Medical Systems, Inc.  
1910 Innovation Park Drive  
Tucson, AZ 85737

D. Michael Young  
Vice President & Chief Intellectual  
Property Counsel  
Roche Diagnostics Operations, Inc.  
9115 Hague Road, Bldg. A  
P.O. Box 50416  
Indianapolis, IN 46250-0416

Roche Diagnostics Corporation  
9115 Hague Road, Bldg. A  
P.O. Box 50457  
Indianapolis, IN 46250-0457

George W. Johnston  
Vice President and Chief Patent Counsel  
Hoffman-La Roche Inc.  
340 Kingsland Street  
Nutley, NJ 07110