UNITED STATES PATENT AND TRADEMARK OFFICE

PUBLIC HEARING ON GENETIC DIAGNOSTIC TESTING

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P R O C E E D I N G S

(9:05 a.m.)

MR. SICHELMAN: Welcome to the University of San Diego. We're very pleased to have the U.S. Patent and Trademark Office here for the public hearing on genetic diagnostic testing. Just in case I haven't introduced myself, I'm Ted Sichelman. I'm the professor here at the law school where I teach a number of patent law courses and a co-author sometimes with Stu Graham before he got to the Patent Office as chief economist. He'll be giving some remarks along with Teresa Stanek Rea, who is now the Deputy Undersecretary of Commerce and the Deputy Director of the Office; Janet Gongola, who is the Patent Reform Coordinator; and George Elliot, who is the Technology Center Director. So those are some pretty high level people here today. We're very pleased to have them. And with that I will turn it over to them. Thank you.

MS. GONGOLA: Thank you for coming to our second Genetic Testing hearing in this beautiful venue of the Joan Kroc Institute for

Peace and Social Justice at the University of San Diego. Thank you to Professor Sichelman for hosting us and helping us to coordinate the Patent Office's visit to this venue.

I am Janet Gongola, the Patent Reform Coordinator. And joining me today from the Patent Office I have to my right the Deputy Undersecretary and Deputy Director of the United States Patent and Trademark Office, Teresa Stanek Rea. Going down the line, next is Dr. Stu Graham, the first Chief Economist for the Patent and Trademark Office. And then, last but not least, is Mr. George Elliot, who is the Technology Center Director for 1600, the biotechnology area. We are all pleased to be here for this important hearing today, and we look forward to a very fulsome and thoughtful discussion with you.

Now, Congress mandated that the Patent and Trademark Office investigate ways that a second opinion genetic test might be made available in situations where there is a gene patent and that patent is licensed to a primary company exclusively to make a first

test. As a result of this mandate, the agency will be exploring the legal and medical issues surrounding second opinion genetic testing, making findings of fact and, if appropriate, offering recommendations to Congress. So we are eager to learn from all of you, our relevant public -- the IP community, patients, medical practitioners, as well as insurance companies -- about our second opinion genetic testing issues. Your input is essential for us to be able to fill our Congressional mandate. And given the breadth of biotechnology interest in the San Diego area, we couldn't think of a better city or a location to host this second genetic testing hearing.

Now, to share with you a little bit more on the background of the genetic testing study, the Patent Office published a notice in the Federal Register in January of this year announcing two hearings and soliciting written comments from all of you. In that Federal Register Notice, we specified particular areas that Congress requested the agency to

investigate and address in our report, and these areas include the lack of second-opinion testing on medical care to patients and recipients of genetic diagnostic testing; the effect of second-opinion testing on patent owners; and the role insurance coverage has had on access to second opinion genetic testing.

On February 16, we held our first hearing in Alexandria, Virginia. Ten witnesses gave prescheduled testimony, and one witness gave unscheduled testimony. Today, I am very pleased that we have eight witnesses who have prescheduled to give testimony. Mr. Len Svensson from BIOCOM; Mr. Richard Marsh, the Executive Vice President, General Counsel, and Secretary of Myriad Genetics; Professor Christopher Holman from the University of Missouri-Kansas City School of Law; Mr. Carlos Candeloro, a Patent Attorney in the biotechnology area; Dr. Bernard Greenspan, Director of Prometheus; Professor Misha Angrist from the Duke Institute for Genomic Science and Policy; Mr. Vern Norviel from the

Wilson Sonsini Law Firm; and Ms. Kimberly Irish, a Program Manager from Breast Cancer Action. We encourage those of you who did not preschedule to give testimony to consider doing so, and we will open the floor to you for that testimony after our prescheduled witnesses are complete.

Lastly, we encourage the IP community that I talked about earlier to consider giving written comments on the subject matter of our study. Written comments may be submitted to genetest@uspto.gov, and they are due by March 26th of this year. We will then prepare our report for Congress based upon the information you share with us through both prescheduled and unscheduled testimony, as well as our own independent research. And our report is due to Congress by June 16th of this year.

Now, with the lay of the land set in front of us, I wish to introduce the Deputy Undersecretary of Commerce and Deputy Director of the Patent and Trademark Office, Teresa Stanek Rea. Deputy Director Rea has enjoyed a

lengthy career in the law focusing her practice before joining the agency in the areas of biotechnology, pharmaceuticals, and chemical arts. She likewise has a thorough understanding of the legal issues related to gene patenting and gene testing. She began her career as a pharmacist and then spent over 25 years in private practice at both an IP boutique and a large multinational general practice firm. Deputy Director Rea will share welcoming remarks with us about the criticality of this study to the legal and medical professions.

MS. REA: Thank you so much, Janet. I should tell all of you at the outset that while Janet Gongola's formal title is Patent Reform Coordinator, all things AIA (America Invents Act) are within the scope of her responsibility at the PTO. So she has a huge slice of our pie right now and we all rely on her for her organization, her perseverance, her intensity, and I think she genuinely enjoys what she does. So we actually have a nickname for her that I would prefer to see in

blogs should any of this appear there and that's the Patent Reform Czarina. So if you will all give me that little benefit I would appreciate it.

So good morning, everybody. I am Teresa Rea, the Deputy Director of the USPTO, and as Janet indicated, we're here today for a hearing on the America Invents Act mandated genetic testing study. I'd like to thank each and every one of you in this room and those of you on the webcast for taking the time today to attend and observe this very important public hearing on genetic diagnostic tests and as well as the accompanying study that the USPTO will be conducting in the short term to actually weigh the impact that independent second-opinion testing has on the ability to provide the highest level of medical care to patients.

Now, as Director Kappos and the entire USPTO team work diligently towards implementing various provisions of the historic America Invents Act, an ongoing dialogue with our user community is vital, not

only for us to remain transparent in the process of enacting the new law but also to ensure that your input helps guide and shape how new provisions in the patent system will actually play out. So each one of you are assuming a very important role in this historic moment. And that is why this study, like the six other reports mandated by Congress, focuses intently on gathering your concerns, your expectations, and your experiences for how exclusive licensing and patents in genetic testing affect the practice of medicine given the importance of this effort to our mission.

I would also especially like to thank Stu Graham once again, Janet Gongola, George Elliot, and Susan Hoffman, the actual coordinator behind the scenes -- Sue, can you just raise your hand? She actually made sure that we started on time and that all the trains are running well -- for their support and all the work that they've done for today's hearing.

And once again I'd like to repeat

that for those who did not have an opportunity to preschedule testimony, we still welcome all of you to chime in and share any thoughts and reactions that you may have just to make sure we encourage a thoughtful and well-rounded discussion.

Now, embedded in the social contract between a patent and the rest of society is a timeless acknowledgement that the American marketplace rewards hard work, innovation, and creativity, and it's that sort of acknowledgment that has allowed new technologies, discoveries, and breakthroughs to be shared with the world. And in a way that's helped us to do everything from cleaning our water to communicating faster and to healing the sick. And in particular, as advancements in the life sciences afford us a renewed lease on life, it is also our responsibility to evaluate how an evolving patent system is keeping pace with the evolution in patient care. Now, admittedly there will be ongoing deliberations over the idea of gene sequence patenting, but that's

not what today is about. Today we gather to specifically explore how we should go about balancing the interests of accessing information about our own health consistent with the interests of patent holders and licensees.

As testimony today will illuminate, making life-altering decisions about ongoing surgery or administering a medical treatment can be immensely difficult when only one test exists for identifying a specific genetic mutation. And that's why it is critical that this study explore the effect an independent second opinion on diagnostic testing would have on existing patent holders and on patient care. Also, the impact that current exclusive licensing arrangements have on the practice of interpreting test results and the performance of testing procedures, as well as the role that costs and insurance coverage has on the overall access to these genetic testing methods.

Now, in the same way, the America Invents Act was an explicit acknowledgement

that the innovations of tomorrow cannot take root in the patent infrastructure of the past. This study advances the United States Patent and Trademark Office's commitment to modernizing our IP system while ensuring that regulations do not establish a false dichotomy between incentives to innovate and adequate access to health care. By addressing these key questions about how the status quo is affecting patient outcomes, we work towards determining how best to provide independent and confirmatory tests and ultimately remove barriers for patient access.

There is a lot at stake here, and today's conversation can provoke strong emotions. We may hear stories about our loved ones, but it's a conversation that must be had. Having spent a considerable amount of my career delving into life science matters, I want to applaud the courage of my dear friend, Congressman Wasserman Schultz for being willing to share her story today, and I want to thank each and every single one of you for sharing your thoughts and experiences. But

ultimately, the dialogue we have today gives us a real opportunity to kick off a new era in how intellectual property rights interact with patient rights, and your contributing insights will not only shape a critical public health consideration of our time but it will also help effectuate change that reaches beyond the health and wellness of the patent system and into the health and wellness of our health care system.

Now, we can be honest and acknowledge the window of time given to us by Congress to complete the study is rather short, but that is why all levels of feedback are particularly important in aggregating a broad range of opinions in how we move forward. And certainly there will be many factors to consider and different perspectives to understand the thoughtful discussion today and assist us in doing just that. We can encourage those watching today via the microsite to consider submitting input through written comments as soon as possible and at the very latest by March 26th because our

congressional report is due to Congress in June of this year. So I would appreciate comments from everywhere that we can, even comments supplementing what we hear today.

And as we dive into the study I'd like to think -- I'd like us all rather to think about and comment on the fundamentals. Are there practical consequences of the current availability of independent second opinion genetic diagnostic tests in terms of patient health, quality of life, and longevity? Second, what entities or institutions, if any, should play an active role in ensuring that independent second opinion genetic diagnostic tests are more widely provided? And third, what policies, if any, should the federal government explore in order to ensure that independent second opinion genetic diagnostic tests are more widely available?

By thinking along these lines and identifying problem areas we will be able to thoughtfully and carefully devise more mechanisms that allow innovators and health

care providers to do what they've done in America for generation after generation -- promote jobs, spur breakthroughs, and most importantly heal those in need. We have an important challenge ahead of us in guiding the implementation of the America Invents Act. And while we are making excellent headway, sharing your experiences and thoughts on second opinion genetic testing will enable the U.S. Patent and Trademark Office to continue preparing a most accurate and well-informed report for Congress.

So I encourage you to be as open as possible because I genuinely look forward to your thoughts and insights of today and in the days to come. And once again, I thank each one of you for spending the time with us today. Thank you again.

MS. GONGOLA: Next, I introduce a video from Congresswoman Debbie Wasserman Schultz. Congresswoman Wasserman Schultz represents the 20th Congressional District of Florida in the House of Representatives. She has been a member of the House of

Representatives for eight years and is currently the chairperson for the Democratic National Committee. Congresswoman Wasserman Schultz is responsible for the inclusion of the genetic testing study in the America Invents Act. In her video presentation, she will explain why she sponsored this aspect of the legislation and what it means to her personally. I think you will find her remarks to be very moving, and it brings a human touch to the America Invents Act.

(Video plays)

MS. WASSERMAN SCHULTZ: Good morning, and thank you to everyone at the U.S. Patent and Trademark Office for working so hard to coordinate this public hearing today. Thank you in advance to Teresa Stanek Rea, Janet Gongola, Stuart Graham, and the entire USPTO legislative team for the incredible work on which you are about to embark. I am so grateful for your attention and dedication to these vital questions of genetic testing, exclusive licensing, and how that affects patient outcomes.

For all of the advocates attending today's hearing, we are so grateful for the devotion you have given to patients undergoing genetic testing throughout your careers. Your insight and commitment have been vital to developing, nurturing, and realizing the potential of genetic tests for improving medical outcomes.

It is such a pleasure to speak with you all for the first public hearing on this important provision from the America Invents Act. I'm truly delighted that you've all dedicated yourselves to this goal, and I look forward to what the results of this study will bring.

I'm thrilled that the study is among the first wave of America Invents Act provisions to be implemented, and that process begins with you, the USPTO and all of the advocates and organizations participating in this hearing. Over the next several months you will have the incredible opportunity to investigate this complicated aspect of patent law in need of a thoughtful remedy.

As you know, this study is a result of a provision in the patent reform law Congress passed last summer that will help engender much needed patient protection and choice vocations undergoing genetic diagnostic tests. My hope is that this study will illuminate ways to remove patient access barriers on second opinions on genetic testing on patented themes.

With the passage of this law, Congress is primarily interested in several important questions. For example, what impact does the current lack of independent second-opinion testing have on the ability to provide the highest level of medical care to patients and recipients of genetic tests? And how does this inhibit innovation for existing tests? What would be the effect of providing an independent second opinion genetic test on existing patent and license holders of an exclusive genetic test? What impact does the current exclusive licensing and patents on genetic testing have on the practice of medicine including but not limited to the

interpretation of testing results and performance of testing procedures? And what is the role that costs and insurance coverage have on access to and provision of genetic diagnostic tests?

These vital questions must be answered because of the complicated reality that we're facing today. Tests are now available for a modality of genetic disorders such as colon cancer, Parkinson's disease, Alzheimer's disease, stroke, and many others. But in approximately 20 percent of all cases only one laboratory can perform the test due to patent exclusivity for the diagnostic testing, and often the actual human gene being tested. Genetic disorders that fall into this patent exclusivity area include breast cancer, and certain neurological diseases such as muscular dystrophy.

I believe that the availability of a second testing procedure in these areas would have several benefits, the most important of which is that it will allow people making life- altering medical decisions based on

these genetic tests to seek out an independent second opinion. By allowing clinical laboratories to confirm the presence or absence of a gene mutation found in a diagnostic test, we can help Americans access the second opinions they truly deserve.

As you may know, I know firsthand the stress of wanting a second opinion but being unable to get it. Several years ago, just after my 41st birthday, I found a lump while doing a routine breast self-exam. It was cancer. Luckily, I found my tumor early and my treatment officers were initially fairly straightforward. I was supposed to have a lumpectomy and radiation and that would have been the end of the story. But an incredibly wise and thoughtful nurse educator asked the right questions about my family's health history that threw my story for a loop. I never would have known that as an Ashkenazi Jewish woman, a Jew of Eastern European descent, with two paternal great aunts who had had breast cancer, that there were some significant red flags in my genetic file.

I did not know that as an Ashkenazi Jew I was five times more likely to have the BRCA1 or BRCA2 genetic mutation. I did not know that carriers of that mutation have up to an 85 percent lifetime chance of getting breast cancer and up to a 60 percent chance of getting ovarian cancer. My nurse suggested that I take the BRCA test and I could not be more grateful for her knowledge and advice. This process, however, presented a new set of challenges and questions for which no woman could ever be prepared. Now, as many of you know there was only one test on the market for the BRCA mutations. The maker of this test not only has a patent on the gene itself; they also have an exclusive license for their laboratories to administer the test. There is absolutely no way for someone who is questioning her genetic risk for breast or ovarian cancer to get a second opinion. This is intensified by the fact that for many women the test results are inconclusive. Imagine being faced with this decision -- your genes hold the key to your survival, having major

body altering surgery could save your life, but the test results fail to give you any answers. What would you do in that situation?

You might say that I was lucky. My test clearly showed that I had the BRCA2 mutation. But there was absolutely nothing I could do to question these results or receive an independent confirmatory test. So I had no choice but to make the life-altering decision to have seven major surgeries, including a double mastectomy and an oophorectomy from a single administration of a single test.

Unfortunately, many women have to face this decision with even less reliable information than I had. No one should ever have to go through this experience without the comfort and the confidence of a second opinion. With so much at stake it is incredibly important that we give everyone in this situation as much certainty as we possibly can. I can assure you it was devastating to me to have to make a decision that was as life altering as a double mastectomy and six other major surgeries

without being able to confirm the results of that genetic test. We owe that much to those whose lives hang in the balance. Many of you helped shape this legislation and now it is your task to make sure that your knowledge and experience can be put into practice to help save lives.

I wish you all the best of luck in this important endeavor, and I look forward to hearing all of your ideas and suggestions. Thank you so much again for being here today and for your dedication to the health and well-being of others.

(End of video)

MS. GONGOLA: Next, I turn the floor over to our Chief economist, Dr. Stu Graham. Dr. Graham previously worked as a professor of economics at Georgia Tech University. He will provide an overview of more details about our genetic testing study.

MR. GRAHAM: Thank you, Janet. Good morning. I am Stuart Graham, chief economist of the USPTO. My office has been given the responsibility to lead this study and I am

very happy to be here along with my colleagues from the USPTO to take testimony today.

In our request for information posted in the Federal Register on January 25 and in this hearing today, we are seeking comments and information on how to best address a specific set of questions related to genetic diagnostic testing. Our interest is in collecting evidence that enables us to best answer the questions posed in the legislation and to provide Director David Kappos with the best evidence possible in order that he may consider what recommendations, if any, are appropriate to make in the final report.

As we enter the sixth decade since the publication of Watson & Crick's seminal findings, medical knowledge has fundamentally changed. There are no fewer than 2,400 genetic diseases for which diagnostic tests have been developed with hundreds of laboratories providing tests for these diseases. From these many sources there are differing organizational forms used to provide primary and secondary tests, many licensing

arrangements and business models, and significant variation in the way the testing results are made available to both patients and caregivers.

While there have been several important recent studies and reports covering issues related to genetic diagnostic testing over recent years, the set of questions posed in the America Invents Act, section 27, have generally been given too little attention or left unaddressed entirely. That is not to suggest that these questions are unimportant. In fact, having adequate evidence with which to formulate reliable answers to these questions would meaningfully inform the current debate about how genetic diagnostic testing is made available to patients by physicians and insurers and the role, if any, that patenting is playing in the availability and reliability of these tests.

To assist with the completion of the study, the USPTO is seeking public comments and conducting public hearings on the circumstances under which independent second

opinion genetic diagnostic testing is currently available or not available to physicians and their patients and about the impact of such availability on the quality of medical care and the practice of medicine, the effect of independent second opinion genetic diagnostic testing on relevant patent and license holders, and the impact on medical costs and insurance coverage.

We are therefore pleased to have an excellent set of speakers today to help us learn more about these issues and I encourage our speakers to provide robust evidence on these questions. Since these questions have been largely unaddressed in previous reports and studies, it is incumbent upon us - so that the USPTO may provide the most meaningful response to the congressional mandate - to collect a robust set of data and the best evidence available to help inform the report. So I do encourage you to point us to reliable evidence upon which we can identify generalizable findings if possible.

In our Federal Register notice, we

provided a detailed set of questions that directly relate to issues raised in the legislation. We encourage those here today and anyone listening to our live stream to consider responding and offering information at the e-mail address provided in the Federal Register notice. In the meantime, let us turn the program over to live comments from several members of the public and representatives of organizations who have expressed an interest in these issues and a willingness to give testimony today. And for that I hand the program back to Janet Gongola.

MS. GONGOLA: I would like to review the protocol for giving witness testimony this morning. I will announce your name and ask you to please come up to the podium, share your remarks, and then remain at the podium when your testimony is complete in the event that the panel has any questions we might like to ask you about your testimony. And then we will follow the order for witness testimony listed in the agenda with one exception. Due to scheduling conflicts, we will begin our

testimony this morning from Len Svensson from BIOCOM. So Mr. Svensson, please come to the podium for your testimony.

MR. SVENSSON: Good morning. Thank you for the opportunity. My name is Leonard Svensson and I'm here this morning to give some testimony on behalf of BIOCOM, specifically in opposition to any amendments to the law that might be proposed to effectively provide a compulsory licensing for purposes of this so-called second opinion.

BIOCOM, as a little bit of background, is a regional life science association representing more than 560 members in Southern California, including biopharmaceutical, medical device, diagnostic, industrial biotech and biofuel companies, as well as universities, research institutes, and patient groups, approximately 60 of which are developing gene-based diagnostics. Rather than reiterate the arguments that have already been presented by many groups in the first hearing and probably are going to be submitted by some other groups later this morning, as a

trade association we would like to present a discussion of the economics of this question -- the economics facing patients, insurance companies, industry, and research institutes who are developing lifesaving diagnostics and therapeutics we're talking about this morning.

Access to medical care, be it diagnostic test or procedure, a therapeutic drug, or treatment in a medical facility is often a question of economics. We're all aware of the complications and expense issues surrounding our current medical insurance system and those issues are particularly problematic for persons that are unemployed, underinsured, and uninsured. But on the other side of this problem is the economics of discovering, developing, gaining approval, and bringing to market the very tests and treatments that are so important to a healthy society. Negative impacts on the economics of discovering and commercializing medical treatments will have a negative impact on the innovative treatments that we all want to see developed. Intellectual property protections

are indispensible components of the financial incentives which are needed to attract the billions of dollars in investment required to fund the high-risk research and development critical to biotech innovation. Let's not forget that it's those investments that bring essential new gene-based diagnostics and therapies to patients suffering from genetic diseases.

Looking at the local family here, Southern California is home to 97,000 people who are directly employed at 3,500 different life science companies. The life science industry in Southern California indirectly generates a total of 248,000 jobs that pay over $17 billion in wages and produce a total of $57 billion of economic activity regionally. BIOCOM's members currently have 21 products on the market with 303 in the pipeline, many of which leverage information to cure diseases. In order to develop these gene-based diagnostics and therapies, the U.S.-based biotechnology companies often, in collaboration with academic researchers,

translate information regarding the genetic-linked diseases and the critical lifesaving treatments.

Without robust patent protection or the ability to control licensing of their innovations, most BIOCOM member companies would never be able to financially recoup their upfront costs and this would greatly inhibit their ability to attract vital investment money. This lack of capital will cause promising discoveries to go undeveloped into therapies and diagnostics. Legislation that undermines the patentability of innovations or the strength of valid patents would no doubt result in the further diversion of investment capital away from biotechnology, the outcome of which would be detrimental to the financial and public health of our nation.

Now, while this is an emotional issue and there have been concerns expressed regarding the scope of patents and the potential for patents to limit innovation, BIOCOM and its members believe that any changes in U.S. patent policy, regulation, or

statutory authority related to gene-based innovations must take into account the critical incentive that patents present to investors. Unlike most industries, the timeframe between idea and revenue-generating product is many years due to regulation and testing to ensure product safety and efficacy. Without extremely strong patent protections, it's unlikely that investors will accept the inherently high risk involved in life science companies. For this reason we are strongly opposed to any changes in law that by way of patent infringement exemption or some other mechanism would effectively provide compulsory licensing for the purpose of a second opinion.

The United States has never had a compulsory licensing regime in its patent laws because we've always recognized that a robust patent system that rewards innovators is the driving force for innovation. Indeed, a survey of countries that do have compulsory licensing provisions will reveal two important consequences. First of all, very few compulsory licenses are actually granted and

utilized because practicing an invention, especially in high specialized medical fields and treatment and diagnostics requires more than just a patent license. It requires a lot of knowledge and technical knowhow. So just enforcing a compulsory license does not even successfully address the perceived problem. Secondly, those countries which do have compulsory licensing provisions are not the countries known for innovations because even the possibility of compulsory licensing stifles investment. The United States simply should not start down that wrong path.

Much of the discussion on the issue has focused on the perceived need for patients to be able to obtain a second opinion. We suggest that this is a classic misnomer that does not properly reflect the real world situation. Under the current situation, patients are fully free to obtain a second medical opinion. Any patient can go to a second doctor and obtain a second opinion on the medical recommendation of the first doctor. No patent or licensing arrangement in

any way inhibits this action of the patient. On the other hand, if the doctor or the patient for some reason haves concerns about the results of the diagnostic assay, the doctor can always ask for a rerun of the test. This type of action takes place every day in our medical system in a wide variety of diagnostic and treatment environments. BIOCOM submits that since patients are currently free to obtain any desired second medical opinion, the push for compulsory licensing is an unwise solution in search of a problem that does not really exist when the real world situation is carefully analyzed. And the potential unintended consequence is an important and innovative new test will not be developed in such an environment.

We strongly urge you to carefully consider the broader implications of any proposal to place limitations or compulsory licenses on licensing arrangements related to these scientific advancements. BIOCOM and its members would be happy to work with you on ways to address actual concerns over the

patenting and genetic-based diagnostics while also avoiding potential detrimental effects on the U.S. Biotechnology industry which relies on the intellectual property protections and patents in order to fund the development of innovative lifesaving diagnostics and therapies. And that's the end of my comments. If you have any questions?

MR. GRAHAM: Thank you, Mr. Svensson for the testimony.

I'm wondering if -- so you've pointed to something that many of the speakers at our first hearing pointed to, and that is this dichotomy between the world in which, you know, we would live either in the current system which doesn't support compulsory licensing or in a system which would devolve into a compulsory licensing system that would undermine all the incentives associated with doing research and the necessary element of profit in our capitalist system that supports innovation. But is there some middle ground? Is there some -- is there some -- or can you imagine some solution that could allow us to

get to a place in which those concerns like Congressman Wasserman Schultz's in accessing second-opinion testing could have that available to them, you know, given the caveat that you just stressed about what it means to get a second opinion, while at the same time not undermining the incentives that you and we and everyone should be so critically concerned with?

MR. SVENSSON: It's a good question. I'm not sure what the middle ground is. I think we've always had a legal system that permits compulsory license in some national emergency. If there was really a national emergency there could be some margin and we've had that available. But we've never had anything where a particular test or disease was considered the national emergency except for, I guess, recently the anthrax raised the concern. The anthrax scare. And the question was, well, should the government do something there? But I think even there private industry was able to step up to the plate and provide the tests and the kits that were

necessary to meet even the national -- perceived national emergency. Private industry was able to meet that need without the need for the government stepping in.

I think if you look around the world at the countries who have tried some compulsory licensing I think you'll see that a lot of scholarly articles are written on it, people that know a lot more than me. And it never results in spurring innovation of drug development. Thailand tried it for AIDS treatments. Brazil has compulsory licensing, and neither one of those countries are known for great innovation in pharmaceuticals. I think Canada is the other country you can look at. I've read some articles about what Canada has done. They have some compulsory licensing and even there it doesn't spur innovation in pharmaceuticals. It doesn't spur new products. Thank you.

MS. GONGOLA: Deputy Director Rea also has a question. Please remain at the podium.

MS. REA: There are some instances

where one might want to visit a second physician for their professional opinion or to re-run a genetic diagnostic test. During the open mike session at the last Genetic Testing Hearing in Alexandria, one speaker commented that there is a relatively high error rate for many genetic diagnostic tests. I assume that you disagree with that statement and that there would be no, or minimal, benefit with re-running the test?

MR. SVENSSON: Well, I understand the concern about tests potentially having an error rate. Before I took the diversion off in patent law I worked in diagnostic testing. And doctors would all the time -- not all the time but oftentimes come back and ask for a rerun of the test because the results were unclear. The controls weren't what they normally were or something else. They didn't look to go to another facility for the test; they wanted us to rerun the same test. And sometimes the results would come out more clearly. But the concern is usually not that the test is unclear because the person didn't

run it well if you rerun it; the problem is tests can only go to a certain level of specificity depending upon the scientific or research development of that kind of test at this time the test is being run. The problem usually is given the data that science can provide at that time, what should the doctor provide as the medical opinion? That's, I think, what usually is the crux of the issue. It's not a concern that facility runs the test doesn't do a good job. If they weren't doing a good job all the time they would go out of business.

MS. REA: But if they were the only company doing that business --

MR. SVENSSON: Right. But I don't think there's a concern frankly, generally out there in diagnostic testing that the tests are not being run well or accurately. We all understand there's some built-in error rate in tests for all kinds of things, whether it's medical or your automobile or anything.

MS. REA: Thank you so much.

MR. ELLIOTT: I do have one

question.

MS. GONGOLA: Yes. Question from Mr. Elliott.

MR. ELLIOTT: With respect to the confirmatory testing that's done by the same company that did the original test, there is -- perhaps it's only a psychological aspect to something especially as serious as BRCA1, BRCA2, that may have little to do with the quality of the original test but much more to do with the comfort of having an independent confirmation of that test. And I think there's a perception that going back to the original company may not provide that independent confirmation. Can you address that?

MR. SVENSSON: I haven't seen any studies that confirm that one way or another. I read Hans Sauer’s testimony in the Washington hearing from Bio on the similar thing and their testimony was that the patient groups that they've talked to, patients are not looking for or complaining about the lack of an ability to get a test run by some other

company or some other diagnostic testing company; that's not been raised as an issue. I understand the emotional pull and the emotional concern about that but that doesn't seem to be what patients are concerned about. The concern is about getting the test run again and then what do I do with the results of the test? And maybe I'd like to talk to a second doctor and have a second doctor tell me in their opinion what should I do as a result in view of these results? I haven't seen any evidence of patients asking for some second laboratory to run the test because they don't believe the results of the first one. I think we ought to look at whether that's actually an issue in the public or whether that's just some perceived emotional issue.

MR. ELLIOTT: Thank you.

MS. GONGOLA: Thank you, Mr. Svensson. Our next witness is Mr. Richard Marsh from Myriad Genetics.

MR. MARSH: Good morning. Myriad Genetics wishes to thank the U.S. Patent and Trademark Office, Professor Sichelman and the

University of San Diego. This truly is a beautiful campus and venue to be here, as well as this panel for the opportunity to respond to the PTO's request for comments on genetic diagnostic testing study that was included as part of the America Invents Act.

Please allow me to introduce myself. I am Richard Marsh. I'm the executive vice president, general counsel, and secretary of Myriad Genetics, Inc. I've been at Myriad for nearly 10 years, serving as an executive officer and overseeing legal matters for the company and its operational subsidiaries. I received a master of laws degree in taxation from Georgetown University, a law degree from Thomas M. Cooley Law School, graduating magna cum laude; a bachelor of science degree in accounting from Brigham Young University, and was previously licensed as a certified public accountant in the District of Columbia.

Myriad is a leading molecular diagnostic company located in Salt Lake City, Utah. We are focused on developing and commercializing novel predictive medicine and

personalized medicine and prognostic medicine tests. As a central reference laboratory, Myriad performs all molecular and diagnostic testing and analysis for our own tests. We believe that the future of testing lies in the shift from a trial and error paradigm to a prevention and personalized medicine paradigm. By understanding the underlying genetic basis of disease, it has been well documented that the individuals who have a greater risk of developing disease can be identified and physicians can use this information to improve patient outcomes and better manage patient health care. In addition, by understanding the genetic differences in each individual, personalized medicine tests can be used to predict whether someone will respond favorably for a particular drug therapy, and what drug best will produce the best results. Myriad's goal is to provide physicians with critical information that can be used to more precisely guide health care management of your patients.

To date, Myriad has launched nine molecular diagnostic tests. Two

representative genetic test services that Myriad offers are the BRACAnalysis test and the COLARIS test. Our BRACAnalysis test is a comprehensive analysis of the BRCA1 and BRCA2 gene assessing a women's risk for developing hereditary breast and ovarian cancer. Our COLARIS test is a comprehensive analysis of the MLH1, MSH2, MSH6, and PMS2 genes for assessing a person's risk of developing colorectal and uterine cancer. In the interest of time, we would refer the PTO to Myriad's website where there is a further description of all of our Myriad molecular diagnostic products and the benefits that they provide.

Myriad employs a number of proprietary technologies, including patented technologies owned or licensed by Myriad to better understand the genetic basis of human disease and the role that genes and other molecular markers play in the onset and prevention of disease. This intellectual property plays a critical and vital role in driving the investment of capital, both human

and financial, in the research, development, and commercialization of molecular diagnostic tests. It is important to recognize the substantial risks and significant investment necessary for molecular diagnostic tests to be successful. To be successful and beneficial to the general public, a genetic test must go through various stages of development. First, the initial research and discovery effort, followed by the process of validating the clinical test to be done in a laboratory at a commercial scale, commercially launching the new test, which includes developing all the associated medical support materials, patient education materials, and marketing materials. Additional clinical trials must then be undertaken to generate peer reviewed publications on the medical necessity and the importance of the new testing. Medical societies must then be educated on the new testing and encouraged to adopt new guidelines regarding testing. And finally, great effort is needed to gain insurance reimbursement for testing which includes demonstrating the

positive pharmacoeconomics of testing.

Twenty years ago, Myriad was a small startup biotech company with the goal to discover and characterize genes associated with hereditary breast and ovarian cancers. Initial funding for Myriad's research and development efforts came largely from outside venture capital and collaborative research contact with pharmaceutical partners based on the promise of a limited period of exclusivity for the fruits, if any, of our research and discovery efforts. While the discovery of the BRCA1 and the BRCA2 genes was monumental, our success and the invaluable benefit delivered to patients has far more to do with the ensuing phases of product development which I just mentioned above. Great discoveries can languish in academic laboratories and scientific publications, and never fully benefit the public, without the significant efforts to develop and commercialize them appropriately for public consumption. This incontrovertible fact is the foundation of the Bayh-Dole Act, a transformative law aimed at

ensuring discoveries reach their full potential.

Molecular diagnostics, like the genetic tests, require an enormous commitment of capital to be developed and launched, and then additional sustained and significant financial support to reach a level of commercial activity and viability at which point patients may benefit. The risk and reward inherent in the ability to obtain exclusive licensed rights within the U.S. patent system is the driving force behind investment in genetic tests and hence their development and commercialization to the general public.

Myriad's story of commercializing BRACAnalysis illustrates these principles. Myriad has spent over $500 million in 17 years in the research, development, and ensuing commercialization and operational support of the BRACAnalysis test before achieving financial break even. Myriad would not have been able to make this capital investment without the promise of exclusive patent rights

and the then hoped for, but unknown, positive return on investment. Hence, patents drive innovation, product introductions, product commercialization and societal adoption of new genetic testing.

The following comments now respond to the four issues or topics that are statutorily required to be examined under the America Invents Act and are based primarily on Myriad's experience with its nine molecular diagnostic tests and more specifically with respect to Myriad's BRACAnalysis and tests.

The first topic: the impact that current lack of independent, second-opinion testing has had on the ability to provide the highest level of medical clarifications. First, an important term to clarify is "second-opinion testing." In the context of genetic testing and this request for comments, the ability of patients to seek a second opinion is an important part of medical care; however, there is a big difference between repeating a diagnostic test to confirm the initial results and getting a second opinion

as to what to do with the results for such a test. For example, if a patient shows a cancerous lesion in her breast and her doctor recommends a lumpectomy, such a patient may seek a second opinion of another doctor to consider an alternative or confirmatory treatment. However, the patient is much less likely to ask for, and insurance will not generally pay for, a repeated MRI. There most likely is not a need. In such an instance it is not the accuracy of the test that the patient likely questions but the plan of action presented by her doctor.

In this respect, second opinions are no less available in the genetic testing field than any other field. Patients are free to seek medical advice and counsel of any health care practitioner as to appropriate medical treatment plans following a genetic test or result. In considering comments to the questions presented in this matter it is important to remember that the term "second-opinion testing" is referring to conducting a second test to confirm the

results of the initial laboratory diagnostic test that was performed.

With respect to Myriad's BRACAnalysis test there is no current lack of independent second opinion such as referenced in the statutory defined topic one. In fact, since 1999, multiple laboratories have performed testing which can confirm reported identification of a deleterious mutation in the BRCA1 or BRCA2 gene. Today, there are multiple laboratories that can conduct the confirmatory genetic diagnostic test. To name just a few, UCLA Diagnostic Molecular Pathology Laboratory; the University of California San Francisco Molecular Diagnostic Laboratory; and the University of Chicago Genetic Services Laboratory. So if a patient receives a BRACAnalysis report of a deleterious mutation, a laboratory independent of Myriad, can perform a confirmatory test for that reported mutation before the patient has any treatment decision including possible prophylactic surgeries.

In addition, in 2001, Myriad

licensed LabCorp the right to conduct single site and multi-site testing, the multi-site test is also referred to as the Ashkenazi panel for testing which Congressman Wasserman Schultz referenced. We granted them a license to that. This license remains in effect today. Therefore, we believe that there has been no adverse impact on medical care due to any alleged lack of second-opinion testing because second-opinion testing is and has been readily available. Even assuming for argument sake second-opinion testing was not available, we do not believe that it would have an adverse impact on patient medical care.

Myriad's laboratory quality systems are highly regulated, being CLIA certified and regularly audited to confirm proficiency in testing. As a result of the high quality of testing provided by Myriad, there has not been a need for second-opinion testing. We believe this is also the case in the general medical community. This is at least evidenced by the fact that Myriad has never received a request by a patient or health care practitioner for

permission for a third party to conduct a second confirmatory test. It has only been on an extremely rare case that Myriad has received, which we have always granted, a request for a patient to have Myriad perform a second confirmatory test.

The lack of demand for confirmatory testing is supported by the testimony of the Association for Molecular Pathology in the first hearing of these proceedings. The executive director of AMP noted that a patent-safe harbor for confirmatory tests would not result in increased access to confirmatory testing because labs will seldom invest in the significant resources needed to develop a test merely for duplicative purposes and health insurers and Medicare will likely not reimburse the cost of the test as it will be viewed as duplicative.

Second, there is no need for a second confirmatory test due to the degree of accuracy and the rigor of Myriad's testing process. Today, Myriad's genetics testing is highly regarded and generally recognized as

the gold standard for diagnostic testing. One example of our rigorous testing is that before reporting out any deleterious mutation, Myriad will retest the sample a second time to confirm the result. Hence, technically, a second confirmatory test is already run by Myriad on every positive report. In this regard, a very important observation is made by the statement of dissent by the Secretary's Advisory Committee on Genetics, Health, and Society in their report released in 2010 by three of the committee members with respect to the quality of testing by sole-source providers such as Myriad. The dissent statement says this: "We do not believe that there is any credible evidence that the quality of testing performed in sole-source laboratories is routinely or demonstrably subpar in any way to that which is done in multiple laboratories, nor do we believe that data indicate that modifying the gene patent system and protections it offers through the exclusive licensing agreements would result in multiple laboratories performing proprietary

tests with better quality and generated by current and developing oversight of quality assurance undertaken by these agencies and the laboratories themselves."

As you are probably aware, the dissenting statement is found at the end of the SACGHS report. We would encourage the PTO to review the entire dissenting statement as it makes several very important observations and cautions about the report and its recommendations. While the underlying studies commissioned by the committee offer valuable data and insights that may be useful to the PTO in their present study, many find that the recommendations proffered by the report are not supported by and in some cases are fairly contrary to the findings of these underlying studies. This statement of dissent provides what Myriad believes are fair observations and comments regarding the report.

Now, the second half of the first statutory topic asks whether the proposed lack of second-opinion testing has any inhibitory impact on innovations to existing testing and

diagnosis. Myriad does not believe so. Innovation is not fueled by running the same test to merely confirm a prior result; rather, innovation is spurred by basic research and by incentives for commercialization which are largely driven by the patent system. Accordingly, Myriad has seen no evidence of inhibition of innovation for existing testing and diagnoses. Myriad consistently develops, validates, and implements new technologies that can provide faster and more sensitive test results. Companies developing new tools are incentivized to do so based upon anticipated utilization of new technologies, which is unaffected whether there are second opinions. Rather, innovation is driven by doctor and patient demand for technologies that satisfy currently unmet clinical needs. If these new innovations to testing are more sensitive, less expensive, more reliable, they have been and will continue to be developed and be adopted.

Now, the second topic: the effect that providing independent second opinion

genetic diagnostic testing would have on existing patent and license holders of exclusive genetic tests. In theory, second opinion confirmatory testing should have no appreciable impact on existing patent and license holders of an exclusive license provided that the second-opinion testing in no way circumvents the initial testing conducted by the patent and license holders. Such exclusive providers will have already derived the benefit from their patented rights to the initial test. However, the real danger to exclusive providers and patent and license holders is gray market erosion of their rights resulting from initial tests performed by unauthorized third parties. If a lab ostensibly extensively offers confirmatory testing under a statutory license but is not required to verify that initial test has been performed by an exclusive provider, this can effectively eviscerate the exclusive provider's patent position by allowing the other lab to perform unauthorized testing under the guise of statutorily sanctioned

testing. Even if the second lab is statutorily required to verify authorized testing before performing confirmatory tests, there must be a mechanism for the exclusive provider to easily confirm this. While Myriad believes there is no need for a statutory scheme to authorize confirmatory testing, these and many other issues would need to be addressed if Congress were to determine there was a need to intervene.

The third topic: the impact that current exclusive licensing and patents on genetic testing has on the practice of medicine. No one can contest that the standard of medical care for the diagnosis, treatment, and reimbursement of hereditary breast and ovarian cancer, sometimes referred to as HBOC syndrome, in the United States is unparalleled to anywhere in the world. Today, a woman with a personal or family history of cancer, who meets medical society criteria, can be tested for the HBOC syndrome and receive timely and accurate results through her health care practitioner to guide the

medical management and her treatment decisions, all at an affordable cost based on insurance reimbursement. This standard of care has been accomplished based on the patenting of the BRCA isolated DNA molecules and the exclusive licensing of such rights to Myriad by the NIH and various academic and research institutions, all who collaboratively participated in this discovery effort.

The incentives of the patent system enable the raising of the investment capital that allowed Myriad to make the research, development, and commercial investment to bring accurate, reliable, and affordable HBOC testing to the general population. Myriad's exclusive licensing of the BRCA patents and commercialization of the BRACAnalysis test have led to advancements in research, medical care, test practicing, patient access, and insurance coverage. For example:

-over 9,000 research papers have been published relating to BRCA1 and BRCA2 gene and increased physician testing for hereditary breast and ovarian cancer;

- Over 18,000 different authors have published on the BRCA genes;

- The number of patients who have received BRCA testing is now approaching one million individuals;

- Approximately 40,000 health care providers have ordered BRCA testing;

- Ninety-five percent of patients have accessed BRACAnalysis testing through private, public, and financial assistance programs;

- Over 2,500 distinct insurance payors have paid for BRCA testing; and

- Eighty thousand individual group plans have paid for BRCA testing.

There are additional benefits of having a single entity exclusively provide particular test results. Such benefits include: uniformity of testing results and procedures; increased volume of test cases for enhanced interpretation of test results; the ability to fund and pursue, at no cost to the individual or family, family member testing of novel variants of uncertain significance for

subsequent classification; the ability to identify subgroups of populations with testing anomalies; better ability to adopt testing standards, whether developed internally or identified through third-party research; and a better ability to negotiate and obtain insurance reimbursement for testing.

Myriad has private insurance coverage for BRACAnalysis for over 200 million covered lives. In addition, for those covered by public insurance, BRACAnalysis is reimbursed by Medicare and by the majority of state Medicaid plans.

Dedicated customer support groups work with insurance companies to facilitate patient reimbursement. Myriad employs over 160 individuals who interact daily with patients and insurance companies to help patients work through the complexities of insurance coverage.

Funding of financial assistance programs for uninsured and underinsured individuals. In the last four years, Myriad has performed free testing for over 4,000 low

income or underinsured patients.

The ability and incentive to undertake and provide patient and physician education. Myriad organizes hundreds of educational meetings for health care practitioners to learn about hereditary breast and ovarian cancer.

Some may argue that patents are not necessary for research and the discovery effort citing the work of academic institutions. However, academic institutions do not have the organization, the infrastructure, the capital, or the mandate to commercialize products. Rather, such institutions rely on licensing their discoveries through commercial entities who will continue the investment of capital and commercialization of products. Since the passage of the Bayh-Dole Act, there has been tremendous growth in the licensing of intellectual property for commercialization with remarkable success both in terms of revenue return to academic institutions as well as a development of new and innovative

medical products and in particular, molecular diagnostic products. Others may suggest that exclusive rights to genetic tests hinder research, restrict innovation, restrict patient access, result in higher prices, and restrict access to confirmatory testing amongst other allegations. In the case of the BRCA diagnostic testing, that is patently false. In fact, the opposite is true. It was noted in a recent study published by the Duke Institute for Genomic Sciences and Policy which found that "it is therefore difficult to attribute reduced access to BRCA testing to patents. We cannot exclude the possibility that Myriad's investments in education about hereditary breast and ovarian cancer testing have actually had the opposite effect of increasing access to testing." The study also noted that "prices for BRCA1 and 2 testing do not reflect an obvious price premium attributed to exclusive patent rights compared with colorectal cancer testing and indeed, Myriad's per unit costs are somewhat lower for BRCA1 and 2 testing and testing for colorectal

cancer susceptibility." The colorectal cancer is one where there are multiple laboratories which provide testing for that.

In the area of personalized medicine, exclusive patent rights will not hinder research or innovation. On the contrary, in order to successfully commercialize a personalized medicine product there must be societal guidelines instructing health care practitioners to undertake testing as a standard of medical care. Societal guidelines are based on research and peer reviewed publications, and exclusive patent holders wanting to commercialize a product are incentivized to promote research and the clinical testing of a product. Equally so, insurance reimbursement will only occur once the payor community is convinced of the medical necessity and positive pharmacoeconomics of testing. Once again, costly research and clinical trials are needed and will be encouraged and conducted by patent holders.

In Myriad's case, we have

collaborated with hundreds of outside researchers and participated in hundreds of research programs and studies through outside researchers' clinical trials. For example, Myriad has provided BRCA testing services at a fraction of the commercial testing price to research conducted by researchers funded by and through the National Cancer Institute. These efforts have resulted in prolific research and publications to create information and knowledge about the BRCA genes.

By way of comparison, BRCA testing is offered exclusively by Myriad in the United States but by a number of different laboratories in Europe. Based on market research conducted by a leading consultant in the diagnostic market with over 200 European laboratories, it is clear that the current service provided in the United States has advantages inherent in the single-source model. There is wider availability of testing for patients in the U.S., especially for those that are unaffected. There are faster

turnaround times for the results in the U.S. due to the economies of scale in a single laboratory -- two weeks versus six months in Europe. And there is a significantly lower rate of uncertain test results -- in the U.S., 3 percent versus 20 percent in Europe. Additionally, we observe that pricing in Europe is consistent with the pricing in the U.S. despite the fact that it is available from multiple laboratories.

The fourth topic: the role the cost of insurance coverage has on access to and provision of diagnostic tests. Although genetic testing is costly, the information provided through testing can provide substantial savings to both the individual patient and the overall health care system. With respect to our specific molecular diagnostic test, Myriad has made substantial investments to educate the payor community on the positive pharmacoeconomics on predisposition testing. This has taken much time, effort, energy, and capital for us to assemble and train a workforce to compile the

necessary pharmacoeconomics data and negotiate with payors for reimbursement of BRACAnalysis testing and other diagnostic tests. As a result, insurance companies almost unanimously cover molecular diagnostic testing. In addition, government health programs like Medicare also provide coverage for BRCA testing and other proven genetic tests. With their reimbursement, genetic testing is affordable to the individual patient. For the vast majority of BRCA patients, the cost of testing and availability of insurance coverage do not create barriers to testing.

Myriad is committed to continue in our efforts to ensure broad access to testing. For example, in order to ensure patients are able to access testing ordered by their physicians, Myriad provides free testing for certain patients based on financial and medical criteria, but by law we cannot perform free testing for an otherwise qualified patient who is a Medicare or Medicaid beneficiary. In this regard, there have been some allegations overstated in the ACLU

lawsuit against Myriad and even referenced in earlier testimony before the PTO that Myriad has rejected or will not provide testing to certain individuals due to their insurance coverage.

The specific allegation is that Myriad rejected the insurance coverage of one of the ACLU plaintiffs who resided in Massachusetts. However, the facts are that this individual was covered by Massachusetts' mandated health care plan and Myriad and Mass Health had not yet entered into an agreement for coverage of BRACAnalysis testing. Hence, Myriad did not reject her insurance coverage; rather, BRACAnalysis was not a covered benefit. When Myriad realized this it sought to provide free testing to this individual under Myriad's patient financial assistance plan, well before the ACLU lawsuit was filed, but was precluded from doing so due to Medicare and Medicaid beneficiary laws.

The good news is two-fold. First, the plaintiff in question, and many other similar situated individuals, did get tested

through free testing provided by Myriad through an unrelated non-profit organization. And second, Mass Health now covers BRACAnalysis testing. Hence, the allegations against Myriad were unfounded. Rather, the underlying cause of the individual's difficulty in getting tested was due to the application of general health care laws and the insurance coverage reimbursement environment.

The statement of dissent to the SACGHS report also comments on this noting the need for an evaluation of "relevant laws, regulations, and policies such as anti-kickback, health care fraud statutes, and government reimbursement policies that are overly burdensome or result in practical barriers on diagnostic companies who would otherwise elect to offer tests at little or no cost based on the financial need."

It is important to note that payor acceptance of new medical treatments does not happen overnight. To the contrary, payors can be slow to adopt new technologies without

extensive education and supporting scientific evidence. In fact, in the mid to late 1990s when Myriad was developing the BRACAnalysis test, there was much apprehension and opposition to conducting genetic testing in general and specifically BRCA testing. We would refer the PTO to a case study undertaken by the Stanford Graduate School of Business dated May 5, 2005, which documents and discusses the opposition to genetic testing in general and the difficulty that Myriad had in developing BRCA testing.

Myriad has spent a great deal of time and resources to ensure payors and physicians are educated on the latest technologies and the benefits to patients in the overall health care system. We believe everyone can benefit from a health care system that values getting the right treatment to the right patient at the right time. Therefore, payors must continue to support coverage and appropriate reimbursement of personalized medical products like BRACAnalysis.

In summary, Myriad believes that

medical care, access, and affordability of genetic testing has tremendously advanced and been to the benefit of all in the United States as the result of the patenting and the exclusive licensing of the BRCA genes. Myriad strongly supports the patent system as a means to bring new medical treatments to patients while providing jobs, revenue, and opportunity to the biotechnology sector in specific and the economy in general. We also believe that the Patent and Trademark Office must ensure the rights of patent holders, and exclusive licensing where applicable, and the underlying purposes of the patent system are respected and preserved, as detailed in its mission which is anchored in Article 1, Section A, Clause 8 of our Constitution. To undermine this prudent system would deny patients and the medical community of new and innovative products which aim to bring the promise of personalized medicine to fruition. We encourage the PTO to base its findings concerning genetic testing not on anecdotal stories or allegations but on well structured,

unbiased studies which Myriad believes will support the conclusion that the quality of patient care has been significantly advanced through the patent system and that any changes thereto should be carefully measured, if any.

Thank you. And I'd be happy to respond to any questions that you might have.

MS. GONGOLA: Thank you, Mr. Marsh. Dr. Graham has a question.

MR. GRAHAM: Thank you, Dr. Marsh. I do appreciate the evidence you've brought to bear on the questions today. It is very helpful. And it will be helpful to us I'm sure in thinking about these issues.

I'd like to press a bit on the issue surrounding the market for second-opinion testing and how demand interacts with the availability of insurance coverage. So I figure you'd be a good person for this since you're an accountant and probably think a lot about these issues. Of course, you know, no business model can survive without an underlying revenue stream associated with it. And of course, that revenue stream in pharma

is a consequence of at least two factors -- patients and/or their stand-in physicians, and the availability of insurance companies to cover that.

So given that your company is interacting certainly with a lot of other companies and probably has -- you've probably in your experience learned some information -- and [your company] has a suite of different tests on both BRCA and other tests. Are you seeing variation among the different tests and the extent to which demand for second-opinion testing may be greater or lesser across different types of tests? And is there more or less likelihood of there being insurance coverage associated with those coverages depending on how much demand there is?

Now, at the same time I do understand, as you said, that oftentimes companies like yours have to go through an educational mission to kind of create the opportunities for insurance companies to support this kind of demand that's out there, and out there for good reasons. But I'm just

trying to get a sense of how this secondary market actually behaves differently across the different types of tests.

MR. MARSH: Thank you, Stuart. I think first you've asked a couple questions so if I don't get them all, come back.

I think the first observation with respect to all of our nine molecular diagnostic products, we have not seen a demand for second-opinion testing. As I mentioned, we've never received a request to have it be done by a third party, be repeated, and only on an isolated case, literally a handful of cases have people asked us to have it be redone with our lab, ourselves. I think that's in part due -- remember, I mean, this is a very highly regulated process. It's strictly a certification process. You have to validate your test and show that it will have reliable results, result after result after result. And that level of certainty I think gives our patients a high degree of comfort that the accuracy of their test is accurate and correct. And so we just have not seen it,

not only with BRACAnalysis but across the suite of all our products. We just haven't seen it or there hasn't been the demand for second-opinion testing for our products.

Your second question I think about the market for second-opinion testing should there be deemed to be a need and maybe other indications for other testing, it's a difficult question because while I appreciate -- I think, George, it was your comment that there could be an individual who receives a positive deleterious mutation test report, and says before I take some very serious prophylactic surgical steps, just for peace of mind I'd like to know. And so I appreciate that desire to have that done. The difficulty is, and this was the testimony of the [AMP] Executive Director, it's very difficult for a commercial lab or for any lab to do the validation process, to spend the time, effort, energy, and dollars to get CLIA certified to be able to give a clinical result back. And so the concern was you're not going to find, as a practical matter, entities that are

willing to set up a facility who is able to do that.

Now, where are the clinical labs coming from today that do offer second-opinion testing? They are out there but they're not commercial scale labs. They are there, which I think is a nice marriage, if you will, because it's a very handful of a few. And so you don't need large commercial scale laboratories. And I think what happens is, is remember with personalized medicine products, research -- you've got to have research and a patent holder, he will do everything he can to encourage research. And so what you have is a number of academic institutions. And you'll notice these entities that do provide where you can get a second opinion test for a confirmatory positive result are largely academic-type institutions which have been doing the underlying research. And so they otherwise do have a laboratory facility which has the ability to do sequencing and otherwise has gone through the rigor of getting a CLIA certification. And so I think there are those

types of labs that are available, but mind you, they are not of a commercial scale to deal with broad-based large scale testing. And so there is a little bit of a practical problem of how do you -- if there is a desire for second-opinion testing, how do you get a commercial site or someone to actually develop such a lab? I think in this case the research community, which will be so critical behind any commercial diagnostic test probably represent for those few individuals who think that whether mentally they want to get that comfort would have I think an access or be able to get that.

The third question I wrote down was insurance. I'm trying to remember what it was. Oh, the insurance community. Reimbursement for second-opinion testing. I think is extremely unlikely that the payor community, the insurance reimbursement community, is going to pay for a second test. It is already extremely difficult to get them to initially compensate for the initial test, if you will. You have to prove medical

necessity. The insurance company is burdened with costs, their cost structure and they are very, very careful to make sure that testing is appropriate for the appropriate individual. The same thing with BRACAnalysis. Every individual shouldn't go get a BRACAnalysis test. It is only those who have a personal and family history, as in the case of Congressman Wasserman Schultz. She was very fortunate to have a very educated nurse practitioner who was aware of the importance to ask any affected person with cancer do you have a personal or family history of cancer? Because it may be suggestive that this is a hereditary condition. And if you meet those red flag criteria you should go get tested.

Insurance will reimburse for that type of test when you meet those types of criteria. When you present the case to an insurance to say I would like to get a second confirmatory test and would you pay for this it is extremely unlikely that insurance would ever pay for that. So hence, you're going to have another practical dilemma of the

affordability of getting a second confirmatory test and the insurance community to pay for a second test.

MS. GONGOLA: Mr. Elliott has a question.

MR. ELLIOTT: It has been argued, and this kind of goes to the resources that you have because you are the licensee. It has been argued that the variants of unknown significance or inconclusive test results are a reflection of the quality of the test. And I just wonder if you could explain a little bit more about what variants of unknown significance are. And this is a three-part question actually. How long have you been doing the family member testing that you do when you find those? And can you tell us approximately how long it generally takes to gather the results that allow you to classify new variants of unknown significance?

MR. MARSH: Thank you, George, for that question. It's very important that people understand that when you sequence DNA, every individual is going to have some form or

type of variation from what we call the wild type or what is the common sequence of BRCA1 or 2 gene. But there are literally, if not tens of thousands of variations in your -- in an individual's DNA sequence. And so when we say a VUS or variant of unknown significance, what it means is that Myriad has identified a polymorphism, a difference or a change from the wild type. So there's nothing inconclusive about the test in the sense that the test was I don't know if you have a change or not. No, the test result is you have a mutation, a polymorphism and that will be identified in the test report as given. So the specificity in the test is exact and is accurate. So that's an important thing to understand, that there's no misinformation or inaccuracy with respect to the test report.

What happens though is that the specific mutation may not yet be known to be whether it's deleterious or not. So anytime you have a mutation it can be anywhere on the spectrum of having no clinical significance -- in other words, it's an inert or it's a

polymorphism, clearly is a mutation, and it's different than what's in the wild type sequence but it has deleterious impact. If you look in the family member's history it's not interconnected. You don't see cancers in the families and after a number of observations we were able to determine that scientifically this is not a deleterious mutation. Otherwise, the mutation could be found to be deleterious, meaning it does have a high probability of being influenced in the genome pathway or in the disease pathway and there's a high degree or risk of cancer reoccurrence. Once again, you look back through the family and look and see how the gene impacts. If there are multiple cancers in the family, as you collect more information about any given VUS (variant of unknown significance) you'll be able to classify it or identify it as being a deleterious or a polymorphism without any impact from being non-deleterious.

So when Myriad first started doing testing, as you can appreciate with any new

molecular diagnostic test, this is an evolutionary test. When we first started testing approximately 40 percent of our test results were unknown. There were new mutations. There were first observations. We didn't know. And from day one, in answer to your second question, we have always had a process of anytime we identify a VUS we contact the patient and we let them know you have a VUS. We do not yet have enough information about this variant to classify it. And the clinical advice is given to a patient, so once again, there's no uncertainty, oh, what do I do; I have this VUS. The medical process and procedure is because it's a VUS they're instructed that you need to base your medical management decisions not based on these test results because it's unknown but on the general management treatment that you would have based on your personal family history that (inaudible) situation. So there's clear specific guidance.

Then the next step that Myriad does is we go out and we test. For free, we

contact the patient and say would you please have any of your family members who have -- we'd like to test all of them because it's a hereditary condition to see what other individuals in the family have that same mutation and then look at their information. Did sister have cancer? Did mother have cancer? Did grandmother have cancer? And we can then collect enough information to determine whether or not it is a deleterious mutation or not. And hence, in time, we classify the gene. We keep a database and we track all our patients. And the day we reclassify -- not reclassify but classify for the first time in the VUS -- we contact the health care provider who ordered the test and we advise them. Generally, that's a difficult question how long it takes. It really depends on how -- the common frequency of the VUS. Today, our VUS rate is 3 percent. So we have seen enough mutations enough of the time that we're very accurate and are able to do it. Hence, that's one of the reasons why a single sole provider is nice. You get enough

samples, can see enough of the cases to be able to make those calls. So 3 percent of the time we have VUS.

So for those you are getting into more rare mutations which means it's more difficult to collect enough family information and see that same mutation and other families to collect their information. And so it can take anywhere from a couple of months to the more rare case of a year or longer. So, I mean, it can take some period of time if not longer to classify it. Again, it's really contingent upon how discreet is that mutation and how many other observations of that mutation have we seen to be able to classify it.

I think did I get everything?

MR. ELLIOTT: I think you covered it. Thank you very much.

MS. GONGOLA: Thank you. Deputy Director Rea has a question.

MS. REA: Sorry. Can you hear me? Thank you so much. I have two very quick issues I'd like to go through. The first one,

was Congressman Wasserman Schultz given incorrect information during her treatment and was there indeed the availability of a second diagnostic test opportunity and they just didn't realize that these academic institutions actually were authorized and licensed by you to do so?

MR. MARSH: Yes. I mean, you asked a two-part question. I don't know what she was actually told and the context of what was told to her but the answer to your second question is yes. Absolutely. She could have gone and been tested by a number of these institutions. If you go to www.genetests.org, I think it's run by the University of Washington. You've kind of got to work your way through the website on testing, current BRCA testing. There's a list of those entities which will do that single site testing for the positive deleterious mutation that she would have been reported out on. Likewise, LabCorp has been licensed to do not only single site testing but also the multisite for the three Ashkenazi Jewish panel

mutations as well. And so she could have gone to an independent laboratory to have confirmed that deleterious report on those -- I don't know what her results were, whether it was one, two, or three or what it was, but she would have been able to confirm that test.

MS. REA: Okay. And the result has been that patients always had that opportunity for a second medical diagnostic test with all of Myriad's products from day one.

MR. MARSH: When you say from all Myriad's products and from day one, we have not tried to keep track. As soon as we launch a product the secondary community is out there. We don't actively go out and license and give people their license.

MS. REA: But you would know if you gave them a license.

MR. MARSH: And we did. I mean, early on from the 1999 to 2000-2001 timeframe we actually went out and licensed third-party laboratories, 8 to 10 institutions who were interested and had licensed to do the single site and multisite testing. Those licenses

expired. As Myriad grew in scope and breadth and capacity to be able to do it all by itself we just went off and ran our business and really didn't try to keep track of it. Until this ACLU lawsuit came up that we stopped and took a second look back at who else is out there testing. We don't police it; we don't look after it, but in hindsight we went back and looked and we identified that there are these multiple laboratories. Largely the research-type institutions who have been doing research around BRACAnalysis. And to do the research, what do you have to do? You have to have patients come in. You sequence their DNA and then you analyze them. So these types of institutions had the capacity within their labs to be doing sequencing. And as we went back and looked we identified these multiple labs. But at least LabCorp is the one example. Since 2001, they've been licensed and to do single site and multi-site testing.

MS. REA: And when did you start testing for the BRCA mutation?

MR. MARSH: Don't hold me to this

but it's approximately 1996 I think is when we first launched BRCA testing.

MS. REA: So there might have been a gap between 1996 and 2001 where the physician community may not have been aware of the opportunity for second diagnostic opinions.

MR. MARSH: Awareness is a different question than availability because there may always, as in the case apparently with Congressman Wasserman Schultz, that the provider may not be accurately informed of what are the options are out there. I don't believe that since when Myriad started launching its product for the first BRACAnalysis test, I'm rather comfortable, although I candidly have not done a timetable to look at it but I'm pretty comfortable that there has always been a laboratory out there doing testing that could have provided confirmatory results.

MS. REA: Thank you. My next issue --

MR. MARSH: Please.

MS. REA: But I want you to educate

me a little bit if you don't mind. I'm not that familiar with the medical diagnostic tests. I just have a dangerous amount of knowledge and the CLIA approval I don't fully understand. But you did indicate in your testimony that you now have a database of a million patients. So you have an awesome database to search for and find these anomalies and mutations. As you obtain data, I'm just curious for CLIA or FDA approval, is that data being dumped into a database in the public domain? Or does that data and information that you have obtained through years of testing with all of these million patients, is that proprietary data to you?

MR. MARSH: It is proprietary data to Myriad. When Myriad first started BRACAnalysis testing there was the creation of what's called the BIC, a public repository of mutation status. Myriad initially participated in the BIC along with the other research facilities and laboratories that were doing testing. And so there was a variety of entities who actually deposited these known

mutations into this public database. I think today Myriad probably represents 80 percent of what's in the public database. We stopped in approximately 2006, I believe, is when we stopped putting information into the public database. I think it's important to note that -- actually, I think that is one of the benefits of a sole provider entity. If you look, for example, to some of the other conditions, colorectal cancer is a common exemplar given the fact that there are multiple laboratories providing testing and everyone holds non-exclusive licenses. You'll note that, because of the competitive nature of multiple labs providing testing, there is no BIC, if you will. There's no repository. The multiple parties don't share data. They don't share what the mutations are because it would be competitive. Because you've got competitors on the other end. One of the benefits of being of a sole licensed model is because of the promise of exclusivity that's provided by the patents it allows, in Myriad's case, for us to initially, as we were trying

to help educate everybody, as I mentioned.

In the 1990s - it was a very interesting environment, if you would like to read that Stanford report about the degree and difficulty, in fact, opposition to doing testing. There were some who would not -- who said giving results to a patient is not appropriate because they don't know what to do with it. They won't know how to react with the results. And there's this tremendous opposition. And so Myriad did everything they could to overcome that to get testing accepted, including trying to get these third party institutions and research labs -- and we can't take all the credit. They were very active and the research community as well and wanted to discover (inaudible). But there was a collegial effort, if you will, and everyone did support that. It largely was driven by Myriad because the preponderance of testing was being done by Myriad. That now is a public database that is available. It doesn't have the full complement of the mutations, particularly the ones more recently, the 3

percent of VUSs in the database and then basically the stuff that is proprietary data that any companies has as a trade secret.

MS. REA: Thank you so much.

MR. MARSH: Thank you.

MS. GONGOLA: Thank you, Mr. Marsh. We have no further questions. You may take a seat.

MR. MARSH: Thank you.

MS. GONGOLA: Our next witness is Professor Christopher Holman from the University of Missouri, Kansas City School of Law.

MR. HOLMAN: Okay. Great. Thank you for allowing me to present here today.

Before becoming a law professor I was a Ph.D. molecular biologist and I cloned genes. After that I became a biotech patent attorney and I wrote some gene patents. But in 2005 I became a law professor. And when I started I noted a huge amount of academic commentary on gene patents and a huge amount of coverage of this notion that gene patents were somehow an exceptional sort of patent and

creating exceptional problems. And particularly at that time I think a lot of the focus was on a so-called patent of gene thickets that was going to block research that involved looking at multiple genes at one time and also hybridization arrays, like the Affymetrix GeneChip as an example, that because you had technologies like that that had lots of genes on them that looked at lots of genes, that these gene patents would be a thicket that would cause a problem for that.

So I decided to look into this and maybe challenge some of these assumptions. So in 2007, I did a study where I tried to identify every single litigation involving human gene patent. Any case where a lawsuit was filed. And people will say, well, there's chilling effects that go beyond lawsuits. That's true maybe. But at least empirically it's something you can get your hands on. You can look at the lawsuits. And what I found is there were relatively few of these lawsuits. Most of them involved therapeutic proteins. So in the majority of cases the gene patents

were acting in a manner analogous to a drug patent that was being used by a company like AMGEN or Genentech to ward off competition for a recombinant biotech drug that maybe they spent a billion dollars developing. Most people don't think that's problematic but they're functioning more like a gene patent -- I mean, a drug patent.

I found absolutely no case where basic research or any sort of research that was looking at multiple genes was the subject of a lawsuit so I think the idea of a patent thicket was not apparent and I think other studies have shown that this idea of a patent thicket is hypothetical but at least in terms of basic research it doesn't seem to be a problem. In terms of genetic diagnostic testing I found six lawsuits. That's all I found, including a couple involving Myriad. But all of these lawsuits happened a while ago. All of them were dismissed very early, so they all settled in some way very early so there was never a substantive decision. So at least when I did that study a few years ago,

there was not a single case where any court had ever addressed any substantive issue in terms of the gene patent and genetic testing.

Since that time I haven't done a systematic study but I know there was a Billups-Rothenberg case a year or two ago out of the Federal Circuit and to my knowledge that's the only genetic testing case involving gene patents that has actually gone that far, and in that case notably all the asserted patent claims were found to be invalid. So as far as I know, there's never been a case where a gene patent has ever been successfully asserted in the context of genetic testing. Which makes me wonder, do they warrant this exceptional sort of treatment? So when I read section 27 there seems to be a section there that gene patents in particular are a problem for genetic testing and for confirmatory testing.

I'm wondering if -- it seems to me that there's an exaggeration. It's maybe an unwarranted assumption that these particular types of patents are causing such a problem.

More recently, I did a study looking at the myth that 20 percent of human genes are patented. And this is a very widespread assumption and I talked to people from China and India who tell me that everybody in India knows that in the U.S. 20 percent of human genes are patented and nobody can do anything with those genes. If you look at the recent Federal Circuit decision involving Myriad, Judge Lourie states that 20 percent of human genes are patented. Judge Bryson goes on in his dissent where he was arguing for patent ineligibility for isolated DNA claims that whole genome sequencing and multiplex testing are particularly at risk and in particular that if someone wants to do whole genome sequencing which is thought to be very important for the development of genetic testing, they will have to obtain thousands of licenses from different gene patent owners at a cost of maybe $100,000. We see Francis Collins, the director of NIH, repeatedly making the statement that he fears that while the cost of doing a whole genome sequence will

drop to $1,000, there will be $100,000 royalty because of all the gene patents. This is a widely held assumption.

So I decided to look into the basis for this assumption that 20 percent of human genes are patented. And what I find is basically there's a single study written and published in Science in 2005 and often it's not cited at all. You see articles in Science that assume that 20 percent of genes are patented. Judge Lourie cites to a Law Review article for the proposition. The Law Review article cites to a National Academy of Science study. But if you trace it back it comes to this single article by Jensen and Murray 2005, "The Intellectual Property Landscape of the Human Genome."

And so what I did is I asked the authors would you mind sharing the list of patents that you found that are the basis for this 20 percent? And they very readily shared the data. It was an Excel spreadsheet and I think interestingly given the prominence that this has taken in the debate, they never

published this and actually until I asked for it a couple years ago nobody had ever asked to see it. And so no patent attorney had ever actually gone through and looked at these patents. No one had ever analyzed the claims.

And so I did that. I also read their supporting online materials for the article, and I think it's kind of telling that if you read the main text of their article it states that 20 percent of human genes are explicitly claimed as US IP. That's the source of this myth. If you read their supporting online materials it's quite accurate. It says 20 percent of known gene sequences are mentioned in U.S. patent claims. And if you look through their methodology what they actually did is they did a nice automated search for patents where there's a SEQ ID number in the claims that corresponds either to, they thought, a human genetic DNA sequence or a protein sequence. They didn't realize that often SEQ ID numbers identify both DNA and protein.

And so that's what they found. I

then decided to actually read the claims in these patents, which really no one has done before. And so I pulled out 533 as a sample of these 4,270 pounds just to make it more manageable. And so I had this random sampling and I looked through and basically you find a huge degree of heterogeneity in what's being claimed but it's really important that you read the patent claims and don't make an assumption that genetic testing is covered by all these patents. What I found is that 139, so I guess over a quarter, have nothing at all to do with claiming a gene. They're mostly protein claims. For example, there's a patent and what it claims is a non-naturally occurring mutant human hemoglobin. So it's claiming a protein that doesn't exist in nature, but according to the interpretation of their study, there's an assumption that nobody can study the human hemoglobin gene or sequence that are due testing because it's patented. But we see that what patented really means is that a non-naturally occurring protein was patented. That's what you see

with a lot of these patents.

Three hundred sixty-six of the 533 had a product claim covering a DNA molecule. Most of these are isolated DNA molecule claims. This is what has gotten a lot of attention. So there are -- quite a few of the patents have those, and what I found is if you read the patents and read the claim set, it's very clear that mostly what the patent drafter was patenting cDNA sequences for the purpose of expressing the protein. For example, making a therapeutic protein. So, for example, the number one assignee of these gene patents in the set was a company called Incyte. Incyte had a business model of looking for -- identifying cDNA sequences and filing patents on them. And if you look at the claims, the claims are directed to full length cDNA molecules, expression vectors, host cells, methods of producing proteins. That's what they're claiming. They're not claims that would cover things like genome sequencing, particularly whole genome sequencing.

For a variety of reasons I think time is limited but if you read my articles I talk about how it's very questionable whether isolated DNA as the defined in the claim is made necessarily in DNA sequencing. DNA sequencing typically involves, you know, analyzing shorter fragments of genomic DNA whereas these claims are usually directed to full length cDNA molecules lacking the introns.

So for a variety of reasons I think that there's a very good argument that could be made that none of these isolated DNA claims would necessarily be infringed by whole genome sequencing or gene sequencing and still be valid because there are issues. If you interpret the claims, they would cover that. There are a lot of issues of compliance with the requirements of patentability. Independently of my work, a gentleman named -- what was his name? W. Nicholson Price II wrote an article, "Unblock the Future: Why Gene Patents Won't Impede Whole Genome Sequencing." Using different methodology but

he came to roughly the same conclusion that it looks like either these isolated DNA claims are either not infringed by genome sequencing in general, or invalid. And in particular with Myriad, I filed a brief in the Myriad case pointing out that some of these claims were directed to full length cDNA molecules whereas their methodology involves amplification of amplicons which are fragments of the full length gene. And then the data is built up but no one actually isolates the full length of the sequence.

Things like that are going on. But what you'll find is many people make the assumption that, well, there's a claim to the isolated gene. And since somebody has patented the gene, nobody can study it. Nobody can do testing. An unwarranted assumption I think because actually to infringe the claim you have to make or use something as defined by the claim. You can't just assume that all testing and all research is off limits. And I think the U.S. Government seems to have taken this position.

I noted during the oral arguments in this Myriad case that the U.S. Government stated the vast majority of the claims to isolated DNA that have been issued by the PTO are "cDNA recombinant DNA process claims and the like" and hence, would not cover genomic DNA, and hence, genomic DNA sequencing. And I think that's consistent with what I saw in my study.

I also found 47 patents had a claim to a method that would cover maybe some form of genetic testing. Mostly these would not cover testing like what Myriad is doing. It wouldn't cover DNA sequencing. They're more an expression of a gene that they are looking at. Out of the 533 patents, I only found 13 that have method claims that actually would cover something like isolating a DNA sequence from a patient, sequencing it, and then making a correlation between a certain specific variation and some kind of disorder or clinical result. So pretty rare.

Another -- so I think this goes for this perception that 20 percent of genes are patented in a way that would necessarily be

infringed by whole genome sequencing. There's just really no evidence of that and it looks like most, if not all of these patents, are not necessarily infringed by things like genome sequencing or genetic testing.

Another article I just wanted to comment on is by H-U-Y-S, Huys I'll pronounce her name, some European researchers published in 2009 in Nature Biotechnology. It makes the statement -- it identifies certain patents including Myriad patents saying that some of these patents they found to be almost impossible to circumvent in doing genetic testing and therefore called blocking patents. And many people have interpreted this as saying, well, these gene patents, you can't get around them. They totally block any type of genetic testing. But once again, just like the Murray-Jensen Science article, if you read the article more carefully and see what they actually did, you see that that's not what they found. That's an unwarranted assumption. What they actually did is as European, I believe non-patent attorneys, they looked at

the claims and compared them to best practice guidelines for currently practiced genetic diagnostic tests.

So they never purported to find that these patents blocked any testing of that gene. In their interpretation though they thought under the currently practiced best practices -- that's what they thought. And I actually met with this lead author and asked her about that. She said, oh, yeah. You're exactly right. People misinterpreted the study. We never purported to find that these patents couldn't be designed around. We just found it for these particular tests. So another example I think of some empirical research is being misinterpreted and over interpreted.

Okay. A few minutes, just a little bit on history. I think there's a lesson in history here. This is not the first time there's been calls for rendering subject matter patent ineligible because of fears on their effect on health and society and research. You look at Diamond v. Chakrabarty

(1980), if you look at amicus briefs that were filed in that case, we had Nobel laureates, we had medical people saying if you allow patents on biotech inventions, you know, modified living organisms, it's going to be devastating for the world and for research and for health. We haven't seen that.

In the 1990s there was a big controversy over medical procedure patents. These have been issued for many years, since the '50s at least they were sanctioned but no one was really aware of it. There was one lawsuit filed and because of that we had a huge amount of Law Review articles and attention in the media and we had the American Medical Association making arguments that we're hearing today in terms of gene patents. They said medical procedure patents are unethical. They're unnecessary for innovation. They're going to increase the costs to patients. They're going to delay sharing of information between doctors. They're terrible. They call for patent ineligibility for medical procedures. Okay.

Congress did not do that. What Congress did is they enacted 287(c) which provided a limited exception for liability so it got -- so basically there would be no remedies against doctors for infringement of these patents. You don't hear anything about these patents. They're still issued. I think they're probably a good thing. And patent -- the rules of patentability do not need to be altered to address the problem.

In terms of gene patents, as I said, 15 years ago all the talk was about basic research. Well, we've seen no evidence of that. And also about these hybridization arrays where you have probes representing thousands of genes. And the idea was, well, if you've got a gene chip hybridization array that has probes representing thousands of genes, isn't that going to necessarily result in the infringement of a thicket of gene patents? Isn't that going to be a problem? Well, I'm not sure what a problem it's been. I do know that when I looked I couldn't find a single example of a gene patent ever being

asserted against the use of the hybridization array. I saw lots of patent litigation involving hybridization arrays but not gene patents. Patents are the more fundamental technologies and that's what I see today with whole genome sequencing. That there are lawsuits being filed between the whole genome sequencing companies. They're not gene patents. They're on the more fundamental technologies. Why are we focusing on gene patents per se when they don't seem to be, you know, there's no evidence, tangible evidence of this problem?

So I think in conclusion I will just say that we do have other doctrines of patentability -- section 102, 103, 112 -- that should be the tools for weeding out patents that shouldn't be issued. I think that we're hearing a lot of testimony today and otherwise as to the beneficial aspects of patents and the potential negative unintended consequences if the standards are changed. And I think that we should just be very careful before making changes in non-policy that could have

these negative unintended consequences, particularly when there seems to be -- the perceived problem seems to be much greater than the actual problem. Thank you.

MS. GONGOLA: Thank you, Professor Holman. Dr. Graham has a question.

MR. GRAHAM: Thank you very much for your commentary and for bringing evidence to bear. I just have a couple quick questions. One is on your study of the Murray and Jensen piece -- Jensen and Murray. Can you identify for us those [patents] that you clearly found or that, you know, in your best estimate as someone who has read the claims, clearly found were the Type 1 errors? Those [patents] they included that should not have been included? But also can you comment on, you know, given your experience with this scientific space whether there might have been Type 2 errors, those that didn't get into their sample because of the method that they chose [but should have been]? That's question number one.

Question number two, if you could

give us an estimate of what you think given your reading of that sample of patent that you read, what is your best estimate of the number of or the percentage of the genome that is now actually effectively patented?

MR. HOLMAN: Okay. The first question, I think that you're right. The answer would be yes. I think that their study was both over inclusive and under inclusive. For example, I did my own -- the Human Gene Patent Litigation Study, I used my own methodology. And basically they were looking for patents that used SEQ ID number in the claims and there actually are quite a few patents that I would call gene patents that are directed towards genes. And these are the genes that don't have a SEQ ID number. And so I actually found that the majority of the litigated human gene patents that I found were not in their dataset. So yes, I think that's right.

In terms of how much is off limit, in a way I think that you cannot literally patent a gene and that zero percent is

off-limits. There's a huge deal of heterogeneity in the claims and so it's very hard. For example, there's a lot of claims that would be any DNA sequence, any fragment of this -- of a sequence long enough to encode a fragment of the protein that's long enough to have functional activity. You don't know what that claim covers just by reading it. You'd have to, you know, and so how do you know how long it is? It would very much depend on the methodology used and so forth. But I think, for example, even if you have a very broad interpretation of what isolated means, most of these fragments that are claimed are probably at least over 200, you know, usually far greater than that. And a lot of these genome sequencing methods involve looking at shorter reads, some shorter fragments. So I think those, you know, you can rule them out.

Let me try to answer. If people want to know numbers, I think it's impossible in my opinion to give numbers. But what I can say is I found a lot of patents that I think

you can unambiguously say would not be infringed by sequencing and genetic testing. And then a lot of patents where there's a whole range. And because we haven't had any litigation there's very little guidance from the court. It's hard to unambiguously say this could not go any further. But I think the vast majority of them, very unlikely they would be found valid and infringed and potentially none of the isolated DNA claims. I think the method claims, there is a limitation because I think with the Myriad decision it's very clear. You can't just claim comparing information. So in terms of getting a second and third test, it's very clear you can't get a patent that would stop somebody, a second health care provider or genetic counselor from looking at the data provided to you and making their own assessment of it. I think to infringe you really would have to have some entity who is actually getting a sample for a patient, a molecular sample, performing the molecular analysis and then taking the extra step of

actually recognizing and being aware, being informed of the significance of that variation.

So I think in a world, for example, where you had a whole genome sequencing company, like China is gearing up to be the largest provider of whole genome sequencing in the world. If you have somebody providing your genome sequence without any analysis, I don't think there's infringement of the claim because of lack of analysis. Whereas, if you have that data now converted from molecule to thumb drive or however you have it, you could share that with anybody and anybody could analyze it and you cannot get a patent that would satisfy our current rules of patent eligibility that would cover analyzing the information. So depending on how things shake out, it's unclear whether any of them would cover testing in any world where there was a kind of disconnect between the provider of the sequencing of the molecule and the provider of the analysis and significance of the information.

MS. GONGOLA: Thank you, Professor Holman. At this point, let's take our morning break. We're going to -- because we're a little behind schedule -- we'll keep it relatively short to five minutes. When we resume from our break, we will hear testimony from Mr. Carlos Candeloro, a patent attorney from the biotechnology area. So five minute break, resume very shortly. Thank you.

(Recess)

MS. GONGOLA: Thank you. Our next witness is Mr. Carlos Candeloro, who is a patent attorney in biotechnology.

MR. CANDELORO: Thank you very much. Good morning, everyone. First I'd like to thank members of Congress and Congresswoman Wasserman Schultz and others responsible for including section 27 in the AIA. The request that this study be conducted is very timely and opportune to the continued advance of our field and protection of genetic testing consumers. I would also like to thank the PTO for organizing these hearings on such a tight schedule and for providing me with the

opportunity to testify. I hope the testimony is of assistance in informing the PTO regarding issues that need to be addressed in the study and writing the report.

I'm going to give a brief introduction about myself. I'm a patent attorney. I've been in patent law for about 15 years. Been involved in drafting and prosecuting nucleic acid invention patents. I've also participated in interferences regarding these nucleic acid invention disputes as to who invented it first. Also, I think drafted one of the first patent applications dealing with gene expression.

Can you hear me? Can people not hear me? Is this better? So where was I? Okay.

I drafted one of the very first patent applications with gene expression profiling and that was for the NIH, Dr. Staudt, I believe. Before becoming a patent attorney I graduated with a degree in genetics from UC Berkeley and I went to graduate school right here up the road at UCSD in the lab of

Dr. Geoff Rosenfeld where we studied, you know, gene expression, transcription factors and regulatory sequences and so I'm familiar with this topic.

I would like to give a brief background of the issues that have been discussed here. I'm not going to go over what the AIA says. I'm just going to review some of the issues that have been raised including: definitional problems with confirmatory testing, problems policing or enforcing people who are confirmatory testing, the rights of consumers who consume genetic testing, issues with government-funded patents versus privately funded patents, problems with diluting patent rights, in particular singling-out genetic testing patents, and issues of public opinion and public perception not only of genetic testing and its cost and potential benefits but the patent system itself, particularly as it relates to health care.

And basically I believe the problem that you're confronted with is maximizing the

benefits of the system and analyzing whether you need to change the system or not so that it can function better. Right?

I'd like to go back as to a little bit of the history as I understand it of how this came about and I'm going to give it a slightly different frame of analysis because I'm going to take a little bit of a contrarian view as to what other people have been saying.

And so we have the HHS report that is titled "Gene Patents and Licensing Practices and Their Impact on Patent Access to Genetic Tests," which I'm assuming everyone is familiar with, and which fingers patents as the culprit of many of the issues the report concluded the genetic testing industry is confronting today.

The report made six recommendations, the first of which was to support the creation of exemptions from patent infringement liability. And I believe that is where this AIA section probably derived from and in it’s a narrower analysis where it goes to confirmatory testing.

I think it's interesting that the report concluded that patenting was creating the greatest obstacles in the field and that in any event, patent protection was not necessary in the field because most of the research was funded by the federal government and the patents were just getting in the way.

Prior speakers, including Thomas Kowalski, Mercedes Meyer, Lori Pressman, and Hans Sauer, have adequately explained - many of the speakers today I think have explained- many of the problems with the report and in particular how the factual findings in the report would not logically lead to the conclusions reached by the report.

And as we'll see in a minute, I will reframe the issues and “attack” the report from a little bit of a different perspective.

Also of interest to the study, I think, is the lawsuit against Myriad. I believe it's of great relevance that the lawsuit was not brought by a competitor, like Affymetrix, claiming that the patent is invalid or not infringed, but rather by the

ACLU and the Association for Molecular Pathology. In that lawsuit, again, the issue of rights of genetic test consumers, patents, and government funding were central or are central. I guess the case is still going on. I think the involvement of the ACLU in the Myriad case should raise a large red flag to the genetic testing industry and the government. As we all know, it was about 100 years ago that the beliefs of the power of science and genetics resulted in the misguided passage of shameful legislation that led to the involuntary sterilization of thousands, including here in California. It is in no small part due to the efforts of civil rights attorneys and/or organizations that that disgraceful chapter of this industry was closed although not forgotten.

On this issue I'd like to refer you to the article published February 13, 2012, in the Genomics Law Reporter, by Dr. Jennifer P. Wagner, a research associate at the University of Pennsylvania Center for the Integration of Genetic Health Care Technologies reporting

that the decision by North Carolina to compensate victims of its eugenics program and with reference to the California and other programs.

I'm really surprised and alarmed that after being saved from the eugenics 1.9 program by these civil rights attorneys and groups, the industry apparently has not gotten the message that maybe there's a big problem lurking here and that the field and its program may have gotten ahead of themselves.

So I'm going to address here the issue of government funding of genetic research which people see as a solution to the problem in that we don't need patents; we just need government funding. And I'm going to make the argument that maybe it is the government funding that is the problem here.

So I think in analyzing that we first need to look and see does the government have a valid interest in funding genetic testing research? Excuse me. Does the government have a valid interest in funding genetic testing research? And I think yes.

You know, one of the major functions of government is to protect its citizens and this type of research can assist with improving health care and decision-making that will improve the quality of life of citizens.

Now, can government funding create problems? We all know from economic theory is that many times government intervention in markets can create misallocation of resources.

And so do we see a problem like that here where maybe there's too much government funding of genetic research and not enough private enterprise with genetic research? And what would be the symptoms that we would see with that?

So one of the things that I think you would see in a situation like that is that the field is getting ahead of itself and its supporting framework is not catching up with it.

And so here we have, for example, something that I believe no one disagreed with, which is that a framework, a regulatory framework for genetic testing is not in place.

And so is this regulatory framework something that would be the function of government to implement? And I believe that yes, this is the function of government to implement regulations like these that will protect consumers and will ensure that these genetic tests are being sold in a proper manner in a way that is helpful to the health of individuals rather than maybe just quackery - overselling, overhyped processes.

And so I think that that in and of itself we see that there has been a misallocation of resources at least in the relative level because to the extent that the industry has gotten this far, regulation has not gotten this far, and so relatively speaking there was a misallocation of resources at least temporally in that the government did not spend enough resources at this point to maybe consider and pass regulations that would affect this testing industry.

Are there other symptoms that we can look at that maybe there is too much

government funding of genetic testing?

And I think that if you look at, for example, all these issues that we're running into today that are named in the AIA, section 27, and in the Federal Register notice, you could probably trace each and every one of those issues to the fact that maybe the science has gotten ahead of the rest of the framework. And so, for example, insurance companies are at a loss as to what to do. Health care providers are at a loss as to what to do. Physicians are at a loss as to what to do with all this data. Consumers are at a loss to what to do with all this data.

And so I believe that, again, [this shows] the government may have misallocated resources. We ran ahead of ourselves with too much funding of genetic research and did not permit the market forces to work and let the private sector through the patent system get the funding that is necessary while government funds these other things that the private industry is not going to fund, for example, education, regulation, and lastly, I believe

it's necessary to fund social sciences and the humanities so that the ethical, moral, and civil rights issues that will be raised and have been raised by genetic testing in the past [can be considered]. And that I believe the ACLU's attack on the industry - although they obviously attacked what they perceived to be a very weak opponent - in trying to make a stance.

But obviously, on a day like today where there's, Guantanamo is still open, where, you know, people are being searched in airports, where it was just ruled that the FBI was searching 3,000 people illegally by planting GPS devices on them, when the federal government is ordering the assassination of U.S. citizens without a court order, the fact that the ACLU decided to spend resources to attack the industry maybe indicates that they perceive that there are civil rights issues here and that the industry has maybe, you know, gone further than it should have in this time and it has not permitted the framework around it to develop.

And I think there are some other problems that arise when there's too much government funding of something like this.

I think it clouds the objectivity of government scientists because of the funding process. They need to always be overhyping and overselling so that they can get more funds, and it clouds their objectivity.

Second, I think it suffocates private funding by front running private industry and placing everything in the public domain and then it does not permit private development by taking away interest provided by patents. And so basically it's like adding too much fertilizer and water to a plant; it's going to suffocate it. And so the patents that were necessary for the field to properly develop as the professor [Prof. Christopher Holman] just mentioned, people did not patent these genes and maybe they should have. People were hurrying to patent as many genes as they could and were not claiming them properly.

And so what happens now? What

happens now is it’s probably difficult to go to a venture capitalist and say we have this market locked down. We can’t get this genetic test out there because people [VC’s] are going to look at those patents and be like, well, this is not going to lock anything down. And so you are going to have to spend a lot of time, money, effort convincing people to buy your genetic test, but as soon as you do that there's going to be competitors and entrants and you will not be able to safeguard your position with these patents. And so that is probably also a result of the government providing too much funding to the genetic industry.

And so I believe that going forward you cannot address a problem of too much government funding of a particular area by modifying the patent system. I think the patent system is working fine and I think that the solution lies elsewhere. We need more government spending on other issues so that we can catch up with where -- and it's very successful. I want to clarify here that

people say, well, you're misallocating resources but it has a pejorative sense. Like, okay, you're throwing money away. And I don't mean it in that sense because obviously the research is there. The knowledge is there. And people are going to be able to use it in the future. The issue is temporally is it the right time to spend this money here and now? And what are the side effects that it will have?

So I had a few solutions here that I already mentioned. The government should devote adequate resources to things private industry will not, including: passing adequate legislation; funding education; funding social science and humanities programs and research on the ethical, moral and civil rights issues raised by adoption of the technology.

And also I think what would be important for the industry, because of the issues with public perception and public opinion that there be maybe a Magna Carta or maybe a Bill of Rights for genetic testing consumers and it would be something - a

document that would be put together by the government, by industry, by insurance companies, civil right groups, and everyone - that will set a set of guidelines. And I think I'm not the first one obviously calling for this so that people feel more secure. And my concern right now is that there is some sort of legislation like this but it all points towards “let's do more genetic testing.” So, for example, there's the federal GINA. There's the California GINA. And they all have to do with, okay, let's safeguard the information, genetic information by keeping it private, by not being able to allow people to use it for different things so that people will get more genetic testing. And I'm not sure that's exactly what is necessary at this point. It's more like, okay, how can we intelligently, properly, in a cost-effective manner use this genetic testing?

For example, just to cite an example- and this is going to be my last example here and I'll conclude - is, for example, I think a lot of people would make

the assumption that, for example, using genetic testing to discriminate in a job application is completely incorrect. Right? Who agrees with that? I see a bunch of hands. But now let's say, for example, this example with the BRCA1 gene, and it seems like what happens is that -- and don't quote me on this. Let's just presume that apparently it renders people more susceptible to deleterious mutations when they're exposed to ionizing radiation. Right? And so let's say that we, for example, know that somebody has this BRCA1 mutation and that exposing them to ionizing radiation is going to more likely than not lead to cancer. Should we not -- wouldn't it be an intelligent policy to say, well, maybe you shouldn't apply for a job where there's a lot of ionizing radiation in the environment? Can't you find another source of income? And so there are uses of genetic information that would be, you know, you would discriminate someone applying for a particular job where they're going to be particularly at risk because of the genetic factors.

And so you cannot make black and white rules. This is going to require a lot more thought than has been put into it. And so that's my point; that maybe we've gone too far too fast and we need to pause. Let the back fill in so that we have all the support system that is necessary.

Thank you very much. And I hope this is informative and can help you when writing the report.

MS. GONGOLA: Our next witness is Bernard Greenspan, Director of Prometheus Labs.

MR. GREENSPAN: Good morning. My name is Bernie Greenspan. I am the director of intellectual property at Prometheus Laboratories. I hold a Ph.D. in biophysics and I'm registered to practice at the USPTO. Prometheus is a diagnostics and therapeutics company in San Diego employing over 500 people. I appreciate the opportunity to speak to you today.

Prometheus is seriously concerned that the U.S. PTO might endorse or that

Congress might enact changes to current patent law that would allow performance of any diagnostic testing in a manner circumventing patent holder rights or negotiated license agreements. We are troubled by the application of the terminology "second opinion" to genetic diagnostic testing. Application of this terminology to diagnostic testing draws an analogy to the subjective realm of physician diagnoses or selection of the course of treatment for a particular patient with a particular clinical condition. This only obscures the underlying issues. It is generally accepted that a patient or an insurance company will want additional opinions on a recommended course of therapy prior to adopting it, especially when that therapy is expensive, invasive, or involves significant risk.

In the case of treatments based on genetic measurements, one might still pursue a second opinion but it would be on the recommended course of therapy rather on the accuracy of the test results. In genetic

testing measurements, uncertainty of the measurement is not the question. The correlation of a particular genetic mutation or single nucleotide polymorphism with a disease or as contribution to the development of a particular pathology is a powerful and potentially lifesaving discovery whether the polymorphism is predictive on its own or in correlation with other biomarkers. What may not be fully appreciated is the fact that the genetic sequence of the target polymorphism once identified will become well characterized and reproducible. Indeed it must be, both to secure patent rights and to demonstrate meaningful results to clinicians who rely on them. Modern gene sequencing technologies are designed to detect and report the presence of very specific changes.

Why then are there some results and diagnostic testing that are reported as inconclusive? We've heard that term today. It would take more time than we have to explain that in its entirety, but the short answer is because the results are a function

of multiple factors, including whether the mutation is germline or somatic. It is also a function of the computational methods used to correlate the signals from the asset with the diagnostic results from the clinical data used to develop the test. Further, it could also be a function of the diversity of the population sampled in the development of the test.

Prior to commercial acceptance of the diagnostic test, all of these factors would have been published and vetted in the scientific and clinical communities. Key opinion leaders and clinicians take this information under advisement when prescribing, interpreting, and charting an individual therapeutic course for each of their patients. A second measurement of an inconclusive result due to these parameters is also not expected to be different from the first test if the data are processed in the same way.

Within the diagnostic testing environment, strict internal quality controls are applied to each measurement to ensure that

validated results are released. Should a particular measurement fail the internal quality indicators, a repeat test is run. If the quality of the sample provided is not sufficient for the test, an additional sample can be requested. These repeat measurements and additional samples are measured without extra cost to the patient or the payor. This is done to ensure the quality and scientific integrity of the results reported back to the physician.

On top of this, the testing laboratory is governed by government regulations and accreditation programs. The Centers for Medicare and Medicaid Services regulate all laboratory testing performed on humans in the U.S. through the Clinical Laboratory Improvement Amendments or CLIA. Commercial laboratories engaged in offering diagnostic tests must undergo licensing through CLIA. In addition, diagnostic testing laboratories are also accredited by the College of American Pathologists or other accrediting bodies. These accreditation

programs involve routine inspections and proficiency testing to assure accuracy and precision of the results. Thus, in this highly regulated and validated environment the likelihood of a repeated genetic measurement producing a different result is as small as the error rate in the measurement technique itself -- virtually zero.

A second measurement, or it has been inappropriately named a second opinion, is fully expected to give the same result whether performed at the same or a different laboratory. If a second measurement does not yield the same result, the problem is a quality issue, certainly not a patent or access issue. The second testing laboratory would have to develop and comply with systems duplicating the innovator laboratory. The results would not be expected to be different and as such the second measurement would only add cost to the overall health care system without yielding new information. It is not clear who would be expected to pay for this process.

Another question that has been raised is the role that cost and insurance play in access and provision of genetic diagnostic tests. It is not clear to us why the Patent Office is being asked to comment on insurance and reimbursement. Nonetheless, an industry perspective may be helpful. When a new diagnostic test is launched by a company, physicians will order the test and payors will pay for the test based on the strength of its supporting scientific data. When the lab submits a claim for the test to the insurer, information may be requested from the innovator. The payor may do their own research and evaluate the scientific merit and benefit to the patient and the payor may even request specific patient information to determine the need for the test.

An insurance company's decision on whether to pay for a new test depends on whether they feel there is sufficient validated clinical evidence and that the test will add benefit to the patient and that it is within the scope of coverage of the plan in

which the patient is enrolled. Apart from the scope of the patient's plan, the reimbursement is determined by virtue of the merit of the scientific evidence of the test, including any uncertainties as previously discussed.

While it is often asserted that patents limit access to and insurance coverage of diagnostic tests, in reality just the opposite is true. Patents and exclusive licenses are required for an innovator to secure the funds needed to generate the scientific evidence that a test is valid and beneficial to patients. These clinical studies are very expensive for us, often costing in the range of $1 to 10 million each. Only when this evidence is available will insurance companies cover and pay for these tests. Taken the other way, a lack of patents and reliance on studies by other organizations would be very unlikely to produce the validated clinical evidence to support commercialization and reimbursement coverage.

Patient access to diagnostic tests is as important to us as it is to the

patients. For this reason our company offers a patient assistance program to provide for those truly in need. This assures that access to important therapeutics and diagnostics is not necessarily limited by a patient's out-of-pocket liability or financial hardship.

On another topic, it is difficult to envision an enforceable patent system in which a non-patent holder or licensee could perform a second laboratory measurement without infringing but would infringe by performing a primary measurement. How would the patent holder ever be able to determine whether the confirming laboratory is also performing primary testing measurements? Who would monitor and police such a system? And at what cost? Current patent law places the burden of stopping infringement squarely on the shoulders of the patent holder. Monitoring and distinguishing non- infringing activities from infringing activities will only add costs and redirect resources from new developments.

The laboratories performing the second measurements will generally not be

innovators themselves and thus will not be subjected to the costs associated with the original clinical validations or the increased costs of monitoring for possible infringement. Will the innovator of the test also be required to turn over to the second laboratory all of its proprietary validation information? Would it also have to surrender the intellectual property embodying the computational methods used to arrive at the reported results? Indeed, what would the limit and scope of the amount of proprietary information taken? A legislative carve out or a taking of intellectual property is not the means to achieve the outwardly professed goal of second measurement tests as a means to drive down cost. Access, costs, and reimbursement are entirely separate issues from patent rights.

Finally, the chilling effect -- you've heard that term a lot -- on research and development of new and innovative tests created by a carve out to allow non-licensed parties to avoid infringement will be

far-reaching. Established companies, university technology transfer offices and job creation by start-up ventures will be faced with the proposition that they will lose proprietary benefits of their patents and discoveries. Robust, intellectual property rights, are the cornerstone of a robust economy in which companies and investors are assured of their ability to control and profit from the significant investments, often in tens of millions of dollars, required for the clinical validation and commercialization of their technologies.

Any steps are taken to weaken those rights while having a presupposed short-term gain in access to current technologies will result in long-term reduction of investments needed to commercialize future innovations, thus creating a decrease in access to future technologies. We encourage the USPTO to take a firm stand against dismantling patent and licensing rights, and we urge that Congress refocus the discussion on the correct aspects of health care reimbursement. Thank you.

MR. GRAHAM: Thank you. Thank you very much. I appreciate the commentary. I want to ask you to comment on a question that I asked Len early on today about the dichotomy that we're often being presented with these hearings, between, you know, the system we have today versus some sort of regime that would support a compulsory license that would, you know, underlay all expenses associated with the patent system.

We did hear at the first hearing some suggestions that there might be a middle ground out there. One of those suggestions took the character of something that sounds like the following: That if there was a -- if there was some sort of safe harbor built in, be it legislation for instance, that would do something along the lines of giving a two-part defense. Say something to the effect of that 'there is no other provider that is providing second-opinion testing' and 'that the accused infringer could demonstrate say that they made a bona fide effort to license from the exclusive patent holder.'

Now, I'm just trying to understand why it is that, you know, that a regime in which there was at least one licensee that was licensed by the patent holder to conduct second-opinion testing, in which the license essentially extracted everything from the licensee, [does not leave the patentee better off]. [That way, the patentee] extracted all the profits, extracted all the data, and even made a requirement that the licensee would, say, validate with the patent holder that the patent holder had done the primary test. Right? To ensure that every time in which there was a second confirmatory test there had already been a primary one initially, which gives all monopoly rights of the primary still to the patent holder, but then also to the extent that -- well we heard today a lot saying that there may not even be a secondary market. But to the extent that there's a secondary market at all, the patentee can still extract everything that he wants out of that secondary [market]. Now, why would a result like that, right, lead to a regime in

which the patentee was worse off?

MR. GREENSPAN: That's a very complicated question to answer. And I think that, you know, we do have some models I think in the pharmaceutical industry that talk about safe harbors. However, those safe harbors lead up to a point where the patent holder still asserts their patent rights as in the approval of genetic drugs. So I'm not quite sure of the details of this safe harbor of which you speak because there's more to it than just saying the patentee will be able to extract everything. We don't know the size of the market. We don't know the size of the market in which perhaps the testing laboratory is operating in. And will they ever recover their costs? So segmenting the market may not be in their best interest or their investors' best interest.

Much more than that I can't say. I would echo the earlier idea of, you know, you talk of a middle ground and I'm not quite certain what that would be. It's very dangerous, I think, to try to define that now.

MS. GONGOLA: Well, thank you, Dr. Greenspan.

MR. GREENSPAN: You're welcome.

MS. GONGOLA: We'll call our next witness. So we have Professor Misha Angrist, who is an Assistant Professor of Practice from Duke Institute for Genomic Sciences and Policy.

MR. ANGRIST: Thank you. I see that I've been an allotted 80 minutes on the schedule. I think I can say what I need to say in an hour. That's a joke.

Thank you for allowing me to testify. My name is Misha Angrist. I had not intended to be here. But having attended the USPTO genetic diagnostic hearings in Alexandria three weeks ago and having listened to testimony this morning, having bitten my tongue so hard as to chew through it, I find that I can no longer contain myself.

I am an assistant professor at the Duke University Institute for Genomic Sciences and Policy. Years ago I was a board-eligible genetic counselor. I hold a Ph.D. in human

genetics from Case Western Reserve University. I am the author of the narrative nonfiction book, Here is a Human Being: At the Dawn of Personal Genomics, which I should say is now out in paperback and makes a swell gift.

I have had my own genome fully sequenced twice. As it happens, I also have a family history of early onset breast and ovarian cancer and two young daughters. I had the Ashkenazi Jewish BRCA mutation panel done by Myriad through DNA Direct in 2008 and again by 23andMe in 2009. I tested negative in both cases and I'm satisfied that I do not carry the three mutations in this panel. In the case of the DNA Direct test, it was covered by insurance, though I still paid $200 for the genetic testing out of pocket, which I was happy to do. But that's not why I'm here.

In 2008, a series of case studies on the role of gene patents and their effects on patient access was commissioned by the Secretary's Advisory Committee on Genetics, Health and Society and overseen by geneticist Jim Evans at the University of North Carolina

and my colleague, Robert Cook-Deegan at Duke. These were published online and in the Journal of Genetics and Medicine in 2010. I was the lead author of the case study on intellectual property and long QT syndrome, a story, that like the BRCA story, involves exclusive licensing by the University of Utah. More on that in a few minutes.

As a policy researcher I am struck by the extent to which these case studies have become a Rorschach Test. Indeed, I was and remain astonished, but perhaps this says more about my own naiveté as I've listened to testimonies both in Alexandria in February and here this morning. The SACGHS report has alternately been maligned as wrong, dismissed as meaningless, held up as finding nothing and then cherry picked when some piece of data could be cited as proof that the current system of IP and genetics is just fine and, you know, there is nothing to see here so move along.

I am reminded of the scene in Annie Hall where Woody Allen is in line at the movie

theater listening to a rather pompous gasbag bloviate on the films of Fellini, the plays of Beckett, and media theories of Marshall McLuhan. Exasperated, Woody reaches behind a movie poster and says, "I happen to have Marshall McLuhan right here." McLuhan appears from behind the poster and immediately begins to excoriate the blowhard saying, "You know nothing of my work."

Well, at the risk of impoliteness I say to those of you who have taken our case studies out of context or otherwise mischaracterized our findings, "you know nothing of my work." Or my colleagues' work for that matter. It is simply not credible that an attentive, objective reader of our case studies of 10 conditions for SACGHS would conclude that there are no problems with how the patent system is functioning in genetic testing for Mendelian conditions.

I would now like to make specific comments which are meant to correct and/or clarify some of the testimony that has been given in Alexandria and here. Please note

that my comments do not address patent eligibility of DNA or broader questions of patenting in biotechnology pertaining to drug development. They are, like the SACGHS report, limited to intellectual property and genetic diagnostics for the Mendelian disorders.

First, to the extent that Myriad has made repeat confirmatory testing available, the company is to be commended. I confess that their testimony this morning is the first I've heard of it. But in the February hearing in Alexandria, the gentleman from the Biotechnology Industry Organization said that getting a breast cancer genetic diagnostic test repeated was not a problem because one could simply go overseas or to a research lab. In the case of BRCA testing, the ability to go overseas, if possible at all, is only possible because the EU chose to fight back against the Myriad patents while the provincial health ministries in Canada essentially told Myriad to take a hike, prompting the company to cede the Canadian market.

Moreover, I find it ironic in the extreme that the defenders of exclusively licensed -- excuse me -- gene patents would commend patients seeking genetic diagnoses to visit academic research labs when it is the exclusive licensees themselves, who since the 1990s, have periodically demanded that such labs cease and desist from returning results to patients. We have a number of these letters and would be happy to share them. That notwithstanding, from the patient's point of view, this is not an adequate solution. Research labs are not, as Myriad's representatives said this morning, commercial scale labs. And as we have documented in our case studies, their turnaround times can be many months.

Other witnesses have pointed out that our BRCA case study showed that Myriad's per-amplicon price was no higher than testing for the diseases where there were multiple providers and therefore, we should conclude that the system works. The pricing argument is true insofar as it goes. The price, in

fact, is indeed equivocal and it's hard to show a definitive effect one way or the other. But whether the test is $4 or $4,000, there remains a single licensee in the U.S., for better or worse, and while payor coverage is very high, it is not universal. Moreover, the sensitivity of Myriad's assay is less than 100 percent. We know, for example, that Mary Claire King's Research Lab at the University of Washington has identified dozens of BRCA mutations that were missed by Myriad, many of which were published in JAMA in 2006.

It should also be said that unlike the NIH-funded Breast Cancer Information Core (the BIC), and unlike the international collaborative MutaDATABASE, Myriad is the only genetic diagnostic lab I know of that does not participate in this database[1]. Unlike databases for virtually every other Mendelian condition I know of, Myriad's mutation data are not open to independent verification,

[1] Correction: Neither Myriad Genetics nor Prevention Genetics participate in MutaDATABASE as of 5 April 2012 (http://www.mutadatabase.org/index.php?option=com_content&view=article&id=78&Itemid=71)

scientific scrutiny, or use by the breast cancer genetics community for interpretation of variants of unknown significance. For Myriad's legal counsel to stand here this morning and take credit for the mutation data resident in the BIC, despite not having contributed data to it for more than seven years -- November 2004 was the company's last significant deposit of data -- is what my mother would call chutzpah. The same nondisclosure of mutation data was practiced by Clinical Data, the company that held the exclusive license to long QT syndrome IP over a period of several years. Only after my colleagues and I started asking obnoxious questions in 2008 did Clinical Data announce with great fanfare that it would release its mutation data.

As a monopoly, Myriad's behavior has direct, unilateral effects on (1) the practice of medicine; (2) who sets the standard in breast cancer genetic diagnostics; and (3) the availability of data that would otherwise be shared. Data, by the way, that could only

have been generated because of research underwritten by American taxpayers since the 1990’s.

Next, it is already clear from the Classen Immunotherapies versus Biogen Idec case, in which the plaintiff argued that a physician infringes Classen's patent simply by reviewing the literature on immunization schedules and the method patent invalidations in AMP versus USPTO that in the eyes of the United States judiciary and the U.S. Court of Appeals for the Federal Circuit in particular, patent claims related to biotech diagnostics have been broader than they should have been for some 15 years. I mean, come on. This is the CAFC we're talking about. The court that is often thought of as the court that, with apologies to Will Rogers, never met a patent it didn't like.

We know that overly broad patents led to monopolies at Myriad, Clinical Data and Athena Diagnostics and perhaps a handful of other companies. If the scope of these companies' patents had been appropriate per

the CAFC, then these firms would have had viable businesses with royalty streams, but not monopolies. If patent holders and physicians are expected to trust the patent system, then the BRCA case does little to inspire that trust. These obvious flaws in how patents were used have real world consequences that cannot be denied.

One of the refrains of the exclusive licensees has been that their way was the only way. The implication is that if it were not for Myriad there would be no analytically valid, clinically valid, clinically useful BRCA testing for American women. This contention is simply -- excuse my French -- bullshit in Babylon. I refer you again to our case studies. Until 2009, genetic testing for long QT syndrome was, like BRCA testing, a monopoly based on exclusively licensed IP from the University of Utah. It was controlled by Clinical Data which has long since sold its long QT testing business to Transgenomic for $15.5 million. Thanks to an intrepid IP attorney, BioReference Laboratories and its

subsidiary, GeneDx, were able to license additional long QT IP from Utah that, for whatever reason, had lain fallow. Thus, four years ago there was one provider of genetic testing for long QT syndrome. It tested for five genes. Today there are two providers of long QT testing, each of which tests for at least 12 genes.

Finally, the case study on cystic fibrosis spearheaded by my Duke colleague, Subhashini Chandrasekharan, is arguably even more instructive. One in 25 non-Latino persons of European descent carries a mutation in the CFTR gene. There are 30,000 CF patients in the U.S.; not a trivial number but well below the 200,000 patient cutoff that the FDA uses to define an orphan disease.

CFTR patent holders, the University of Michigan, the Hospital for Sick Children in Toronto, and Johns Hopkins University, with input from the CF Foundation (i.e., CF patients), opted to license genetic testing for CF broadly rather than exclusively. How could this possibly work? Who would take up

the mantle of such a financially dismal prospect? Quite a few people actually. Today, according to the NIH Genetic Testing Registry, there are 67 CLIA certified providers of CF testing. We've yet to hear of any systematic complaints from patients or physician about poor insurance coverage, high prices, lack of access, and inability to obtain second opinions or slow turnaround times. A 2011 independent study of proficiency testing in CF by the Centers for Disease Control and Prevention showed that 45 laboratories using molecular assays to detect CFTR mutations from dried blood spots; a more difficult task than identifying mutations from whole blood, were performing satisfactorily with incorrect assessments of blinded samples occurring less than 1 percent of the time.

In closing, the SACGHS case studies were undertaken in good faith and without an ideological pro- or anti-patent agenda and indeed, nowhere did they consider patent eligibility questions or any issues beyond those bearing on how intellectual property and

its deployment have affected the development and dissemination of genetic testing to patients suffering from any of a set of 10 Mendelian conditions. The case studies documented both the successes (e.g., comparable pricing, a high rate of third-party coverage), and inadequacies (e.g., undisclosed mutation data, inadequate sensitivity of the current system and its evolution since the 1990s).

While they are by no means perfect, the studies offer an empirical account of the role that intellectual property has played in the realm of genetic diagnostics thus far; indeed, there may be no more compelling evidence of this than the willingness of stakeholders with an interest in genetic diagnostics, be it financial or in the health of their loved ones to appeal to the objectivity and meticulousness of our work.

Thank you for your attention.

MS. GONGOLA: Thank you, Dr. Angrist. Dr. Graham has a question.

MR. GRAHAM: Thank you for your

(inaudible).

I'm interested in the case studies because they do provide us with some views into -- or potentially -- some views into evidence that thus far we've gotten relatively less evidence about. I think to the extent that we're trying to collect evidence, the types of evidence that would be useful -- but the representatives of which have been less likely to come here have been patients themselves, physicians, and any representatives or those that can speak meaningfully about the insurance industry. So can you educate us as to what method you used in your case studies and the extent to which those particular interests were studied? And if so, how? And to the extent possible what those particular interests taught you in the case studies?

MR. ANGRIST: Sure. Well, obviously this was qualitative research. It was NIH funded. We had human subjects' approval and everyone who we interviewed consented. Some of the commentary was obviously off the

record, but we essentially set out to interview as many stakeholders as we could. Obviously, I can speak best to the case of long QT syndrome. The long QT syndrome IP changed hands at least three times and began with a startup, whose name is escaping me right at the moment. It was originally called Kiva Genetics and subsequently that company went under. Its assets were sold to Genaissance Pharmaceutical and subsequently, Genaissance had its assets acquired by Clinical Data, which then sold its business to Transgenomic in 2010. We spoke to company officers and to the physicians. So in the case of long QT, [the physicians were] particularly cardiac geneticists and other cardiologists who are apt to be the ones to order this testing. And then we set up an online survey on a patient website that is particular to people suffering from cardiac arrhythmias. And I think we got somewhere between 20 and 30 respondents and we asked them who provided their test. Was it covered? How did they feel about it? What was the

diagnosis? Was it definitive? Was it a VUS? Did they wind up having a defibrillator implanted, et cetera.

MR. GRAHAM: Did you learn either in your case study or are you aware of any other of those case studies in which any information was collected on second opinion diagnostic testing and possibly not covered by you in the case studies themselves?

MR. ANGRIST: Well, again, I'll limit my comments to long QT because at that time Clinical Data was the only provider. If there were any confirmatory testing it would be done by a research lab. The proficiency testing lab that, under CLIA regulations, Clinical Data would send blinded samples to, was the Mayo Clinic. There's a wonderful cardiologist there who is arguably the world's expert on long QT syndrome, but it should also be noted that he is a paid consultant to Clinical Data or he was. So I think the problem, if there was a problem, it had less to do with quality control and more to do with, I would say, fewer eyes looking at the

same mutation. And long QT syndrome is particularly difficult because something like 10 percent of patients is compound heterozygotes, meaning they have two mutations contributing to their phenotype. And I even had one physician tell me -- and this is one of the heavyweights -- he said, "You know what? Unless it's a relative of someone with a known pathogenic mutation, I don't like to order genetic testing because it just opens a can of worms."

And so I would argue that anything that does more to crowd source analysis of mutations that we don't understand is beneficial.

MS. GONGOLA: Thank you, Dr. Angrist. You may be seated.

And we'll call our next witness, Vern Norviel, who is a partner at the law firm of Wilson, Sonsini, Goodrich, and Rosati.

MR. NORVIEL: Madam Undersecretary, thank you for the opportunity today. Again, my name is Vern Norviel. I am a partner at Wilson Sonsini. I've been an early employee

and general counsel of several biotechnology companies. I helped start Affymetrix as an example. I'm also a past member of the Patent Office Public Advisory Committee. I'm an adjunct professor at Berkeley and I've helped in the formation of probably hundreds of life science companies, many of which I believe are dramatically impacting and improving health care today. Of these companies, many are involved with or directly related to genetic testing and this is providing direct translation of research from universities in our country to patient care. I'm also on the board of directors of one of the world's leading research institutions in Parkinson's disease, which is called the Parkinson's Institute.

I'm pleased to offer a perspective on gene patents and diagnostics tests today. I'll be speaking almost exclusively from the view of a smaller innovative life science company which I think is somewhat unusual for today anyway.

I have general counsel disclaimers

now. I will not be representing any company or my firm specifically. These are my personal views based on my experience in the manner of which genetic IP is used. I also will be -- I do want to point out I probably will be talking somewhat from the point of view of patients. Let me just mention that I had a very beautiful wife that I just to cancer six years ago and genetic testing played a very important role in her treatment decisions, including by one of the members of her tumor board was actually on the group that wrote the paper that was being discussed in the last testimony. And by the way, he dissented from those views.

So I want to address two other questions that are in the Federal Register and hopefully no one has addressed all of them. These, largely boil down to how do genes play a role in genetic testing today? So after we started lots of the companies, it's my observation that most innovative diagnostic tests today -- and this does not apply to just genetic diagnostic tests, I don't exactly

understand why these are being singled out -- but these tests arise almost entirely from the bench top of incredible research from incredible universities in our country, mostly funded by the NIH and other government institutions in the United States.

Now, many of these innovations will and can dramatically improve health care. But there's a problem and it's a big problem-- these innovations are simply not ready to be transferred to give to a patient. To translate this research requires many millions of dollars to reach the clinic in a genetic test and so far as I know, the only viable source that anybody's found for me or any of my companies so far to do that translation is the venture capital industry. But there is a major problem with that in life science startups today and that is access to capital. As a result of many factors, not the least of which is this horrible economy, venture capital has become more and more difficult to access. In life science, a large ration of the companies are founded from these

university NIH-funded efforts, but they're far too early even for the venture capital industry.

A few months ago a forum was held in San Francisco called the Bio Investor Forum and the last section of the conference was, I believe, quite tellingly called "Opportunity or Apocalypse: Prophecies for 2010." So things are tough even as they are. Let me tell you, they're very tough. It's very difficult to get these efforts translated from the bench to the clinic. And very simply put, if anything is done to make these companies unable to fully protect their IP, they will become less investable and these innovations simply won't reach patients. It's just that simple.

So this issue does really matter, not the least of which was relevant to my life, to my late wife. She had the very fundamental benefit of having access to all of my friends in science, and we had a tumor board that was some of the leading scientists in the world; and she did obtain genetic

testing. Unfortunately, the very large majority of cancer victims in our country do not have access to that, and so this issue really matters. It's life and death.

So, and I'm going to point out that very much unlike the high technology and software industries, the need for patent protection is essential in the venture capital investment area in life science. It's practically common knowledge that in my business there is essentially no drug, and no diagnostic, is moved through the development process without patent protection-- and it's very simple math. The returns just won't be there to do it. The investment in life science products, such as a diagnostic is huge compared to a social networking or semiconductor product. Social, what do you call it? Social networking? Whatever the words are, the buzz words in the dot-com industry like my son likes to use aren't relative in my industry. There are big regulatory hurdles. No rational investor would put money in these businesses unless

they could have a short-term of exclusivity on which they could make a significant return on their investment.

So the answer to your question in number two and nine is this: Patents play a pivotal role in funding virtually every innovative genetic test made available today and these tests simply won't happen without strong patents. It's just that simple. I apologize for sounding too dramatic but I have lived through this. But these patents make these tests available and without the test patients will die.

I suspect buried in the question is the reverse question. Do these patents slow down innovative young companies that move these tests from the bench to the clinic? I think that's a question that has been occasionally commented on. It's interesting because I've represented again hundreds of these companies and there's a great deal of drama (I call it) right now surrounding these genetic tests, and I feel comfortable in saying that I've never seen a company slow

down as a result of a gene patent. Now, why is it there's so much drama but a person like me that see hundreds of these companies and can make such an extreme statement? Part of the reason is simply found in time. Most of the genome was sequenced and published almost 20 years ago now today. We're getting older. There just aren't any more genes to patent.

I work in this area for a living and I can tell you with certainly that the issue of gene patents passed us by and is somewhat old news. I had my personal complete genome sequenced. I think I was the first lawyer and they're still trying to figure out what's wrong with lawyers. They haven't figured that part out yet. But there were no patent threats when I had my entire genome sequenced. It was very simple.

Now what do companies do instead? Well, what they're doing instead is developing specific tests, for example, to pick the right drug for the right patient, using genetic variation perhaps amongst many genes. And the VCs again won't invest in these companies if

they are knocking off a test that is patented by someone else. So the system works pretty well because what do these companies do? They do new innovative tests. They move the ball forward or they work around the patents that have been in place around genetic information. What it all comes down to is the system is working just like those founding fathers wanted. The genetic tests are no different than other tests, a pregnancy test or whatever. These patents are, in fact, not only helping provide innovation -- the dollars to provide innovative tests but they're also providing the system that everyone worked on 300 years ago to produce a system that would push the technology envelope. And it works beautifully.

I think also when we worry about the patent issues here that have been discussed, we need to keep in mind our larger place in history. Keep in mind the patents that we file today only have a life of 20 years from the filing date. Given the long lead time for product development and regulatory approval in

life science, these patents, if we're lucky, tend to have a real life from the time a test is introduced of, in my experience, about 10 years. That's the real number. Many of the basic patents that I offered in the field have long ago expired, such as on the DNA chip, green fluorescent proteins-- very basic research tools in the world today. Ten years is actually a very short time in the bigger scheme of history in our lives, and allowing a company to recoup its investment in these tests so they are available in the first instance is very important. These tests are available not just for the next 10 years but for the patients that are dying of cancer for the next 50 years.

Now, I would be the first to say that we need to be very careful about quality in these tests. There's no question in my mind about that. I think someone referred to a question in the Federal Register notice that we also need to be very careful about how the results are interpreted, and provided in genetic counseling and so on. All of these

are very important issues and with my late wife, it worried me a great deal that I was having to operate outside the system. I would have far preferred that these tests were available from a company such as some of the ones that have talked today by an order of magnitude. But that wasn't an option for me and we did what we had to do. We need to be careful not to cut ourselves off at the knees by weakening these patents on these tests such that the gene tests and other tests are not available in the first instance.

So that's my comments and I'll be thrilled to take any questions.

MS. GONGOLA: Question from Dr. Graham.

MR. GRAHAM: Thank you, Mr. Norviel. And thank you for coming and giving us testimony here. I know - with thanks - that you also gave testimony at the hearing some months ago on international patent protection, so I just acknowledge that.

MR. NORVIEL: Thank you.

MR. GRAHAM: We appreciate you

bringing information to us in both these venues.

I'll ask you as well to comment on the same question that I asked Mr. Greenspan some moments ago. To the extent that your comments are directed at least in part to the incentive effects that patents offer to investors -- and certainly all the study that I've done and I think there's a [body of] credible study out there that suggests that patents are indeed extremely important in these industries -- at the same time though if a middle solution could lead to an equilibrium in which companies that wouldn't under other circumstances allow for second-opinion testing [are providing these tests], how could that ever be worse for the investors to not only have the promise of monopoly rents on the first primary product being offered [to the patentee] but also in a secondary market in what is essentially a different product, a second test? Wouldn't all investors think that that's a better deal, more of a reason to fund, and why wouldn't investors prefer that,

or what are the risks associated with that? What is it that the patentee may not want in terms of what it would have to offer up to another entity to allow that entity to do a second opinion test?

MR. NORVIEL: Right. So I was going to actually answer that question even if you hadn't asked. So I guess great minds think alike.

I think that there are two things. I think we first have to really determine whether there's a problem that needs to be fixed here and if the patent system is the right place to fix it. Again, I'm all for having high quality tests and that applies to not just diagnostics tests for use in genetics but gosh, a pregnancy test. You don't want to have a screw up there, right? And so I think quality is of the utmost importance for all of these tests. Diagnostics for genetics are no different and I do not dispute that one iota. We have agencies to deal with that. Perhaps that system needs to be worked more. But I think we should first ask whether this is a

problem that needs to be solved.

Second, if there was a system, I think Mr. Greenspan said something about the answer. “Well, gosh, that's very uncertain” I don't know what that the question means, and that I think was the answer to the question.

Let me tell you about a typical venture IP diligence session. Sometimes I work for the venture capitalists and I look these companies over and say these companies are actually okay or not. It's usually the last thing they look at, and it's make or break. Now, the uncertainty around that, sometimes I believe if I'm in the room with these venture guys and I even wiggle too much while I'm presenting and saying it's okay, I think that that scares them. I mean, if my body language can create enough uncertainty around this that they will become reluctant to put $10 or $20 million in one of these companies, unless we can come up with a system where the economic return is equally insured they will not invest. There's another thing that is very important to keep in mind which

is when you're building a company you start with “test A” and always part of the investment is to have that as a place to build infrastructure, build customer contacts for test B and C and D and E and F. So these “option values” are very important to a venture person. If two of those people are getting that option value if is of less value than if there's one person. And plus, anything less than certain, again, if my body language messes these investments up sometimes, you just have just to be really careful not to do what I think Mr. Greenspan said which is “I don't know what that means,” if you tell that to a VC it's over.

Thank you.

MS. GONGOLA: Thank you very much. You may be seated, and we'll take our last prescheduled witness, Kimberly Irish, who is a Program Manager at Breast Cancer Action.

MS. IRISH: Thank you. Thank you for the opportunity to speak today. My name is Kimberly Irish and I represent Breast Cancer Action or BCAction. And I bring a

different perspective today than we've heard yet.

BCAction is a national education and advocacy organization that carries the voices of women affected by breast cancer -- living with and at-risk of the disease -- in order to inspire and compel the changes necessary to end the breast cancer epidemic. We represent over 40,000 members nationwide, some of whom have a known BRCA mutation, some of whom do not know if they have a BRCA mutation, and some of whom have no known mutation. We accomplish our mission through working on our three program priority areas -- putting patients first, where we advocate for more effective and less toxic breast cancer treatments by shifting the balance of power in the Food and Drug Administration's drug approval process away from the pharmaceutical industry and toward the public interests; creating healthy environments, where we work to decrease involuntary environmental exposures that put people at risk for breast cancer; and eliminating social inequities,

where we work to create awareness that it is not just genes but social injustices that lead to disparities in breast cancer incidence and outcomes. We are also plaintiffs in the lawsuit against Myriad Genetics.

Breast Cancer Action opposes gene patents because they harm women in five key ways. They harm women who have not been able to get information about whether or not they have a mutation that increases their risk of breast and ovarian cancer. Some women can't get the test because of the monopoly and high cost. The test may not look at some women's particular mutation (because even the second test combined with the first doesn't look at every possible mutation, just the common ones). Women who have the test with an indeterminate result are also harmed, because it is not clear from this whether their risk of breast and ovarian cancer increases.

Women who were able to get genetic testing and have a clear result are also harmed because, as Congresswoman Wasserman Schultz described, they should have access to

independent second-opinion testing before making decisions about organ-removing surgery.

Finally, both groups of women suffer when there are impediments to potentially lifesaving research. Not all patients are equally harmed. Sometimes things go dramatically wrong and women are unable to get the information that they need. I'll talk about that. Other times, it seems that things worked as they should have when women are able to get information on their mutation. But even in the seemingly "best case" scenarios there are important ways that gene patents harm women. Let me explain.

The first reason that Breast Cancer Action opposes Myriad Genetics' patents on the BRCA1 and BRCA2 genes is that the monopoly means that too many women can't access this expensive test. Myriad's monopoly also means that there is no competition present from other companies whatsoever. There are no other options for patients to choose from, so the cost remains high and out of reach for far too many women. Because of the patents Myriad

Genetics holds on these genes, the company can charge whatever it wants for testing, though other labs say that they could charge far less. Make no mistake about it -- genetic diagnostic testing is expensive. Myriad Genetics' BRACAnalysis test costs approximately $3,500, with the supplemental BRCA large rearrangement test in high risk patients (or BART) costing an additional $700. Although some health insurance companies will cover the cost (or a portion of the cost) of testing, not all companies do. Each insurance company must negotiate with Myriad individually -- and we hear stories of women, including a plaintiff in the lawsuit against Myriad, as noted earlier, whose insurance did not have a contract for services for the test. In addition, the BART test is not always covered by insurance, even if the first test is. For women without health insurance, and according to the U.S. Department of Health and Human Services, that number is more than 17 million women between the ages of 18 and 64 -- the test is simply not affordable. Uninsured

and underinsured women deserve to have the same opportunity to access testing that women with insurance coverage have.

Second, only some mutations are evaluated in Myriad's standard "comprehensive BRCAnalysis." For some high risk women, in particular women of Latin American and Hispanic ancestry, about 10 percent of the mutations (called large rearrangements) are missed by the standard BRACAnalysis test. Testing for large rearrangements requires a separate test that is often not covered by insurance.

A third issue is that current testing has limitations in what it can detect. That is, the two tests combined still only look at some of the possible mutations, and there are others of unknown significance. Myriad's test results can be indeterminate -- one study found that as many as 10 percent of people tested had an indeterminate test result, a disproportionate number of those women are women of color. What are women supposed to do when the results are unclear?

Should they have prophylactic surgeries? Will their insurance cover increased screenings?

A fourth critical problem with Myriad's patents is that independent second-opinion testing is not widely available, if at all. And like the professor from Duke who spoke earlier, today is the first I've heard that other labs can conduct the testing. So if someone tests negative or positive for BRCA gene mutations, how do they know that this finding is accurate? For a time, Myriad reported that its method of testing resulted in a high false negative rate -- as much as 12 percent. Before making life-altering decisions, wouldn't you want to have the option of a second opinion confirming the results?

Nancy S., a Breast Cancer Action member, who tested positive for the BRCA mutations, was not offered second- opinion testing by her doctor because it wasn't an option. In fact, none of BCActions members have reported that they could access second-opinion testing or that they even knew

that it was an option. Women who are at significant hereditary risk and base important screening and other decisions on negative results, or are considering life-altering prophylactic surgeries (where organs or other body parts are removed) should be able to access second-opinion testing on which to base these significant decisions. Just as women want to be able to access second opinions from doctors, it is understandable that they may want access to independent second-opinion testing as well. Women of color (including African-American and Asian-American women) are more likely than white women to receive uncertain test results, creating many questions about which follow up steps they should take, such as: "Does an indeterminate result warrant prophylactic surgery?" and "Does it justify increased monitoring? And if so, will insurance pay for it?"

Runi Limary, an Asian-American woman and plaintiff in the lawsuit challenging Myriad's patents, received ambiguous results when she had genetic testing done. Runi was

told that this "variant of uncertain significance" has been seen in Asian women, and that these ambiguous results seem to come up more for women of color.

The fifth issue is the limits on future research that may benefit women. Breast Cancer Action believes that current and future research, which has the potential to save many lives, should not be limited by Myriad Genetics' monopoly on BRCA1 and BRCA2 genes and testing. Last year over 230,000 women were diagnosed with invasive breast cancer. Forty thousand women still die of the disease each year. Up to 10 percent may be associated with hereditary risk, including known and as-yet-unknown BRCA mutations. We, our families, and our friends, cannot wait for better prevention, treatment, and surgery. Limits that inhibit other labs from doing tests and research that could save the lives of our mothers, our sisters, friends, daughters, wives, and partners are simply not acceptable.

When women cannot access testing,

when the test fails to provide conclusive evidence about a particular mutation, when the test provides an indeterminate result, when second-opinion testing is not accessible, and when creativity and innovation in research is limited that could potentially save lives, we all suffer. Breast Cancer Action urges an end to gene patents so that women's health comes first.

Thank you.

MR. GRAHAM: Thank you very much for your testimony and for bringing the voice of patients -- which I think we've heard through you in these hearings -- to us.

I'm sure you'll recognize that we have our responsibility, a twofold responsibility in this report. One is to report on genetic testing - and the availability of second opinion genetic testing on a wide range of possible genetic disorders. And the other is to answer questions specifically about the availability of those second opinion tests. And I would like to have more evidence if you have it from your

own organizations of those patients -- and I take it very seriously your suggestions that certain members of our communities are disproportionately unable to access the information that they need in order to make adequate health decisions. What's the incidence of the desire to get that second-opinion testing? And in some sense, what evidence do you have that absent patents there would suddenly be a huge market and available markets to provide this for the people that desire this information, or that insurance companies would be willing to fund those? Because other things we've heard today suggest that is unlikely to happen.

MS. IRISH: Thank you. That's a really great question.

We hear from patients, from women every day who are considering these life-altering surgeries and other, you know, treatment methods that they're considering. And what we hear is that women want information. They want to be fully informed and to feel like they've gotten a chance to

ask multiple doctors, multiple experts about their options before they're able to make a decision because these are such weighty decisions. They're going to be -- could potentially be a mastectomy, a double mastectomy, you know, possibly removing ovaries or other possible treatments. So what we hear is that women want information.

From the women that we've heard from who have had the BRACAnalysis testing done they were very surprised that they weren't offered a second-opinion testing. They had hoped that, you know, that they would have been offered something like that so that they could have that option. I think generally people don't know that that is an option right now. That's what we've heard; that women were surprised to know that that was, you know, that was possible. And as I said, and I think the professor from Duke said, it was the first that I heard today that that was -- that other labs are able to do that kind of second time testing.

I think to the second part of your

question I'm not sure that insurance companies -- it sounds like other people have said that, too -- that it doesn't sound like insurance companies would probably pay for second-opinion testing. I don't have more information on that. But I do know that we have some, a few patients that we work with, some women who were asking to submit written comments before the March 26th deadline. And so we'll certainly encourage them to do so.

MR. GRAHAM: Thank you.

MS. IRISH: Thank you.

MS. GONGOLA: I have a question. Did you maintain any databases or records about the cost and the difficulty procuring insurance coverage for any of these testing that you can share with us? Or other sources where we might obtain that information?

MS. IRISH: We do have some information but, you know, it's not something that we really have the capacity to do sort of a large-scale study or research on. We collect information as it's given to us by women who call us with questions, and so it's

probably not -- I'm guessing it's not of the large-scale variety that would be more helpful, but I'd be happy to look into what we do have and provide that in our written comments that we're planning to provide.

MS. GONGOLA: That would be very good. Thank you. Okay. Well, thank you very much, Ms. Irish.

MS. IRISH: Thank you. Thank you for the opportunity to speak.

MS. GONGOLA: We are now going to open the floor for unscheduled testimony. And I know for sure we have one witness to give unscheduled testimony. And if there are others, please certainly raise your hand, and we will take you in due course. Do we have others who are interested in unscheduled testimony?

We'll call our first unscheduled witness, Professor Brenda Simon, who is a Non-resident Fellow at Stanford Law School and a Professor at Thomas Jefferson Law School.

MS. SIMON: Thanks very much for having me. I'm Brenda Simon. I currently am

a professor at Thomas Jefferson and a nonresident fellow at Stanford Law School as you mentioned. I practiced both patent litigation and prosecution for about seven years before I decided to go into academia. And I wanted to talk a little bit further about the issue of quality assessment of genetic testing.

So we talked a little bit about the ambiguity of this term "second opinion," but what I want to talk about in terms of quality assessment is this idea of objective assessment of screening methods. So this isn't just about Myriad. This goes broader as the gentleman from Duke talked about with the testing of LQTS and other syndromes. So even if Myriad has, as we heard today, opened up its licensing of laboratories behind just its own laboratories in Utah, we want to think of this in a broader scale, not just in terms of Myriad but in terms of really genetic diagnostic testing more broadly. I wanted to for the interest of time, I know we're running a little bit over, refer the panel to and the

study to this issue I discussed in great detail in an article I published last year in the Houston Law Review entitled "Patent Cover-up," that addresses this issue of using patents to prevent the objective analysis and quality testing of patented technology.

In short, I argue that we do need to allow for quality assessment of patented technology to protect the flow of information. This would balance concerns about free riding with the need for information vital to decision-making and personal health. It's just not clear that the scope of patent protection was intended to expand beyond the technology to the data that's generated as the result of it as well as providing a cover for objective assessment of patented technologies.

We heard a bit about the ways in which genetic testing methods are certified but there have been several commentators who talked about the lack of sufficient peer review and oversight for these testing methods. Many are not subject to the type of comprehensive FDA approval that we have for

other technologies, including medical devices, general CLIA certification is not specific to assessing the objective analysis of these methods. We have heard how gene patents are often exclusively licensed or licensed to a small number of laboratories. This limits analysis of the testing methods and discoveries. Many exclusive licensees refuse to provide a written policy that would enable researchers to go ahead unfettered with the research or would allow for objective quality testing.

The question has arisen is there actually a market for this? Would there be providers that would come out and do this? I don't know that that is something we need to answer at this point. I don't know that we need to get that far in determining whether to grant an exception or limited defense for second opinion or objective assessment to ask whether that market would come forth, kind of the ‘if you build it, it will come’ type of Field of Dreams analysis. If there's a limited market out there for second opinions,

if there's a written defense that would be provided we would assume that laboratories would come into being that would offer these second opinions without having to get to that empirical analysis just yet.

Because of restrictions on testing and objectively assessing genetic methods, clinical geneticists can't assess the analytic and clinical validity of sequencing methods. Namely, they can't determine if methods are accurate in identifying mutations and predicting risk. These restrictions also hinder the assessment of the test's clinical utility which is the likelihood that a test will significantly improve outcomes for a patient. This is particularly true if variations of unknown significance, or VUS, if the data and the analysis are limited to one provider that has patent protection, is the necessary incentive going to be there to go ahead and conduct further research to figure out what these given variations of unknown significance actually mean?

Now, we heard the argument today

that limitations on testing can ensure consistent quality across the laboratories, but I suggest that perhaps the level of quality is consistently lower overall than it might otherwise be if we had independent and objective assessment and broader peer evaluation. As I have set forth in the paper "Patent Cover-Up," in some circumstances, even when patent holders have permitted license for testing, they've often required prior approval before test results can be published, limiting the ability to evaluate claims that patent holders are making about their technology.

So I suggest that we need to allow use of a patented invention for quality assessment of technology covered by that patent. Quality assessment would include activities necessary to identify and analyze limitations of the patented invention. And when we think about patent law, providing information hardly cuts against the traditional proprietary justifications that we have underlying one patent law. Allowing quality assessment from an objective source

doesn't undercut the patent holder's ability to obtain a return on investment because they can still charge their chosen price for the first test. Permitting quality assessment strikes a reasonable balance between the normal exploitation of the patent and the legitimate interests of the public.

MS. GONGOLA: Thank you very much, Dr. Simon. Do we have questions? Questions? Thank you. You may be seated.

MS. SIMON: Thank you.

MS. GONGOLA: Do we have any others in the audience who would like to make a statement, make a comment, follow-up remarks of any sort?

Oh, okay. Well, to all of our witnesses and to those of you who came in attendance today and joining us on the webcast, I sincerely thank you. You have put a tremendous amount of information in our hands to prepare us to write our report for Congress. And your input is very much appreciated.

Now, for those of you who might

still like to make a comment or who think of more information you've heard and you want to respond to after today, please remember that we are still accepting comments through March 26th, and you should use the e-mail address genetest@uspto.gov to submit this information to us.

And so I will now, unless there's any further commentary from the floor, officially close the genetic testing hearing, and wish you all safe travels home. So thank you again.

(Whereupon, at 12:52 p.m., the PROCEEDINGS were adjourned.)

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I, Carleton J. Anderson, III do hereby certify that the forgoing electronic file when originally transmitted was reduced to text at my direction; that said transcript is a true record of the proceedings therein referenced; that I am neither counsel for, related to, nor employed by any of the parties to the action in which these proceedings were taken; and, furthermore, that I am neither a relative or employee of any attorney or counsel employed by the parties hereto, nor financially or otherwise interested in the outcome of this action.

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