UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF NEW YORK

ASSOCIATION FOR MOLECULAR PATHOLOGY; AMERICAN COLLEGE OF MEDICAL GENETICS; AMERICAN SOCIETY FOR CLINICAL PATHOLOGY; COLLEGE OF AMERICAN PATHOLOGISTS; HAIG KAZAZIAN, MD; ARUPA GANGULY, PhD; WENDY CHUNG, MD, PhD; HARRY OSTRER, MD; DAVID LEDBETTER, PhD; STEPHEN WARREN, PhD; ELLEN MATLOFF, M.S.; ELSA REICH, M.S.; BREAST CANCER ACTION; BOSTON WOMEN'S HEALTH BOOK COLLECTIVE; LISBETH CERIANI; RUNI LIMARY; GENAE GIRARD; PATRICE FORTUNE; VICKY THOMASON; KATHLEEN RAKER,

Plaintiffs,

-against-

UNITED STATES PATENT AND TRADEMARK OFFICE; MYRIAD GENETICS; LORRIS BETZ, ROGER BOYER, JACK BRITTAIN, ARNOLD B. COMBE, RAYMOND GESTELAND, JAMES U. JENSEN, JOHN KENDALL MORRIS, THOMAS PARKS, DAVID W. PERSHING, and MICHAEL K. YOUNG, in their official capacity as Directors of the University of Utah Research Foundation,

Defendants.

No. 09 Civ. 4515 (RWS)

ECF Case

DEFENDANTS' RESPONSIVE STATEMENT AND COUNTERSTATEMENT TO PLAINTIFFS' RULE 56.1 STATEMENT OF MATERIAL FACTS

Pursuant to the Federal Rules of Civil Procedure ("Fed. R. Civ. P.") and Local Civil Rule 56.1, Defendants Myriad Genetics ("Myriad") and Lorris Betz, Roger Boyer, Jack Brittain, Arnold B. Combe, Raymond Gesteland, James U. Jensen, John Kendall Morris, Thomas Parks, David W. Pershing, and Michael K. Young in their official capacity, or alleged to have been named in their official capacity, as directors of the University of Utah Research Foundation (the "Directors") (collectively, Myriad and the Directors are referred to as the "Defendants"), hereby

submit this Responsive Statement And Counterstatement To Plaintiffs' Rule 56.1 Statement Of Material Facts.

1. Plaintiff ASSOCIATION FOR MOLECULAR PATHOLOGY (AMP) is a not-for-profit scientific society dedicated to the advancement, practice, and science of clinical molecular laboratory medicine and translational research based on the applications of genomics and proteomics. AMP members participate in basic and translational research aimed at broadening the understanding of gene/protein structure and function, disease processes, and molecular diagnostics, and provide clinical medical services for patients, including diagnosis of breast cancer. AMP believes that a single gene "is a product of nature and should not be patentable . . . Gene patents can serve as a disincentive to innovation in molecular testing, because they deny access to a vital baseline of genomic information that cannot be 'invented around.'" D. Sobel ¶¶ 2, 4-5.

RESPONSE TO PARAGRAPH 1:

The evidence cited by Plaintiffs does not support this statement. In addition, the evidence offered by Plaintiffs is inadmissible. Fed. R. Evid. 701, 702, 802. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Isolated DNA molecules are patent eligible subject matter. Doll ¶¶ 26, 34; Linck ¶¶ 14-17, 43, 47, 49; Straus ¶¶ 26, 29-34. Without the promise of a period of market exclusivity provided by patents and the infusion of venture and risk capital derived therefrom, companies that capitalize on innovation simply would not be created. Their products would not be brought to market, to the clinic, and most importantly, to patients. This of course, holds true for companies such as Myriad and its *BRCA1/2* diagnostic tests. Intellectual property is essential to innovation in health care. Reilly ¶¶ 18, 34, 51, 52, 62; Critchfield ¶¶ 67, 68; Linck ¶¶ 73, 271.

2. Plaintiff AMERICAN COLLEGE OF MEDICAL GENETICS (ACMG) is a private, non-profit voluntary organization of clinical and laboratory geneticists. The Fellows of the ACMG are doctoral level medical geneticists and other physicians involved in the practice of medical genetics. With more than 1300 members, the ACMG's mission is to improve health through the practice of Medical Genetics. In order to fulfill this mission, the ACMG strives to 1) define and promote excellence in medical genetics practice and the integration of translational research into practice; 2) promote and provide medical genetics education; 3) increase access to medical genetics services and integrate genetics

into patient care; and 4) advocate for and represent providers of medical genetics services and their patients. It is ACMG's position that "Genes and their mutations are naturally occurring substances that should not be patented." D. Watson ¶¶ 2, 4-5.

RESPONSE TO PARAGRAPH 2:

The evidence cited by Plaintiffs does not support this statement. In addition, the evidence offered by Plaintiffs is inadmissible. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); Fed. R. Civ. P. 56(e); Fed. R. Evid. 701; 702; and 802.

To the extent a response is required, Defendants dispute this statement.

Isolated DNA molecules are patent eligible subject matter. Doll ¶¶ 26, 34 Linck ¶¶ 14-17, 43, 47, 49; Straus ¶¶ 29-34. Patents such as the patents-in-suit have served to advance research and the practice of medicine and benefit patients. Reilly ¶¶ 38, 43; Linck ¶¶ 27-28, 71, 73; Critchfield ¶¶ 2-18, 65, 68; Tavtigian ¶¶ 14-17; Doll ¶¶ 45-46; Bone ¶¶ 10-11; Frieder ¶ 13; Schlessinger ¶¶ 31-32.

3. Founded in 1922, the plaintiff AMERICAN SOCIETY FOR CLINICAL PATHOLOGY (ASCP) is the largest and oldest organization representing the medical specialty of pathology and laboratory medicine. The ASCP has 130,000 members working as pathologists and laboratory professionals. ASCP members design and interpret the tests that detect disease, predict outcome, and determine the appropriate therapy for the patient. The ASCP is recognized for its excellence in continuing professional education, certification of laboratory professionals, and advocacy—championing causes at the state and federal levels. ASCP is a not-for-profit entity organized for scientific and educational purposes and dedicated to patient safety, public health, and the practice of pathology and laboratory medicine. ASCP believes "the practice of gene patenting harms patients, impedes advances in medicine, and limits those in the practice of pathology and laboratory medicine from doing what they are educated to do – provide high quality health care and engage in research that will enhance the practice of medicine and patient care." D. Ball ¶¶ 2, 5.

RESPONSE TO PARAGRAPH 3:

The evidence cited by Plaintiffs does not support this statement. In addition, the evidence offered by Plaintiffs is inadmissible. Fed. R. Evid. 701, 702, and 802. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Isolated DNA molecules are patent eligible subject matter. Doll ¶¶ 26, 34; Linck ¶¶ 14-17, 43, 47, 49; Straus ¶¶ 29-34. Patents such as the patents-in-suit have served to advance research and the practice of medicine and benefit patients. Reilly ¶¶ 38, 43; Critchfield ¶¶ 2-18, 65, 68; Linck ¶¶ 27-28, 71, 73; Tavtigian ¶¶ 14-17; Doll ¶¶ 45-46; Bone ¶¶ 10-11; Frieder ¶ 13, Schlessinger ¶¶ 31-32.

4. Plaintiff COLLEGE OF AMERICAN PATHOLOGISTS (CAP) is a national medical society representing more than 17,000 pathologists who practice anatomic pathology and laboratory medicine in laboratories worldwide. The College's Commission on Laboratory Accreditation is responsible for accrediting more than 6,000 laboratories domestically and abroad, and approximately 23,000 laboratories are enrolled in CAP's proficiency testing programs. It is the world's largest association composed exclusively of board-certified pathologists and pathologists in training worldwide and is widely considered the leader in laboratory quality assurance. CAP is an advocate for high-quality and cost-effective medical care. CAP "believes that genes and their variants (to include mutations) are naturally occurring substances and should not be patented." D. Scott ¶¶ 2, 4-5.

RESPONSE TO PARAGRAPH 4:

The evidence cited by Plaintiffs does not support this statement. In addition, the evidence offered by Plaintiffs is inadmissible. Fed. R. Evid. 701; 702; and 802. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Isolated DNA molecules are patentable subject matter under applicable United States patent law and regulations. Doll ¶¶ 26, 34; Linck ¶¶ 14-17, 43, 47, 49; Straus ¶¶ 26, 29-34. Patents such as the patents-in-suit have served to advance research and the practice of medicine and benefit patients. Reilly ¶¶ 38, 43; Critchfield ¶¶ 2-18, 65, 68; Linck ¶¶ 27-28, 71, 73; Tavtigian ¶¶ 14-17; Doll ¶¶ 45-46; Bone ¶¶ 10-11; Frieder ¶ 13, Schlessinger ¶¶ 31-32.

5. Plaintiff HAIG KAZAZIAN, MD, is the Seymour Gray Professor of Molecular Medicine in Genetics in the Department of Genetics at the University of Pennsylvania School of Medicine. He is a human genetics researcher and the previous chair of the Department.

> Dr. Kazazian and Arupa Ganguly, another plaintiff, designed tests to screen the *BRCA1* and *BRCA2* genes in their lab and provided screening to approximately 500 women per year starting in 1996 until they were forced to stop offering testing by Myriad. D. Kazazian ¶¶ 1-5.

RESPONSE TO PARAGRAPH 5:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

It has been, and still is, Myriad's policy and practice to allow scientists to conduct research studies on the *BRCA1* and *BRCA2* genes freely. Critchfield ¶¶ 3; Li ¶¶ 3-6; Baer ¶¶ 3-6; Parvin ¶ 3-6; Sandbach¶¶ 3-7. During a personal meeting with Plaintiff Dr. Haig Kazazian sometime between 1999 and 2000, Dr. Critchfield told Dr. Kazazian that he is free to do academic research on the *BRCA1* and *BRCA2* genes including sequencing the genes and detecting mutations in the genes. Critchfield ¶ 22. The commercial nature of Dr. Kazazian's *BRCA*-related activities in the 1990s has been readily admitted by Dr. Kazazian. Kazazian ¶ 8.

On or about May 29, 1998, Myriad sent a letter to Dr. Kazazian. The letter offered a collaborative license to the University of Pennsylvania Medical Center to perform *BRCA1* testing in connection with United States Patent Numbers 5,693,473 (the "'473 patent"); 5,709,999 (the "'999 patent"); 5,710,001 (the "'001 patent") 5,747,282 (the "'282 patent"); and 5,753,441 (the "'441 patent"). Ganguly Exh. 2.

On or about August 26, 1998, O'Melveny & Myers LLP sent a letter to Dr. Kazazian. The letter states that Dr. Kazazian is "engaged in commercial testing activities that infringe Myriad's patents" and that such activities should be ceased "[u]nless and until such a license arrangement is complete." Ganguly Exh. 3.

The general counsel of the University of Pennsylvania advised Dr. Kazazian to stop *BRCA* commercial testing. Kazazian ¶ 7.

6. Plaintiff ARUPA GANGULY, PhD, is an Associate Professor in the Department of Genetics at the Hospital of the University of Pennsylvania. Dr. Ganguly's work previously included *BRCA1/2* screening for both research and clinical purposes. She was compelled to stop *BRCA* screening after Myriad accused her lab of violating the patents. D. Ganguly ¶¶ 1, 3-4.

RESPONSE TO PARAGRAPH 6:

Disputed.

It has been, and still is, Myriad's policy and practice to allow scientists to conduct research studies on the *BRCA1* and *BRCA2* genes freely. Critchfield ¶¶ 3; Li ¶¶ 3-6; Baer ¶¶ 3-6; Parvin ¶ 3-6; Sandbach ¶¶ 3-7. During a personal meeting with Plaintiff Dr. Haig Kazazian sometime between 1999 and 2000, Dr. Critchfield told Dr. Kazazian that he is free to do academic research on the *BRCA1* and *BRCA2* genes including sequencing the genes and detecting mutations in the genes. Critchfield ¶ 22. The commercial nature of Dr. Kazazian's *BRCA*-related activities in the 1990s has been readily admitted by Dr. Kazazian. Kazazian ¶ 8.

On or about May 29, 1998, Myriad sent a letter to Dr. Kazazian. The letter offered a collaborative license to the University of Pennsylvania Medical Center to perform *BRCA1* testing in connection with United States Patent Numbers 5,693,473 (the "'473 patent"); 5,709,999 (the "'999 patent"); 5,710,001 (the "'001 patent") 5,747,282 (the "'282 patent"); and 5,753,441 (the "'441 patent"). Ganguly Exh. 2.

On or about August 26, 1998, O'Melveny & Myers LLP sent a letter to Dr. Kazazian. The letter states that Dr. Kazazian is "engaged in commercial testing activities that infringe Myriad's patents" and that such activities should be ceased "[u]nless and until such a license arrangement is complete." Ganguly Exh. 3.

The general counsel of the University of Pennsylvania advised Dr. Kazazian to stop *BRCA* commercial testing. Kazazian ¶7.

7. Plaintiff WENDY CHUNG, MD, PhD, is an Associate Professor of Pediatrics at Columbia University. Dr. Chung is a human geneticist whose current research includes research on the *BRCA1* and *BRCA2* genes. Because of the patents, Dr. Chung currently cannot tell research subjects in her studies the results of their *BRCA1/2* tests and cannot offer clinical *BRCA* testing services. D. Chung ¶¶ 1-9, 11-13, 16.

RESPONSE TO PARAGRAPH 7:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Dr. Chung identifies herself as "the Herbert Irving Professor of Pediatrics and Medicine in the Division of Molecular Genetics at Columbia University in New York." D. Chung, ¶1.

It has been, and still is, Myriad's policy and practice to allow scientists to conduct research studies on the *BRCA1* and *BRCA2* genes freely. Critchfield ¶ 3; Li ¶¶ 3-6; Baer ¶¶ 3-6; Parvin ¶ 3-6; Sandbach¶¶ 3-7.

The majority of academic researchers operating laboratories (as opposed to CLIA-certified laboratories) do not believe that they should share test results with subjects outside of the standard clinical setting. Reilly ¶¶ 57-59.

8. Plaintiff HARRY OSTRER, MD, is a Professor of Pediatrics, Pathology and Medicine and Director of the Human Genetics Program in the Department of Pediatrics at New York University School of Medicine. Dr. Ostrer's work has focused on understanding the genetic basis of development and disease, including disorders of sexual differentiation and genetic susceptibility to breast and prostate cancer and malignant melanoma. Dr. Ostrer is actively engaged in identifying genes that convey risk of breast cancer and that may mitigate the effects of mutations in the *BRCA1* and *BRCA2* genes. Dr. Ostrer is also the Director of the Molecular Genetics Laboratory of NYU Medical Center, one of the largest academic genetic testing laboratories in the United States. Because of the patents, Dr. Ostrer currently cannot tell research subjects in his studies the results of their *BRCA1/2* tests and cannot offer clinical *BRCA* testing services. D. Ostrer ¶¶ 1-4, 8, 10, 12.

RESPONSE TO PARAGRAPH 8:

Disputed.

It has been, and still is, Myriad's policy and practice to allow scientists to conduct research studies on the *BRCA1* and *BRCA2* genes freely. Critchfield ¶ 3; Li ¶¶ 3-6; Baer ¶¶ 3-6; Parvin ¶ 3-6; Sandbach¶¶ 3-7.

Dr. Ostrer confuses research with clinical medicine. The majority of academic researchers operating laboratories (as opposed to CLIA-certified laboratories) do not believe that they should share test results with subjects outside of the standard clinical setting. Reilly ¶¶ 57-59.

9. Plaintiff DAVID LEDBETTER, PhD, is a Professor of Human Genetics and Director of the Division of Medical Genetics at the Emory University School of Medicine. Dr. Ledbetter is a genetic researcher. Research in his laboratory focuses on the molecular characterization of human developmental disorders. Dr. Ledbetter directs the Emory Genetics Laboratory which provides testing services for individuals with or at risk for genetic diseases. Because of the patents, Dr. Ledbetter cannot offer comprehensive *BRCA* genetic testing to patients. D. Ledbetter ¶¶ 1-8, 16.

RESPONSE TO PARAGRAPH 9:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

10. Plaintiff STEPHEN T. WARREN, PhD, is the William Patterson Timmie Professor of Human Genetics, Chairman of the Department of Human Genetics, and Professor of Biochemistry and Professor of Pediatrics at Emory University. He is a past President of the American Society of Human Genetics. He personally supervises genetic research at Emory. He is also responsible for the laboratories at the Emory Genetics Laboratory. These laboratories would offer *BRCA* genetic testing but for the patents. D. Ledbetter ¶¶ 1, 16.

RESPONSE TO PARAGRAPH 10:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

The cited paragraph from Dr. Ledbetter's declaration merely states that "[t]he Chair of our Department at Emory is plaintiff Stephen Warren." Ledbetter ¶ 1.

11. Plaintiff ELLEN MATLOFF, M.S., is Director of the Yale Cancer Genetic Counseling Program. Ms. Matloff advises women on the desirability of obtaining an analysis of their genes to determine if the women have the genetic mutations that correlate with an increased risk of breast and/or ovarian cancer. If she determines that such an analysis is warranted and the individual woman concurs, Ms. Matloff arranges for the analysis and then advises the woman of the significance of the results. Ms. Matloff would like to have the option to send patient samples to laboratories other than Myriad Genetics for *BRCA1/2* sequencing. D. Matloff ¶¶ 1-4, 11.

RESPONSE TO PARAGRAPH 11:

Admitted.

12. Plaintiff ELSA W. REICH, M.S., is a Professor in the Department of Pediatrics at New York University. She is a genetic counselor. She helps women decide whether to be tested for mutations in the *BRCA1* and *BRCA2* genes. If they need testing, she sends samples to defendant Myriad and explains the results for the women. Ms. Reich would like to have the option to send patient samples to laboratories other than Myriad Genetics for *BRCA1/2* sequencing. Reich ¶¶ 1-3, 8.

RESPONSE TO PARAGRAPH 12:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Dr. Reich states in her declaration that "[i]f [she] learned that the *BRCA* patents owned by Myriad were invalidated, [she] would potentially alter [her] testing choices in numerous ways." Reich ¶7.

13. Plaintiff BREAST CANCER ACTION (BCA) is a national organization of approximately 30,000 members based in San Francisco, California. Breast Cancer Action is dedicated to carrying the voices of people affected by breast cancer in order to inspire and compel the changes necessary to end the breast cancer epidemic. Its members include breast cancer survivors, family members of people diagnosed with breast cancer and other people affected by or concerned about breast cancer. BCA advocates for policy changes directed at achieving prevention, finding better treatments, and reducing the incidence of breast cancer; provides information about breast cancer to anyone who needs it via newsletters, web sites, e- mail and a toll-free number; and organizes people to get

involved in advocacy to advance its policy goals. BCA believes that the *BRCA* gene patents interfere with people's ability to participate fully in decisions relating to breast cancer treatment and to gain access to information about breast cancer and quality health care. D. Brenner ¶¶ 1-4.

RESPONSE TO PARAGRAPH 13:

The evidence cited by Plaintiffs does not support this statement. In addition, the evidence cited by Plaintiffs is inadmissible. Fed. R. Evid. 701; 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

It has been, and still is, Myriad's policy and practice to allow scientists to conduct research studies on the *BRCA1* and *BRCA2* genes freely. Critchfield ¶ 3; Li ¶¶ 3-6; Baer ¶¶ 3-6; Parvin ¶ 3-6; Sandbach ¶¶ 3-7.

Patents such as the patents-in-suit have served to advance research and the practice of medicine and benefit patients. Reilly ¶¶38, 43; Critchfield ¶¶ 2-18, 65, 68; ; Linck ¶¶ 27-28, 71, 73; Tavtigian ¶¶ 14-17; Doll ¶¶ 45-46; Bone ¶¶ 10-11; Frieder ¶ 13, Schlessinger ¶¶ 31-32.

14. Plaintiff BOSTON WOMEN'S HEALTH BOOK COLLECTIVE (BWHBC), doing business as Our Bodies Ourselves (OBOS), is a nonprofit, public interest women's health education, advocacy, and consulting organization. OBOS provides clear, accurate information about health, sexuality and reproduction from a feminist and consumer perspective. OBOS vigorously advocates for women's health by challenging the institutions and systems that block women from full control over their bodies and devalue women's lives. OBOS's long-standing commitment to serve only in the public interest and its bridge-building capacity are its hallmarks. In addition, OBOS staff provide information to members of the public about genetic analysis. OBOS believes that the *BRCA* gene patents are a barrier to a woman's ability to know about her body and make informed health decisions. D. Norsigian ¶¶ 1-4, 7.

RESPONSE TO PARAGRAPH 14:

The evidence cited by Plaintiffs does not support this statement. In addition, the evidence cited by Plaintiffs is inadmissible. Fed. R. Evid. 701, 702, 802. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

It has been, and still is, Myriad's policy and practice to allow scientists to conduct research studies on the *BRCA1* and *BRCA2* genes freely. Critchfield ¶ 3; Li ¶¶ 3-6; Baer ¶¶ 3-6; Parvin ¶ 3-6; Sandbach¶¶ 3-7.

Patents such as the patents-in-suit have served to advance research and the practice of medicine and benefit patients. Reilly ¶¶38, 43; Critchfield ¶¶ 2-18, 65, 68; Linck ¶¶ 27-28, 71, 73; Tavtigian ¶¶ 14-17; Doll ¶¶ 45-46; Bone ¶¶ 10-11; Frieder ¶ 13, Schlessinger ¶¶ 31-32.

15. Plaintiff LISBETH CERIANI is a 43-year-old single mother who was diagnosed with cancer in both breasts in May 2008. Ms. Ceriani is insured through MassHealth, a Medicaid insurance program for low-income people. Her oncologist and genetic counselor recommended that she obtain *BRCA1* and *BRCA2* genetic testing, because she may need to consider further surgery in order to reduce her risk of ovarian cancer. However, Myriad will not accept the MassHealth coverage. Ms. Ceriani is unable to pay the full cost out-of-pocket. D. Ceriani ¶¶ 1-5.

RESPONSE TO PARAGRAPH 15:

The evidence cited by Plaintiffs does not support this statement. In addition, the evidence cited by Plaintiffs is inadmissible. Fed. R. Evid. 802. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Since 1996 when BRAC*Analysis*® was launched, Myriad has had a financial assistance program directly providing free testing to low income, uninsured patients. Just in the last four years, more than 3,000 patients have received free *BRCA* testing under this program (about 55 tests a month). In addition, Myriad also makes free testing available to needy patients through independent nonprofit organizations such as the Cancer Resource Foundation ("CRF") in Massachusetts. See http://www.breastcancerrna.org/helping-hand/#genetic. In fact, through the CRF, MassHealth patients such as Plaintiff Ceriani may receive BRAC*Analysis*® testing at no charge. Critchfield ¶ 33; Rusconi ¶ 6; Ogaard ¶ 4-6.

16. Plaintiff RUNI LIMARY is a 32-year-old Asian-American woman who was diagnosed with aggressive breast cancer in 2005. Ms. Limary obtained *BRCA* testing through Myriad and received the following result: "genetic variant of uncertain significance." D. Limary ¶¶ 1-5.

RESPONSE TO PARAGRAPH 16:

Admitted.

17. Plaintiff GENAE GIRARD is a 39-year-old woman who was diagnosed with breast cancer in 2006. Shortly after her diagnosis, she obtained *BRCA1*/*BRCA2* genetic testing from Myriad and tested positive for a deleterious mutation on the *BRCA2* gene. She sought a second opinion of that test result but learned that Myriad is the only laboratory in the country that can provide full *BRCA* sequencing. D. Girard ¶¶ 1-7.

RESPONSE TO PARAGRAPH 17:

Disputed.

Myriad has never prohibited a "second opinion" on *BRCA* mutation testing, which has been available to patients like Plaintiff Girard since late 1990s. Critchfield ¶ 64. In the clinic, the term "second opinion" is used to refer to the interpretation of diagnostic tests and their implications for treatment. It would be quite unusual to have a patient's DNA sequenced a second time in a second laboratory. If, however, there were any doubts regarding the accuracy of the test, re-sequencing with the proper controls would normally be performed by the original provider. The term, second opinion, generally refers to the interpretation of a test result and which therapeutic options to follow based thereon. Once a patient has his or her genes sequenced, *e.g.*, the *BRCA1* and/or *BRCA2* genes, the patient generally does not get his or her genes re-sequenced. In the absence of any doubts regarding the accuracy of the original test, re-sequencing of the patient's genes would be an unnecessary use of resources. Reilly ¶¶ 54, 55.

There are multiple laboratories available for confirmatory testing under patent licenses from Myriad. Many of these labs have been performing testing for specific *BRCA* mutations for the past ten years. For example, testing for specific *BRCA* mutations is available in both the

University of Chicago Genetic Services Laboratories and Yale DNA Diagnostic Laboratories. Information on their testing services for *BRCA* mutations is readily accessible on Internet. Critchfield ¶ 62; Lessman ¶ 4.

18. Plaintiff PATRICE FORTUNE is a 48-year-old woman who was diagnosed with breast cancer in February 2009. Ms. Fortune is insured through Medi-Cal. Her oncologist and genetic counselor recommended that she obtain *BRCA1*/*BRCA2* genetic testing, including the supplemental testing that is offered by Myriad separate from its standard test, but told her that Myriad would not accept her insurance. Ms. Fortune is unable to pay the full cost out-of-pocket. D. Fortune ¶¶ 1-5.

RESPONSE TO PARAGRAPH 18:

Disputed.

Since 1996 when BRAC*Analysis*® was launched, Myriad has had a financial assistance program directly providing free testing to low income, uninsured patients. Just in the last four years, more than 3,000 patients have received free *BRCA* testing under this program (about 55 tests a month). In addition, Myriad also makes free testing available to needy patients through independent nonprofit organizations such as the Cancer Resource Foundation ("CRF") in Massachusetts. See http://www.breastcancerrna.org/helping-hand/#genetic. Critchfield ¶ 33.

19. Plaintiff VICKY THOMASON is a 52-year-old woman who was diagnosed with ovarian cancer in 2006. She obtained *BRCA1*/*BRCA2* genetic testing from Myriad in 2007 and was found to be negative for mutations covered by that test. Her genetic counselor advised her about additional *BRCA* genetic testing offered by Myriad that looks for other large genetic rearrangements that are not included in Myriad's standard full sequencing test, but informed her that her insurance would not cover the full cost of that test. Ms. Thomason is unable to afford the extra cost. D. Thomason ¶¶ 1-8.

RESPONSE TO PARAGRAPH 19:

Admitted.

20. Plaintiff KATHLEEN RAKER is a 41-year-old woman whose mother and maternal grandmother died from breast cancer. She obtained *BRCA1*/*BRCA2* genetic testing from Myriad in 2007 and was found to be negative for mutations covered by that test. Her genetic counselor advised her about additional *BRCA* genetic testing offered by Myriad that looks for other large genetic rearrangements that are not included in Myriad's standard full sequencing test, but informed her that it was unclear whether her insurance

would not cover the full cost of that test. Ms. Raker is unable to afford the extra cost. D. Raker ¶¶ 1-9.

RESPONSE TO PARAGRAPH 20:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Ms. Raker's declaration states that she is "a 42-year-old woman." Raker ¶ 2.

21. Dr. John Sulston, Nobel Prize winner for Physiology or Medicine and Chair of the Institute for Science, Ethics, and Innovation at the University of Manchester (UK), is qualified to express expert opinions in the area of human genetics. D. Sulston ¶¶ 1-9.

RESPONSE TO PARAGRAPH 21:

Admitted.

22. Dr. Wayne Grody, Professor in the Department of Pathology and Laboratory Medicine, Pediatrics, and Human Genetics at the UCLA School of Medicine, is qualified to express expert opinions in the area of human genetics. D. Grody ¶¶ 1-3.

RESPONSE TO PARAGRAPH 22:

Admitted.

23. Dr. Debra Leonard, Professor of Pathology and Laboratory Medicine at Weill Cornell Medical College and New York-Presbyterian Hospital, is qualified to express expert opinions in the area of human genetics. D. Leonard ¶¶ 1-10.

RESPONSE TO PARAGRAPH 23:

Admitted.

24. Dr. Christopher Mason, Post-doctoral Associate in the Program on Neurogenetics at Yale University, is qualified to express expert opinions in the area of human genetics. D. Mason ¶¶ 1-3.

RESPONSE TO PARAGRAPH 24:

Admitted.

25. Dr. Susan Love, Clinical Professor of Surgery at the University of California at Los Angeles and President of the Dr. Susan Love Research Foundation, is qualified to express expert opinions in the area of breast cancer treatment and research. D. Love ¶¶ 1-7.

RESPONSE TO PARAGRAPH 25:

Admitted.

26. Dr. Elizabeth Swisher, Associate Professor of Obstetrics and Gynecology at the University of Washington School of Medicine, is qualified to express expert opinions in the area of human genetics. D. Swisher ¶¶ 1-9.

RESPONSE TO PARAGRAPH 26:

Admitted.

27. Dr. Shobita Parthasarathy, Assistant Professor of Public Policy at the University of Michigan School of Public Policy, is qualified to express expert opinions in the area of the history of human genetic testing and research. D. Parthasarathy ¶¶ 1-7.

RESPONSE TO PARAGRAPH 27:

Admitted.

28. Dr. Myles Jackson, the Dibner Family Professor of the History and Philosophy of Science and Technology at the Polytechnic Institute of New York University, reviewed 12 court cases involving patents that were challenged, including 9 Supreme Court cases to compare the scientific principles and products either granted or denied patents. Dr. Jackson is qualified to express expert opinions in the area of science and patents. D. Jackson ¶¶ 1-6.

RESPONSE TO PARAGRAPH 28:

Disputed.

Dr. Jackson is not qualified by training or experience to testify as an expert in the area of science and patents. Fed. R. Evid. 702. He has an undergraduate degree from Cornell University in German literature, with a minor in biological sciences (with a specific concentration in molecular and cell biology), D. Jackson, ¶ 3; and a Ph.D. in the history and philosophy of science, D. Jackson, ¶ 4. He is not a lawyer and admits that he is not qualified to give opinions on the legal distinctions made in the opinions of the court cases that he reviewed. Jackson ¶6.

29. Dr. Mildred Cho, Associate Director of the Stanford Center for Biomedical Ethics, is qualified to express expert opinions on the need or lack thereof for gene patents to spur

research into genes and the effect of such patents on research and clinical practice. D. Cho ¶¶ 1-8.

RESPONSE TO PARAGRAPH 29:

Admitted.

30. Dr. Madhuri Hegde, Senior Laboratory Director at the Emory Genetics Laboratory, is qualified to express expert opinions in the area of human genetics. D. Hegde ¶¶ 1-5.

RESPONSE TO PARAGRAPH 30:

Admitted.

31. Dr. Roger Hubbard, President and Chief Executive Officer of Molecular Pathology Laboratory Network, Inc., is qualified to express expert opinions in the area of human genetics. D. Hubbard ¶¶ 1-6.

RESPONSE TO PARAGRAPH 31:

Admitted.

32. Dr. Jeffrey Kant, Director of the Division of Molecular Diagnostics at the University of Pittsburgh Medical Center, is qualified to express expert opinions in the area of human genetics. D. Kant ¶¶ 1-3.

RESPONSE TO PARAGRAPH 32:

Admitted.

33. Dr. Haig Kazazian is qualified to express expert opinions in the area of human genetics. D. Kazazian ¶¶ 1-3.

RESPONSE TO PARAGRAPH 33:

Admitted.

34. Dr. Arupa Ganguly is qualified to express expert opinions in the area of human genetics. D. Ganguly ¶¶ 1-3.

RESPONSE TO PARAGRAPH 34:

Admitted.

35. Dr. Wendy Chung is qualified to express expert opinions in the area of human genetics. D. Chung ¶¶ 1-7.

RESPONSE TO PARAGRAPH 35:

Admitted.

36. Dr. Harry Ostrer is qualified to express expert opinions in the area of human genetics. D. Ostrer ¶¶ 1-3.

RESPONSE TO PARAGRAPH 36:

Admitted.

37. Dr. David Ledbetter is qualified to express expert opinions in the area of human genetics. D. Ledbetter ¶¶ 1-6.

RESPONSE TO PARAGRAPH 37:

Admitted.

38. Ms. Ellen Matloff is qualified to express expert opinions in the area of human genetics. D. Matloff ¶¶ 1-4.

RESPONSE TO PARAGRAPH 38:

Admitted.

39. Ms. Elsa Reich is qualified to express expert opinions in the area of human genetics. D. Reich ¶¶ 1-2.

RESPONSE TO PARAGRAPH 39:

Admitted.

GENES

40. Genes and human genetic sequences are not inventions of humans. They are naturally occurring and are products of nature. D. Sulston ¶ 10; D. Ostrer ¶ 14; D. Chung ¶ 25; D. Mason ¶ 33; D. Ledbetter ¶ 27; D. Leonard ¶ 15.

RESPONSE TO PARAGRAPH 40:

The statement is not relevant. Fed. R. Evid. 402. Because Plaintiffs have failed to offer admissible evidence, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Isolated DNA molecules are patent eligible inventions under current applicable laws and regulations. Linck ¶¶ 14-17, 43, 47, 49; Doll ¶¶ 26, 34; Straus ¶¶ 26, 29-34.

41. Genes are the basic units of heredity in all living organisms. A gene is a segment of DNA, the molecule that makes life possible. DNA encodes the instructions for the development and functioning of each of our cells. D. Sulston ¶ 11.

RESPONSE TO PARAGRAPH 41:

The statement is not relevant. Fed. R. Evid. 402. Because Plaintiffs have failed to offer admissible evidence Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

The term "gene" has been used to describe the unit that is responsible for the inheritance of a discrete trait. Kay ¶142; Straus ¶ 20. In molecular terms, a gene is an aggregate of several segments of a chromosome. Kay ¶142. Factors other than native DNA, so-called epigenetic factors, can influence native DNA and consequently the presentation of a trait. Kay ¶132.

42. Each human gene has its place on one of the twenty-four chromosomes (numbered 1-22, plus the X and Y sex chromosomes), which together constitute the whole genome. D. Sulston ¶ 15.

RESPONSE TO PARAGRAPH 42:

The statement is not relevant. Fed. R. Evid. 402. Because Plaintiffs have failed to offer admissible evidence Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

A small fraction of human genes are located on the mitochondrial chromosome. Kay ¶144; Schlessinger ¶ 23.

43. Scientists have long recognized the role of genes in heredity. But it wasn't until 1953 – the year that Watson and Crick identified the double-helix structure of DNA – that the scientific community came to understand how DNA plays its role. This central discovery

for modern biology made it immediately apparent that the structure embodies a linear digital code. This code – nucleic acid sequence – gets copied more or less faithfully from one generation to the next. D. Sulston ¶ 13; D. Mason ¶¶ 8-10, 13.

RESPONSE TO PARAGRAPH 43:

The statement is not relevant. Because Plaintiffs have failed to offer admissible evidence to support this statement, Defendants need not offer contradictory evidence. Fed. R. Evid. 402. Local Civil Rule 56.1; and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

The genetic code was not elucidated until the early 1960's. The physical structure of the DNA molecule by itself does not reveal how the DNA molecule functions. Kay ¶160.

Cells divide throughout a person's life. The chromosomes, and with them genes and the DNA of which they are comprised, are also duplicated. Kay ¶145.

44. The genetic code is similar to the English alphabet, except that it consists of four letters (A, T, C, and G) rather than 26 (A through Z). The letters of the genetic alphabet correspond to 4 chemical bases (adenine (A), thymine (T), cytosine (C) and guanine (G)). Each gene is typically thousands of bases long, and its sequence of As, Ts, Cs and Gs usually encodes a protein. The code is a set of three-letter words – for example TTT, CAG – each of which corresponds to one of the twenty amino acids that are the building blocks of proteins. D. Sulston ¶¶ 14-15.

RESPONSE TO PARAGRAPH 44:

Disputed.

Three consecutive bases in an mRNA molecule constitute a codon, which codes for a specific amino acid of the 20 amino acids. Kay ¶¶157, 158.

The genetic code describes which codons code for which amino acids. For example, the codon adenine-thymine-guanine encodes the amino acid methionine. Kay ¶158. The genetic code is very much dependent on the cellular environment. Kay ¶159; Link ¶ 45.

The repeating units of DNA are known as nucleotides. The standard nucleotide in vertebrate DNA contains four different types of bases, i.e., adenine, cytosine, guanine, and

thymine. Scientists often denote nucleotides by the first letter of the names of their bases: "A" for adenine, "C" for cytosine, "G" for guanine, and "T" for thymine. Kay ¶14; Schlessinger ¶ 12.

45. When the body creates proteins, it relies on the processes of transcription and translation. During transcription, the DNA unwinds itself inside the cell and a temporary copy is created called a messenger RNA (mRNA). This mRNA contains sections that are unnecessary for the creation of proteins. These regions, known as introns, are removed by the body as a natural process because they will not be necessary for creation of a protein. The regions that remain are called exons and are necessary for creation of a protein. Translation is the naturally- occurring process of converting the processed mRNA into a protein. The tri-nucleotide segments of mRNA (codons) are converted into amino acids, which create the poly-peptide (protein). In other words, the DNA represented by three letters creates a single amino acid. The amino acids, when linked together, create a protein and the protein does the work of the body. D. Mason ¶¶ 11-12.

RESPONSE TO PARAGRAPH 45:

Disputed.

During transcription of RNA from DNA, a discrete segment of the DNA unwinds and the bases of the DNA molecule act as "clamps" that hold the bases of the newly forming RNA in place while the chemical bonds of the sugar-phosphate backbone are formed. Kay ¶150.

The bases of the mRNA serve as clamps to hold the amino acids in place while the chemical bonds between the individual amino acids are formed. Kay ¶157. Three consecutive bases in an mRNA molecule constitute a codon, which codes for a specific amino acid. Kay ¶157.

Pre-mRNA contains nucleotides that are eliminated during a process called splicing. The segments of the pre-mRNA that are spliced out are called introns, and the remaining segments, called exons, are ligated together. Introns can contain regulatory sequences. Kay ¶151; Schlessinger ¶ 14.

mRNA serves as a template to assemble a protein. Kay ¶157.

46. The genome is contained within almost every cell of the body. It defines obvious traits such as skin tone, eye color, and sex, but also directs the manifestation of very complex traits such as Alzheimer's disease. There are approximately 25,000 genes that make up the human genome. D. Mason ¶¶ 4-5; *see* D. Sulston ¶¶ 10-11.

RESPONSE TO PARAGRAPH 46:

The statement is not relevant. Fed. R. Evid. 402. Because Plaintiffs have failed to offer admissible evidence Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

47. A genetic sequence is the sequence of letters of a specified section of the human genome. D. Sulston ¶ 16; D. Mason ¶ 13; D. Chung ¶ 10.

RESPONSE TO PARAGRAPH 47:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

A molecule of isolated DNA is typically represented by the linear order of its nucleotides, *i.e.*, its "nucleotide sequence" or simply, its "sequence." Kay ¶126; Linck ¶ 45.

48. A genetic sequence is biological information. Like strings of alphabetic text, the genetic sequences are the same regardless of the medium. Whether the data reside in the DNA of an organism, a computer, or as letters on a printed page, the information is the same. The physical form in which they occur is unimportant; what matters is the informational content. D. Sulston ¶ 16.

RESPONSE TO PARAGRAPH 48:

Disputed.

DNA, which stands for deoxyribonucleic acid, is a type of chemical compound called a nucleic acid. Kay ¶14. A nucleotide sequence is not merely information or letters of the English alphabet – the nucleotide sequence defines the structure and chemical properties of a particular DNA molecule based on the linear order of nucleotides in that particular DNA molecule. Kay ¶ 126; Schlessinger ¶ 19; Linck ¶¶ 45, 46.

49. The information contained in the genetic sequence is a product of nature. The informational content of a human genetic sequence is fixed. While many inventive steps may have been necessary to allow scientists to extract and read a genetic sequence, the ordering of the 4 letters is determined by nature. D. Sulston ¶ 17.

RESPONSE TO PARAGRAPH 49:

Disputed.

Isolated DNA is different in kind, not merely different in degree of purity, from any composition found in nature. Kay ¶138; Linck ¶ 47; Doll ¶ 27-29, 33. DNA as it is found in the human body, *i.e.*, native DNA, is one integral component of chromosomes. Kay ¶ 131; Doll ¶ 27; Schlessinger ¶¶ 11, 27. Native DNA does not have the chemical, structural, functional properties that make isolated DNA so useful to the molecular biologist. Kay ¶ 139; Linck ¶ 47; Doll ¶¶ 28-29; Schlessinger ¶¶ 27, 30.

50. Genes are so basic to science that any restriction that prevents scientists from looking at the genes themselves or examining the effects of the genes is fundamentally inconsistent with the advancement of human knowledge. D. Sulston ¶¶ 28, 37; D. Ostrer ¶ 14; D. Chung ¶ 25; D. Swisher ¶ 21; D. Ledbetter ¶ 27; D. Love ¶ 19.

RESPONSE TO PARAGRAPH 50:

The statement is not relevant. Fed. R. Evid. 402. Because Plaintiffs have failed to offer admissible evidence Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Patents such as the patents-in-suit have served to advance research and the practice of medicine and benefit patients. Reilly ¶¶ 38, 43; Critchfield ¶¶ 2-18, 65, 68; Linck ¶¶ 27-28, 71, 73; Tavtigian ¶¶ 14-17; Doll ¶¶ 45-46; Bone ¶¶ 10-11; Frieder ¶ 13; Schlessinger ¶¶ 31-32.

The incentives provided by patents fuel discovery and commercialization in emerging technologies such as medical diagnostics, resulting in social and health benefits for future generations. Reilly ¶ 62.

51. Except for identical twins, no two humans are genetically the same. Variation in the human genome is very common, and each person is estimated to be 99.5% similar, or to have one to five differences every 1000 base pairs (bp). D. Mason ¶ 14; D. Sulston ¶ 12.

RESPONSE TO PARAGRAPH 51:

The statement is not relevant. Fed. R. Evid. 402. Because Plaintiffs have failed to offer admissible evidence to support this statement, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

52. Small scale variation can occur, manifested as slight sequence differences between the same genes in different individuals. Thus, for example, a sequence of a gene represented by . . .GACTCG. . . might contain a variation that omits the first C (GATCG) or that adds an extra C at that point (GACCTCG) or that reverses the order of two of the letters (CCATCG). D. Mason ¶ 16.

RESPONSE TO PARAGRAPH 52:

Disputed.

A nucleotide sequence is not merely information or letters of the English alphabet – the nucleotide sequence defines the structure and chemical properties of a particular DNA molecule based on the linear order of nucleotides in that particular DNA molecule. Kay ¶126; Linck ¶ 46.

53. Large scale variation can also occur in the genome, such as the addition or deletion of substantial chromosomal regions. Thus, a particular gene may omit several hundred letters at one point or may add several hundred letters where they do not normally exist. Structural variants also can occur, so that up to millions of nucleotides can be missing or duplicated. These extra copies or missing copies of the genome that are larger than 1000 bp are called copy number variants. D. Mason ¶¶ 15, 18.

RESPONSE TO PARAGRAPH 53:

Disputed.

A nucleotide sequence is not merely information or letters of the English alphabet – the nucleotide sequence defines the structure and chemical properties of a particular DNA molecule based on the linear order of nucleotides in that particular DNA molecule. Kay ¶126; Linck ¶ 46.

54. Some variants appear to have little or no effect on the body's processes. There are also variants whose significance is currently unknown ("variants of uncertain significance").

Other variants that interfere with a body's processes, including those that appear to correlate with an increased risk of particular diseases, are called mutations. Mutations can be in the form of the insertion or deletion of a single letter, or rearrangements, deletions or repeated segments of groups of letters. D. Mason ¶ 19; D. Sulston ¶ 18.

RESPONSE TO PARAGRAPH 54:

Disputed.

Silent mutations or those resulting in conservative amino acid substitutions would not generally be expected to disrupt protein function. Kay ¶76. Without knowing the correlation between DNA sequence and a disease state, the nucleotide sequence of DNA by itself in a chromosome of a person does not say anything about the disease susceptibility of that person. Rather, extensive statistical analysis is required to identify those alterations in a nucleotide sequence that correlate with a particular medical condition. Nucleotide sequences of a large group of people have to be painstakingly sequenced, analyzed, and correlated with the presence or absence of disease in the carrier of the sequence. This process can take many years. Kay ¶ 190.

55. Genetic sequencing is the process by which one "reads", or determines the ordering of the 4 letters (A, T, C, and G) within a specified part of the genome. In order to sequence, or read a gene, one has to remove it from the cell of an organism and place it in a form so that it can be replicated outside of the body. Most commonly, scientists use a technique called PCR to replicate small segments of the gene many times over. Amplifying these segments allows scientists to read out the genetic code. D. Sulston ¶¶ 20, 25; D. Chung ¶ 10.

RESPONSE TO PARAGRAPH 55:

Disputed.

Sequencing is used to determine the primary structure of a DNA molecule. Kay ¶ 138.

We admit that sequencing requires that the DNA be removed from a cell in order to be sequenced. Kay ¶¶ 178, 186-187.

Sequencing is not simply "reading" a series of letters through a microscope. A DNA sequence cannot be determined by mere inspection. Instead, a series of extractions and chemical reactions must be performed. Kay ¶176. In order to initiate a DNA sequencing reaction, at least part of the sequence of the target DNA molecule must be known. Kay ¶177.

The use of PCR requires knowledge of at least part of the sequence of the target DNA molecule to design specific primers. Kay ¶184.

56. Sequencing of a gene can be done by several processes that are well-known and understood by scientists. Anyone skilled in molecular biology has the knowledge and methods to sequence and examine any part of the human genome. D. Chung ¶ 10; D. Mason ¶¶ 24-30; D. Swisher ¶¶ 23-24; D. Kant ¶ 5; D. Sulston ¶¶ 20-21, 23; D. Ledbetter ¶¶ 21-22; D. Leonard ¶ 18.

RESPONSE TO PARAGRAPH 56:

Disputed.

In order to initiate a DNA sequencing reaction, at least part of the sequence of the DNA molecule must be known. Kay ¶177. Without knowing the correlation between DNA sequence and a disease state, the nucleotide sequence of DNA by itself in a chromosome of a person does not say anything about the disease susceptibility of that person. Rather, extensive statistical analysis is required to identify those alterations in a nucleotide sequence that correlate with a particular medical condition. Nucleotide sequences of a large group of people have to be painstakingly sequenced, analyzed, and correlated with the presence or absence of disease in the carrier of the sequence. This process can take many years. Kay ¶190.

57. Scientists and clinicians sequence and analyze genes literally every day. D. Chung ¶¶ 10-11; D. Hegde ¶¶ 6-7; D. Hubbard ¶¶ 3-6; D. Mason ¶¶ 22, 31; D. Sulston ¶¶ 21-22; D. Ledbetter ¶¶ 9-10, 22.

RESPONSE TO PARAGRAPH 57:

The statement is not relevant. Fed. R. Evid. 402. Because Plaintiffs have failed to offer admissible evidence Defendants need not offer contradict ory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

58. The process of sequencing is designed simply to illuminate the information that nature has dictated in that person's genome. In that respect, sequencing is essentially no different than looking at something through a microscope. It takes something created by nature but too small to be seen and makes it visible. D. Mason ¶ 23; D. Sulston ¶ 18

RESPONSE TO PARAGRAPH 58:

Disputed.

Sequencing is not simply "reading" a series of letters through a microscope. A DNA sequence cannot be determined by mere inspection. Instead, a series of extractions and chemical reactions must be performed. Kay ¶176. In order to initiate a DNA sequencing reaction, at least part of the sequence of the target DNA molecule must be known. Kay ¶177.

59. The process of sequencing a gene does not change the informational content of that gene. The resultant sequence is informationally and functionally identical to the sequence found inside the body. D. Sulston ¶ 27; D. Chung ¶ 10; D. Mason ¶¶ 32-33.

RESPONSE TO PARAGRAPH 59:

Disputed.

Isolated DNA is different in kind, not merely different in degree of purity, from any composition found in nature. Kay ¶138; Linck ¶ 47; Doll ¶ 27-29, 33. DNA as it is found in the human body, *i.e.*, native DNA, is one integral component of chromosomes. Kay ¶ 131; Doll ¶ 27; Schlessinger ¶¶ 11, 27. Native DNA does not have the chemical, structural, functional properties that make isolated DNA so useful to the molecular biologist. Kay ¶ 139;.Doll ¶¶ 28-29; Schlessinger ¶¶ 27, 30.

After diagnostic sequencing, the patient's sample, such as blood or tissue, is no longer blood or tissue but is has been processed to obtain DNA. The DNA has then been subjected to a sequencing reaction. At the end, instead of blood or tissue, the clinician has the chemical structure of a small portion of the patient's DNA. Kay ¶185.

60. The alterations or mutations in the gene that scientists are able to see after sequencing the gene were made by nature, not by the process of sequencing or by scientists, and the effect of those alterations or mutations is dictated by nature, not by any scientist. D. Sulston ¶ 27; D. Chung ¶ 10.

RESPONSE TO PARAGRAPH 60:

Disputed.

Sequencing is not simply "reading" a series of letters through a microscope. A DNA sequence cannot be determined by mere inspection. Instead, a series of extractions and chemical reactions must be performed. Kay ¶176. In order to initiate a DNA sequencing reaction, at least part of the sequence of a DNA molecule has to be known. Kay ¶177.

After diagnostic sequencing, the patient's sample, such as blood or tissue, is no longer blood or tissue but is has been processed to obtain DNA. The DNA has then been subjected to a sequencing reaction. At the end, instead of blood or tissue, the clinician has the chemical structure of a small portion of the patient's DNA. Kay ¶185.

61. Gene sequencing sometimes involves cDNA or complementary DNA. mRNA that is the result of the natural process of transcription (*see supra* ¶ 45) is reverse-transcribed into cDNA. Thus, the coding effect of a cDNA is the same as that of the original DNA from which it was originally derived. Thus, cDNA means a purely coding polynucleotide sequence that is produced from RNA that has had all of its non-coding regions (called introns) removed. D. Leonard ¶ 75.

RESPONSE TO PARAGRAPH 61:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

cDNA is structurally and functionally different from native DNA or mRNA in the human body. cDNA is not mirror of mRNA nor is it identical to native DNA found in the body. Kay ¶¶167-171; Schlessinger ¶ 15; Linck ¶48; Doll ¶ 32, 33. During a process called "alternative splicing," different combinations of exons from the same pre-mRNA molecule can be spliced together yielding alternative mRNA products. Kay ¶152; Linck ¶ 48.

62. Complementary DNA does not exist in the body but is simply a mirror of the RNA which does exist in the body. In the body, certain of the nucleotides, represented by the letters, always bind or attach to certain other nucleotides or letters. G always links to C, and A always links to T. If the RNA in the body is a G, then the cDNA in the lab is a C. Knowing that the cDNA is a C tells a scientist without exception that the RNA was a G. In other words, the cDNA is a sequence of nucleotides that "complements" the RNA. Because the RNA was a mirror of the DNA, the cDNA is again identical to the DNA. The only difference is the introns have been removed. Thus, the functional sequence of the cDNA is identical to the functional sequence of the DNA. D. Mason ¶¶ 28-29, 32.

RESPONSE TO PARAGRAPH 62:

Disputed.

cDNA is structurally and functionally different from native DNA or mRNA in the human body. cDNA is not mirror of mRNA nor is it identical to native DNA found in the body. Kay ¶¶167-171; Schlessinger ¶ 15; Doll ¶ 32, 33. During a process called "alternative splicing," different combinations of exons from the same pre-mRNA molecule can be spliced together yielding alternative mRNA products. Kay ¶152; Linck ¶ 48.

63. The sequence of a cDNA is dictated not by scientists but by nature. Even though the structure of cDNA does not exist in precisely the same form in the body, for literally all practical and information-based purposes its sequence is identical to that in the body. D. Mason ¶ 32.

RESPONSE TO PARAGRAPH 63:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Isolated cDNA is an artificial construct. cDNA is not mirror of mRNA nor is it identical to native DNA found in the body. Kay ¶167; Schlessinger ¶ 15; Doll ¶ 32. during a process called "alternative splicing," different combinations of exons from the same pre-mRNA molecule can be spliced together yielding alternative mRNA products. Kay ¶152; Linck ¶ 48.

64. "Isolated DNA" is a fragment of DNA that is separated from other cellular components. This separation could be accomplished through a number of well known techniques. D. Grody ¶ 13; D. Leonard ¶ 33.

RESPONSE TO PARAGRAPH 64:

Disputed.

At least part of the sequence of the gene of interest must be known to allow the researcher or clinician to isolate and sequence the specific gene of interest. Kay ¶182.

65. "Isolating and purifying" a gene (removing it from the body and placing it in a form so that it can be sequenced and possibly used in other ways) is simply copying it into another format. D. Sulston ¶ 26.

RESPONSE TO PARAGRAPH 65:

Disputed.

At least part of the sequence of the gene of interest must be known to allow the researcher or clinician to isolate and sequence the specific gene of interest. Kay ¶182.

66. Gene sequencing is used in diagnostic testing. Gene sequences are examined to determine if they contain any alterations or mutations that have been associated with a particular condition. D. Chung ¶ 10; D. Swisher ¶¶ 23-26; D. Mason ¶ 21; D. Sulston ¶ 24.

RESPONSE TO PARAGRAPH 66:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Sequencing is not simply "reading" a series of letters through a microscope. A DNA sequence cannot be determined by mere inspection. Instead, a series of extractions and chemical reactions must be performed. Kay ¶176. In order to initiate a DNA sequencing reaction, at least part of the sequence of a DNA molecule must be known. Kay ¶177.

After diagnostic sequencing, the patient's sample, such as blood or tissue, is no longer blood or tissue but is has been processed to obtain DNA. The DNA has then been subjected to a sequencing reaction. At the end, instead of blood or tissue, the clinician has the chemical structure of a small portion of the patient's DNA. Kay ¶185.

67. Scientists often refer to the "wild-type" or "normal" gene, which is the gene without variations. However, the notion that there exists a gene without variations is increasingly misleading. Newfound recognition of the high frequency of variation between individuals has implications for the definition (and patenting) of genes: such variation reinforces the emerging idea that no single DNA sequence can adequately capture either the human genome or a single gene, both of which occur naturally in a variety of forms. D. Mason ¶ 17.

RESPONSE TO PARAGRAPH 67:

Disputed.

Plaintiffs' expert Dr. Grody states that "[t]he ordinary or customary meaning of the phrase 'wild type' to one of ordinary skill in the art at the time of the application for the patents in suit would have meant the most common typical version of, for example, a gene." D. Grody, ¶46.

68. Gene sequences can have alterations from the wild-type sequence that are caused by nature. D. Chung ¶ 10; D. Mason ¶ 20; D. Sulston ¶¶ 19, 27; D. Ledbetter ¶ 26.

RESPONSE TO PARAGRAPH 68:

Disputed.

Isolated DNA molecules are patent eligible subject matter. Doll ¶¶ 26, 34; Linck ¶¶ 14-17, 43, 47, 49; Straus ¶¶ 26, 29-34

69. Full sequencing is often the method used to identify when there is a substitution of one of the letters at a single point or where the insertion or deletion of a small number of bases has occurred. D. Swisher ¶ 23.

RESPONSE TO PARAGRAPH 69:

Disputed.

A nucleotide sequence is not merely information or letters of the English alphabet – the nucleotide sequence defines the structure and chemical properties of a particular DNA molecule based on the linear order of nucleotides in that particular DNA molecule. Kay ¶126. Site-specific sequencing, as opposed to full length sequencing, is often used to identify an alteration at a specific nucleotide position. Kay ¶180; Linck ¶ 46.

70. Full sequencing can miss large genomic rearrangements where whole sections of the gene have been deleted or moved to a different part of the sequence. Other tests have been developed that better detect large rearrangements. D. Swisher ¶¶ 23-24; D. Ledbetter ¶¶ 16-17.

RESPONSE TO PARAGRAPH 70:

Admitted.

71. When alterations or mutations are found in a gene sequence, they can be further investigated to see if they have any significance such as for increasing the propensity to a particular disease. D. Chung ¶ 10; D. Sulston ¶ 24.

RESPONSE TO PARAGRAPH 71:

Disputed.

The nucleotide sequence of DNA by itself in a chromosome of a person does not say anything about the disease susceptibility of that person. Rather, extensive statistical analysis is required to identify those alterations in a nucleotide sequence that correlate with a particular medical condition. Nucleotide sequences of a large group of people have to be sequenced and correlated with the presence or absence of disease in the carrier of the sequence. Kay ¶190.

72. The significance of alterations in a gene sequence is caused by nature. D. Chung, ¶ 10; D. Mason ¶ 20; D. Sulston ¶ 27; D. Ledbetter ¶ 26.

RESPONSE TO PARAGRAPH 72:

Disputed.

Alterations may be caused by artificial environmental factors. Kay ¶189.

The nucleotide sequence of DNA by itself in a chromosome of a person does not say anything about the disease susceptibility of that person. Rather, extensive statistical analysis is required to identify those alterations in a nucleotide sequence that correlate with a particular medical condition. Nucleotide sequences of a large group of people have to be sequenced and correlated with the presence or absence of disease in the carrier of the sequence. Kay ¶190.

73. The significance of any person's genetic sequence, including its relationship to any disease, is dictated by nature. D. Mason ¶ 32.

RESPONSE TO PARAGRAPH 73:

Disputed.

The nucleotide sequence of DNA by itself in a chromosome of a person does not say anything about the disease susceptibility of that person. Rather, extensive statistical analysis is required to identify those alterations in a nucleotide sequence that correlate with a particular medical condition. Nucleotide sequences of a large group of people have to be sequenced and correlated with the presence or absence of disease in the carrier of the sequence. Kay ¶190.

74. From the beginning of the Human Genome Project, an international project initiated in 1990 with the aim of sequencing an entire human genome, most scientists and even some private companies recognized the importance of keeping the genome freely available to all. In 1994, the pharmaceutical company Merck funded a massive drive to generate genetic sequences and place them into public databases. D. Sulston ¶¶ 22, 29.

RESPONSE TO PARAGRAPH 74:

The statement is not relevant. Fed. R. Evid. 402. Because Plaintiffs have failed to offer admissible evidence Defendants need not offer contradictory evidence. Local Civil Rule 56.1; and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Isolated DNA molecules are patent eligible subject matter. Doll ¶¶ 26, 34; Linck ¶¶ 14-17, 43, 47, 49; Straus ¶¶ 26, 29-34.

Patents such as the patents-in-suit have served to advance research and the practice of medicine and benefit patients. Reilly ¶¶38, 43; Critchfield ¶¶ 2-18, 65, 68; Linck ¶¶ 27-28, 71, 73; Tavtigian ¶¶ 14-17; Doll ¶¶ 45-46; Bone ¶¶ 10-11; Frieder ¶13; Schlessinger ¶¶ 31-32.

The patenting of human isolated DNA molecules is not in conflict with the notion that science would advance more rapidly if researchers are allowed to take advantage of free access to knowledge. Part of the *quid pro quo* of the patent system is that inventors, in exchange for a limited period of patent exclusivity, must provide a sufficient description of the patented invention so that others may improve upon it. Reilly ¶ 24, Doll ¶ 44.

75. In 1996, a group of 50 of the most prominent geneticists in the world who were involved with the sequencing of the human genome adopted the Bermuda principles which included the mandate that all "human genomic sequence information should be freely available and in the public domain in order to encourage research and development and to maximize its benefit to society." D. Sulston ¶ 33.

RESPONSE TO PARAGRAPH 75:

The statement is not relevant. Fed. R. Evid. 402. Because Plaintiffs have failed to offer admissible evidence Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Isolated DNA molecules are patent eligible subject matter regulations. Doll ¶¶ 26-34; Linck ¶¶ 14-17, 43, 47, 49; Straus ¶¶ 26, 29-34.

Patents on isolated DNA promote research and advance clinical development. Patents such as the patents-in-suit have served to advance research and the practice of medicine and

benefit patients. Reilly ¶¶ 38, 43; Critchfield ¶¶ 2-18, 65, 68; Linck ¶¶ 27-28, 71, 73; Tavtigian; ¶¶ 14-17; Doll ¶¶ 45-46; Bone ¶¶ 10-11; Frieder ¶ 13; Schlessinger ¶¶ 31-32.

The patenting of human isolated DNA molecules is not in conflict with the notion that science would advance more rapidly if researchers are allowed to take advantage of free access to knowledge. Part of the *quid pro quo* of the patent system is that inventors, in exchange for a limited period of patent exclusivity, must provide a sufficient description of the patented invention so that others may improve upon it. Reilly ¶ 24; Doll ¶ 44.

BRCA1/2 **GENES**

76. Mutations on the *BRCA1* and *BRCA2* genes have been associated with a predisposition to develop breast and ovarian cancer. *BRCA1* is a particular portion of DNA found on chromosome 17. *BRCA2* is a particular portion of DNA found on chromosome 13. D. Leonard ¶ 39.

RESPONSE TO PARAGRAPH 76:

Disputed.

The *BRCA1* gene is an aggregate of several segments of a chromosome. Some segments regulate the activity of the *BRCA1* gene. From other segments, *BRCA1* pre-mRNA and then mRNA is produced. From the mRNA, *BRCA1* protein is typically produced. Kay ¶24. The *BRCA2* gene is an aggregate of several segments of a chromosome. Some segments regulate the activity of the *BRCA2* gene. From other segments, *BRCA2* pre-mRNA and then mRNA is produced. From the mRNA, *BRCA2* protein is typically produced. Kay ¶31.

77. Breast cancer is the most frequently diagnosed cancer worldwide, and is heavily publicized as the leading cause of cancer death for women in Britain and the second leading cause of cancer death for women in the United States. D. Parthasarathy ¶ 8.

RESPONSE TO PARAGRAPH 77:

The statement is not relevant. In addition, Plaintiffs have failed to cite admissible evidence which supports this statement. Fed. R. Evid. 402; 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

78. The relationship between mutations in the *BRCA1/2* genes and breast and ovarian cancer incidence is complex. Estimates for elevated risk of breast cancer for women who have *BRCA1* or *BRCA2* mutations have ranged from 3 to 86 percent. Male carriers of mutations are also at increased risk of breast and prostate cancers. D. Love ¶ 10; D. Parthasarathy ¶ 9.

RESPONSE TO PARAGRAPH 78:

Plaintiffs have failed to cite admissible evidence which supports this statement. Fed. R. Evid. 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Dr. Love states that "woman who have *BRCA1* or *BRCA2* mutations have an elevated risk of breast cancer—anywhere between 50 to 80 percent--as well as a lifetime risk of ovarian cancer between 20 and 50 percent." D. Love ¶ 10

79. Ovarian cancer is the eighth most common cancer in women and causes more deaths in the Western world than any other gynecologic cancer. D. Swisher ¶ 10.

RESPONSE TO PARAGRAPH 79:

The statement is not relevant. In addition, Plaintiffs have failed to cite admissible evidence which supports this statement. Fed. R. Evid. 402; 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

80. Between 10 and 15% of ovarian cancers are inherited genetically. For women who are diagnosed under the age of 50 years old, approximately 80% of inherited ovarian cancers are caused by *BRCA1* mutations and approximately 20% are caused by *BRCA2* mutations. Women with inherited *BRCA1* mutations have a 40-52% cumulative risk of ovarian cancer by the time they reach 70 years old. For women with inherited *BRCA2* mutations, the risk is approximately 15-25%. D. Swisher ¶ 11.

RESPONSE TO PARAGRAPH 80:

Plaintiffs have failed to cite admissible evidence which supports this statement. Fed. R. Evid. 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

81. *BRCA1/2* mutations and the correlations between the mutations and the increased risk of disease are created by nature. D. Mason ¶ 20.

RESPONSE TO PARAGRAPH 81:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

The nucleotide sequence of DNA by itself in a chromosome of a person does not say anything about the disease susceptibility of that person. Rather, extensive statistical analysis is required to identify those alterations in a nucleotide sequence that correlate with a particular medical condition. Nucleotide sequences of a large group of people have to be sequenced and correlated with the presence or absence of disease in the carrier of the sequence. Kay ¶190.

82. The existence of *BRCA1/2* mutations is an important factor in clinical care of breast and/or ovarian cancer. A patient will not only learn her risk for hereditary breast and ovarian cancer, but also can gain information that may be useful in determining prevention and treatment options. This information is useful for women who are facing difficult decisions regarding whether or not to undergo prophylactic surgery, hormonal therapy, chemotherapy, and other measures. D. Swisher ¶ 12; D. Love ¶¶ 8-19.

RESPONSE TO PARAGRAPH 82:

The statement is not relevant. Fed. R. Evid. 402. Because Plaintiffs have failed to offer admissible evidence Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

83. Testing results for the *BRCA1/2* genes can be an important factor in structuring an appropriate course of cancer treatment. Certain forms of chemotherapy can be more effective in treating *BRCA* mutation carriers. D. Swisher ¶ 13; D. Love ¶ 18.

RESPONSE TO PARAGRAPH 83:

The statement is not relevant. Fed. R. Evid. 402. Because Plaintiffs have failed to offer admissible evidence Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

84. Myriad Genetics offers multiple forms of *BRCA1/2* testing to the general public. Its standard test is a full sequencing test called Comprehensive BRACAnalysis. In 2006, it started offering a supplemental test to Comprehensive BRACAnalysis called the BRACAnalysis Rearrangement Test ("BART"). Unless a patient meets certain criteria, the patient must pay an extra fee for BART. Myriad also offers more limited forms of testing. D. Swisher ¶¶ 29-30; D. Reich ¶ 10; D. Parthasarathy ¶ 26.

RESPONSE TO PARAGRAPH 84:

The statement is not relevant. Fed. R. Evid. 402. Because Plaintiffs have failed to offer admissible evidence to support this statement, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

In 2002 Myriad supplemented its full sequencing analysis with a large rearrangement panel (LRP) for detecting five common large rearrangement mutations. Since then, Myriad has included the LRP panel in every comprehensive BRAC*Analysis*® test it performs. Critchfield ¶ 49. Myriad launched in 2006 the BART™ (BRAC*Analysis*® Rearrangement Test) assay which can detect virtually all large rearrangement mutations in the *BRCA1* and *BRCA2* genes. Critchfield ¶ 51.

85. Many researchers, clinicians, and molecular pathologists have the personnel, equipment, and expertise to sequence and analyze genes, including the *BRCA1* and *BRCA2* genes. D. Kazazian ¶ 11; D. Ganguly ¶¶ 3, 10, 14; D. Chung ¶¶ 11-12, 18; D. Ostrer ¶¶ 8-9; D. Ledbetter ¶¶ 16-18; D. Hegde ¶¶ 8-12; D. Mason ¶ 22; D. Kant ¶ 5.

RESPONSE TO PARAGRAPH 85:

The statement is not relevant. Fed. R. Evid. 402. Because Plaintiffs have failed to offer admissible evidence to support this statement, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Myriad's full sequencing test has been recognized as the "gold standard" for *BRCA* mutation testing. Critchfield ¶ 37. Myriad has been continuously improving its testing process. Critchfield ¶ 37. In 2002 Myriad supplemented its full sequencing ananlysis with a large rearrangement panel (LRP) for detecting five common large rearrangement mutations. Critchfield ¶ 49. Myriad launched in 2006 the BART™ (BRAC*Analysis*® Rearrangement Test) assay which can detect virtually all large rearrangement mutations in the *BRCA1* and *BRCA2* genes. Critchfield ¶ 51.

86. The United States Patent and Trademark Office (USPTO) granted the patent claims at issue in this case. Patent 5,747,282 (Claims 1, 2, 5, 6, 7, and 20), Patent 5,837,492 (Claims 1, 6, and 7), Patent 5,693,473 (Claim 1), Patent 5,709,999 (Claim 1), Patent 5,710,001 (Claim 1), Patent 5,753,441 (Claim 1), Patent 6,033,857 (Claims 1 and 2).[1]

RESPONSE TO PARAGRAPH 86:

Admitted.

87. Patents prevent anyone from using what has been patented. 35 U.S.C. § 271.

RESPONSE TO PARAGRAPH 87:

Disputed.

Only for a limited time, patents prevent anyone from using what has been patented without a license, after which the patented invention is donated to the public to be freely used. Doll ¶ 44.

[1] Hereinafter, references to "The patents" includes all of the patents at issue in this case. The patents are attached as Exhibits 1-7 of the Declarations of Daniel B. Ravicher.

88. Uses of the genes at stake in the patent claims in this case include research into or clinical testing of the *BRCA1* and *BRCA2* genes. D. Sobel ¶¶ 3-5; D. Watson ¶¶ 3-5; D. Ball ¶¶ 2-5; D. Scott ¶¶ 2-5.

RESPONSE TO PARAGRAPH 88:

The statement is not relevant. In addition, the evidence cited by Plaintiffs is inadmissible. Fed. R. Evid. 402, 701, 702. Because Plaintiffs have failed to offer admissible evidence Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

The claimed isolated *BRCA1* or *BRCA2* DNA molecules of the Myriad patents are chemical compositions that have a specific utility, *e.g.*, molecular diagnostics. Linck ¶ 45.

89. The patent claims at issue in this case do not claim specific methods of sequencing genes. The patents.

RESPONSE TO PARAGRAPH 89:

There is no evidence cited by Plaintiff to support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

90. If someone had the ability to sequence her own genes, she could utilize non- patented methodologies to sequence those genes, but could be infringing if she sequenced her own *BRCA1* and *BRCA2* genes. D. Norsigian ¶ 7.

RESPONSE TO PARAGRAPH 90:

The statement is not relevant. Because Plaintiffs have failed to offer admissible evidence Fed. R. Evid. 402, 701, 702. Defendants need not offer contradictory evidence. Local Civil Rule 56.1; and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

The claimed isolated *BRCA1* or *BRCA2* DNA molecules of the Myriad patents are chemical compositions that have a specific utility, *e.g.*, molecular diagnostics. Linck ¶ 45.

91. A patent on a gene sequence and any mutations of that gene applies regardless of the person from whom the gene is taken or the sequencing process that is used. D. Sulston ¶ 27.

RESPONSE TO PARAGRAPH 91:

The evidence cited by Plaintiffs to support this statement is inadmissible. Fed. R. Evid. 701, 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Isolated DNA molecules are patent eligible subject matter. Doll ¶¶ 26, 34; Linck ¶¶ 14-17, 43, 47, 49; Straus ¶¶ 26, 29-34.

92. Certain of the patent claims at issue in this case cover the *BRCA1* and *BRCA2* genes without known alterations or mutations. D. Ravicher, Exs. 1, 6 (Patents '282 (Claims 1, 2, 5, 6) and '492 (Claim 1)).

RESPONSE TO PARAGRAPH 92:

Disputed.

Isolated DNA molecules are patentable subject matter under applicable United States laws and regulations. Doll ¶¶ 26, 34; Linck ¶¶ 14-17, 43, 47, 49; Straus ¶¶ 26, 29-34.

93. The *BRCA1* and *BRCA2* genes are naturally-occurring and the sequence of nucleotides in them is created by and dictated by nature. They are products of nature. *See supra* ¶¶ 40-50.

RESPONSE TO PARAGRAPH 93:

Disputed.

Isolated DNA molecules are patentable subject matter under applicable United States laws and regulations. Doll ¶¶ 26, 34; Linck ¶¶ 14-17, 43, 47, 49; Straus ¶¶ 26, 29-34.

94. The patents are on wild-type *BRCA1* and *BRCA2* human genes. None of the claim language covers genes that have been engineered by humans – their sequence and function are dictated by nature. D. Grody ¶¶ 10-33, 46-48; D. Leonard ¶¶ 30-53, 66-68.

RESPONSE TO PARAGRAPH 94:

Plaintiffs have failed to cite admissible evidence which supports this statement. Fed. R. Evid. 701, 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Isolated DNA molecules are patent eligible subject matter. Doll ¶¶ 26, 34; Linck ¶¶ 14-17, 43, 47, 49; Straus ¶¶ 26, 29-34.

95. The claims that are on genes are on "isolated DNA." Isolated DNA is just a fragment of DNA that has been separated from other things in order to be read. D. Grody ¶ 13; D.Leonard ¶ 33.

RESPONSE TO PARAGRAPH 95:

Plaintiffs have failed to cite admissible evidence which supports this statement. Fed. R. Evid. 701, 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Isolated DNA molecules are patent eligible subject matter. Doll ¶¶ 26, 34; Linck ¶¶ 14-17, 43, 47, 49; Straus ¶¶ 26, 29-34.

96. The process of sequencing a gene does not change the informational content of that gene. The isolated sequence is informationally and functionally identical to the sequence found inside the body. D. Sulston ¶ 27; D. Chung ¶ 10; D. Mason ¶ 32-33.

RESPONSE TO PARAGRAPH 96:

Disputed.

Isolated DNA is very much informationally different in kind from native DNA and mRNA. Kay ¶172; Doll ¶¶ 27-29, 33. Once a DNA molecule is isolated, it gains new properties. Kay ¶134; Linck ¶ 47; Doll ¶¶ 27-30.

97. Certain of the patent claims cover the *BRCA1* and *BRCA2* genes in their altered or mutated form or gene alterations or mutations. D. Ravicher, Exs. 1, 2, 6 (Patents '473 (Claim 1), '282 (Claim 7), and '492 (Claims 6 and 7)).

RESPONSE TO PARAGRAPH 97:

Disputed.

Isolated DNA molecules are patent eligible subject matter. Doll ¶¶ 26, 34; Linck ¶¶ 14-17, 43, 47, 49; Straus ¶¶ 26, 29-34.

98. Some of Myriad's patents cover mutations that were found by other scientists. Myriad filed for a patent on the *BRCA2* gene a day before a team of British researchers published the *BRCA2* sequence in the scientific journal, *Nature*. Scientists in the breast cancer genetic community tend to credit this team for being the first to sequence *BRCA2* rather than Myriad. D. Sulston ¶¶ 30-32; D. Parthasarathy ¶¶ 12-13.

RESPONSE TO PARAGRAPH 98:

The evidence cited by Plaintiffs to support this statement is inadmissible. Fed. R. Evid. 402, 602, 802. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Isolated DNA molecules are patent eligible subject matter. Doll ¶¶ 26, 34; Linck ¶¶ 14-17, 43, 47, 49; Straus ¶¶ 26, 29-34.

The Institute of Cancer Research published a *BRCA2* structure that was incomplete at one end and contained a fatal error at the other. Tavtigian ¶ 7. Myriad and its collaborators discovered that the Ashkenazi mutation (6174delT) is a founder mutation commonly found among Ashkenazi Jews from central and eastern Europe. Tavtigian ¶ 20.

99. The *BRCA1* and *BRCA2* gene sequences with mutations are naturally-occurring and products of nature. *See supra* ¶¶ 51-54, 60-72.

RESPONSE TO PARAGRAPH 99:

The statement is not relevant. Fed. R. Evid. 402. In addition, Plaintiffs have failed to cite admissible evidence which supports this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Isolated DNA molecules are patent eligible subject matter. Doll ¶¶ 26, 34; Linck ¶¶ 14-17, 43, 47, 49; Straus ¶¶ 26, 29-34.

100. The "altered" or "mutated" DNA covered by the patent claims refers to naturally-occurring alterations or mutations in the *BRCA1* and *BRCA2* genes. D. Grody ¶¶ 37-39, 46-48; D. Leonard ¶¶ 57-59, 66-68.

RESPONSE TO PARAGRAPH 100:

Plaintiffs have failed to cite admissible evidence which supports this statement. Fed. R. Evid. 701, 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Paragraph 37 of the declaration of Dr. Grody states that "the terms 'mutated' and 'mutation' inherently mean made by nature and usually inherited from a parent." D. Grody, ¶ 37 Paragraph 66 of the declaration of Dr. Leonard states that "'mutated' means a 'harmful alteration' and does not include non-harmful alterations like polymorphisms. So, a 'mutated' gene is one that is altered in a way that has some harmful effect." D. Leonard ¶ 66.

Isolated DNA molecules are patent eligible subject matter. Doll ¶¶ 26, 34; Linck ¶¶ 14-17, 43, 47, 49; Straus ¶¶ 26, 29-34.

Alterations are defined in these patents as all forms of mutations including deletions, insertions and point mutations in the coding and noncoding regions. Deletions may be of the entire gene or of only a portion of the gene. Point mutations may result in stop codons,

frameshift mutations or amino acid substitutions. Somatic mutations are those which occur only in certain tissues, *e.g.*, in the tumor tissue, and are not inherited in the germline. Germline mutations can be found in any of a body's tissues and are inherited. If only a single allele is somatically mutated, an early neoplastic state is indicated. However, if both alleles are somatically mutated, then a late neoplastic state is indicated. The finding of *BRCA1* mutations thus provides both diagnostic and prognostic information. A *BRCA1* allele which is not deleted (*e.g.*, found on the sister chromosome to a chromosome carrying a *BRCA1* deletion) can be screened for other mutations, such as insertions, small deletions, and point mutations. It is believed that many mutations found in tumor tissues will be those leading to decreased expression of the *BRCA1* gene product. However, mutations leading to non-functional gene products would also lead to a cancerous state. Point mutational events may occur in regulatory regions, such as in the promoter of the gene, leading to loss or diminution of expression of the mRNA. Point mutations may also abolish proper RNA processing, leading to loss of expression of the *BRCA1* gene product, or to a decrease in mRNA stability or translation efficiency. Kay ¶60.

101. Certain of the patent claims cover “analyzing” or looking at the genes. D. Ravicher, Ex. 3 (Patent ‘999 (Claim 1)).

RESPONSE TO PARAGRAPH 101:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

To analyze a sequence of the *BRCA* gene, DNA must be isolated from the sample and sequenced prior to identifying variations in the DNA. Linck ¶ 82.

In the context of the method of claim 1 of the '999 Patent, the term "analyzing a sequence of a *BRCA1* gene or *BRCA1* RNA from a human sample or analyzing a sequence of *BRCA1* cDNA made from mRNA from said human sample with the proviso that said germline alteration is not a deletion of 4 nucleotides corresponding to base numbers 4184-4187 of SEQ ID NO:1" necessarily involves first isolating nucleic acids from a human and determining the sequence of the *BRCA1* gene or portions thereof. Kay ¶70.

102. "Analyzing" a *BRCA1* gene sequence for an alteration, as described in '999 cl. 1, simply refers to any method of looking at a *BRCA1* nucleotide sequence and inherently presumes that the sequence is already provided. There are numerous methods for looking at or analyzing a sequence. D. Grody ¶¶ 43-45; D. Leonard ¶¶ 63-65.

RESPONSE TO PARAGRAPH 102:

The evidence cited by Plaintiffs to support this statement is inadmissible. Fed. R. Evid. 701, 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

To analyze a sequence of the *BRCA* gene, DNA must be isolated from the sample and sequenced prior to identifying variations in the DNA. Linck ¶ 82.

In the context of the method of claim 1 of the '999 Patent, the term "analyzing a sequence of a *BRCA1* gene or *BRCA1* RNA from a human sample or analyzing a sequence of *BRCA1* cDNA made from mRNA from said human sample with the proviso that said germline alteration is not a deletion of 4 nucleotides corresponding to base numbers 4184-4187 of SEQ ID NO:1" necessarily involves first isolating nucleic acids from a human and determining the sequence of the *BRCA1* gene or portions thereof. Kay ¶70.

103. Claim 1 of patent '999 patents looking at the *BRCA1* gene for alterations even if that person used a non-patented methodology to do so, including simply looking at a given sequence and thinking about whether it contains an alteration. Patent '999 (Claim 1).

RESPONSE TO PARAGRAPH 103:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

To analyze a sequence of the *BRCA* gene, DNA must be isolated from the sample and sequenced prior to identifying variations in the DNA. Linck ¶ 82.

In the context of the method of claim 1 of the '999 Patent, the term "analyzing a sequence of a *BRCA1* gene or *BRCA1* RNA from a human sample or analyzing a sequence of *BRCA1* cDNA made from mRNA from said human sample with the proviso that said germline alteration is not a deletion of 4 nucleotides corresponding to base numbers 4184-4187 of SEQ ID NO:1" necessarily involves first isolating nucleic acids from a human and determining the sequence of the *BRCA1* gene or portions thereof. Kay ¶70.

104. Certain of the patent claims cover comparing two genes and then thinking that they are the same or different. D. Ravicher, Exs. 4, 5, 7 ((Patents '001 (Claim 1), '441 (Claim 1), and '857 (Claims 1 and 2)).

RESPONSE TO PARAGRAPH 104:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Myriad's method claims involve several transformative manipulations of tissue or blood and the DNA to detect a genetic mutation in the *BRCA1* or *BRCA2* gene. Thus, the method claims involve "an act, or series of acts, performed upon the subject matter to be transformed and reduced to a different state or thing," and therefore are to statutory subject matter. Linck ¶ 101. The methods of claim 1 of the '001 patent, claim 1 of the '441 patent, and claims 1 and 2 of the '857 patent necessarily involve first isolating nucleic acids from the tissue sample of said subject

and from a wild-type sample from a different human subject and determining the sequence of the *BRCA1* gene or portions thereof from both samples. Kay ¶¶64-67.

105. "Comparing" two genetic sequences, as described in '001 cl. 1, '441 cl. 1, and '857 cls. 1 and 2, means looking at two or more sequences to see if they are different in any way. "Comparing" two sequences inherently presumes that such sequences are already provided. D. Grody ¶¶ 40-42; D. Leonard ¶¶ 60-62.

RESPONSE TO PARAGRAPH 105:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Myriad's method claims involve several transformative manipulations of tissue or blood and the DNA to detect a genetic mutation in the *BRCA1* or *BRCA2* gene. Thus, the method claims involve "an act, or series of acts, performed upon the subject matter to be transformed and reduced to a different state or thing," and therefore are to statutory subject matter. Linck ¶ 101. The methods of claim 1 of the '001 patent, claim 1 of the '441 patent, and claims 1 and 2 of the '857 patent necessarily involve first isolating nucleic acids from the tissue sample of said subject and from a wild-type sample from a different human subject and determining the sequence of the *BRCA1* gene or portions thereof from both samples. Kay ¶¶64-67.

106. Claim 1 of patents '001, '441, and '857 patent the mental process of comparing two given genetic sequences and thinking "these two genes are the same" or "these two genes are different." D. Ravicher, Exs. 4, 5, 7 (Patents '001 (Claim 1), '441 (Claim 1), and '857 (Claims 1 and 2)).

RESPONSE TO PARAGRAPH 106:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Myriad's method claims involve several transformative manipulations of tissue or blood and the DNA to detect a genetic mutation in the *BRCA1* or *BRCA2* gene. Thus, the method claims involve "an act, or series of acts, performed upon the subject matter to be transformed and reduced to a different state or thing," and therefore are to statutory subject matter. Linck ¶ 101. The methods of claim 1 of the '001 patent, claim 1 of the '441 patent, and claims 1 and 2 of the '857 patent necessarily involve first isolating nucleic acids from the tissue sample of said subject and from a wild-type sample from a different human subject and determining the sequence of the *BRCA1* gene or portions thereof from both samples. Kay ¶¶64-67.

107. Claim 2 of '857 patents comparing a gene with the wild-type gene, wherein an alteration in the gene indicates a predisposition to breast cancer. D. Ravicher, Ex. 7 (Patent '857 (Claim 2)).

RESPONSE TO PARAGRAPH 107:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Myriad's method claims involve several transformative manipulations of tissue or blood and the DNA to detect a genetic mutation in the *BRCA1* or *BRCA2* gene. Thus, the method claims involve "an act, or series of acts, performed upon the subject matter to be transformed and reduced to a different state or thing," and therefore are to statutory subject matter. Linck ¶ 101. The methods of claim 1 of the '001 patent, claim 1 of the '441 patent, and claims 1 and 2 of the '857 patent necessarily involve first isolating nucleic acids from the tissue sample of said subject and from a wild-type sample from a different human subject and determining the sequence of the *BRCA1* gene or portions thereof from both samples. Kay ¶¶64-67.

108. Claim 2 of patent '857 patents the mental process of comparing two genes and recognizing that an alteration in the gene "indicates a predisposition to" breast cancer. *Id*. Patent '857 (Claim 2).

RESPONSE TO PARAGRAPH 108:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Myriad's method claims involve several transformative manipulations of tissue or blood and the DNA to detect a genetic mutation in the *BRCA1* or *BRCA2* gene. Thus, the method claims involve "an act, or series of acts, performed upon the subject matter to be transformed and reduced to a different state or thing," and therefore are to statutory subject matter. Linck ¶ 101. The methods of claim 1 of the '001 patent, claim 1 of the '441 patent, and claims 1 and 2 of the '857 patent necessarily involve first isolating nucleic acids from the tissue sample of said subject and from a wild-type sample from a different human subject and determining the sequence of the *BRCA1* gene or portions thereof from both samples. Kay ¶¶64-67.

109. Patents on correlations or associations between a gene sequence and a greater risk of disease allow the patent holder to control the use of that medical fact. D. Leonard ¶ 19.

RESPONSE TO PARAGRAPH 109:

The evidence cited by Plaintiffs to support this statement is inadmissible. Fed. R. Evid. 701, 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Myriad's claimed methods are not based on a mathematical algorithm but rather on the application of their discovery that a particular DNA sequence is associated with certain cancers to provide a diagnostic tool for such cancers. Linck ¶ 103.

110. Claim 20 of '282 patents an abstract method for comparing cell growth rates to screen for a possible cancer therapeutic. The claim covers comparing the growth rates of two cells contained an altered *BRCA1* gene, one of which has been exposed to the possible cancer therapeutic. Patent '282 (Claim 20).

RESPONSE TO PARAGRAPH 110:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

In the context of the method of claim 20 of the '282 Patent, the term "comparing the growth rate of said host cells" and wherein one host cell is a "transformed eukaryotic host cell" necessarily involves first transforming the cells, i.e., introducing a polynucleotide into the cell. Kay ¶63; Linck ¶ 84.

111. The act of comparing covered by '282 claim 20 means simply looking at two or more things – such as cells – to determine if there is a difference between them – such as growth rates. *See* D. Grody ¶¶ 40-42; D. Leonard ¶¶ 60-62.

RESPONSE TO PARAGRAPH 111:

The evidence cited by Plaintiffs to support this statement is inadmissible. Fed. R. Evid. 701, 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

In the context of the method of claim 20 of the '282 Patent, the term "comparing the growth rate of said host cells" and wherein one host cell is a "transformed eukaryotic host cell" necessarily involves first transforming the cells, i.e., introducing a polynucleotide into the cell. Kay ¶63; Linck ¶ 84.

112. Claim 20 of patent '282 patents the mental process of comparing the cell growth rates and "this chemical had a therapeutic impact" on a cell with a *BRCA1* altered gene or "this chemical did not have a therapeutic impact." D. Ravicher, Ex. 1 (Patent '282 (Claim 20)).

RESPONSE TO PARAGRAPH 112:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

In the context of the method of claim 20 of the '282 Patent, the term "comparing the growth rate of said host cells" and wherein one host cell is a "transformed eukaryotic host cell" necessarily involves first transforming the cells, i.e., introducing a polynucleotide into the cell. Kay ¶63; Linck ¶ 84.

113. The USPTO granted these patent claims pursuant to a formal written policy that permits the patenting of "isolated and purified" genes and pursuant to a practice that permits such patents and the patenting of correlations created by nature between natural elements of the body and a predisposition to disease. Utility Examination Guidelines, 66 Fed. Reg. 1,093 (Jan. 5, 2001).

RESPONSE TO PARAGRAPH 113:

Disputed.

"Isolated" DNA molecules do not occur in nature and are different from the complex naturally occurring native DNA. *See* the legal analysis in the 1995 Utility Guidelines in effect when the Myriad's patents issued. Linck ¶ 47; Doll ¶ 27-29.

114. It is scientifically inaccurate to compare DNA and genes to chemicals. One cannot "invent" a slightly different gene than that which occurs in nature – whether natural or mutated – in the way that one can invent a slightly different chemical. Because one can invent around chemicals, i.e. can synthetically produce new and better chemicals, but cannot invent around genes, they are not comparable. D. Jackson ¶¶ 12-16, 49.

RESPONSE TO PARAGRAPH 114:

Dr. Jackson is not qualified by training or experience to testify as an expert in the area of science and patents. As a result, the evidence cited by Plaintiffs is not admissible. Fed. R. Evid. 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

The ability to invent around an invention is *not* a statutory patentability requirement nor is it an underlying purpose of the patent system. Doll ¶ 49; Linck ¶ 271. DNA, which stands for deoxyribonucleic acid, is a type of chemical compound called a nucleic acid. Kay ¶125.

115. The dye that was declared unpatentable in *Cochrane v. Badische*, 111 U.S. 293 (1884), is scientifically analogous to the patent claims at issue in this case. In both instances, the patent sought was over a product, not a process, and in both instances, the product is functionally identical to the product in nature. D. Jackson ¶¶ 7-16.

RESPONSE TO PARAGRAPH 115:

Dr. Jackson is not qualified by training or experience to testify as an expert in the area of science and patents. As a result, the evidence cited by Plaintiffs is not admissible. Fed. R. Evid. 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

In Cochrane, the court's holding of invalidity of the reissue patent was based, in part, on the fact that artificial alizarine synthetically produced was identical in its properties and composition to alizarine previously produced by other methods. Linck ¶ 63.

116. As with *Cochrane*, the paper pulp that was declared unpatentable in *The Wood- Paper Patent*, 90 U.S. 566 (1874), is scientifically analogous to the patent claims at issue in this case. Even though the pulp in that patent was superior in purity to previous wood pulp, it was identical in function. D. Jackson ¶¶ 17-25.

RESPONSE TO PARAGRAPH 116:

Dr. Jackson is not qualified by training or experience to testify as an expert in the area of science and patents. As a result, the evidence cited by Plaintiffs is not admissible. Fed. R. Evid. 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

The pulp product claimed in Wood-Paper had been in common public use and the court's holding turned on the "novelty" statutory requirement. Linck ¶ 63.

117. The adrenaline that was declared patentable in *Parke-Davis and Co. v. H.K. Mulford*, 189 F. 95 (S.D.N.Y. 1911), *aff'd* 196 F.496 (2nd Cir. 1912), is not scientifically analogous to the patent claims at issue in this case because the process for purifying the adrenaline relies solely on human intervention, while genes and their splicing can occur naturally without human intervention. D. Jackson ¶¶ 26-31.

RESPONSE TO PARAGRAPH 117:

Dr. Jackson is not qualified by training or experience to testify as an expert in the area of science and patents. As a result, the evidence cited by Plaintiffs is not admissible. Fed. R. Evid. 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Like the purified adrenaline of *Parke-Davis*, the isolated DNA molecules of the Myriad claims are different "in kind" from naturally occurring counterparts. Linck ¶ 51.

118. The bacteria grouping that was declared unpatentable in *Funk Brothers v. Kalo*, 333 U.S. 127 (1948), is scientifically analogous to the patent claims at issue in this case because the bacteria grouping, though structurally different from any grouping found in nature, continued to perform in their natural way, just as the patented genes function in the same way as genes in nature. D. Jackson ¶¶ 32-34.

RESPONSE TO PARAGRAPH 118:

Dr. Jackson is not qualified by training or experience to testify as an expert in the area of science and patents. As a result, the evidence cited by Plaintiffs is not admissible. Fed. R. Evid. 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

The Supreme Court in *Funk* recognized that the claims covered a new composition but denied the patent because it found the combination of bacteria to be an obvious combination of known, commercially available products. Linck ¶ 42.

119. The patented B-12 in *Merck and Co. v. Olin Mathieson*, 253 F.2d 156 (4th Cir. 1958) is not scientifically analogous to the patent claims at issue in this case. The B-12 patent did not cover all uses of B-12 but the patent claims here cover all uses of the genes. In addition, the function of the patented B-12 was different from that found in nature, while the function of the patented genes in this case is identical to that found in nature. D. Jackson ¶¶ 35-37.

RESPONSE TO PARAGRAPH 119:

Dr. Jackson is not qualified by training or experience to testify as an expert in the area of science and patents. As a result, the evidence cited by Plaintiffs is not admissible. Fed. R. Evid. 702. In addition, the evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Paragraph 37 of the declaration by Dr. Jackson states that "the patent in that case did not cover all *forms* of the vitamin" (emphasis added). Jackson ¶ 37.

The ability to invent around an invention is not a statutory patentability requirement nor is it an underlying purpose of the patent system. Doll ¶ 49; Linck ¶ 271. Isolated DNA is very much *informationally* different in kind from native DNA and mRNA. Kay ¶172; Doll ¶¶ 27-29. Once a DNA molecule is isolated, it gains new properties. Kay ¶134; Linck ¶ 47; Doll ¶¶ 27-30.

120. The tungsten that was declared unpatentable in *G.E. v. De Forest Radio*, 28 F.2d 641 (3rd Cir. 1928), is scientifically analogous to the patent claims at issue in this case. Purification of tungsten was insufficient to alter the fact that the function of the tungsten, like the functions of genes, was dictated by nature and it was therefore unpatentable. D. Jackson ¶¶ 38- 40.

RESPONSE TO PARAGRAPH 120:

Dr. Jackson is not qualified by training or experience to testify as an expert in the area of science and patents. As a result, the evidence cited by Plaintiffs is not admissible. Fed. R. Evid. 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

In *General Electric*, the issue of patentability of tungsten turned on the "novelty" requirement. As the court properly notes, in *General Electric*, the patentee had not sought a patent for a "new" composition of matter. Rather, patentee had claimed a product that later proved to be tungsten – an old product. Linck ¶ 65.

121. The new bacterium that was declared patentable in *Diamond v. Chakrabarty*, 447 U.S. 303 (1980), is not scientifically analogous to the patent claims at issue in this case. The bacterium was newly created and genetically engineered. D. Jackson ¶ 41.

RESPONSE TO PARAGRAPH 121:

Dr. Jackson is not qualified by training or experience to testify as an expert in the area of science and patents. As a result, the evidence cited by Plaintiffs is not admissible. Fed. R. Evid. 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Isolated DNA molecules are patent eligible subject matter. Doll ¶¶ 26, 34; Linck ¶¶ 14-17, 43, 47 49; Straus ¶¶ 26, 29-34.

122. The mathematical algorithms that were declared unpatentable in *Parker v. Flook*, 437 U.S. 584 (1978) and *Gottschalk v. Benson*, 409 U.S. 63 (1972) are scientifically analogous to the patent claims at issue in this case. The patent claims in those cases attempted to preclude all uses of the algorithms just as the gene "composition" claims in this case preclude all uses of the genes and the method claims prevent all methods of comparing genes. D. Jackson ¶¶ 42-45, 47-48.

RESPONSE TO PARAGRAPH 122:

Dr. Jackson is not qualified by training or experience to testify as an expert in the area of science and patents. As a result, the evidence cited by Plaintiffs is not admissible. Fed. R. Evid. 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Myriad's method claims do not involve a mathematical algorithm as that term was used in *Benson* and *Flook* or a software program for performing a mathematical algorithm. Neither do they involve pure information. Rather, they involve chemical molecules that are capable of many complex reactions yet to be fully understood, including replication, transcription and translation. Linck ¶ 97.

123. The mathematical algorithm that was declared unpatentable in *Diamond v. Diehr*, 450 U.S. 175 (1981) is not scientifically analogous to the patent claims at issue in this case for the opposite reason. It did not preclude all uses of the algorithm. D. Jackson ¶¶ 46-48.

RESPONSE TO PARAGRAPH 123:

Dr. Jackson is not qualified by training or experience to testify as an expert in the area of science and patents. As a result, the evidence cited by Plaintiffs is not admissible. Fed. R. Evid. 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

The evidence offered by Plaintiffs does not support this statement.

The claimed subject matter in *Diehr* was a process for curing rubber which included a mathematical algorithm and a programmed digital computer. Respondents did not seek a patent on a mathematical algorithm but rather on a process for curing rubber. Recognizing that "an application of a law of nature or mathematical algorithm to a known structure or process may well be deserving of patent protection," id., the Court held Diehr's claims eligible for patenting.

Similarly, Myriad's method claims are to an application of a law of nature—a method for detecting a germline alteration linked to breast and ovarian cancer—and not to the law of nature itself. Linck ¶ 104. The ability to invent around an invention is not a statutory patentability requirement nor is it an underlying purpose of the patent system. Doll ¶ 49; Linck ¶ 271.

124. A specific method used to sequence genes is a process that could be patented if it met other patentability requirements. Patents on processes do not apply to the data - such as the genes - flowing through them. This is analogous to claiming a small thing viewed through the common microscope. D. Leonard ¶ 17; D. Sulston ¶ 23.

RESPONSE TO PARAGRAPH 124:

The evidence cited by Plaintiffs to support this statement is inadmissible. Fed. R. Evid. 402, 701, 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

The claimed isolated *BRCA1* or *BRCA2* DNA molecules of the Myriad patents are chemical compositions that have a specific utility, *e.g.*, molecular diagnostics. Linck ¶ 45.

ENFORCEMENT OF PATENTS

125. Dr. Kazazian and the University of Pennsylvania received several cease and desist letters from defendant Myriad as a result of work that was being done in the Genetic Diagnostic Laboratory of the Department of Genetics. Dr. Kazazian was also told by defendant Myriad's Chief Science Officer during an in-person meeting that Myriad planned to stop the *BRCA* testing activity that Dr. Ganguly and he were performing. In November 1998, Myriad sued the University of Pennsylvania for infringing the *BRCA* patents. *Myriad Genetics v. University of Pennsylvania,* 2:98-cv-00829 (D. Utah) (filed November 19, 1998). As a result, the laboratory directed by Dr. Kazazian was and is prohibited from doing routine screening for *BRCA1* and *BRCA2* genes for research or part of clinical practice without Myriad's permission as a direct result of the patents challenged by this action. D. Kazazian ¶¶ 4-7; D. Ganguly ¶¶ 4-10; D. Parthasarathy ¶ 28.

RESPONSE TO PARAGRAPH 125:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

It has been, and still is, Myriad's policy and practice to allow scientists to conduct research studies on the *BRCA1* and *BRCA2* genes freely. Critchfield ¶¶3; Li ¶¶ 3-6; Baer ¶¶ 3-6; Parvin ¶ 3-6; Sandbach¶¶ 3-7. During a personal meeting with Plaintiff Dr. Haig Kazazian sometime between 1999 and 2000, Dr. Critchfield told Dr. Kazazian that he is free to do academic research on the *BRCA1* and *BRCA2* genes including sequencing the genes and detecting mutations in the genes. Critchfield ¶ 22. The commercial nature of Dr. Kazazian's *BRCA*-related activities in the 1990s has been readily admitted by Dr. Kazazian. Kazazian ¶8.

On or about May 29, 1998, Myriad sent a letter to Dr. Kazazian. The letter offered a collaborative license to the University of Pennsylvania Medical Center to perform *BRCA1* testing in connection with United States Patent Numbers 5,693,473 (the "'473 patent"); 5,709,999 (the "'999 patent"); 5,710,001 (the "'001 patent") 5,747,282 (the "'282 patent"); and 5,753,441 (the "'441 patent"). D. Ganguly, Exh. 2.

On or about August 26, 1998, O'Melveny & Myers LLP sent a letter to Dr. Kazazian. The letter states that Dr. Kazazian is "engaged in commercial testing activities that infringe Myriad's patents" and that such activities should be ceased "[u]nless and until such a license arrangement is complete." D. Ganguly, Exh. 3.

The general counsel of the University of Pennsylvania advised Dr. Kazazian to stop *BRCA* commercial testing. D. Kazazian, ¶7.

126. Dr. Kazazian and Dr. Ganguly were screening for *BRCA* mutations using a different methodology than that used by Myriad, but were precluded from using that methodology by Myriad because the patents are on the genes themselves, not on the methodology for screening. D. Kazazian ¶ 9; D. Parthasarathy ¶ 23.

RESPONSE TO PARAGRAPH 126:

The evidence cited by Plaintiffs to support this statement is inadmissible. Fed. R. Evid. 701, 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

It has been, and still is, Myriad's policy and practice to allow scientists to conduct research studies on the *BRCA1* and *BRCA2* genes freely. Critchfield ¶¶3; Li ¶¶ 3-6; Baer ¶¶ 3-6; Parvin ¶ 3-6; Sandbach¶¶ 3-7. During a personal meeting with Plaintiff Dr. Haig Kazazian sometime between 1999 and 2000, Dr. Critchfield told Dr. Kazazian that he is free to do academic research on the *BRCA1* and *BRCA2* genes including sequencing the genes and detecting mutations in the genes. Critchfield ¶ 22. The commercial nature of Dr. Kazazian's *BRCA*-related activities in the 1990s has been readily admitted by Dr. Kazazian. Kazazian ¶8.

On or about May 29, 1998, Myriad sent a letter to Dr. Kazazian. The letter offered a collaborative license to the University of Pennsylvania Medical Center to perform *BRCA1* testing in connection with United States Patent Numbers 5,693,473 (the "'473 patent"); 5,709,999 (the "'999 patent"); 5,710,001 (the "'001 patent") 5,747,282 (the "'282 patent"); and 5,753,441 (the "'441 patent"). D. Ganguly, Exh. 2.

On or about August 26, 1998, O'Melveny & Myers LLP sent a letter to Dr. Kazazian. The letter states that Dr. Kazazian is "engaged in commercial testing activities that infringe Myriad's patents" and that such activities should be ceased "[u]nless and until such a license arrangement is complete." D. Ganguly, Exh. 3.

The general counsel of the University of Pennsylvania advised Dr. Kazazian to stop *BRCA* commercial testing. D. Kazazian, ¶7.

The claimed isolated *BRCA1* or *BRCA2* DNA molecules of the Myriad patents are chemical compositions that have a specific utility, *e.g.*, molecular diagnostics. Linck ¶ 45.

127. Myriad sent a letter to Barbara Weber, principal investigator on a project sponsored by the National Cancer Institute, regarding how Myriad's patent position might impact research sponsored by the Institute. As a result of that letter, the University of Pennsylvania laboratory that was doing *BRCA* analyses for Dr. Weber, stopped doing those analyses. D. Ganguly ¶ 12.

RESPONSE TO PARAGRAPH 127:

The evidence cited by Plaintiffs to support this statement is inadmissible. Fed. R. Evid. 602, 802. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

The *BRCA* testing by Dr. Ganguly offered to the Cancer Genetics Network Project led by Dr. Barbara Weber was commercial in nature and not research. D. Ganguly ¶¶ 12, 13. The principal involvement by Dr. Ganguly in the Project was conducting DNA testing on the *BRCA1* and *BRCA2* genes for fees. D. Ganguly ¶¶ 12, 13. The Genetic Diagnostic Laboratory was acting as a core testing lab just like other commercial core labs. Critchfield ¶ 21.

128. Myriad sent a letter to Georgetown University demanding that Georgetown stop sending genetic samples to the University of Pennsylvania laboratory. As a result of that letter, the University of Pennsylvania laboratory that was doing *BRCA* analyses for Georgetown stopped doing those analyses. D. Ganguly ¶ 13.

RESPONSE TO PARAGRAPH 128:

The evidence cited by Plaintiffs to support this statement is inadmissible. Fed. R. Evid. 602, 802. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

It has been, and still is, Myriad's policy and practice to allow scientists to conduct research studies on the *BRCA1* and *BRCA2* genes freely. Critchfield ¶¶3; Li ¶¶ 3-6; Baer ¶¶ 3-6;

Parvin ¶ 3-6; Sandbach¶¶ 3-7. During a personal meeting with Plaintiff Dr. Haig Kazazian sometime between 1999 and 2000, Dr. Critchfield told Dr. Kazazian that he is free to do academic research on the *BRCA1* and *BRCA2* genes including sequencing the genes and detecting mutations in the genes. Critchfield ¶ 22. The commercial nature of Dr. Kazazian's *BRCA*-related activities in the 1990s has been readily admitted by Dr. Kazazian. Kazazian ¶8.

129. Myriad and Oncormed, another company that undertook *BRCA*-related activity, were involved in a series of lawsuits against each other regarding patents that covered various aspects of the *BRCA1* gene sequence. D. Parthasarathy ¶ 27.

RESPONSE TO PARAGRAPH 129:

The evidence cited by Plaintiffs to support this statement is inadmissible. Fed. R. Evid.602, 701, 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

130. Sometime in or around December 2000, the director of the Yale DNA Diagnostics Lab received a cease and desist letter from Myriad concerning *BRCA1/2* genes. As a result of that letter, Yale ceased doing *BRCA1/2* testing. D. Matloff ¶ 7.

RESPONSE TO PARAGRAPH 130:

The evidence cited by Plaintiffs to support this statement is inadmissible. Fed. R. Evid. 802. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Testing for specific *BRCA* mutations is available in both the University of Chicago Genetic Services Laboratories and Yale DNA Diagnostic Laboratories. Critchfield ¶ 62.

131. In 2005, Ms. Matloff contacted Myriad to obtain permission so that the Yale DNA Diagnostic Lab could do screening for mutations caused by large rearrangements, which Myriad was not then doing. Myriad denied permission. D. Matloff ¶ 8.

RESPONSE TO PARAGRAPH 131:

The statement is not relevant. Fed. R. Evid. 402. Because Plaintiffs have failed to offer admissible evidence to support this statement, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

It has been, and still is, Myriad's policy and practice to allow scientists to conduct research studies on the *BRCA1* and *BRCA2* genes freely. Critchfield ¶¶3; Li ¶¶ 3-6; Baer ¶¶ 3-6; Parvin ¶ 3-6; Sandbach¶¶ 3-7. During a personal meeting with Plaintiff Dr. Haig Kazazian sometime between 1999 and 2000, Dr. Critchfield told Dr. Kazazian that he is free to do academic research on the *BRCA1* and *BRCA2* genes including sequencing the genes and detecting mutations in the genes. Critchfield ¶ 22. The commercial nature of Dr. Kazazian's *BRCA*-related activities in the 1990s has been readily admitted by Dr. Kazazian. Kazazian ¶8.

132. Myriad wrote to Dr. Ostrer prohibiting him from engaging in any *BRCA1* or *BRCA2* testing unless he entered a license, and even then the company would only allow him to do all but the most limited *BRCA1* and *BRCA2* testing. Dr. Ostrer refused that license because it was too narrow to allow him to do any meaningful *BRCA*-related activity. D. Ostrer ¶ 7.

RESPONSE TO PARAGRAPH 132:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

Disputed.

Dr. Osterer states in his declaration that "Myriad was offering [him] a very limited license only to do single mutation tests and multiple mutation panels (up to four mutations) for patients of Ashkenazi Jewish descent." Osterer ¶ 7.

133. A valid scientific survey of laboratory directors in the United States revealed that 25% had stopped performing a clinical test because of a gene patent or license. D. Cho ¶¶ 11-15.

RESPONSE TO PARAGRAPH 133:

The statement is not relevant. In addition, the evidence cited by Plaintiffs does not support this statement. Further, the evidence cited by Plaintiffs is inadmissible. Fed. R. Evid. 402, 702, 802. Because Plaintiffs have failed to cite admissible evidence to support this statement, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Patents such as the patents-in-suit have served to advance research and the practice of medicine and benefit patients. Reilly ¶¶38, 43; Critchfield ¶¶ 2-18, 65, 68; Linck ¶¶ 27-28, 71, 73; Tavtigian ¶¶ 14-17; Doll ¶¶ 45-49; Bone ¶¶ 10-11; Frieder ¶ 13; Schlessinger ¶¶ 31-32.

134. A valid scientific survey of laboratory directors in the United States revealed that of those who stopped performing a clinical test because of a gene patent or license, the largest number stopped doing *BRCA1* and *BRCA1* testing (and the same number stopped ApoE testing). D. Choi ¶ 16.

RESPONSE TO PARAGRAPH 134:

The statement is not relevant. In addition, the evidence cited by Plaintiffs does not support this statement. Further, the evidence cited by Plaintiffs is inadmissible. Fed. R. Evid. 402, 702, 802. Because Plaintiffs have failed to cite admissible evidence which supports this statement, Defendants need not offer contradictory evidence. Local Civil Rule 56.1; and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Paragraph 16 of the declaration of Dr. Cho states that "[m]ore laboratories had stopped performing *BRCA1* and *BRCA2* tests than any other test, with the exception of Apolipoprotein E," without giving the reason "because of a gene patent or license."

Patents such as the patents-in-suit have served to advance research and the practice of medicine and benefit patients. Reilly ¶¶38, 43; Critchfield ¶¶ 2-18, 65, 68; Linck ¶¶ 27-28, 71, 73; Tavtigian ¶¶ 14-17; Doll ¶¶ 45-49; Bone ¶¶ 10-11; Frieder ¶ 13; Schlessinger ¶¶ 31-32.

135. Nine labs reported that they had stopped performing tests for *BRCA1* and *BRCA2* in response to a valid scientific survey of laboratory directors in the United States. D. Cho ¶ 16.

RESPONSE TO PARAGRAPH 135:

The statement is not relevant. In addition, the evidence cited by Plaintiffs does not support this statement. Further, the evidence cited by Plaintiffs is inadmissible. Fed. R. Evid. 402, 702, 802. Because Plaintiffs have failed to cite admissible evidence which supports this statement, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Patents such as the patents-in-suit have served to advance research and the practice of medicine and benefit patients. Reilly ¶¶38, 43; Critchfield ¶¶ 2-18, 65, 68; Linck ¶¶ 27-28, 71, 73; Tavtigian ¶¶ 14-17; Doll ¶¶ 45-49; Bone ¶¶ 10-11; Frieder ¶ 13; Schlessinger ¶¶ 31-32.

136. Labs have avoided or refrained from developing tests for *BRCA1* or *BRCA2* as a direct result of the gene patents held by Myriad. D. Ostrer ¶ 6; D. Ledbetter ¶¶ 14-16.

RESPONSE TO PARAGRAPH 136:

The statement is not relevant. In addition, the evidence offered by Plaintiffs does not support this statement. Further, the evidence offered by Plaintiffs is inadmissible. Fed. R. Evid. 402, 701, 702. Because Plaintiffs have failed to cite admissible evidence which supports this statement, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Paragraph 16 of the declaration of Dr. Ledbetter states that "[o]ur lab explicitly avoided the *BRCA1* and *BRCA2* genes," without giving the reason "as a direct result of the gene patents held by Myriad." Ledbetter ¶ 16.

It has been, and still is, Myriad's policy and practice to allow scientists to conduct research studies on the *BRCA1* and *BRCA2* genes freely. Critchfield ¶¶3; Li ¶¶ 3-6; Baer ¶¶ 3-6; Parvin ¶ 3-6; Sandbach¶¶ 3-7.

137. Other studies of other gene patents also reveal that labs frequently stop developing or offering clinical tests for disease as a result of gene patents. In a valid scientific survey of labs in the United States, 26% stopped doing testing for hemochromatosis as a result of gene patents. D. Cho ¶¶ 17-20.

RESPONSE TO PARAGRAPH 137:

The statement is not relevant. In addition, the evidence cited by Plaintiffs does not support this statement. Further, the evidence cited by Plaintiffs is inadmissible. Fed. R. Evid. 402, 701, 702. Because Plaintiffs have failed to cite admissible evidence which supports this statement, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Paragraph 16 of the declaration of Dr. Ledbetter states that "[o]ur lab explicitly avoided the *BRCA1* and *BRCA2* genes," without giving the reason "as a direct result of the gene patents held by Myriad." Ledbetter ¶ 16.

It has been, and still is, Myriad's policy and practice to allow scientists to conduct research studies on the *BRCA1* and *BRCA2* genes freely. Critchfield ¶¶3; Li ¶¶ 3-6; Baer ¶¶ 3-6; Parvin ¶ 3-6; Sandbach¶¶ 3-7.

138. Researchers, clinicians, and pathologists are aware that Myriad has sent cease and desist letters over the patent claims at issue in this case or are aware that it prohibits virtually all clinical testing of the *BRCA1/2* genes. D. Kazazian ¶¶ 5-11; D. Ganguly ¶¶ 4-14; D. Chung ¶ 15; D. Hegde ¶ 10; D. Matloff ¶¶ 5-7; D. Ostrer, ¶¶ 4-7; D. Swisher ¶ 28; D.

Hubbard ¶¶ 7-8; D. Kant ¶ 4; D. Ledbetter ¶ 13; D. Reich ¶¶ 3, 5; D. Parthasarathy ¶¶ 28-31.

RESPONSE TO PARAGRAPH 138:

The statement is not relevant. In addition, the evidence cited by Plaintiffs does not support this statement. Further, the evidence cited by Plaintiffs is inadmissible. Fed. R. Evid. 402, 701, 702. Because Plaintiffs have failed to cite admissible evidence which supports this statement, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Paragraph 16 of the declaration of Dr. Ledbetter states that "[o]ur lab explicitly avoided the *BRCA1* and *BRCA2* genes," without giving the reason "as a direct result of the gene patents held by Myriad." Ledbetter ¶ 16.

It has been, and still is, Myriad's policy and practice to allow scientists to conduct research studies on the *BRCA1* and *BRCA2* genes freely. This has been commonly understood by academic scientists in the field. Critchfield ¶¶3; Li ¶¶ 3-6; Baer ¶¶ 3-6; Parvin ¶ 3-6; Sandbach¶¶ 3-7.

139. Researchers, clinicians, and pathologists are prohibited from sequencing and analyzing the *BRCA1* and *BRCA2* genes because of the patents at issue in this case. D. Ganguly ¶ 14; D. Chung ¶¶ 13, 17, 18; D. Ostrer ¶¶ 6-8; D. Hegde ¶ 10; D. Swisher ¶¶ 34-35; D. Hubbard ¶ 9; D. Kant ¶ 6; D. Ledbetter ¶¶ 16, 18; D. Reich ¶¶ 3, 5.

RESPONSE TO PARAGRAPH 139:

The evidence cited by Plaintiffs does not support this statement. Further, the evidence cited by Plaintiffs is inadmissible. Because Plaintiffs have failed to cite admissible evidence which supports this statement, Defendants need not offer contradictory evidence. Fed. R. Evid. 701, 702; Local Civil Rule 56.1; and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Paragraph 16 of the declaration of Dr. Ledbetter states that "[o]ur lab explicitly avoided the *BRCA1* and *BRCA2* genes," without giving the reason "as a direct result of the gene patents held by Myriad." Ledbetter ¶ 16.

It has been, and still is, Myriad's policy and practice to allow scientists to conduct research studies on the *BRCA1* and *BRCA2* genes freely. This has been commonly understood by academic scientists in the field. Critchfield ¶¶3; Li ¶¶ 3-6; Baer ¶¶ 3-6; Parvin ¶ 3-6; Sandbach¶¶ 3-7.

140. Myriad does not permit researchers to tell patients involved in research the results of their *BRCA1/2* testing. D. Ostrer ¶ 10; D. Chung ¶ 13.

RESPONSE TO PARAGRAPH 140:

The statement is not relevant. In addition, the evidence cited by Plaintiffs does not support this statement. Further, the evidence cited by Plaintiffs is inadmissible. Fed. R. Evid. 402, 602. Because Plaintiffs have failed to cite admissible evidence which supports this statement, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

The majority of academic researchers operating laboratories (as opposed to CLIA-certified laboratories) do not believe that they should share test results with subjects outside of the standard clinical setting. Reilly ¶¶ 57-59.

141. The *BRCA1/2* patents prevent physicians from testing for breast and ovarian cancer genetic risk (*BRCA1/2* sequencing). D. Leonard ¶ 14; D. Swisher ¶ 34

RESPONSE TO PARAGRAPH 141:

The evidence cited by Plaintiffs to support this statement is inadmissible. Fed. R. Evid. 701, 702, 802. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

EFFECTS OF *BRCA1/2* GENE PATENTS

142. For a period of years, the testing done by Myriad did not reveal all known mutations in the *BRCA1* and *BRCA2* genes or utilize known methodologies that would have revealed those additional mutations. D. Chung ¶ 19; D. Matloff ¶ 8; D. Swisher ¶ 26; D. Limary ¶ 7; D. Thomason ¶ 6; D. Raker ¶¶ 7-8; D. Ledbetter ¶ 16; D. Parthasarathy ¶ 29.

RESPONSE TO PARAGRAPH 142:

Disputed.

In the late 1990s, Myriad and the research community recognized the need for testing "large rearrangements" in the *BRCA1* and *BRCA2* genes. Large genomic rearrangements occur in a small percentage of all patients tested for hereditary breast and ovarian cancer. Nevertheless, Myriad immediately began researching and developing a commercially viable high quality process for detecting large rearrangements in the genes. As a result, in 2002 Myriad supplemented its full sequencing analysis with a large rearrangement panel (LRP) for detecting five common large rearrangement mutations. Since then, Myriad has included the LRP panel in every comprehensive BRAC*Analysis*® test it performs. In the meantime, Myriad continued its research and development work with a goal to provide a test that could detect all large rearrangement mutations, even those extremely rare ones. The commercially available MLPA (Multiplex Ligation dependent Probe Amplification) kit often used by academic researchers is for research use only and not approved for clinical testing by the FDA. Moreover, it is incapable of detecting certain rearrangements with smaller sizes. Critchfield ¶¶ 49, 50.

143. During this period, people who received Myriad's test may have gotten false negative results. A scientifically valid study from 2006 concluded that 12% of those from high risk families with breast cancer and with negative test results from Myriad carried cancer-predisposing genomic deletions or duplications in one of those genes. This result reinforced other similar studies done over the years. D. Swisher ¶¶ 25-26.

RESPONSE TO PARAGRAPH 143:

Disputed.

Myriad's full sequencing test has been recognized as the "gold standard" for *BRCA* mutation testing. Critchfield ¶ 37. Myriad has been continuously improving its testing process. Critchfield ¶ 37.

144. The Myriad test that Ms. Thomason, Ms. Raker, and Ms. Limary received did not look for all known large rearrangements in the *BRCA* genes. D. Thomason ¶ 6; D. Raker ¶¶ 7-8; D. Limary ¶ 7.

RESPONSE TO PARAGRAPH 144:

Plaintiffs have failed to cite admissible evidence which supports this statement. Fed. R. Evid. 802. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Myriad's full sequencing test has been recognized as the "gold standard" for *BRCA* mutation testing. Critchfield ¶ 37. Myriad has been continuously improving its testing process. Critchfield ¶ 37.

145. Myriad now offers a separate test called BART which looks for additional large rearrangements in the coding sequences of both *BRCA1* and *BRCA2*. This test is offered with the standard test for a limited number of women, but most women must pay an extra fee for it. D. Swisher ¶¶ 29-30; D. Reich ¶ 10; D. Matloff ¶ 14.

RESPONSE TO PARAGRAPH 145:

The statement is not relevant. Fed. R. Evid. 402. Because Plaintiffs have failed to cite admissible evidence to support this statement, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

BART is a complex test with a high cost associated with it, and large genomic rearrangements occur in a small percentage of all patients tested for hereditary breast and ovarian cancer. Nevertheless, Myriad has made BART™ available to all patients who want to be tested. At the present time, for high risk patients, BART™ is performed together with our full sequencing analysis and LRP (for common large rearrangements) at no additional charge. For low risk patients who do not meet certain clinical criteria developed based on published literature, BART™ is also available at a cost. Today, Myriad is still investing heavily to develop a new version of BART™ with a significantly lowered cost and increased efficiency. Myriad is striving to provide an improved BART™ that is commercially viable to all patients at little cost. Critchfield ¶¶ 52, 53.

146. The BART test is not available to many women who should have access to it as a result of the strict criteria Myriad has adopted and the price Myriad charges for the test. Myriad's standard way of offering genetic testing is a partial testing strategy because it does not reflexively offer large rearrangement testing for all women who receive negative full sequencing test results. D. Swisher ¶¶ 30-31, 33; D. Reich ¶ 10; D. Matloff ¶ 14; D. Ledbetter ¶ 16.

RESPONSE TO PARAGRAPH 146:

The statement is not relevant. Fed. R. Evid. 402. Because Plaintiffs have failed to cite admissible evidence to support this statement, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

BART is a complex test with a high cost associated with it, and large genomic rearrangements occur in a small percentage of all patients tested for hereditary breast and ovarian cancer. Nevertheless, Myriad has made BART™ available to all patients who want to be tested. At the present time, for high risk patients, BART™ is performed together with our full sequencing analysis and LRP (for common large rearrangements) at no additional charge. For

low risk patients who do not meet certain clinical criteria developed based on published literature, BART™ is also available at a cost. Today, Myriad is still investing heavily to develop a new version of BART™ with a significantly lowered cost and increased efficiency. Myriad is striving to provide an improved BART™ that is commercially viable to all patients at little cost. Critchfield ¶¶ 52, 53.

147. The sensitivity and specificity of BART has never been fully and independently validated. D. Swisher ¶ 32.

RESPONSE TO PARAGRAPH 147:

The statement is not relevant. Fed. R. Evid. 402. Because Plaintiffs have failed to cite admissible evidence to support this statement, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

The commercially available MLPA (Multiplex Ligation-dependent Probe Amplification) kit often used by academic researchers is for research use only and not approved by the FDA. Moreover, it is incapable of detecting certain rearrangements in smaller sizes. Critchfield ¶ 50. In studies by outside researchers, BART™ has exhibited superior performance over other methods including MLPA. Critchfield ¶ 51.

148. Other methods for looking for *BRCA* large rearrangements, such as one called MLPA, are performed around the world. Myriad has never published comparisons of BART with MLPA. D. Swisher ¶ 33.

RESPONSE TO PARAGRAPH 148:

The statement is not relevant. In addition, the evidence cited by Plaintiffs is inadmissible. Fed. R. Evid. 402, 602. Because Plaintiffs have failed to cite admissible evidence which supports this statement, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

The commercially available MLPA (Multiplex Ligation-dependent Probe Amplification) kit often used by academic researchers is for research use only and not approved by the FDA. Moreover, it is incapable of detecting certain rearrangements in smaller sizes. Critchfield ¶ 50. In studies by outside researchers, BART™ has exhibited superior performance over other methods including MLPA. Critchfield ¶ 51.

149. Other labs are in a position to offer more comprehensive testing than Myriad's standard test and would do so were it not for Myriad's patents. Some labs would use newer testing methods (such as microarray analysis) that are expected to result in improved testing quality and efficiency. Other labs would reflexively conduct large rearrangement testing after a negative test result is received through full sequencing. D. Ledbetter ¶¶ 17-18; D. Chung ¶ 18; D. Ostrer ¶ 9.

RESPONSE TO PARAGRAPH 149:

Disputed.

Myriad's full sequencing test has been recognized as the "gold standard" for *BRCA* mutation testing. Critchfield ¶ 37. Myriad has been continuously improving its testing process. Critchfield ¶37.

BART is a complex test with a high cost associated with it, and large genomic rearrangements occur in a small percentage of all patients tested for hereditary breast and ovarian cancer. Nevertheless, Myriad has made BART™ available to all patients who want to be tested. At the present time, for high risk patients, BART™ is performed together with our full sequencing analysis and LRP (for common large rearrangements) at no additional charge. For low risk patients who do not meet certain clinical criteria developed based on published literature, BART™ is also available at a cost. Today, Myriad is still investing heavily to develop a new version of BART™ with a significantly lowered cost and increased efficiency. Myriad is striving to provide an improved BART™ that is commercially viable to all patients at little cost.

Myriad makes free testing available to needy patients through independent non-profit organizations. Due to their efforts, over 90% of the tests Myriad performs are covered by insurance at over 90% of the test cost. Critchfield ¶¶ 32, 33, 52, 53.

150. In the event the patents were invalidated, other labs would immediately consider and/or begin offering genetic testing to include all known methods of analysis of the genes. D. Ledbetter ¶ 18; D. Ostrer ¶ 9; D. Kant ¶ 6; D. Hegde ¶¶ 10-11; D. Chung ¶¶ 17-18; D. Hubbard ¶ 9; D. Ganguly ¶ 14.

RESPONSE TO PARAGRAPH 150:

Disputed.

Myriad's full sequencing test has been recognized as the "gold standard" for *BRCA* mutation testing. Critchfield ¶ 37. Myriad has been continuously improving its testing process. Critchfield ¶ 37.

151. When Ms. Limary was tested by Myriad, she was given the following test result: "genetic variant of uncertain significance." D. Limary ¶ 5.

RESPONSE TO PARAGRAPH 151:

Admitted.

152. Variants of uncertain significance in the *BRCA1* and *BRCA2* genes are reported disproportionately for members of minority groups. D. Chung ¶ 20; D. Ostrer ¶ 12; D. Matloff ¶ 9; D. Limary ¶ 8.

RESPONSE TO PARAGRAPH 152:

Plaintiffs have failed to cite admissible evidence to support this statement. Fed. R. Evid. 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Myriad has an in-house review committee for variant classification, and has developed a systematic approach to provide clinical interpretations for detected sequence variants based on generally accepted scientific data and analysis of its own database. We also continuously

improve upon this approach based on research advances and accumulated experience. Because of all these efforts, the VUS reporting rate at Myriad has decreased markedly, as we reported recently. In particular, between 2002 and 2006, a decrease of almost 50% was accomplished in major ethnic minority groups. Critchfield ¶ 58.

153. A lack of independent *BRCA1/2* testing and analysis undermines the ability of the scientific community to determine the meaning of variants of uncertain significance. Other labs would do extensive analyses for patients in the face of a result of "variant of uncertain significance." D. Chung ¶ 21; *see* D. Ostrer ¶ 12.

RESPONSE TO PARAGRAPH 153:

Plaintiffs have failed to cite admissible evidence to support this statement. Fed. R. Evid. 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Myriad constantly reexamines all remaining VUS previously reported to patients in an attempt to clarify the clinical significance of the variants based on new information gained in research and clinical testing. As soon as a clarification is accomplished for a patient, Myriad generates and sends an updated report to the patient's healthcare provider, thus providing the doctor and patient with the most up-to-date scientific information about that patient's particular hereditary cancer risk. In fact, it is estimated that Myriad has in total clarified about 850 VUS for about 21,000 patients, all of whose physicians have been notified with an updated report. Just between the beginning of 2008 and the present, Myriad has reclassified 502 VUS for 13,127 patients. Myriad has also made critical data available to noted international researchers and helped them analyze their VUS models in their research. The published research results have the potential of improving the diagnostic testing for the other genes. Critchfield ¶¶ 57, 59.

154. Myriad does not routinely perform genetic testing on tumor specimens preserved in paraffin from deceased family members, even though such testing can often provide

valuable genetic information for living relatives and is often necessary for accurate test interpretation. Such testing could be performed in other research laboratories and would be, were it not for the patents issue in this case. D. Chung ¶ 24.

RESPONSE TO PARAGRAPH 154:

Disputed.

Myriad's full sequencing test has been recognized as the "gold standard" for *BRCA* mutation testing. Critchfield ¶ 37.

155. Because only Myriad performs full sequencing in the United States, women who receive a negative result cannot know for certain what the rate of false negatives might be. Women who receive a positive result cannot confirm the lab's findings or seek a second opinion on the interpretation of those results. D. Ledbetter ¶ 23; D. Ostrer ¶ 11.

RESPONSE TO PARAGRAPH 155:

Disputed.

Myriad has never prohibited a "second opinion" on BRCA mutation testing, which has been available to patients like Plaintiff Girard since late 1990s. Critchfield ¶ 64. In the clinic, the term "second opinion" is used to refer to the interpretation of diagnostic tests and their implications for treatment. It would be quite unusual to have a patient's DNA sequenced a second time in a second laboratory. If, however, there were any doubts regarding the accuracy of the test, re-sequencing with the proper controls would normally be performed by the original provider. The term, second opinion, generally refers to the interpretation of a test result and which therapeutic options to follow based thereon. Once a patient has his or her genes sequenced, *e.g.*, the *BRCA1* and/or *BRCA2* genes, the patient generally does not get his or her genes re-sequenced. In the absence of any doubts regarding the accuracy of the original test, re-sequencing of the patient's genes would be an unnecessary use of resources. Reilly ¶¶ 54, 55.

156. After receiving a test from Myriad that indicated she was positive for a deleterious mutation on her *BRCA2* gene, Ms. Girard sought confirmatory testing of that test result but learned that Myriad is the only laboratory in the country that may provide full sequencing. The patents on the *BRCA* genes block her from getting a second full

sequencing test done. Ms. Girard has been forced to make significant medical decisions for herself based on a test result that has not been verified by another laboratory. A second opinion on Ms. Girard's test results is also crucial for her immediate family's options and screening. D. Girard ¶¶ 4-9.

RESPONSE TO PARAGRAPH 156:

Disputed.

There are multiple laboratories available for confirmatory testing under patent licenses from Myriad. Many of these labs have been performing testing for specific *BRCA* mutations for the past ten years. For example, testing for specific *BRCA* mutations is available in both the University of Chicago Genetic Services Laboratories and Yale DNA Diagnostic Laboratories. Information on their testing services for *BRCA* mutations is readily accessible on Internet. Critchfield ¶ 62; Lessman ¶ 4.

157. *BRCA* genetic testing is one of the very few tests performed as part of breast cancer care and prevention for which a doctor or patient cannot get a second confirmatory test done through another laboratory. D. Love ¶ 12.

RESPONSE TO PARAGRAPH 157:

Plaintiffs have failed to cite admissible evidence to support this statement. Fed. R. Evid. 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

There are multiple laboratories available for confirmatory testing under patent licenses from Myriad. Many of these labs have been performing testing for specific *BRCA* mutations for the past ten years. For example, testing for specific *BRCA* mutations is available in both the University of Chicago Genetic Services Laboratories and Yale DNA Diagnostic Laboratories. Information on their testing services for *BRCA* mutations is readily accessible on Internet. Critchfield ¶ 62.

158. Before taking major surgical steps, Ms. Ceriani would want a second opinion concerning her *BRCA1/2* status. D. Ceriani ¶¶ 9, 11.

RESPONSE TO PARAGRAPH 158:

Disputed.

There are multiple laboratories available for confirmatory testing under patent licenses from Myriad. Many of these labs have been performing testing for specific *BRCA* mutations for the past ten years. For example, testing for specific *BRCA* mutations is available in both the University of Chicago Genetic Services Laboratories and Yale DNA Diagnostic Laboratories. Information on their testing services for *BRCA* mutations is readily accessible on Internet. Critchfield ¶ 62; Lessman ¶ 4.

159. Ms. Fortune would want a second opinion concerning her *BRCA1/2* status. D. Fortune ¶ 7.

RESPONSE TO PARAGRAPH 159:

Disputed.

There are multiple laboratories available for confirmatory testing under patent licenses from Myriad. Many of these labs have been performing testing for specific *BRCA* mutations for the past ten years. For example, testing for specific *BRCA* mutations is available in both the University of Chicago Genetic Services Laboratories and Yale DNA Diagnostic Laboratories. Information on their testing services for *BRCA* mutations is readily accessible on Internet. Critchfield ¶ 62; Lessman ¶ 4.

160. Other pathologists, clinical laboratory scientists, medical professionals, and researchers could provide the testing now done by the patent holders at a cost less than that charged by the patent holders. D. Kazazian ¶ 8; D. Matloff ¶¶ 12, 14; D. Ostrer ¶ 8; D. Reich ¶¶ 6, 8, 13.

RESPONSE TO PARAGRAPH 160:

The statement is not relevant. Fed. R. Evid. 402. Because Plaintiffs have failed to offer admissible evidence to support this statement, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

The relative price of BRACAnalysis® is actually lower than the gene sequencing-based genetic tests offered by those diagnostic labs run by the geneticist plaintiffs Kazazian and Ganguly (the Genetic Diagnostic Laboratory at the University of Pennsylvania), and Ledbetter and Warren (Emory Genetics Laboratory). Critchfield ¶ 35.

161. The *BRCA1/2* testing being done by Yale DNA Diagnostics Lab prior to receipt of Myriad's cease and desist letter cost less than Myriad charges. D. Matloff ¶ 7.

RESPONSE TO PARAGRAPH 161:

The statement is not relevant. In addition, the evidence offered by Plaintiffs is inadmissible. Fed. R. Evid. 402, 802. Because Plaintiffs have failed to cite admissible evidence which supports this statement, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

The relative price of BRACAnalysis® is actually lower than the gene sequencing-based genetic tests offered by those diagnostic labs run by the geneticist plaintiffs Kazazian and Ganguly (the Genetic Diagnostic Laboratory at the University of Pennsylvania), and Ledbetter and Warren (Emory Genetics Laboratory). Critchfield ¶ 35.

162. The *BRCA1/2* testing being done by the University of Pennsylvania Genetic Diagnostic Laboratory prior to receipt of Myriad's cease and desist letters cost less than Myriad charges. D. Kazazian ¶ 8.

RESPONSE TO PARAGRAPH 162:

Disputed.

The relative price of BRACAnalysis® is actually lower than the gene sequencing-based genetic tests offered by those diagnostic labs run by the geneticist plaintiffs Kazazian and Ganguly (the Genetic Diagnostic Laboratory at the University of Pennsylvania), and Ledbetter and Warren (Emory Genetics Laboratory). Critchfield ¶ 35.

Plaintiffs Kazazian and Ganguly used the CSGE (Conformation-Sensitive Gel Electrophoresis) approach in the late 1990's for mutation detection in *BRCA1* and *BRCA2*. In one comparative study by the Breast Cancer Information Core (BIC) Consortium, the CSGE laboratory participating in the study missed as many as 40% of mutations in *BRCA1* and *BRCA2*. In that study, four different less expensive methods were compared to Myriad's method. Myriad's full sequencing approach was recognized as the "gold standard" for mutation detection for *BRCA1* and *BRCA2*. Critchfield ¶¶ 42, 43.

163. The *BRCA1/2* testing offered by OncorMed was cheaper for patients than the testing offered by Myriad. D. Parthasarathy ¶ 24.

RESPONSE TO PARAGRAPH 163:

The statement is not relevant. In addition, the evidence cited by Plaintiffs is inadmissible. Fed. R. Evid. 402, 602, 802. Because Plaintiffs have failed to cite admissible evidence which supports this statement, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

The relative price of BRACAnalysis® is actually lower than the gene sequencing-based genetic tests offered by those diagnostic labs run by the geneticist plaintiffs Kazazian and

Ganguly (the Genetic Diagnostic Laboratory at the University of Pennsylvania), and Ledbetter and Warren (Emory Genetics Laboratory). Critchfield ¶ 35.

164. Ms. Ceriani's genetic counselor submitted a blood sample to Myriad on her behalf. However, Ms. Ceriani was notified that Myriad would not process the sample. Even though Ms. Ceriani's insurance company, MassHealth, has informed her that it would cover the *BRCA* genetic test, Myriad will not accept the MassHealth coverage. Ms. Ceriani is unable to pay the full cost out-of-pocket and, to date, has not been tested. D. Ceriani ¶¶ 5-7.

RESPONSE TO PARAGRAPH 164:

Disputed.

Myriad also makes free testing available to needy patients through independent non-profit organizations such as the Cancer Resource Foundation ("CRF") in Massachusetts. Critchfield ¶ 33.

Until Myriad is approved by each state as a "participating provider," Myriad cannot offer testing to that state's Medicaid patients. Myriad has been pursuing Medicaid coverage for years and has secured "participating provider" status in 25 states. Unfortunately, Myriad has not yet been granted "participating provider" status in some states, which may create gaps in coverage for some patients. However, Myriad provides free testing to independent non-profit institutions. In addition, Myriad also makes free testing available to needy patients through independent nonprofit organizations such as the Cancer Resource Foundation ("CRF") in Massachusetts. See http://www.breastcancerrna.org/helping-hand/#genetic. In fact, through the CRF, MassHealth patients such as Plaintiff Ceriani may receive BRAC*Analysis*® testing at no charge. Rusconi ¶¶ 6; Critchfield ¶ 33; Ogaard ¶ 6.

165. Ms. Fortune is insured through Medi-Cal. Her oncologist and genetic counselor recommended that she obtain *BRCA1*/*BRCA2* genetic testing but told her that Myriad would not accept her insurance. Ms. Fortune is unable to pay the full cost out-of-pocket and, to date, has not been tested. D. Fortune ¶¶ 4-5.

RESPONSE TO PARAGRAPH 165:

Disputed.

Since 1996 when BRACAnalysis® was launched, Myriad has had a formal financial assistance program directly providing free testing to low-income and uninsured patients. Critchfield ¶ 33; Ogaard ¶¶ 4, 5.

Until Myriad is approved by each state as a "participating provider," Myriad cannot offer testing to that state's Medicaid patients. Myriad has been pursuing Medicaid coverage for years and has secured "participating provider" status in 25 states. Unfortunately, Myriad has not yet been granted "participating provider" status in some states, which may create gaps in coverage for some patients. Rusconi ¶ 5.

166. Myriad's BART test is not covered by many insurers, and for most patients, they must pay separately for BART on top of the fee for the standard Comprehensive BRACAnalysis test. D. Reich ¶ 10.

RESPONSE TO PARAGRAPH 166:

The statement is not relevant. In addition, the evidence cited by Plaintiffs does not support this statement. Further, the evidence cited by Plaintiffs is inadmissible. Fed. R. Evid. 402, 602. Because Plaintiffs have failed to cite admissible evidence which supports this statement, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Paragraph 10 of the declaration of Ms. Reich states that "many insurers to not cover this test when it is and [sic] 'add on.'"

For high risk patients, BART™ is performed together with our full sequencing analysis and LRP (for common large rearrangements) at no additional charge. Critchfield ¶ 52.

167. Ms. Raker's genetic counselor advised her about additional *BRCA* genetic testing that looks for other large genetic rearrangements that are not included in Myriad's standard full sequencing test, but informed her that it was unclear whether her insurance would cover the cost of that test. Ms. Raker is unable to afford the extra cost and, to date, has not received this testing. Without these results, she cannot determine the best course of medical care for herself. D. Raker ¶¶ 7-11.

RESPONSE TO PARAGRAPH 167:

Disputed.

For high risk patients, BART™ is performed together with our full sequencing analysis and LRP (for common large rearrangements) at no additional charge. Critchfield ¶ 52.

168. Ms. Thomason has not been able to afford the additional *BRCA* testing recommended by her genetic counselor. D. Thomason ¶ 8.

RESPONSE TO PARAGRAPH 168:

Disputed.

For high risk patients, BART™ is performed together with our full sequencing analysis and LRP (for common large rearrangements) at no additional charge. Critchfield ¶ 52.

Myriad makes free testing available to needy patients through independent non-profit organizations. Critchfield ¶ 33; Ogaard ¶¶ 4-6; Rusconi ¶ 6.

169. Genetic counselors would recommend additional women for testing and additional tests if the cost came down. D. Matloff ¶¶ 13-14; D. Reich ¶ 6-13.

RESPONSE TO PARAGRAPH 169:

Disputed.

The relative price of BRAC*Analysis*® is actually lower than the gene sequencing-based genetic tests offered by those diagnostic labs run by the geneticist plaintiffs Kazazian and Ganguly (the Genetic Diagnostic Laboratory at the University of Pennsylvania), and Ledbetter and Warren (Emory Genetics Laboratory). Critchfield ¶ 35. Myriad makes free testing available to needy patients through independent non-profit organizations. Critchfield ¶ 33; Ogaard ¶¶ 4-6;

Rusconi ¶ 6. Due to their efforts, over 90% of the tests Myriad performs are covered by insurance at over 90% of the test cost. Critchfield ¶ 32; Ogaard ¶ 3; Frieder ¶12.

170. Data sharing is key to the future of genetic discoveries and bio informatics. D. Sulston ¶ 36.

RESPONSE TO PARAGRAPH 170:

The statement is not relevant. In addition, the evidence cited by Plaintiffs is inadmissible. Fed. R. Evid. 402, 702. Because Plaintiffs have failed to offer admissible evidence Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Part of the *quid pro quo* of the patent system is that inventors, in exchange for a limited period of patent exclusivity, must provide a sufficient description of the patented invention so that others may improve upon it. Reilly ¶ 24; Doll ¶ 44; Tavtigian ¶¶ 15-17. Myriad is the largest contributor to the BIC database, and has made a total of more than 20,000 submissions to the database. Myriad has published the largest clinical series of mutation risk in the *BRCA1* and *BRCA2* genes based on its experience from the largest scale of genetic testing ever conducted in the world. The mutation risk data has been tabulated and posted on Myriad's website and is frequently updated by Myriad and freely available to researchers throughout the world. Critchfield ¶¶ 11, 12.

171. The Breast Cancer Information Core (BIC), an international resource, is an open access, on-line database that is a central repository for information about *BRCA* genes and *BRCA* genetic variants. It helps facilitate identification of deleterious mutations (mutations associated with a higher risk of cancer) and provides a mechanism to collect and distribute data about genetic variants. The value of the BIC comes from the amount and quality of data provided by the scientific community. D, Swisher ¶¶ 15, 17; D. Chung ¶ 22; D. Ostrer ¶ 13.

RESPONSE TO PARAGRAPH 171:

The statement is not relevant. Fed. R. Evid. 402. Because Plaintiffs have failed to offer admissible evidence to support this statement, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Part of the *quid pro quo* of the patent system is that inventors, in exchange for a limited period of patent exclusivity, must provide a sufficient description of the patented invention so that others may improve upon it. Reilly ¶ 24; Doll ¶ 44; Tavtigian ¶¶ 15-17. Myriad is the largest contributor to the BIC database, and has made a total of more than 20,000 submissions to the BIC database. Myriad has published the largest clinical series of mutation risk in the *BRCA1* and *BRCA2* genes based on its experience from the largest scale of genetic testing ever conducted in the world. The mutation risk data has been tabulated and posted on Myriad's website and is frequently updated by Myriad and freely available to researchers throughout the world. Critchfield ¶¶ 11, 12.

172. By gathering information about variants of uncertain significance in one place, the BIC plays an important role in helping to elucidate these variants. D. Swisher ¶ 18.

RESPONSE TO PARAGRAPH 172:

The statement is not relevant. Fed. R. Evid. 402. Because Plaintiffs have failed to cite admissible evidence Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Myriad is the largest contributor to the BIC database, and has made a total of more than 20,000 submissions to the database. Critchfield ¶ 11.

When Myriad detects a VUS, it reports the variant to the patient as a "genetic variant of uncertain significance." The uncertainty about the cancer risk of such variants at the time of their detection arises not because of any limitation in the test, but because of the limits of current scientific knowledge. This is independent of the testing method. Any lab uncovering the same variant, such as those of Plaintiffs Ledbetter or Ganguly, would need to report the exact same result because of the limited scientific knowledge. In fact, there is widespread consensus among cancer geneticists that the VUS problem is challenging. It has been estimated that about one-third of the genetic variants in *BRCAl* and 50% of those found in *BRCA2* reported by the Breast Cancer Information Core (BIC) Consortium are or have been considered genetic variants of unknown clinical significance. The VUS problem is not unique to *BRCA* testing. It is also·common in many other genetic tests such as sequencing analysis of the *CFTR* gene (for cystic fibrosis), the *MLH1*and *MSH2* genes (for hereditary nonpolyposis colorectal cancer), the *CDKN2A* gene (for hereditary melanoma), and the *APC* gene (for familial adenomatous polyposis or FAP). Critchfield ¶¶ 55, 56.

173. Myriad does not share its data with BIC. D. Swisher ¶ 19.

RESPONSE TO PARAGRAPH 173:

The statement is not relevant. Fed. R. Evid. 402. Because Plaintiffs have failed to offer admissible evidence to support this statement, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Myriad is the largest contributor to the BIC database, and has made a total of more than 20,000 submissions to the database. Critchfield ¶ 11.

174. If other researchers had access to the data Myriad has collected as a result of its exclusive testing, additional information about the nature of the *BRCA1/2* variants and their

significance might be known. D. Sulston ¶ 36; D. Swisher ¶¶ 20-21; D. Matloff ¶ 9; D. Ostrer ¶¶ 12-13; D. Chung ¶¶ 21-22; D. Ledbetter ¶ 20.

RESPONSE TO PARAGRAPH 174:

The statement is not relevant. Fed. R. Evid. 402. Because Plaintiffs have failed to offer admissible evidence to support this statement, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Myriad is the largest contributor to the BIC database, and has made a total of more than 20,000 submissions to the database. Critchfield ¶ 11. When Myriad detects a VUS, it reports the variant to the patient as a "genetic variant of uncertain significance." The uncertainty about the cancer risk of such variants at the time of their detection arises not because of any limitation in the test, but because of the limits of current scientific knowledge. This is independent of the testing method. Any lab uncovering the same variant, such as those of Plaintiffs Ledbetter or Ganguly, would need to report the exact same result because of the limited scientific knowledge. In fact, there is widespread consensus among cancer geneticists that the VUS problem is challenging. It has been estimated that about one-third of the genetic variants in *BRCA1* and 50% of those found in *BRCA2* reported by the Breast Cancer Information Core (BIC) Consortium are or have been considered genetic variants of unknown clinical significance. Myriad has also made critical data available to noted international researchers and helped them analyze their VUS models in their research. The published research results have the potential of improving the diagnostic testing for the other genesCritchfield ¶¶ 55, 56, 57.

175. Gene patents inhibit research. D. Sulston ¶ 37; D. Cho ¶ 24.

RESPONSE TO PARAGRAPH 175:

Disputed.

Patents such as the patents-in-suit have served to advance research and the practice of medicine and benefit patients. Reilly ¶¶ 38, 43; Linck ¶¶ 27-28, 71, 73; Critchfield ¶¶ 2-18, 65, 68; Tavtigian ¶¶ 14-17; Doll ¶¶ 45-46; Bone ¶¶ 10-11; Frieder ¶ 13; Schlessinger ¶¶ 31-32.

176. A scientifically valid survey of laboratory directors in the United States revealed that 53% decided not to develop a new clinical test because of a gene patent or license, 67% believed that gene patents decreased an ability to do research. A second study concluded that 46% of respondents believed that gene patents delayed or limited their research. D. Cho ¶ 10

RESPONSE TO PARAGRAPH 176:

Disputed.

Patents such as the patents-in-suit have served to advance research and the practice of medicine and benefit patients. Reilly ¶¶ 38, 43; Linck ¶¶ 27-28, 71, 73; Critchfield ¶¶ 2-18, 65, 68; Tavtigian ¶¶ 14-17; Doll ¶¶ 45-46; Bone ¶¶ 10-11; Frieder ¶ 13; Schlessinger ¶¶ 31-32.

177. Gene patents are deleterious to unraveling the role of genes in medical conditions. D. Sulston ¶ 38.

RESPONSE TO PARAGRAPH 177:

Disputed.

Patents such as the patents-in-suit have served to advance research and the practice of medicine and benefit patients. Reilly ¶¶ 38, 43; Linck ¶¶ 27-28, 71, 73; Tavtigian ¶¶ 14-17; Critchfield ¶¶ 2-18, 65, 68; Doll ¶¶ 45-46; Bone ¶¶ 10-11; Frieder ¶ 13; Schlessinger ¶¶ 31-32.

Today, scientists understand that functional *BRCA1* and *BRCA2* proteins prevent mutations and cancer through homologous recombination by repairing doublestranded DNA damages. Critchfield ¶ 14.

178. New sequencing technologies are beginning to offer the option of faster and less expensive sequencing of single genes, multiple genes, and even the entire human genome. Patents on one or more genes may impede scientists' ability to develop a comprehensive test for complex diseases or provide a person with an analysis of his or her entire genome. D. Sulston ¶ 38; D. Ledbetter ¶ 24.

RESPONSE TO PARAGRAPH 178:

Disputed.

Myriad's full sequencing test has been recognized as the "gold standard" for *BRCA* mutation testing. Critchfield ¶ 37.

179. Gene patents directly interfere with the ability of physicians and researchers to investigate complex diseases. For example, *BRCA1* and *BRCA2* may be associated with cancers other than breast and ovarian cancer, or even other diseases, but so long as the patents on these genes remain, no one will be able to include these genes in tests for other disease predispositions. D. Ledbetter ¶¶ 24-25.

RESPONSE TO PARAGRAPH 179:

Disputed.

It has been, and still is, Myriad's policy and practice to allow scientists to conduct research studies on the *BRCA1* and *BRCA2* genes freely. Critchfield ¶¶3; Li ¶¶ 3-6; Baer ¶¶ 3-6; Parvin ¶ 3-6; Sandbach¶¶ 3-7. Patents such as the patents-in-suit have served to advance research and the practice of medicine and benefit patients. Reilly ¶¶38, 43; Linck ¶¶ 27-28, 71, 73; Tavtigian ¶¶ 14-17; Critchfield ¶¶ 2-18, 65, 68; Doll ¶¶ 45-46; Bone ¶¶ 10-11; Frieder ¶ 13; Schlessinger ¶¶ 31-32.

180. Imagine if Watson and Crick had patented the double-helix structure when they discovered it. D. Parthasarathy ¶ 28.

RESPONSE TO PARAGRAPH 180:

The statement is not relevant. Fed. R. Evid. 402. Because Plaintiffs have failed to offer admissible evidence Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

181. Gene patents inhibit clinical diagnostic laboratories from providing clinical tests and services. D. Cho ¶ 24.

RESPONSE TO PARAGRAPH 181:

Plaintiffs have failed to cite admissible evidence to support this statement. Fed. R. Evid. 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

182. Geneticists have refrained from developing and improving tests for diseases as a result of the impediment of gene patents. D. Ledbetter ¶¶ 14-15.

RESPONSE TO PARAGRAPH 182:

The evidence cited by Plaintiffs is inadmissible. Fed. R. Evid. 701, 702. Because Plaintiffs have failed to cite admissible evidence which supports this statement, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Patents are essential in obtaining capital investment in the development and commercialization of technological breakthroughs. Linck ¶¶ 27, 28, 73, 85, 271; Reilly ¶ 16.

183. Gene patents are not necessary to create incentives for initial discoveries or the development of commercial applications, including diagnostics. D. Cho ¶ 25; D. Leonard ¶¶ 20-21.

RESPONSE TO PARAGRAPH 183:

The evidence cited by Plaintiffs is inadmissible. Fed. R. Evid. 702. Because Plaintiffs have failed to cite admissible evidence which supports this statement, Defendants need not offer contradictory evidence. Fed. R. Evid. 702; Local Civil Rule 56.1; and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Patents are essential in obtaining capital investment in the development and commercialization of technological breakthroughs. Linick ¶¶ 27, 28, 73, 85, 271; Reilly ¶ 16.

Myriad would not have made the investment of more than 200 million dollars in raising patient and physician awareness alone without the protection provided by the exact patents the Plaintiffs are challenging. Critchfield ¶ 25.

184. Patents have not been necessary for rapid introduction of genetic testing. Clinical genetic testing has been offered for genetic testing prior to a patent being issued. D. Cho ¶ 21

RESPONSE TO PARAGRAPH 184:

The evidence cited by Plaintiffs does not support this statement. In addition, the evidence cited by Plaintiffs is inadmissible. Fed. R. Evid. 702. Because Plaintiffs have failed to offer admissible evidence which supports this statement, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Patents are essential in obtaining capital investment in the development and commercialization of technological breakthroughs. Reilly ¶ 16; Linck ¶¶ 27, 28, 73, 85, 271.

185. A study of gene patents issued in the U.S. for genetic diagnostics showed that 67% of these patents were issued for discoveries funded by the U.S. government. D. Cho ¶ 22.

RESPONSE TO PARAGRAPH 185:

Disputed.

A survey published in 2009 by BIO of 150 biotechnology member companies in the therapeutic and diagnostic healthcare industry revealed that the majority of companies (61%) stated they generally in-license projects that are in the pre-clinical or Phase I stage of development, and thus still require substantial R&D investment and commercialization risk by the licensee. A substantial majority (77%) of the respondents without approved products indicated that they expect to spend 5-15 years and over $100 million developing a commercial product. These expenditures dwarf any initial research funding by the federal government. Reilly ¶ 22; Doll ¶46.

186. Another study showed that 63% of patents on gene sequences resulted from federally supported research. D. Leonard ¶ 22.

RESPONSE TO PARAGRAPH 186:

Plaintiffs have failed to cite admissible evidence to support this statement. Fed. R. Evid. 702. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

A survey published in 2009 by BIO of 150 biotechnology member companies in the therapeutic and diagnostic healthcare industry revealed that the majority of companies (61%) stated they generally in-license projects that are in the pre-clinical or Phase I stage of development, and thus still require substantial R&D investment and commercialization risk by the licensee. A substantial majority (77%) of the respondents without approved products indicated that they expect to spend 5-15 years and over $100 million developing a commercial product. These expenditures dwarf any initial research funding by the federal government. Reilly ¶ 22; Doll ¶ 46.

187. Significant federal funds were provided to support research to find the *BRCA* genes. The National Institutes of Health (NIH) funded a six-person National Institute of Environmental Health Sciences research team. NIH also provided approximately $2 million in research grants to the University of Utah for this research. NIH contributed one-third of the funding for *BRCA1*'s discovery. D. Parthasarathy ¶ 18.

RESPONSE TO PARAGRAPH 187:

The statement is not relevant. Fed. R. Evid. 402. Because Plaintiffs have failed to offer admissible evidence Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

A significant amount of private investment in Myriad led to the discovery of *BRCA1* and *BRCA2*. The expectation of patent protection provided incentive for research in the discovery of the genes. Skolnick ¶ 14-16.

188. Patient care is promoted where more than one lab offers a particular genetic test utilizing different methodologies. D. Ostrer ¶ 11; D. Swisher ¶¶ 32-35; D. Leonard ¶ 24.

RESPONSE TO PARAGRAPH 188:

The statement is not relevant. Fed. R. Evid. 402. Because Plaintiffs have failed to offer admissible evidence Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Myriad's full sequencing test has been recognized as the "gold standard" for *BRCA* mutation testing. Critchfield ¶ 37.

189. It is important for more than one lab to offer a particular genetic test in order to ensure that the testing being done is quality testing and the results are accurate. D. Chung ¶ 23; D. Swisher ¶¶ 32-35; D. Ledbetter ¶ 23; D. Reich ¶¶ 9, 11; D. Leonard ¶ 24; D. Parthasarathy ¶¶ 29, 31; D. Ostrer ¶ 11.

RESPONSE TO PARAGRAPH 189:

The statement is not relevant. Fed. R. Evid. 402. Because Plaintiffs have failed to offer admissible evidence Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Myriad's full sequencing test has been recognized as the "gold standard" for *BRCA* mutation testing. Critchfield ¶ 37.

190. More than one lab should offer a particular genetic test because clinical laboratory testing takes place in a broader context of patient care and services. Allowing only one lab to offer testing means that one lab dictates the standards for patient care in testing for that disease. D. Parthasarathy ¶¶ 30, 31.

RESPONSE TO PARAGRAPH 190:

The statement is not relevant. Fed. R. Evid. 402. Because Plaintiffs have failed to offer admissible evidence to support this statement, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Myriad's full sequencing test has been recognized as the "gold standard" for *BRCA* mutation testing. Critchfield ¶ 37.

Without the promise of a period of market exclusivity provided by patents and the infusion of venture and risk capital derived therefrom, companies that capitalize on innovation simply would not be created. Their products would not be brought to market, to the clinic, and most importantly, to patients. This of course, holds true for companies such as Myriad and its *BRCA1/2* diagnostic tests. Intellectual property is essential to innovation in health care. Reilly ¶¶ 18, 34, 51, 52, 62; Critchfield ¶¶ 67, 68; Linck ¶¶ 73, 271.

191. Research should allow for subjects to be told the results of their genetic testing as this can lead to valuable insights concerning their behavior. D. Ostrer ¶ 10.

RESPONSE TO PARAGRAPH 191:

The statement is not relevant. In addition, the evidence cited by Plaintiffs is inadmissible. Fed. R. Evid. 402, 702. Because Plaintiffs have failed to cite admissible evidence which supports this statement, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

The majority of academic researchers operating laboratories (as opposed to CLIA-certified laboratories) do not believe that they should share test results with subjects outside of the standard clinical setting. Reilly ¶¶ 57-59.

192. Ethical standards require that physicians be able to provide genetic test results to research subjects, where such results are requested. D. Chung ¶ 14.

RESPONSE TO PARAGRAPH 192:

The statement is not relevant. In addition, the evidence cited by Plaintiffs is inadmissible. Fed. R. Evid. 402, 702. Because Plaintiffs have failed to cite admissible evidence which supports this statement, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

The majority of academic researchers operating laboratories (as opposed to CLIA-certified laboratories) do not believe that they should share test results with subjects outside of the standard clinical setting. Reilly ¶¶ 57-59.

EFFECT OF PATENTS ON PLAINTIFFS

193. AMP sues on behalf of its members, some of whom are ready, willing, and able to engage in research and clinical practice involving the *BRCA1* and *BRCA2* genes if the patents are invalidated. D. Sobel ¶ 3; D. Hegde ¶¶ 6-12.

RESPONSE TO PARAGRAPH 193:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Plaintiffs cite only to one declaration as a members of AMP. Paragraph 11 of Dr. Hegde's declaration states that he would "begin sequencing *BRCA1* and *BRCA2* genes as quickly as possible." Hegde ¶ 11.

194. ACMG sues on behalf of its members, some of whom are ready, willing, and able to engage in research and clinical practice involving the *BRCA1* and *BRCA2* genes if the patents are invalidated. D. Watson ¶ 3; D. Chung ¶¶ 4, 17-18; D. Ostrer ¶¶ 3, 8-9; D. Ledbetter ¶¶ 4, 18.

RESPONSE TO PARAGRAPH 194:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Paragraph 17 of Dr. Chung's application states that she "would immediately take steps to begin clinical testing;" paragraph 8 of Dr. Ostrer's declaration states that he "would immediately take steps to begin clinical testing;" and paragraph 18 of Dr. Ledbetter states that he "would immediately begin offering c omprehensive *BRCA1* and *BRCA2* testing."

195. ASCP sues on behalf of its members, some of whom are ready, willing, and able to engage in research and clinical practice involving the *BRCA1* and *BRCA2* genes if the patents are invalidated. D. Ball ¶ 2; D. Hubbard ¶ 2.

RESPONSE TO PARAGRAPH 195:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

196. CAP sues on behalf of its members, some of whom are ready, willing, and able to engage in research and clinical practice involving the *BRCA1* and *BRCA2* genes if the patents are invalidated. D. Scott ¶ 3; D. Kant ¶¶ 4-6.

RESPONSE TO PARAGRAPH 196:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Paragraph 6 of the declaration of Dr. Kant states "I would immediately consider doing full gene testing for the *BRCA1* and *BRCA2* genes." Kant ¶ 6.

197. The laboratory of Dr. Haig Kazazian and Dr. Arupa Ganguly at the University of Pennsylvania has all of the resources and technological capability to offer *BRCA* testing. If the patents are invalidated, they would immediately consider resuming *BRCA* testing. D. Kazazian ¶ 11; D. Ganguly ¶ 14.

RESPONSE TO PARAGRAPH 197:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Paragraph 11 of the declaration of Dr. Kazazian states that "[i]f Dr. Ganguly and I were to learn that Myriad's *BRCA* patents no longer had legal effect and we decided to resume *BRCA* testing, we would be able to do so within a matter of a few weeks."

198. Dr. Wendy Chung's laboratory at Columbia University has the personnel, expertise and facilities to do *BRCA* sequencing. If the patents are invalidated, she would offer clinical testing of the *BRCA* genes, including *BRCA* testing that is more comprehensive than that which Myriad offers. Dr. Chung would be in a position to tell the subjects in her research their genetic test results. Her lab would share the results of its work with the BIC database. D. Chung ¶¶ 17-18.

RESPONSE TO PARAGRAPH 198:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Myriad's full sequencing test has been recognized as the "gold standard" for *BRCA* mutation testing. Critchfield ¶ 37. Myriad has been continuously improving its testing process. Critchfield ¶ 37.

199. Dr. Harry Ostrer's laboratory at New York University has the personnel, expertise and facilities to do *BRCA* sequencing. If the patents are invalidated, he would offer clinical testing of the *BRCA* genes. He would inform participants in his research program about the results of their *BRCA1/2* genetic screening. His lab would share the results of its work with the BIC database. D. Ostrer ¶¶ 8-13.

RESPONSE TO PARAGRAPH 199:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

The diagnostic labs run by Dr. Harry Ostrer is within a major university typically serving only patients within the major affiliated teaching hospitals. Dr. Ostrer would not have been able to do what Myriad has done in raising awareness and understanding of *BRCA* testing and reaching needy individuals even in rural communities. Critchfield ¶ 30; Frieder ¶ 13.

200. The laboratories directed by Stephen Warren and David Ledbetter at Emory University School of Medicine have all of the personnel and expertise to offer *BRCA* genetic testing. If the patents are invalidated, they would offer clinical testing of the *BRCA1/2* genes, including testing that is more comprehensive and relies on different methodology than that offered by Myriad. They would contribute their research and clinical data to the public. They could have a *BRCA* testing program in operation within weeks. D. Ledbetter ¶¶ 9-12, 16-28; D. Hegde ¶¶ 10-12.

RESPONSE TO PARAGRAPH 200:

The evidence cited by Plaintiffs does not support this statement. In addition, the evidence cited by Plaintiffs is inadmissible. Fed. R. Evid. 602. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); Fed. R. Civ. P; 56(e);

To the extent a response is required, Defendants dispute this statement.

Myriad's full sequencing test has been recognized as the "gold standard" for *BRCA* mutation testing. Critchfield ¶ 37. Myriad has been continuously improving its testing process. Critchfield ¶ 37

201. If the patents are invalidated, Ellen Matloff would immediately take steps to send samples to labs other than Myriad and advise patients regarding increased genetic testing options. D. Matloff ¶¶ 10-15.

RESPONSE TO PARAGRAPH 201:

Disputed.

The relative price of BRACAnalysis® is actually lower than the gene sequencing-based genetic tests offered by those diagnostic labs run by the geneticist plaintiffs Kazazian and Ganguly (the Genetic Diagnostic Laboratory at the University of Pennsylvania), and Ledbetter

and Warren (Emory Genetics Laboratory). Critchfield ¶ 35. Myriad makes free testing available to needy patients through independent non-profit organizations. Critchfield ¶ 33. Due to their efforts, over 90% of the tests Myriad performs are covered by insurance at over 90% of the test cost. Critchfield ¶ 32; Frieder ¶ 12.

202. If the patents are invalidated, Elsa Reich would immediately take steps to send samples to labs other than Myriad and advise patients regarding increased genetic testing options, including the availability of confirmatory testing. D. Reich ¶¶ 7-15.

RESPONSE TO PARAGRAPH 202:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Paragraph 7 of the declaration of Ms. Reich states that she "would potentially alter [her] testing choices in numerous ways." Reich ¶ 7.

There are multiple laboratories available for confirmatory testing under patent licenses from Myriad. Many of these labs have been performing testing for specific *BRCA* mutations for the past ten years. For example, testing for specific *BRCA* mutations is available in both the University of Chicago Genetic Services Laboratories and Yale DNA Diagnostic Laboratories. Information on their testing services for *BRCA* mutations is readily accessible on Internet. Critchfield ¶ 62.

203. Breast Cancer Action (BCA) sues on its own behalf and on behalf of its members, some of whom are ready, willing, and able to order testing and analysis at laboratories other than Myriad Genetics if the patents are invalidated. If the patents are invalidated, BCA would immediately use its existing resources to publicize other laboratories for *BRCA* genetic testing and research opportunities. The interests advanced by this case are central to the mission of BCA. D. Brenner ¶¶ 4-9.

RESPONSE TO PARAGRAPH 203:

The evidence cited by Plaintiffs does not support this statement. In addition, the evidence cited by Plaintiffs is inadmissible. Fed. R. Evid. 602. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); Fed. R. Civ. P; 56(e);

To the extent a response is required, Defendants dispute this statement.

Because of Myriad's efforts with patient and physician outreach, Myriad now routinely receive patient samples from everywhere in all 50 states. More than 40,000 physicians and genetic counselors have used the BRACAnalysis® test. Over 400,000 patients who meet testing criteria have been tested at Myriad for mutations in the *BRCA1* and *BRCA2* genes. Patient awareness and access to important genetic testing has been significantly enhanced as a result of the patent grants at issue in this case. Critchfield ¶ 29; Frieder ¶ 13; Bone ¶¶ 10-11.

204. If the patents are invalidated, Boston Women's Health Book Collective (BWHBC) would immediately use its existing resources to publicize other laboratories for *BRCA* genetic testing and research opportunities. The interests advanced by this case are completely in line with the mission of BWHBC. D. Norsigian ¶¶ 5-8.

RESPONSE TO PARAGRAPH 204:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Because of Myriad's efforts with patient and physician outreach, Myriad now routinely receive patient samples from everywhere in all 50 states. More than 40,000 physicians and genetic counselors have used the BRACAnalysis® test. Over 400,000 patients who meet testing criteria have been tested at Myriad for mutations in the *BRCA1* and *BRCA2* genes. Patient awareness and access to important genetic testing has been significantly enhanced as a result of the patent grants at issue in this case. Critchfield ¶ 29; Frieder ¶ 13; Bone ¶¶ 10-11.

205. Ms. Ceriani has not been able to obtain the *BRCA* genetic testing recommended by her doctor and genetic counselor. If the patents are invalidated, Ms. Ceriani is ready, willing, and able to utilize any additional resources for testing and research, including being tested by a plaintiff physician or geneticist. D. Ceriani ¶¶ 5-11.

RESPONSE TO PARAGRAPH 205:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d) and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Paragraph 8 of Ms. Ceriani's declaration states that "I would like to obtain genetic testing through another lab that would accept my insurance." Ceriani ¶ 8.

206. Ms. Limary wants to access additional resources for *BRCA* testing and research that could reveal the significance of the variant in her genes, including whether the variant is correlated with an increased risk of breast or ovarian cancer. If the patents are invalidated, Ms. Limary is ready, willing, and able to utilize immediately any additional resources for testing and research, including being tested by a plaintiff physician or geneticist. D. Limary ¶¶ 5-9.

RESPONSE TO PARAGRAPH 206:

Disputed.

Myriad has an in-house review committee for variant classification, and has developed a systematic approach to provide clinical interpretations for detected sequence variants based on generally accepted scientific data and analysis of its own database. We also continuously improve upon this approach based on research advances and accumulated experience. Because of all these efforts, the VUS reporting rate at Myriad has decreased markedly, as we reported recently. In particular, between 2002 and 2006, a decrease of almost 50% was accomplished in major ethnic minority groups. Myriad constantly reexamines all remaining VUS previously reported to patients in an attempt to clarify the clinical significance of the variants based on new information gained in research and clinical testing. As soon as a clarification is accomplished for a patient, Myriad generates and sends an updated report to the patient's healthcare provider, thus

providing the doctor and patient with the most up-to-date scientific information about that patient's particular hereditary cancer risk. In fact, it is estimated that Myriad has in total clarified about 850 VUS for about 21,000 patients, all of whose physicians have been notified with an updated report. Just between the beginning of 2008 and the present, Myriad has reclassified 502 VUS for 13,127 patients. There are multiple laboratories available for confirmatory testing under patent licenses from Myriad. Many of these labs have been performing testing for specific *BRCA* mutations for the past ten years. For example, testing for specific *BRCA* mutations is available in both the University of Chicago Genetic Services Laboratories and Yale DNA Diagnostic Laboratories. Information on their testing services for *BRCA* mutations is readily accessible on Internet. Critchfield ¶¶ 58, 59, 62; Lessman ¶ 4.

207. Ms. Girard has not been able to obtain confirmatory, full sequencing testing through another laboratory of her *BRCA* positive result. If the patents are invalidated, Ms. Girard is ready, willing, and able to utilize any additional resources for testing and research, including obtaining confirmatory testing from a plaintiff physician or geneticist. D. Girard ¶¶ 4-10.

RESPONSE TO PARAGRAPH 207:

Disputed.

Myriad has an in-house review committee for variant classification, and has developed a systematic approach to provide clinical interpretations for detected sequence variants based on generally accepted scientific data and analysis of its own database. We also continuously improve upon this approach based on research advances and accumulated experience. Because of all these efforts, the VUS reporting rate at Myriad has decreased markedly, as we reported recently. In particular, between 2002 and 2006, a decrease of almost 50% was accomplished in major ethnic minority groups. Myriad constantly reexamines all remaining VUS previously reported to patients in an attempt to clarify the clinical significance of the variants based on new information gained in research and clinical testing. As soon as a clarification is accomplished for

a patient, Myriad generates and sends an updated report to the patient's healthcare provider, thus providing the doctor and patient with the most up-to-date scientific information about that patient's particular hereditary cancer risk. In fact, it is estimated that Myriad has in total clarified about 850 VUS for about 21,000 patients, all of whose physicians have been notified with an updated report. Just between the beginning of 2008 and the present, Myriad has reclassified 502 VUS for 13,127 patients. There are multiple laboratories available for confirmatory testing under patent licenses from Myriad. Many of these labs have been performing testing for specific *BRCA* mutations for the past ten years. For example, testing for specific *BRCA* mutations is available in both the University of Chicago Genetic Services Laboratories and Yale DNA Diagnostic Laboratories. Information on their testing services for *BRCA* mutations is readily accessible on Internet. Critchfield ¶¶ 58, 59, 62, Lessman ¶ 4.

Physicians using Myriad's tests for their patients do not feel the need for "second opinion" testing. Frieder ¶ 11; Bone ¶ 8.

There are multiple laboratories available for confirmatory testing under patent licenses from Myriad. Many of these labs have been performing testing for specific *BRCA* mutations for the past ten years. For example, testing for specific *BRCA* mutations is available in both the University of Chicago Genetic Services Laboratories and Yale DNA Diagnostic Laboratories. Information on their testing services for *BRCA* mutations is readily accessible on Internet. Critchfield ¶ 62.

208. Ms. Fortune has not been able to obtain the *BRCA* genetic testing recommended by her doctor and genetic counselor. If the patents are invalidated, Ms. Fortune is ready, willing, and able to utilize any additional resources for testing and research, including being tested by a plaintiff physician or geneticist. D. Fortune ¶¶ 4-9.

RESPONSE TO PARAGRAPH 208:

The evidence cited by Plaintiffs to support this statement is inadmissible. Fed. R. Evid. 802. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1(d); Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Myriad makes free testing available to needy patients through independent non-profit organizations. Critchfield ¶ 33; Rusconi ¶ 6; Ogaard ¶¶ 4-6. Due to their efforts, over 90% of the tests Myriad performs are covered by insurance at over 90% of the test cost. Critchfield ¶ 32; Ogaard ¶ 3; Frieder ¶ 12.

209. Ms. Thomason has not been able to obtain additional large rearrangement testing of her *BRCA1/2* genes. If the patents are invalidated, Ms. Thomason is ready, willing, and able to utilize any additional resources for testing and research that would become accessible to her, including being tested by a plaintiff physician or geneticist. D. Thomason ¶¶ 4-10.

RESPONSE TO PARAGRAPH 209:

Disputed.

BART is a complex test with a high cost associated with it, and large genomic rearrangements occur in a small percentage of all patients tested for hereditary breast and ovarian cancer. Nevertheless, Myriad has made BART™ available to all patients who want to be tested. At the present time, for high risk patients, BART™ is performed together with our full sequencing analysis and LRP (for common large rearrangements) at no additional charge. For low risk patients who do not meet certain clinical criteria developed based on published literature, BART™ is also available at a cost. Due to their efforts, over 90% of the tests Myriad performs are covered by insurance at over 90% of the test cost. Critchfield ¶¶ 32, 33, 52, 53; Ogaard ¶ 3; Frieder ¶ 12.

210. Ms. Raker has not been able to obtain additional large rearrangement testing of her *BRCA1/2* genes. If the patents are invalidated, Ms. Raker is ready, willing, and able to

utilize any additional resources for testing and research that would become accessible to her, including being tested by a plaintiff physician or geneticist. D. Raker ¶¶ 5-12.

RESPONSE TO PARAGRAPH 210:

The evidence cited by Plaintiffs does not support this statement. Thus, Defendants need not offer contradictory evidence. Local Civil Rule 56.1 and Fed. R. Civ. P. 56(e).

To the extent a response is required, Defendants dispute this statement.

Paragraph 9 of Ms. Raker's declaration states that she has "often fallen behind in making payments [for insurance], and as a result, [her] coverage is unstable and insecure." Raker ¶ 9.

BART is a complex test with a high cost associated with it, and large genomic rearrangements occur in a small percentage of all patients tested for hereditary breast and ovarian cancer. Nevertheless, Myriad has made BART™ available to all patients who want to be tested. At the present time, for high risk patients, BART™ is performed together with our full sequencing analysis and LRP (for common large rearrangements) at no additional charge. For low risk patients who do not meet certain clinical criteria developed based on published literature, BART™ is also available at a cost. Today, Myriad is still investing heavily to develop a new version of BART™ with a significantly lowered cost and increased efficiency. Myriad is striving to provide an improved BART™ that is commercially viable to all patients at little cost. Myriad makes free testing available to needy patients through independent non-profit organizations. Due to their efforts, over 90% of the tests Myriad performs are covered by insurance at over 90% of the test cost. Critchfield ¶¶ 32, 33, 52, 53; ¶ Ogaard 3.

There are multiple laboratories available for confirmatory testing under patent licenses from Myriad. Many of these labs have been performing testing for specific *BRCA* mutations for the past ten years. For example, testing for specific *BRCA* mutations is available in both the University of Chicago Genetic Services Laboratories and Yale DNA Diagnostic Laboratories.

Information on their testing services for BRCA mutations is readily accessible on Internet.

Critchfield ¶ 62; Lessman ¶ 4.

Dated: New York, New York
December 23, 2009

JONES DAY

By: /s/ Brian M. Poissant
Brian M. Poissant
Barry R. Satine
Laura A. Coruzzi
222 East 41st Street
New York, NY 10017
(212) 326-3939

Gregory A. Castanias (admitted *pro hac vice*)
51 Louisiana Avenue, N.W.
Washington, DC 20001-2113
(202) 879-3939

Attorneys for Defendants Myriad Genetics, Lorris Betz, Roger Boyer, Jack Brittain, Arnold B. Combe, Raymond Gesteland, James U. Jensen, John Kendall Morris, Thomas Parks, David W. Pershing, and Michael K. Young

CERTIFICATE OF SERVICE

This is to certify that on December 23, 2009, a true and correct copy of the foregoing document has been served on all counsel of record via the court's ECF system.

/s/ Brian M. Poissant
Brian M. Poissant