U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
OFFICE FOR CIVIL RIGHTS
HEALTH INFORMATION PRIVACY COMPLAINT
200 Independence Avenue, SW, HHH Building
Washington, DC 20201

COMPLAINANTS

Barbara Zeughauser
Ken Deutsch
Runi Limary
AnneMarie Ciccarella

Counsel for Complainants:
Sandra S. Park
Lenora M. Lapidus
American Civil Liberties Union
125 Broad St. 18th Floor
New York, NY 10004
(212) 519-7871
spark@aclu.org

Please direct all communications regarding this Complaint to Sandra Park, counsel for Complainants. Each Complainant submits a consent form, attached hereto.

COMPLAINT FILED AGAINST:

Myriad Genetics Laboratories, Inc.
320 Wakara Way
Salt Lake City, UT 84108
(800) 469-7423

PRELIMINARY STATEMENT

1. This Complaint is submitted by patients who sought, and were denied, access to their own genetic information in violation of the Health Insurance Portability and Accountability Act ("HIPAA") Privacy Rule, 45 C.F.R. § 164.524.[1] The past and ongoing HIPAA violations thwarted the patients' ability to timely access data they could use to examine their own hereditary risk and contribute to research efforts.

2. Complainants are four patients who obtained testing from Myriad Genetics Laboratories, Inc. ("Myriad") to determine their hereditary risk for breast, ovarian, and other cancers and to guide potential treatment options. Myriad performed the testing for these patients. In February 2016, each patient sought access to his or her genetic information from Myriad, including access to all genetic variants identified as part of the testing process. *See* Ex. 1. In March, for each Complainant, Myriad refused to provide any genetic information beyond a copy of their test report. Myriad defined the Designated Record Set as excluding the patients' own genetic information. *See* Ex. 2.

[1] 79 Fed. Reg. 7,290 (Feb. 6, 2014); 65 Fed. Reg. 82,606 (Dec. 28, 2000); U.S. Dep't of Health & Human Services, Individuals' Rights Under HIPAA to Access Their Health Information 45 C.F.R. § 164.524 (Jan. 2016) [hereinafter, HHS 2016 Guidance], http://www.hhs.gov/hipaa/for-professionals/privacy/guidance/access/index.html.

3. As HHS' regulations and guidance make clear, all patients have the right to access their own health information under HIPAA, including their genomic information generated by a clinical laboratory. HHS stated in its most recent guidance: Patients have a right to access "a copy of the completed test report, the full gene variant information generated by the test, as well as any other information in the designated record set concerning the test."[2]

4. Complainants sought access to their genetic data for two primary reasons: to confirm Myriad's interpretation of variants identified in their genes and proactively monitor their own cancer risk and that of their family members as clinical interpretation of genomic information evolves; and to share their data with the broader research community. Complainants especially are focused on gaining access to a complete list of all variants identified in their genes by Myriad, including all variants that Myriad identified but did not disclose in its test reports. Additional background about the importance of patient access to this information and the specific circumstances of each Complainant is provided in the Addendum to this Complaint.

5. Myriad violated the Complainants' HIPAA rights by refusing to provide a copy of their entire Designated Record Set, including their genetic data, as requested by the Complainants. Under HIPAA, patients are entitled to a copy of their entire MRI, X-rays, or physical exam records – not just the portion chosen by a hospital or laboratory. Likewise, the Complainants are entitled to access all of their genetic information.

6. On May 18, 2016 after 4pm ET, three months after Complainants' requests and on the eve of the planned filing of this complaint, Myriad sent new correspondence to each Complainant, returning additional genetic variant information to them. *See, e.g.*, Ex. 3. Myriad did not, however, return the data pursuant to HIPAA's obligations to provide patients with access to their genetic information. Instead, Myriad stated it "wanted to voluntarily follow up regarding additional information." It did not rescind the prior position it had taken that the Designated Record Set excluded their genetic information. Thus, Myriad continues to violate HIPAA by maintaining a position that denies patients access to this data.

7. Complainants request that OCR open an investigation into these HIPAA past and continuing violations and pursue and obtain the relief afforded by law, including timely patient access to genetic information.

JURISDICTION

8. OCR has jurisdiction over this Complaint because Complainants were denied access to their health information by Myriad in violation of the HIPAA Privacy Rule. These denials occurred within 180 days of the filing of this Complaint.

9. Myriad is covered by HIPAA because it provides genetic testing and electronically transmits health information in connection with transactions for which HHS has adopted standards.

[2] HHS 2016 Guidance, *supra* note 1.

HIPAA VIOLATIONS

10. Under the HIPAA Privacy Rule, patients have a right to access protected health information ("PHI") in their Designated Record Set ("DRS"), which is defined as including medical, insurance, and billing records as well as other records "used, in whole or in part, by or for the covered entity to make decisions about individuals."[3] HHS explained that the DRS includes records "that are normally used, and are reasonably likely to be used, to make decisions about individuals," and "records that are, in fact, used, in whole or in part, to make decisions about individuals."[4] The 2014 HIPAA regulations issued by HHS make clear that providers of laboratory tests are subject to the Privacy Rule § 164.524.[5]

11. In order to assess an individual's hereditary cancer risk, Myriad performs genetic sequencing on the BRCA1 and BRCA2 genes (and in the case of MyRisk, on 25 genes, including BRCA1 and BRCA2) to determine whether a patient has or does not have any mutations that Myriad believes increase his or her susceptibility to cancer. The testing procedure generates the patient's genetic sequence for the genes of interest, which is then compared with a reference sequence to identify any variants and to interpret whether any of those variants may influence the patient's cancer risk. *All* of these data—including all genetic variants identified, whether pathogenic (deleterious), likely (suspected) pathogenic, benign, likely benign (favor polymorphism), or of unknown pathogenicity—are therefore part of an individual's DRS.

12. This conclusion was recently reinforced by HHS in guidance issued on January 7, 2016, where it stated that: "The designated record set includes not only the laboratory test reports but also the underlying information generated as part of the test, as well as other information concerning tests a laboratory runs on an individual. For example, a clinical laboratory that is a HIPAA covered entity and that conducts next generation sequencing (NGS) of DNA on an individual must provide the individual, upon the individual's request for PHI concerning the NGS, with a copy of the completed test report, *the full gene variant information generated by the test, as well as any other information in the designated record set concerning the test*."[6]

13. Myriad has adopted a policy of refusing to return patients' genetic information beyond what it discloses in the test report. In response to the Complainants' requests for various types of genetic information and citation of HHS' amendments to the HIPAA regulations, Ex. 1, Myriad said: "It is important to note, however, that those amendments did not expand the definition of the Designated Record Set, e.g., to include any of the additional items listed in your letter. We have therefore not provided information or files outside the above detailed Designated Record Set." Ex. 2.

[3] 45 C.F.R. § 164.501.
[4] 65 Fed. Reg. 82,642, 82,606 (Dec. 28, 2000).
[5] 79 Fed. Reg. 7,290 (Feb. 6, 2014).
[6] HHS 2016 Guidance, *supra* note 1 (emphasis added). *See also* Barbara J. Evans et al., *Regulatory changes raise troubling questions for genomic testing*, 16 Genetics in Med. 799 (Nov. 2014).

14. Myriad's March responses to Complainants did not make clear the types of genetic data it maintains with respect to its patients. It appeared, however, that it does retain information about genetic variants that it does not disclose in the test report. It said: "As to your request for a 'list of all variants,' while we do not generate VCF files, the enclosed test report lists all clinically actionable or potentially clinically actionable results revealed in your test-that is, variations from each tested gene's normal sequences as well as results whose clinical significance is unknown." Ex. 2. The Complainants' requests for their genetic information, however, were not limited to specific types of files like VCF files or to the variants that Myriad determined were clinically actionable or potentially clinically actionable. Thus, the Complainants did not receive information about variants identified by Myriad but not included in the test report.

15. Myriad misconstrued Complainants' requests for their genetic information by suggesting that they seek information outside of the DRS. The DRS is defined according to HHS regulations to include all records *used or reasonably likely to be used* to make decisions about individuals.

16. Myriad relied on the genetic information it obtained from patients through the testing process to make decisions about what is reported to the patient. For every patient, Myriad's testing will identify genetic variants, and it will characterize each of these variants, including labeling most of them as benign. For example, as described in the Technical Specifications for its MyRisk test, Myriad assigns both a functional interpretation (reflecting whether or not the variant is predicted to result in a significant change to normal protein production and/or function) and a clinical interpretation (reflecting whether or not the variant is predicted to be associated with significantly increased risk for one or more cancer types) *for each variant identified*. *See* Ex. 5. Myriad considers and classifies all variants in its assessment of risk – including variants it interprets to be benign – and thus all of these data necessarily must be viewed as part of the DRS. While it does not report benign variants to the patients, Myriad uses this information to issue its test report.

17. Myriad appears to believe that it is obligated under HIPAA to provide only data about variants that it considers "clinically actionable" or "potentially clinically actionable." However, patient access under HIPAA does not turn on a laboratory's narrow reading of what is actionable genetic information, which can also change over time. In the context of genetic testing, the decision about a patient's potential cancer risk depends on analyzing all of his or her variant information, as Myriad's own technical specifications disclose. A determination that all identified variants are benign (a negative test report) is used to make decisions about a patient – *i.e.*, that measures such as increased surveillance or prophylactic surgery may not be warranted. Myriad thus violated HIPAA by refusing to provide records relating to variants that were identified during the testing process but that it did not include in the test report because Myriad classified them as benign. If Myriad is in error about this

classification, the patients have no recourse unless they can obtain the underlying data about their variants.

18. Myriad's most recent communication in the late afternoon of May 18, 2016 demonstrates that Myriad does keep additional variant information on patients and that it can be provided to them. For each patient, Myriad returned additional genetic information that it had not provided Complainants in its initial response to their request, including lists of variants and sequence information. *See, e.g.*, Ex. 3. Myriad did not, however, return the data pursuant to HIPAA's obligations to provide patients with access to their genetic information. Instead, Myriad stated it "wanted to voluntarily follow up regarding additional information" that was not included in the previous DRS, thereby distinguishing the new information from the DRS. Complainants do not know, given Myriad's prior position and its failure to acknowledge the scope of the DRS, whether this data comprises all of their genetic information that is part of the DRS, or whether there may be additional genetic information that should properly be considered part of the DRS but has not yet been returned to them. In addition, Myriad noted in its letter that the patients "might find this information helpful as you discuss your medical information with your healthcare provider," reinforcing the notion that this information is properly part of the DRS.

19. Patients have a right to access their genetic information, regardless of the purpose for which they seek it, under the HIPAA Privacy Rule. As explained further by Dr. Rehm, the Global Alliance for Genomics and Health, and Breast Cancer Action, this access is increasingly valuable both for patients' personal health care and for research. Exs. 6-8. As genetic testing becomes a routine part of care and scientific understanding of genetic variants evolves, access to genetic information beyond the test report will enhance some patients' ability to make medical decisions and to proactively monitor their health in the future. More broadly, there is a growing focus within precision medicine on patient-centered approaches to responsibly generating and sharing genetic data for research purposes. Patients' access to their genetic information pursuant to HIPAA aligns with these overarching medical and scientific goals.

20. Myriad violated HIPAA by refusing to timely provide Complainants' genetic information, which under HIPAA regulations is part of their DRS, and by maintaining the position that patients do not have a right to access genetic information under HIPAA. Moreover, in their communications with Complainants, they have not changed their position that genetic information falls outside of the DRS.

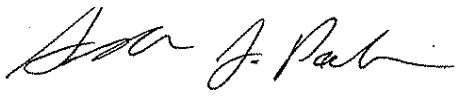
RELIEF REQUESTED

21. Complainants request that OCR open an investigation into the past and continuing HIPAA violations described above and find violations under the Privacy Rule.

22. Relief should include, but is not limited to: A determination that patients have a right to access their genetic information from testing laboratories and regarding violations of Complainants' rights; confirmation that Complainants have been given access to all of their

own genetic information that comprises the DRS; adoption by Myriad of a policy consistent with HHS regulations and guidance providing for patients' access to their own genetic information; and any and all other appropriate corrective actions, monetary penalties, and relief provided by law.

Respectfully submitted,



Sandra S. Park
Lenora M. Lapidus
Counsel for Complainants

May 19, 2016

ADDENDUM

BACKGROUND

1. Patients increasingly obtain genetic testing as part of their medical care. One type of genetic testing offered to patients is aimed at determining whether patients have a hereditary risk for different types of cancer. Patients can use this information in making decisions about surveillance, prevention, and treatment.

2. The BRCA1 and BRCA2 genes are two genes highly associated with inherited cancer risk. Women who have certain mutations on these genes have significantly elevated risks for experiencing breast and ovarian cancers in their lifetimes. These genes also have been connected to increased risks for pancreatic and prostate cancers, among others. In addition to BRCA1 and BRCA2, there are dozens of other genes also associated with hereditary cancers, including breast and ovarian cancers.

3. Myriad has offered genetic testing of the BRCA1 and BRCA2 genes for twenty years. They were the exclusive providers of clinical testing for seventeen years because they held patents on the BRCA1 and BRCA2 genes and used their patent protection to prevent other U.S. laboratories from offering testing to patients.

4. The process of genetic testing uncovers the patient's genetic information. One type of information is the patient's genetic sequence – the sequence of nucleotides (A, C, T, and G) that make up the patient's genetic code. That sequence is then compared to a reference sequence, and where a patient's sequence differs, a genetic variant is identified. Every patient has variants on the BRCA1 and BRCA2 genes. Most of these variants are thought to be benign. Some have been correlated with an increased risk of developing cancer. For others, the clinical significance of the variant is as of yet unknown, most likely because the variant has not been identified in a sufficient number of patients to make a determination either way. *See* Ex. 6.

5. Scientific understanding of genomics – and of the BRCA genes, specifically – is still at an early stage, and knowledge about genetic variants is rapidly evolving. Scientific understanding of the clinical significance of any given variant falls along a gradient, ranging from those in which the variant is almost certainly pathogenic to those that are almost certainly benign.[1]

6. Variant interpretation is often challenging. Geneticists weigh multiple types of evidence that may be available on each variant, and exercise professional judgment to arrive at a

[1] *See, e.g.,* Sue Richards et al., *Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology* (2015), https://www.acmg.net/docs/Standards_Guidelines_for_the_Interpretation_of_Sequence_Variants.pdf [hereinafter, ACMG and AMP Standards].

conclusion.[2] Therefore, it is no surprise that variants are interpreted differently by different laboratories.[3] While BRCA1 and BRCA2 are two of the most well-studied genes, many variants in these genes remain of uncertain significance.[4] Furthermore, interpretation of variants are known to change in light of new clinical and scientific information, as more tests are done and more is learned about variants discovered in patients followed over time.[5] In addition, some variants classified as benign and likely benign are sometimes later found to be low level contributors to disease risk; this is determined by comparing variant frequencies in large populations of people who have experienced the disease and those who have not. Ex. 5.

7. While professional associations like the American College of Medical Genetics and Genomics and the Association for Molecular Pathology have developed guidelines for variant classification, each laboratory can use its own criteria. The ACMG and AMP Standards recommend classifying variants as "pathogenic," "likely pathogenic," "uncertain significance," "likely benign," and "benign," but these categories belie layers of analysis on which experts may differ. Myriad uses its own system and terminology to classify variants, as further described below. The test report it issues to patients reflects this classification.

8. Moreover, each laboratory uses different software to identify and interpret genomic variants. Myriad's software is proprietary, and thus others cannot easily verify whether a variant Myriad has identified is clinically significant.

9. For its BRACAnalysis® test, which tests the BRCA1 and BRCA2 genes, Myriad uses the following terminology to classify variants: "positive for a deleterious mutation," "genetic variant, suspected deleterious," "genetic variant of uncertain significance," "genetic variant, favor polymorphism," and "no deleterious mutation detected." "Positive for a deleterious mutation" indicates variants that Myriad describes as highly correlated with increased cancer risk; "genetic variant, suspected deleterious" indicates variants for which the available evidence indicates a likelihood of pathogenicity; "genetic variant of uncertain significance" indicates variants for which the association with cancer risk is as yet unknown; "genetic variant, favor polymorphism" indicates genetic variants for which available evidence indicates that the variant is highly unlikely to contribute to cancer risk; and "no deleterious mutation detected" indicates genetic variants for which published data demonstrate an absence of substantial cancer risk. In its Technical Specifications for BRACAnalysis®, Myriad notes that it will report variants in the first four categories. Accordingly, patients will receive information only about variants that Myriad identifies if they fall into the first four categories in their test reports. Genetic variants that fall into the last category, resulting in a

[2] ACMG and AMP Standards, *supra* note 1.
[3] *See* Ex. 6; Melanie G. Pepin et al., *The challenge of comprehensive and consistent sequence variant interpretation between clinical laboratories*, 18 Genetics in Medicine 20 (2016).
[4] *See* S. Richter et al., *Variants of unknown significance in BRCA testing: impact on risk perception, worry, prevention and counseling*, 24 Annals of Oncology vii69 (2013).
[5] *See* Ex. 6; Heidi Rehm et al., *ClinGen—The Clinical Genome Resource*, New England J. of Med. (May 27, 2015).

"no deleterious mutation detected" test report, are not disclosed to the patient. As for this last category, Myriad also states: "Data on polymorphic variants are available upon request." *See* Ex. 4. Despite this statement, Myriad did not provide data on variants requested by Complainants.

10. For its MyRisk® test, which tests 25 genes including BRCA1 and BRCA2, Myriad describes use of multiple interpretive criteria in its Technical Specifications. First, it provides a functional interpretation of variants by classifying them in one of four categories: "deleterious mutation"; "genetic variant, suspected deleterious"; "genetic variant of uncertain significance"; and "genetic variant, favor polymorphism" and "genetic variant, polymorphism." Variants in the first three categories are reported, while variants in the last category are not. Second, for each variant identified, Myriad assigns a clinical interpretation by classifying them according to five categories: "high cancer risk," "elevated cancer risk," "clinical significance unknown," "special interpretation," and "clinically insignificant." Variants in the first four categories are reported to patients, while variants in the last category are not. Myriad also provides summary interpretations that either state "clinically significant mutation identified" or "no clinically significant mutation identified." *See* Ex. 5.

11. Thus, Myriad's system for classifying and reporting variants is test-specific. A patient who obtains BRACAnalysis® will receive information about a variant that Myriad classifies as a "genetic variant, favor polymorphism" in his or her test report, while a patient who obtains MyRisk® will not.

12. Classification of some BRCA variants has changed over time: for example, variants of uncertain significance have been reclassified as benign or pathogenic.[6] The classification of variants, including benign variants, is not a set, irrevocable designation.

13. The test report provides only a small fraction of the patient's genetic information obtained during the testing process by Myriad. As described above, Myriad does not report to patients all variants that it has identified in the patient. Patients undergoing testing of their BRCA1 and BRCA2 genes would be expected to have benign variants in these two genes, which together are approximately 165,000 base-pairs in length. *See* Ex. 6.

14. While information about benign variants is not typically required for a patient to gain an understanding of their cancer risk, patients may nonetheless wish to obtain this information. Genetic variants currently categorized as benign could be re-classified in the future as scientific knowledge of cancer genomics evolves, or as research explores connections between those variants and other medical conditions. Patients may also wish to share this information with the research community. As explained by Dr. Rehm, investigation of benign variants and their prevalence in different populations may uncover that they are, in

[6] Mitzi L. Murray et al., *Follow-up of carriers of BRCA1 and BRCA2 variants of unknown significance: Variant reclassification and surgical decisions*, 13 Genetics in Med. 998 (2011).

fact, associated with elevated levels of cancer risk. *See* Ex. 6. The only way to explore these connections is for the data to be available to researchers.

15. Different types of genetic data may be beneficial for research purposes depending on the testing obtained. For example, with patients who obtain panel testing – where particular genes are highly interrogated to diagnose particular genetic conditions or risks – the list of variants identified in the patient is likely to be of most value to researchers. On the other hand, with patients who obtain whole exome sequencing, the raw genetic sequence information may be most useful for research because whole exome sequencing is focused on generating a person's entire genetic sequence and less focused on identifying particular variants. It is thus important that patients who request their genetic information pursuant to HIPAA have access to all the information properly considered part of the DRS. *See* Ex. 6.

16. Complainants are particularly motivated to obtain their genetic data because Myriad refuses to share its data with the larger scientific community. For seventeen years, Myriad controlled patents on the BRCA1 and BRCA2 genes, allowing it to monopolize clinical testing of these genes in the United States and to amass an enormous amount of information about the genes from the patients it tested. Myriad based its business model on exclusive control over clinical BRCA1 and BRCA2 data, calling itself a "genetic information business."[7] It has claimed that its proprietary data gives them a competitive advantage.[8]

17. In 2013, the U.S. Supreme Court invalidated Myriad's patents in *Association for Molecular Pathology v. Myriad Genetics*, 133 S. Ct. 2107 (2013). As a result, numerous laboratories today offer testing of the BRCA1 and BRCA2 genes. Many of these laboratories regularly submit their data to ClinVar, a public, freely accessible archive operated by the National Center for Biotechnology Information at the National Institutes of Health that collects reports about human genetic variants and their clinical significance, with supporting evidence.[9] They also participate in scientific collaborations like the BRCA Challenge, a demonstration project of the Global Alliance for Genomics and Health aimed at advancing the understanding of the genetic basis of breast and other cancers by pooling data on BRCA genetic variants from around the world.[10] These initiatives allow laboratories to share data and scientists to apply multiple and varied methods for interpreting variants on available data. Myriad does not participate.[11] It thus withholds the genetic data of the patients it has

[7] Kevin Davies & Michael White, *Breakthrough: The Race to Find the Breast Cancer Gene* 166 (1996) (quoting Myriad Genetics' 1994 press release).
[8] Turna Ray, *BRCA Variant Data Release From Global Alliance Expands Researchers' Access to Public Data*, GenomeWeb, Apr. 5, 2016.
[9] National Center for Biotechnology Information, http://www.ncbi.nlm.nih.gov/clinvar/intro/ (last visited May 5, 2016).
[10] Ex. 7; *BRCA Challenge*, Global Alliance for Genomics & Health, https://genomicsandhealth.org/work-products-demonstration-projects/brca-challenge-0 (last visited May 5, 2016).
[11] *See* Exs. 6-7; Turna Ray, *Genomic Variant Data Sharing Gains Support; Collaboration Seen as Key to Interpretation Challenge*, GenomeWeb, May 2, 2016.

tested[12] from research initiatives aimed at exploring the connections between these genes, a variety of cancers, and the development of more effective diagnostic methods and potential therapies.

18. Responsible sharing and pooling of genetic data is essential to discerning the significance of genetic variants and advancing scientific research and medical care. For that reason, a priority of the Precision Medicine Initiative launched by the National Institutes of Health is to develop patient-centered approaches to collecting genetic data.[13] The Global Alliance for Genomics and Health has brought together more than 400 organizational members around the world to enable data sharing in order to improve patient diagnoses and prevention of disease. Ex. 7. Aetna, a major health insurance provider, has required companies offering BRCA1 and BRCA2 to submit their variants to a public database such as ClinVar if their test was approved for coverage after January 2015.[14] Indeed, Myriad has acknowledged public databases in its own work on BRCA1 and BRCA2 interpretation.[15]

COMPLAINANTS AND MYRIAD'S RESPONSE TO THEIR REQUESTS

19. Complainants are all patients who received genetic testing of their BRCA1 and BRCA2 genes from Myriad Genetics and who requested, and were denied access to, their genomic data.

20. Barbara Zeughauser and Ken Deutsch are cousins with an extensive history of cancers in their family, including breast, ovarian, lung, and pancreatic cancers. Zeughauser's mother died of breast cancer and had a brother, Deutsch's father, who died of pancreatic cancer. Zeughauser's and Deutsch's shared grandmother also died of pancreatic cancer.

    Zeughauser is a 63-year-old woman living in Maryland. She obtained BRACAnalysis® from Myriad in 2009 and tested positive for a rare deleterious BRCA1 mutation. Deutsch is a 54-year-old man living in Massachusetts. He was diagnosed with metastatic bladder cancer in 2014 and tested positive through Myriad for the same deleterious mutation as Zeughauser. He obtained testing because some courses of cancer treatment are thought to be more successful in those with BRCA mutations. Other relatives also have tested positive.

    Currently, ClinVar contains only three submissions about this variant with summary evidence on seven individuals. Both Zeughauser and Deutsch want access to their genomic data in order to contribute to research initiatives. They strongly believe that data about patients' BRCA1 and BRCA2 genetic information should be shared with the scientific community to advance the understanding of the relationships between variants and different

[12] Myriad Genetics, https://www.myriad.com/healthcare-professionals/about-genetic-testing/overview/ (last visited Apr. 11, 2016).
[13] *Precision Medicine Initiative Cohort Program*, Nat'l Inst. of Health, https://www.nih.gov/precision-medicine-initiative-cohort-program (last visited May 5, 2016).
[14] Ray, *supra* note 11.
[15] *See* J.M. Eggington et al., *A comprehensive laboratory-based program for classification of variants of uncertain significance in hereditary cancer genes*, Clinical Genetics 4 (Nov. 5, 2013) (discussing publicly available databases containing whole-exome sequencing data).

cancers as well as to develop treatment protocols. They are particularly concerned that withholding data about rare variants, such as the BRCA1 deleterious mutation on their genes, will impede research because so little information is available about these variants. They recognize that their own family has benefitted from learning about the BRCA1 variant but that much more research could be done on BRCA variants to advance medical options.

21. Runi Limary is a 39-year-old Asian-American woman living in Texas who was diagnosed with aggressive breast cancer while she was in her late 20s. She obtained BRACAnalysis® from Myriad in 2007 and received a report indicating a BRCA1 genetic variant of uncertain significance. She learned that the variant has been observed in only a few other women, also of Asian descent. This result left her in limbo as she did not know whether her variant did or did not increase her future risk for breast or ovarian cancer. Myriad released another report in 2011 reclassifying the variant as "genetic variant, favor polymorphism." There is only one submission about her variant in ClinVar. She is deeply concerned that Myriad maintains and interprets data about variants like hers and that information is not shared with the scientific community. She believes every person should have access to their own data to be able to make the best decisions for themselves.

22. AnneMarie Ciccarella is a woman in her 50s living in New York who was diagnosed with invasive breast cancer in 2006. She obtained BRACAnalysis® from Myriad, and received a test report indicating a variant of uncertain significance on her BRCA1 gene and another variant of uncertain significance on her BRCA2 gene. The BRCA1 variant of uncertain significance has only four reported submissions to ClinVar, with conflicting interpretations of pathogenicity. The BRCA2 variant of uncertain significance only has one submission in ClinVar. In 2010, Myriad reclassified the BRCA1 variant as a "genetic variant, favor polymorphism," and in 2012, as benign. In 2015, Myriad reclassified the BRCA2 variant as a "genetic variant, favor polymorphism." She wants access to her genetic information in order to be able to better monitor scientific advancements in understanding her genes and to contribute her data to global efforts aimed at improving interpretation of BRCA1 and BRCA2 variants.

23. All of the patients submitted requests for their genetic data to Myriad in February 2016. *See, e.g.*, Ex. 1. The patients requested their entire Designated Record Set, including but not limited to: records relating to clinical interpretation of variants identified; raw genomic sequencing reads; assembled sequences of the genes examined; list of all variants identified, including benign variants, variants of uncertain significance, and pathogenic variants; and results of any large-scale rearrangement/insertion/deletion analysis conducted. The requests each cited regulations and guidance from HHS as mandating patient access to their genomic information – 79 Fed. Reg. 7,290 (Feb. 6, 2014); 65 Fed. Reg. 82,606 (Dec. 28, 2000); U.S. Dep't of Health & Human Services, Individuals' Rights Under HIPAA to Access Their Health Information (Jan. 2016), http://www.hhs.gov/hipaa/for-professionals/privacy/guidance/access/index.html.

24. The Complainants received virtually identical responses from Myriad in March 2016. While Myriad provided test request forms, billing information, and test reports, it specifically rejected their requests for their genomic data. In its responses to each of the patients, it said:

"Per your request and in accordance with 45 C.F.R. § 164.524, we have enclosed your entire Designated Record Set in electronic form. We are foregoing any permissible fee related to the fulfillment of your request. To the extent that certain information has been created, your Designated Record Set may (or may not) include:

- [Test request form (TRF)]
- Test results report
- Case notes
- Personal health records submitted by you
- Billing remittance advices and records of payments
- Billing statements
- Forms signed by you
- Health information created or maintained by Myriad's Business Associates

You will note that, in accordance with the amendments to 45 C.F.R. § 164.524(a)(1)(iii) that were published on February 6, 2014 (and which were effective as of April 7, 2014), we are now permitted to include a copy of your completed test report in response to your request. **It is important to note, however, that those amendments did not expand the definition of the Designated Record Set, e.g., to include any of the additional items listed in your letter. We have therefore not provided information or files outside the above detailed Designated Record Set.**

It is important to note that Myriad's customary practice is not to maintain much, if any, of the items you requested that are outside of the Designated Record Set. As you may appreciate, the rise in demand for genetic testing, as well as the increase in complexity of the testing, has led to an increase in the volume of data for laboratories. Such volume is both administratively burdensome and costly to maintain in a secure manner. Further, Myriad's sequencing and data analysis processes are largely custom and do not retain the types of files you requested (e.g., BAM, SAM, CRAM). **As to your request for a "list of all variants," while we do not generate VCF files, the enclosed test report lists all clinically actionable or potentially clinically actionable results revealed in your test-that is, variations from each tested gene's normal sequences as well as results whose clinical significance is unknown.**"

See Ex. 2 (emphasis added).

25. Myriad thus asserted that the Designated Record Set does not include patients' genetic information, such as information about variants that are not clinically actionable or potentially clinically actionable.

26. On May 18, 2016, three months after Complainants' requests and on the afternoon before the planned filing of this complaint, Myriad sent new correspondence to each Complainant, returning additional genetic variant information to them. *See, e.g.*, Ex. 3. Myriad did not, however, state that it was returning the data pursuant to HIPAA's obligations to provide patients with access to their genetic information. Instead, Myriad stated it "wanted to voluntarily follow up regarding additional information" that was not included in the previous Designated Record Set.

Exhibit List

1. February 2016 letter from Complainant requesting genetic information pursuant to HIPAA
2. March 2016 letter from Myriad Genetics denying Complainant's request for genetic information
3. May 18, 2016 letter from Myriad Genetics
4. Myriad's Technical Specifications for BRACAnalysis
5. Myriad's Technical Specifications for MyRisk
6. Supporting letter from Dr. Heidi Rehm, Director of the Laboratory for Molecular Medicine at Partners Healthcare Personalized Medicine and Associate Professor of Pathology at Harvard Medical School
7. Supporting letter from Global Alliance for Genomics & Health
8. Supporting letter from Breast Cancer Action

Exhibit 1

Myriad Genetics Laboratories, Inc.
Privacy Officer
Compliance Department
320 Wakara Way
Salt Lake City, UT 84108
compliance@myriad.com

Dear Myriad:

I am writing to request my entire Designated Record Set, as defined by HIPAA.

Recent regulations and guidance from the U.S. Department of Health & Human Services make clear that under HIPAA, patients have a right to genomic information that laboratories obtain during the testing process as well as any information used to make decisions about genetic test results. 79 Fed. Reg. 7,290 (Feb. 6, 2014); 65 Fed. Reg. 82,606 (Dec. 28, 2000); U.S. Department of Health & Human Services, Individuals' Rights Under HIPAA to Access Their Health Information (Jan. 2016), http://www.hhs.gov/hipaa/for-professionals/privacy/guidance/access/index.html.

I therefore request my entire Designated Record Set, including but not limited to: records relating to clinical interpretation of variants; raw genomic sequencing reads; assembled sequences of the genes examined (assembled sequences of amplicons for BRACAnalysis or BAM/SAM/CRAM files for MyRisk or other next-generation sequencing); list of all variants identified, including benign variants, variants of uncertain significance, and pathogenic variants (VCF files if available, or list of identified variants in genes examined); and results of any large-scale rearrangement/insertion/deletion analysis conducted.

Please send this information to me as soon as possible, and in any case within 30 days, in electronic, machine-readable form via email at [redacted] or indicate a site from which I might download the files. If this request or any part of it is denied, please provide a written explanation for the denial.

Thank you.

Sincerely,

[redacted]

February 13, 2016

Exhibit 2

3/11/2016

[redacted]

Re: Medical Records Request

Dear [redacted]

This letter is in response to your Designated Record Set request, which Myriad received on February 13, 2016.

Per your request and in accordance with 45 C.F.R. § 164.524, we have enclosed your entire Designated Record Set in electronic form. We are foregoing any permissible fee related to the fulfillment of your request. To the extent that certain information has been created, your Designated Record Set may (or may not) include:

- [Test request form (TRF)]
- Test results report
- Case notes
- Personal health records submitted by you
- Billing remittance advices and records of payments
- Billing statements
- Forms signed by you
- Health information created or maintained by Myriad's Business Associates

You will note that, in accordance with the amendments to 45 C.F.R. § 164.524(a)(1)(iii) that were published on February 6, 2014 (and which were effective as of April 7, 2014), we are now permitted to include a copy of your completed test report in response to your request. It is important to note, however, that those amendments did not expand the definition of the Designated Record Set, e.g., to include any of the additional items listed in your letter. We have therefore not provided information or files outside the above detailed Designated Record Set.

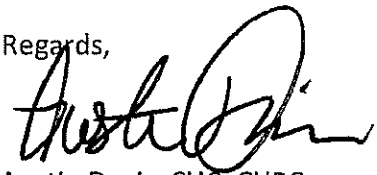
It is important to note that Myriad's customary practice is not to maintain much, if any, of the items you requested that are outside of the Designated Record Set. As you may appreciate, the

Myriad Genetic Laboratories, Inc. / 320 Wakara Way / Salt Lake City, UT 84108 / 801-584-3600

rise in demand for genetic testing, as well as the increase in complexity of the testing, has led to an increase in the volume of data for laboratories. Such volume is both administratively burdensome and costly to maintain in a secure manner. Further, Myriad's sequencing and data analysis processes are largely custom and do not retain the types of files you requested (e.g., BAM, SAM, CRAM). As to your request for a "list of all variants," while we do not generate VCF files, the enclosed test report lists all clinically actionable or potentially clinically actionable results revealed in your test—that is, variations from each tested gene's normal sequences as well as results whose clinical significance is unknown.

Should you have any questions or concerns regarding your request or the items included in our response, please don't hesitate to contact me at audavis@myriad.com or 801-584-3035. Additionally, Myriad would be happy to assist you in better understanding the clinical meaning of your test results and your individual medical management options based on your test results. Again, please let me know if you would like any additional assistance or information.

Regards,



Austin Davis, CHC, CHPC
Privacy Manager | Myriad Genetic Laboratories

Myriad Genetic Laboratories, Inc. / 320 Wakara Way / Salt Lake City, UT 84108 / 801-584-3600

Exhibit 3

myriad®
WHEN DECISIONS MATTER

5/18/2016

[redacted]

Re: Designated Record Set Request

Dear [redacted]

On February 23, 2016 you submitted a Designated Record Set request under HIPAA. We responded on March 22, 2016 by transferring to you several items comprising the Designated Record Set. We also encouraged you to reach back out to us if you had questions or concerns about our response, including the items included in your Designated Record Set, your test results, etc.

We wanted to take this opportunity to follow up with you regarding your request. Since we sent our response, one of our industry associations, the American Clinical Laboratory Association, met with the Office of Civil Rights of the Department of Health and Human Services ("OCR") to discuss patient test records that may now be provided directly to patients. Myriad had the opportunity of participating in that meeting as well. While Myriad anticipates further discussions with OCR, we wanted to voluntarily provide you additional information which is not included in your Designated Record Set response we previously sent. Accordingly, please find attached hereto all the variant information generated by the BRACA*nalysis*® test we performed for you. While this additional information does not contain any clinically actionable results, you might find this information helpful as you discuss your medical information with your healthcare provider.

Regarding your request for other sequence information (e.g., "raw genomic sequencing reads"), please note that due to the passage of time and our data retention practices we no longer possess this data, and thus cannot provide you with this information for your test. We still have, and have included here, raw data for the BART® (large rearrangement) test we ran on your sample.

Since test results have only recently been permitted to be disclosed directly to patients, as an additional resource to you, please be advised that Myriad has a staff of genetic counselors who can help explain your laboratory test results, including interpretation of variants. However, we

Myriad Genetic Laboratories, Inc. / 320 Wakara Way / Salt Lake City, UT 84108 / 801-584-3600

encourage you to always discuss your medical management decisions with your primary healthcare provider. Again, we encourage you or your health care provider to contact Myriad with any questions or additional information you stand in need of for your medical management decisions.

Regards,

Austin Davis, CHC, CHPC
Privacy Manager | Myriad Genetic Laboratories

Myriad Genetic Laboratories, Inc. / 320 Wakara Way / Salt Lake City, UT 84108 / 801-584-3600

Exhibit 4

BRAC*Analysis*® Technical Specifications
Myriad Genetic Laboratories, Updated: October 2, 2013
TEST RESULTS SHOULD BE USED ONLY AFTER REVIEW OF THE FOLLOWING SPECIFICATIONS:

Description of Analysis

Integrated BRAC*Analysis*®:

This test comprises both Comprehensive BRAC*Analysis*® and BRAC*Analysis*® Rearrangement Test (BART).

Comprehensive BRAC*Analysis*®:

BRCA1: Full sequence determination in both forward and reverse directions of approximately 5,400 base pairs comprising 22 coding exons and approximately 750 adjacent base pairs in the non-coding intervening sequences (introns). Exons 1 and 4, which are non-coding, are not analyzed. The wild-type *BRCA1* gene encodes a protein comprised of 1863 amino acids.

BRCA2: Full sequence determination in both forward and reverse directions of approximately 10,200 base pairs comprising 26 coding exons and approximately 900 adjacent base pairs in the non-coding intervening sequence (intron). Exon 1, which is non-coding, is not analyzed. The wild-type *BRCA2* gene encodes a protein comprised of 3418 amino acids.

The non-coding intronic regions of *BRCA1* and *BRCA2* that are analyzed do not extend more than 20 base pairs proximal to the 5' end and 10 base pairs distal to the 3' end of each exon.

This analysis may also include detection of the following five specific large genomic rearrangements of the *BRCA1* gene (5-site rearrangement panel): a 3.8-kb deletion of exon 13 and a 510-bp deletion of exon 22 described in individuals of Dutch ancestry (Petrij-Bosch, A et al., *BRCA1* genomic deletions are major founder mutations in Dutch breast cancer patients. *Nat Gen* 1997; 17:341-345), a 6-kb duplication of exon 13 described in individuals of European (particularly British) ancestry (The *BRCA1* Exon 13 Duplication Screening Group. The Exon 13 duplication in the *BRCA1* gene is a founder mutation present in geographically diverse population. *Am J Hum Gen* 2000; 67:207-212), a 7.1-kb deletion of exons 8 and 9 described in individuals of European ancestry (Rohlfs EM et al., An Alu-mediated 7.1 kb deletion of *BRCA1* exons 8 and 9 in breast and ovarian cancer families that results in alternative splicing of exon 10. *Genes Chr & Cancer* 2000; 28:300-307), and a 26-kb deletion of exons 14-20 (Myriad).

BRAC*Analysis*® Rearrangement Test (BART): All coding exons of *BRCA1/BRCA2*, limited flanking intron regions, and their respective promoters are examined for evidence of deletions and duplications by either multiplex quantitative PCR analysis or microarray comparative genomic hybridization analysis (microarray-CGH).

Single Site BRAC*Analysis*®: DNA sequence analysis for a specified variant in *BRCA1* and/or *BRCA2*. Analysis for one of the five *BRCA1* large genomic rearrangements described above may include analysis for all five rearrangements. When the single site mutation is a *BRCA1*/*BRCA2* deletion or duplication mutation other than the five common *BRCA1* large genomic rearrangements described, multiplex quantitative PCR or microarray comparative genomic hybridization analysis (i.e. BRAC*Analysis* Rearrangement Test) of all coding exons, limited flanking intron regions and the promoter regions of *BRCA1/BRCA2* is performed to assess large rearrangements. In some cases, long range PCR analysis and/or sequencing of the resulting PCR product is used to detect specific, previously reported insertions.

Multisite 3 BRAC*Analysis*®: DNA sequence analysis of specific portions of *BRCA1* exon 2, *BRCA1* exon 20 and *BRCA2* exon 11 designed to detect the mutations 187delAG and 5385insC in *BRCA1* and 6174delT in *BRCA2*.

Description of Method:

Patient samples are assigned a unique bar-code for robotic specimen tracking. DNA is extracted and purified from peripheral blood samples or buccal mouthwash samples, submitted for molecular testing.

Sequence analysis: Aliquots of patient DNA are each subjected to polymerase chain reaction (PCR) amplification (35 reactions for *BRCA1*, 47 reactions for *BRCA2*). The amplified products are each directly sequenced in forward and reverse directions using fluorescent dye-labeled sequencing primers. Chromatographic tracings of each amplicon are analyzed by a proprietary computer-based review followed by visual inspection and confirmation. Genetic variants are detected by comparison with a consensus wild-type sequence constructed for each gene. All potential clinically significant variants are independently confirmed by repeated PCR amplification of the indicated gene region(s) and sequence determination as above.

5-site Rearrangement Panel: The five specific *BRCA1* rearrangements described above are detected by recombination-specific PCR using primers specific for the normal gene as well as for the rearrangement.

Full Gene *BRCA1*/*BRCA2* Large Rearrangement Analysis (BRAC*Analysis* Rearrangement Test): Genomic DNA from patients is analyzed by either multiplex quantitative PCR or microarray-CGH analysis to determine copy number abnormalities indicative of deletion or duplication mutations across the *BRCA1* and *BRCA2* genes. For multiplex quantitative PCR, twelve fluorescently labeled multiplex PCR reactions are designed to interrogate all exons and the respective promoters of *BRCA1* and *BRCA2*, with a minimum of two amplicons per target region. Proprietary software analysis is used to normalize the copy number of individual amplicons in the *BRCA1* gene against *BRCA2*, plus three control genes.

For microarray-CGH analysis, approximately 1700 probes have been designed to interrogate all coding exons, limited flanking intron regions, and the respective promoters of *BRCA1* and *BRCA2*. Each probe is analyzed using proprietary software that compares the ratio of bound patient DNA to that of a reference DNA to indicate regions of altered copy number. The microarray design includes probes to detect deletions and duplications in multiple genes tested by MGL; however, a data masking feature is used to limit the analysis only to specific genes for which testing has been requested.

Patient samples positive for deletions or duplications are confirmed by repeat multiplex quantitative PCR or microarray analysis of the *BRCA1*/*BRCA2*genes. For multiplex quantitative PCR, rearrangement positive samples are further assessed for sequence polymorphisms affecting the PCR primer binding sites, to minimize the possibility of false positive results.

Performance Characteristics:

Analytical specificity: The incidence of a false report of a genetic variant or mutation resulting from technical error is considered negligible because of independent confirmation of all genetic variants (see above). The incidence of a false report of a genetic variant or mutation resulting from errors in specimen handling and tracking is estimated from validation studies to be less than one percent (<1%). No false positive results were obtained through the large rearrangement

testing process using microarray-CGH on a set of 313 individual samples that were previously examined for deletions and duplications in *BRCA1* and *BRCA2* by multiplex quantitative PCR.

Analytical sensitivity: Failure to detect a genetic variant or mutation in the analyzed DNA regions may result from errors in specimen handling and tracking, amplification and sequencing reactions, or computer-assisted analysis and data review. The rate of such errors is estimated from validation studies to be less than one percent (<1%). The analytical sensitivity of DNA sequencing performed in both directions is estimated to be >99.98%. In addition, all samples that were previously examined by alternative methods to be positive for deletions or duplications in *BRCA1*/*BRCA2* were correctly identified by the full gene large rearrangement analysis by multiplex quantitative PCR (BRAC*Analysis* Rearrangement Test).

The large rearrangement testing process using microarray-CGH correctly identified all 37 positives among 313 samples that were previously examined for deletions and duplications in *BRCA1* and *BRCA2* by multiplex quantitative PCR. Furthermore, these validation studies correctly identified two instances of an Alu insertion specific to the Portuguese population (156_157insAlu), among the 313 samples previously tested for large rearrangements.

Overall test accuracy: For a patient with at least a 10% probability of a positive test based on a personal or family history of cancer, the chance of an incorrect test result is less than 1%.

Limitations of method: There may be limited portions of either *BRCA1* or *BRCA2* for which sequence determination can be performed only in the forward or reverse direction. Unequal allele amplification may result from rare polymorphisms under primer sites. Comprehensive BRAC*Analysis* includes testing for only the five specific large genomic rearrangements specified above. The BRAC*Analysis* Rearrangement Test described above using either multiplex quantitative PCR or microarray-CGH will detect deletion and duplication rearrangements involving the promoter and coding exons of *BRCA1*/*BRCA2*, but will not detect some types of errors in RNA transcript processing, regulatory mutations, or balanced rearrangements (i.e. inversions). The Portuguese founder mutation in BRCA2, 156_157insAlu, can be detected by multiplex quantitative PCR and microarray-CGH; however, other insertions that do not result in duplications will generally not be detected.

Among patients who underwent BRAC*Analysis* Rearrangement Testing, the proportion of clinically significant defects in *BRCA1* and *BRCA2* attributable to genomic rearrangements identified specifically by the BRAC*Analysis* Rearrangement Test is estimated to be 5-8% (Judkins, T. et al., Clinical Significance of Large Rearrangements in *BRCA1* and *BRCA2*.*Cancer* 2012; 118(21):5210-5216).

Description of Nomenclature:

All mutations and genetic variants are named according to the convention of Beaudet and Tsui. (Beaudet AL, Tsui LC. A suggested nomenclature for designating mutations. *Hum Mut* 1993; 2:245-248). Nucleotide numbering starts at the first transcribed base of *BRCA1* and *BRCA2* based on GenBank entries U14680 and U43746, respectively. (Under these conventions, the two mutations commonly referred to as "185delAG" and "5382insC" are named 187delAG and 5385insC, respectively.)

Interpretive Criteria:

The classification and interpretation of all variants identified in the assay reflects the current state of scientific understanding at the time the report is issued. In some instances, the classification and interpretation of variants may change as scientific information becomes available.

"Positive for a deleterious mutation": Includes clinically significant nonsense and frameshift mutations that prematurely truncate the protein. In addition, specific missense mutations and non-coding intervening sequence (IVS) mutations are recognized as deleterious on the basis of data derived from linkage analysis of high risk families, functional assays, statistical analysis, biochemical evidence and/or demonstration of abnormal mRNA transcript processing.

Deletions and duplications of an entire exon(s) identified by the BRAC*Analysis* Rearrangement Test may also be interpreted to be deleterious. Deleterious large genomic rearrangements include single exon and multi exonic deletions and duplications that are out of frame. In frame deletions/duplications are interpreted on an individual basis and the specific evidence supporting the classification of these mutations is included in the individual patient report.

"Genetic variant, suspected deleterious": Includes genetic variants for which the available evidence indicates a likelihood, but not proof, that the mutation is deleterious. The specific evidence supporting such an interpretation will be summarized for individual variants on each such report.

"Genetic variant, favor polymorphism": Includes genetic variants for which available evidence indicates that the variant is highly unlikely to contribute substantially to cancer risk. The specific evidence supporting such an interpretation will be summarized for individual variants on each such report.

"Genetic variant of uncertain significance": Includes missense mutations and mutations that occur in analyzed intronic regions whose clinical significance has not yet been determined, as well as nonsense and frameshift mutations that occur very close to the normal stop codon, unless otherwise documented (Mazoyer S et al., *Nature Genetics* 1996; 14:253-254).

"No deleterious mutation detected": Includes genetic variants for which published data demonstrate absence of substantial clinical significance. Includes truncating mutations in *BRCA2* that occur at and distal to amino acid 3326 (Mazoyer S et al., *Nature Genetics* 1996; 14:253-254). Also includes mutations in the protein-coding region that neither alter the amino acid sequence nor are predicted to significantly affect exon splicing, and base pair alterations in non-coding portions of the gene that have been demonstrated to have no deleterious effect on the length or stability of the mRNA transcript. Data on polymorphic variants are available upon request.

There may be uncommon genetic abnormalities in *BRCA1* and *BRCA2* that will not be detected by BRAC*Analysis*® (see **Limitations of method**, above). This analysis, however, is believed to rule out the majority of abnormalities in these genes which are believed to be responsible for most hereditary susceptibility to breast and ovarian cancer.

"Specific variant/mutation not identified": Indicates that specific and designated mutations or variants are not present in the individual being tested.

Change of mutation/variant classification and issuance of amended reports: Whenever there is a change in the classification of a mutation/variant within a patient's test result, an amended report will be provided by Myriad Genetic Laboratories.

(please see reverse side for Description of Analysis and Performance Characteristics)

Exhibit 5

Myriad myRisk™ Hereditary Cancer Technical Specifications
Myriad Genetic Laboratories
Effective: 18 February 2016

TEST RESULTS SHOULD BE USED ONLY AFTER REVIEW OF THE FOLLOWING SPECIFICATIONS:

Description of Analysis:

The Myriad myRisk™ Hereditary Cancer test includes germline DNA-based next generation sequencing (NGS) analysis of a panel of genes related to Hereditary Cancer. Large Rearrangement (LR) testing for deletions and duplications is performed primarily by NGS dosage analysis. Sequence analysis of the coding regions is performed using NGS for the following genes: *APC, ATM, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A* (*p16* and *p14ARF*), *CHEK2, MLH1, MSH2, MSH6, MUTYH, NBN, PALB2, PMS2, PTEN, RAD51C, RAD51D, SMAD4, STK11, TP53*. For the *EPCAM* gene, only large rearrangement analysis is performed (*EPCAM* deletions that affect adjacent *MSH2* gene expression are associated with Lynch syndrome). Portions of non-coding intronic regions are also analyzed by sequencing analysis and typically do not extend more than 20 base pairs (bp) proximal to the 5' end and 10 bp distal to the 3' end of each exon.

Description of Method:

Patient samples are assigned a unique bar-code for robotic-assisted continuous sample tracking. Genomic DNA is extracted and purified from either peripheral blood samples or buccal saliva samples submitted for molecular testing.

DNA sequence analysis by NGS
The samples are prepared through a PCR-based target-enrichment strategy for subsequent next generation sequencing. Aliquots of patient genomic DNA are sonicated. The fragmented DNA is dispersed in oil into picoliter- sized aqueous droplets that are merged with a dropletized target enrichment primer library. The resulting emulsion of microdroplets is subjected to PCR amplification. Emulsion PCR products are purified and subjected to secondary PCR to incorporate sequencing adaptors for NGS and indexing barcodes for individual sample tracking. Barcoded samples from up to 96 patients are pooled and loaded onto massively-parallel next generation sequencers for 2 x 150 base paired-end reads. Primer design and data analysis were optimized for NGS analysis of genes with known pseudogene regions. Supplementary workflows were developed to analyze the *PMS2* and *CHEK2* genes as described below.

Supplementary sample preparation and NGS of PMS2 and CHEK2
Long Range (LoRa) PCR is used for initial amplification of *PMS2* and *CHEK2* gene regions to avoid well-characterized pseudogenes. Aliquots of patient DNA are subjected to gene-specific LoRa amplification of: 1) *PMS2* exons 1-5; 2) *PMS2* exon 9; 3) *PMS2* exons 11-15; 4) *CHEK2* exons 10-14. The four separate LoRa amplicons are diluted and subjected to secondary PCR to incorporate sequencing adaptors for NGS and indexing barcodes for individual sample tracking. The barcoded samples are pooled and loaded onto massively-parallel next generation sequencers for 2 x 150 base paired-end reads.

NGS Data Analysis and Confirmation
A combination of commercial and laboratory-developed software is used for NGS data processing, which includes base-calling, alignment, variant identification, annotation, and quality metrics. Genetic variants are reviewed by computer software and human reviewers. The minimum depth of coverage used for sequence determination by NGS is 50x per base. All clinically significant variants identified by NGS and regions that do not meet NGS quality metrics are independently confirmed with orthogonal, site-specific Sanger sequencing.

Large Rearrangement Analysis
Genomic DNA from patients is analyzed by NGS dosage analysis to determine copy number abnormalities indicative of deletion or duplication mutations. Additionally, this method is used to evaluate samples for an Alu insertion in *BRCA2* exon 3, a Portuguese founder mutation, c.156_157insAlu. NGS dosage analysis uses normalized read counts from sequencing amplicons to determine gene copy number. Pseudogenes are avoided through primer design and alignment filters for NGS data analysis. For *PMS2* exons 12-15 and flanking regions, this approach is supplemented by dosage quantification involving previously defined paralogous sequence variants (PSVs) between *PMS2* and its highly homologous pseudogene *PMS2CL*. Approximately 2,000 amplicons for NGS are used to interrogate coding exons and limited flanking intron regions of tested genes. Functionally characterized promoter regions of certain genes are also analyzed for gross deletion or duplication (*APC, BMPR1A, BRCA1, BRCA2, MLH1, MSH2, MSH6, PTEN, SMAD4, STK11* and *TP53)*. For NGS dosage analysis, the normalized ratio of each amplicon is compared across patients to identify regions of altered copy number. Patient samples positive for deletions or duplications are confirmed by repeat testing using one or more methods, which can include NGS dosage analysis, Multiplex Ligation-dependent Probe Amplification (MLPA), or microarray comparative genomic hybridization (microarray-CGH) analysis. For microarray-CGH analysis, approximately 9,600 probes interrogate coding exons, limited flanking intron regions, and promoters of tested genes. Microarray probe design was optimized to avoid known pseudogene regions, which includes the use of flanking intron probes in certain genes. Probe signals are analyzed using laboratory developed software that compares the ratio of bound patient DNA to that of a differentially labeled reference DNA to identify regions of altered copy number. In addition to large rearrangements detected by NGS, a 10 Mb inversion mutation involving *MSH2* exons 1-7 is detected by targeted PCR and Sanger sequencing analysis across the 5' inversion breakpoint.

Single Site Analysis
DNA sequencing or large rearrangement analysis is performed for the specified variant in *APC, ATM, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A* (*p16* and *p14ARF*), *CHEK2, EPCAM, MLH1, MSH2, MSH6, MUTYH, NBN, PALB2, PMS2, PTEN, RAD51C, RAD51D, SMAD4, STK11* or *TP53*. Single site testing for sequencing mutations is performed using Sanger sequencing. When the single site mutation is a deletion or duplication mutation, microarray–CGH analysis, NGS dosage analysis, or MLPA is used. In some cases, long-range PCR analysis and/or sequencing of the resulting PCR product is used to detect specific, previously reported insertions.

Performance Characteristics:

Analytical Validation Publication: Judkins et al. BMC Cancer (2015) 15:215 DOI 10.1186/s12885-015-1224-y

Analytical specificity
The incidence of a false report of a genetic variant or mutation resulting from technical error is considered negligible because of independent confirmation of all clinically significant genetic variants (see above). The incidence of a false report of a clinically significant genetic variant or mutation resulting from errors in specimen handling and tracking is estimated from validation studies to be less than one percent (<1%).

Analytical sensitivity
Failure to detect a genetic variant or mutation in the analyzed DNA regions may result from errors in specimen handling and tracking, amplification and sequencing reactions, or computer-assisted analysis and data review. The rate of such errors is estimated from validation studies to be less than one percent (<1%). The analytical sensitivity of next-generation sequencing for genes in the myRisk test was 100% (99.96%-100%, 95% C.I.) and the analytical specificity was 100% (99.99%-100%, 95% C.I.) based on complete concordance in comparative studies to validated reference methods performed on 238 individual anonymized DNA samples extracted from blood or saliva with 9,303 identified sequence variants for genes in the myRisk test.

Large Rearrangement Validation
Validation studies for large rearrangement detection using NGS dosage analysis were performed using DNA samples extracted from blood and buccal saliva samples. These included 308 samples that had previously tested positive for large rearrangement mutations, which were all successfully detected by NGS dosage analysis of the genes in the myRisk panel. All reviewable results for large rearrangements were 100% concordant.

Test reproducibility
The 1st comparative analytical validation study included a reproducibility sample set comprised of 4 individual anonymized DNA samples extracted from blood, collectively carrying 199 sequence variants confirmed by Sanger sequencing. The 2nd study included a reproducibility sample set comprised of anonymized DNA extracted from 4 contributors who donated paired blood and saliva samples, collectively carrying 121 sequence variants which were found to be concordant between saliva and blood. In both studies, each of the 4 anonymized samples was sequenced by NGS in triplicate across three batches (i.e., 4 samples x 9 replicates each) which demonstrated 100% reproducibility.

Exhibit 5

Limitations of method
Unequal allele amplification may result from rare polymorphisms under PCR primer sites. The presence of pseudogenes may complicate the detection of rare sequencing and large rearrangement mutations in certain genes. There may be uncommon genetic abnormalities such as specific insertions, inversions, and certain regulatory mutations that will not be detected by myRisk. This analysis, however, is believed to rule out the majority of abnormalities in the genes analyzed. Genetic testing results on blood or buccal saliva samples may not reflect the germline genetic status of patients with a hematologic malignancy, or patients who underwent allogeneic bone marrow transplants. In such cases, please contact Medical Services to discuss re-submission of an appropriate sample type.

Description of Nomenclature:

All mutations and genetic variants are referenced to cDNA positions on their respective primary transcripts and named according to the HGVS convention (J Mol Diagn. 2007 Feb;9(1):1-6). Transcript IDs are indicated on patient reports with their associated variants (Table 1).

Interpretive Criteria:

Functional Variant Interpretations
A functional interpretation is assigned to each variant identified. This interpretation reflects whether or not the variant is predicted to result in a significant change to normal protein production and/or function. It may not necessarily reflect cancer risk (see Clinical Variant Interpretations).

"Deleterious mutation": Includes most nonsense and frameshift mutations that occur at/or before the last known deleterious amino acid position of the affected gene. In addition, specific missense mutations and non-coding intervening sequence (IVS) mutations are recognized as deleterious on the basis of data derived from linkage analysis of high risk families, functional assays, biochemical evidence, statistical evidence, and/or demonstration of abnormal mRNA transcript processing.

"Genetic variant, suspected deleterious": Includes genetic variants for which the available evidence indicates a high likelihood, but not definitive proof, that the mutation is deleterious. The specific evidence supporting an interpretation will be summarized for individual variants on the Genetic Test Result.

"Genetic variant of uncertain significance": Includes missense variants and variants that occur in analyzed intronic regions whose functional significance has not yet been determined, as well as nonsense and frameshift mutations that occur distal to the last known deleterious amino acid positions of the affected genes.

"Genetic variant, favor polymorphism" and "Genetic variant, polymorphism": Includes genetic variants for which available evidence indicates that the variant is highly unlikely to alter protein production and/or function or contribute substantially to cancer risk. Variants of this type are not reported.

Clinical Variant Interpretations
A clinical interpretation is assigned to each variant identified. This interpretation reflects whether or not the variant is predicted to be associated with significantly increased risk for one or more cancer types.

"High Cancer Risk": Includes genetic variants for which absolute cancer risk is predicted to be higher than ~5% with a ~3-fold or higher increased relative risk over that of the general population. Strong data is available to support gene-specific risk estimates, although actual variant-specific risks may differ.

"Elevated Cancer Risk": Includes genetic variants for which there is sufficient data to indicate that the specific variant increases risk for one or more cancers over that of the general population. These risks may be lower than those conveyed by "High Cancer Risk" variants or may be supported by less solid, but still significant, data.

"Clinical Significance Unknown": Includes genetic variants for which there is insufficient data to determine whether or not the variant is associated with increased cancer risk.

"Clinically Insignificant": Includes genetic variants for which available evidence indicates that the variant is highly unlikely to significantly contribute to cancer risk. Variants of this type are not reported.

"Special Interpretation": Includes genetic variants with more complex clinical interpretations. Specific interpretations will be provided for each variant on the Genetic Test Result.

Summary Interpretations

"Clinically significant mutation identified": Includes Genetic Test Results in which one or more genetic variants, which are associated with the potential to alter medical intervention, were identified."

"No clinically significant mutation identified": Includes Genetic Test Results in which either no genetic variants were identified or all identified variants were classified as "Clinical Significance Unknown" or "Clinically Insignificant."

Change of interpretation and issuance of amended reports

The classification and interpretation of all variants identified in the assay reflect the current state of scientific understanding at the time the report is issued. In some instances, the classification and interpretation of such variants may change as new scientific information becomes available. Whenever there is a clinically significant change in the classification of a variant within a patient's test result, an amended report will be provided by Myriad Genetic Laboratories.

Table 1: Transcript IDs associated with myRisk genes

Gene Name	Transcript ID
APC	NM_000038.5
ATM	NM_000051.3
BARD1	NM_000465.3
BMPR1A	NM_004329.2
BRCA1	NM_007294.3
BRCA2	NM_000059.3
BRIP1	NM_032043.2
CDH1	NM_004360.3
CDK4	NM_000075.3
CHEK2	NM_007194.3
EPCAM	NM_002354.2
MLH1	NM_000249.3
MSH2	NM_000251.2
MSH6	NM_000179.2
MUTYH (alpha5)	NM_001128425.1
MUTYH (alpha3)	NM_001048171.1
NBN	NM_002485.4
P14ARF	NM_058195.3
P16	NM_000077.4
PALB2	NM_024675.3
PMS2	NM_000535.5
PTEN	NM_000314.4
RAD51C	NM_058216.2
RAD51D	NM_002878.3
SMAD4	NM_005359.5
STK11	NM_000455.4
TP53	NM_000546.5

http://www.ncbi.nlm.nih.gov/refseq/

References:

Judkins T et al. *BMC Cancer* (2015) 15:215

https://www.myriadpro.com/

Exhibit 6

Laboratory for Molecular Medicine
Partners Healthcare Personalized Medicine
65 Landsdowne Street, Cambridge, MA 02139
Tel: 617-768-8291; Fax: 617-768-8513
hrehm@partners.org

Heidi L. Rehm, PhD, FACMG
Associate Professor of Pathology
Brigham & Women's Hospital
Harvard Medical School

May 17, 2016

U.S. Department of Health and Human Services
Office for Civil Rights
200 Independence Avenue, SW, Suite 515F, HHH Building
Washington, DC 20201

To Whom It May Concern:

I submit this letter in support of the HIPAA complaint filed by patients regarding patient access to genetic information.

I am the Director of the Laboratory for Molecular Medicine at Partners Healthcare Personalized Medicine and Associate Professor of Pathology at Harvard Medical School and Brigham & Women's Hospital. The CLIA accredited lab that I run offers a range of genetic sequencing services for both direct clinical use and to support research programs. I also am involved in a number of efforts aimed at public pooling of genetic data in order to facilitate research and clinical understanding of genetic variants, including ClinGen, the Clinical Genome Resource Program, funded by the National Institutes of Health. This involves laboratories submitting their variant interpretations to ClinVar, a free and open variant database allowing comparison of variant interpretations to identify and resolve differences, enabling improved care of patients. I am also involved in leading the Matchmaker Exchange program which facilitates sharing rare disease patient data to help identify new causes of disease.

I support the right of patients to access their genomic data. In our laboratory, we provide patients with access to their genetic information upon request. For patients who receive panel testing, where we are focusing on certain genes connected with particular diseases, we include all likely benign variants on the test report in case these variants are later reclassified as disease associated, and we also allow patients access upon request to a list of all of the genetic variants we identified, including benign variants. For those who receive whole genome sequencing, we typically provide the entire genetic sequence upon request.

While HIPAA makes clear that patients can access their data for any reason, there are at least three compelling, well-founded reasons why patients may want access. First, patients may want to confirm the interpretation of their genetic testing results. Second, patients may wish to retain a complete list of their genetic variants so they can monitor scientific findings related to those variants over time. Third, patients may want to share their data to advance research.

The process of genetic testing involves interrogating particular segments of a patient's DNA (or the entire sequence in the case of whole genome sequencing) to determine the sequence of nucleotides (A, C, T, and G) that make up the patient's genetic code. That sequence is then compared to a reference sequence, and where a patient's sequence differs, a genetic variant is identified. Each variant is then clinically interpreted. While there have been major advancements in deciphering the genetic bases of human disease, for the majority of the more

than 80 million genetic variants that have been uncovered in the human genome, we have no clear understanding of their role in human health and disease.

Every patient has numerous genetic variants, including in the BRCA1 and BRCA2 genes. Many of these variants are thought to be benign, or not connected to disease or susceptibility to disease, and some variants have been correlated with an increased risk of disease by scientists, but many others are of uncertain clinical significance.

The determination by a laboratory that a patient has particular variants but all are benign is typically reported as a "negative" test result, with no information provided to the patient that variants were identified and characterized as benign. In the context of testing the BRCA genes, this result generally leads a patient and the physician to conclude that there is no elevated risk for cancer and thus they need not pursue additional surveillance or prophylactic surgery.

Until recently there have been no standards for how genetic variants should be interpreted, and laboratories have developed their own systems and judgments. The American College of Medical Genetics and Genomics and the Association for Molecular Pathology recently published a set of guidelines for classifying variants as "pathogenic," "likely pathogenic," "uncertain significance," "likely benign," and "benign."[1] However, application of the guidelines is not mandatory and even when applying such standards, labs still arrive at different conclusions given the subjectivity of applying the rules.[2] Laboratories also differ in the information they provide to patients in reporting their genetic test results. Some may choose to report only those variants that they believe are pathogenic, likely pathogenic, or of uncertain significance, while others may also report variants that are likely benign.

Laboratories can and do differ in interpreting variants, including variants thought to be benign or likely benign. As a result, our research has shown that in some cases, patients are receiving inconsistent and sometimes inaccurate information that can lead to patient harm. In a 2015 publication, we reported that 17% of variants interpreted by more than one laboratory were interpreted differently.[3] Patients therefore may want access to their genetic information in order to confirm a laboratory's clinical interpretation of their cancer risk.

Furthermore, variants are regularly re-classified. Sometimes variants initially classified as likely benign or benign can later be found to be risk factors for disease once data is combined across larger cohorts. Such variants have already been shown to be associated with increased risk for breast cancer.[4] Patients may wish to retain a copy of their complete list of variant calls so that they can monitor developments in scientific knowledge that may impact their risk.

Finally, patients may want access to their data so they can share it with the research community. Scientists rely on publicly available databases to inform how they interpret a genetic variant given that only a paucity of variant data is available through publications. A key factor in the ability of scientists to determine the clinical significance of a variant is whether they

---

[1] Richards et al., *Standards and guidelines for the interpretation of sequence variants*, Genetics in Medicine (Mar. 5, 2015).
[2] Amendola et al., *Performance of ACMG-AMP Variant Interpretation Guidelines among Nine Laboratories in the Clinical Sequencing Exploratory Research Consortium*, The Am. J. of Human Genetics (2016), http://dx.dol.org/10.1016/j.ahjg.2016.03.024.
[3] Heidi Rehm et al., *ClinGen – the Clinical Genome Resource* – N. Engl. J. Med. (May 27, 2015).
[4] Walsh et al., *Genomic Biomarkers for Breast Cancer Risk*, Adv. Exp. Med. Biol. 2016; 882:1-32. doi: 10.1007/978-3-319-22909-6_1.

can examine a large amount of data about that variant – including how often it has been identified in patients and whether they have experienced particular diseases, like cancer. Our lack of consistent, clear and clinically relevant annotation of human genetic variation is due, in part, to the so-called silo effect, in which various commercial and academic entities maintain isolated, sometimes proprietary, databases of variant interpretations. This prevents the sharing of critical knowledge that could benefit patients, families, health care providers, diagnostic laboratories, and payers.[5] It has been shown that comparing data to enable consensus efforts is the best approach to arrive at consistent variant interpretation.[6] Recognizing this issue, some healthcare providers have begun to only order services from laboratories who share their data and Aetna, a major health insurer, began requiring labs to submit to ClinVar if they wanted reimbursement for their BRCA tests.[7]

To the best of my knowledge, Myriad does not contribute genetic variant data to ClinVar and stopped contributing data about the BRCA1 and BRCA2 genes to the Breast Cancer Information Core more than a decade ago. It thus retains data about the BRCA1 and BRCA2 genetic variants it identifies in patients in its exclusive, proprietary database, even while acknowledging reliance on public databases in its own work.[8] In my opinion, Myriad's data exclusivity impoverishes the scientific and clinical understandings of the genes.

Myriad's website includes its "Policy on Genetic Information."[9] The Policy states: "Myriad's laboratory processes including variant classification and variant databases are subject to regulatory oversight from either CLIA (Clinical Laboratory Improvement Amendments) or the U.S. Food and Drug Administration. Consistent with this regulatory oversight, we are not allowed to release our variant databases because they may only be used to interpret clinical test results for patients tested in our laboratories." In my opinion and in consultation with FDA staff, this statement is incorrect and seriously misleading. Laboratories around the world, including my own, regularly contribute data about genetic variants to efforts like ClinVar and many others. Neither CLIA nor the FDA prohibits the release of variant data. Indeed, the federal government encourages and incentivizes genomic data-sharing.

Thank you for your consideration.

Sincerely,

Heidi Rehm

Heidi L. Rehm, Ph.D., FACMG
Chief Laboratory Director, Laboratory for Molecular Medicine, Partners Personalized Medicine
Medical Director, Broad Institute Clinical Research Sequencing Platform
Associate Professor of Pathology, Brigham and Women's Hospital and Harvard Medical School

[5] Rehm et al., *supra* note 3.
[6] Amendola et al., *supra* note 2.
[7] Turna Ray, *Genomic variant data sharing gains support; Collaboration seen as key to interpretation challenge*, GenomeWeb, May 2, 2016.
[8] *See* J.M. Eggington et al., *A comprehensive laboratory-based program for classification of variants of uncertain significance in hereditary cancer genes*, Clinical Genetics 4 (Nov. 5, 2013) (discussing reliance on publicly available databases containing whole-exome sequencing data).
[9] https://www.myriad.com/myriad-cares-2/policy-on-genetic-information/.

Exhibit 7

Global Alliance
for Genomics & Health
Collaborate. Innovate. Accelerate.

May 12, 2016

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
OFFICE FOR CIVIL RIGHTS
200 Independence Avenue, SW, Suite 515F, HHH Building
Washington, DC 20201

To whom it may concern,

We are writing in support of the administrative complaint submitted by patients seeking access to their *BRCA1* and *BRCA2* genetic information. As leaders of the Global Alliance for Genomics and Health (GA4GH), we believe that variant aggregation and patient access to genomic and clinical data are critical steps in the effort to improve human health through genomic medicine.

The GA4GH consists of more than 400 organizational members and more than 600 individual members from around the globe who are working together to establish a common framework of harmonized approaches to enable effective and responsible sharing of genomic and clinical data. We work to illustrate the value of data sharing in real world contexts by catalyzing demonstration projects such as the BRCA Challenge, whose specific aim is to advance understanding of the genetic basis of breast and other cancers by pooling data on *BRCA1/2* genetic variants from around the world. Improved understanding of genetic variation in these genes has the potential to improve patient diagnoses and prevention of disease.

Founded in part on the principle of respect for the data sharing and privacy preferences of participants, GA4GH takes a humans rights approach to the issue of patient engagement: as stated in our *Framework for Responsible Sharing of Genomic and Health Related Data*, Article 27 of the 1948 *Universal Declaration of Human Rights* guarantees the rights of every individual in the world "to share in scientific advancement and its benefits" (including to freely engage in responsible scientific inquiry). For this reason, we believe that patients have a human right to access their own data in order to contribute to any research that would benefit from those data.

As such, we are committed to ensuring that patient access to genomic and health related data align with the goals of the BRCA Challenge. Patients who obtain their data from Myriad can immediately support research by sharing their information directly with the BRCA Exchange, the web portal built by the BRCA Challenge. Several other private labs that offer BRCA testing are already reflexively sharing variant-level data with public databases such as ClinVar, consistent with patient consent. The BRCA Challenge has aggregated those data, and is also currently collaborating with Ambry, Invitae, Counsyl,

Exhibit 7

Global Alliance for Genomics & Health
Collaborate. Innovate. Accelerate.

GeneDx, Color Genomics, and others, to pilot the aggregation of some case-level data in a secure computing environment for improved pathogenicity classification. Data from Myriad remain a gaping void in the world's knowledge about *BRCA*-related cancers.

For precision medicine to realize its promise of transforming human health, researchers and clinicians must have access to large-scale datasets on the order of many millions of genomic and clinical cases. Millions of data points are needed to achieve statistically robust evidence linking genomic information with phenotypes, diagnoses, and treatment responses. Furthermore, data sets must contain information across all levels of pathogenicity, from benign to deleterious in order to reveal differences in health and disease. No single institution is capable of compiling such volumes on its own, so data aggregation is imperative.

All variant calls and raw sequencing files are used in assessing a patient's hereditary risk for BRCA-related cancers, so these data should be considered part of a patient's Designated Record Set (DRS). Access to these data is critical for the global community to learn from clinical genomic research and to achieve better health outcomes as a result. For this reason, the GA4GH recommends that OCR clarify that the DRS explicitly includes variant calls and raw sequencing files, giving patients the right under HIPAA to routinely access them and thus contribute to research and improved health.

Best regards,

Thomas Hudson
Chair, Steering Committee
Global Alliance for Genomics and Health

Peter Goodhand
Executive Director
Global Alliance for Genomics and Health

Exhibit 8

BREAST CANCER ACTION

May 13, 2016

U.S. Department of Health and Human Services
Office for Civil Rights
200 Independence Avenue, SW, Suite 515F, HHH Building
Washington, DC 20201

To whom it may concern,

We submit this letter in support of the HIPAA complaint filed by patients regarding access to genetic information.

Breast Cancer Action (BCAction) is a national education and activist organization working to achieve health justice for all women at risk of and living with breast cancer. We advocate for systemic change to stop breast cancer before it starts, while also addressing the needs of women at risk of and living with breast cancer. With 60,000 members nationwide, we are a patient watchdog working to put public health and patient needs first.

In 2009, we were a plaintiff in the suit brought against Myriad Genetics to challenge the company's patent claims on the human BRCA1 and BRCA2 genes, the *Association for Molecular Pathology v. Myriad Genetics, Inc*. In June 2013 the U.S. Supreme Court ruled unanimously in our favor that genes found in nature are not patentable. Soon after the ruling the cost of commercial testing dropped and more women were able to get access to this potentially life-saving information.

Our interest in this issue goes beyond the extremely important issue of cost and access. We are also deeply concerned about the ways that the patent monopoly held by Myriad Genetics for nearly 20 years impeded scientific and medical progress.

Despite the significant progress that identification of the BRCA 1/2 genes sparked for families with strong histories of breast and ovarian and other cancers, many questions remain. For example, some families carry variants of uncertain significance (VUS), which labs have not yet classified as linked or not linked to increased risk of cancer. Such families urgently want answers about these rare mutations. Other families have a strong history of cancer even without carrying a recognized deleterious mutation. Additionally, even for families with a known deleterious mutation, questions remain why some individuals get cancer while others do not.

As a patient watchdog, we recognize that in order to answer these and other patient questions, researchers and clinicians must have access to properly protected and anonymized data from millions of individuals. Although there are a number of labs seeking to address these and other issues, so long as Myriad Genetics continue to hold hostage vast quantities of data accumulated under an unjust patent, advancements will be delayed.

We believe that access to these data is critical for the medical and scientific community to learn from clinical genomic research and to advance medical options for women living with and at risk of breast cancer. For this reason, BCAction believes that all patients should have the same right to access genetic information as she would to records about physical exams, mammograms, MRIs, and other medical procedures. No company should be able to withhold a patient's genetic information

657 Mission Street, Suite 302 San Francisco, California 94105
Tel: 415.243.9301 Toll free: 1.877.2STOPBC Fax: 415-243-3996
Web: www.bcaction.org www.thinkbeforeyoupink.org Email: info@bcaction.org

from her. All patients should have the right to access their own genetic information which would allow them to monitor any scientific developments that might affect them and their families as well as contribute their data to research.

We urge you to affirm patient rights to their genetic information under HIPAA.

Sincerely,

Karuna Jagger
Executive Director
Breast Cancer Action