UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF NEW YORK

ASSOCIATION FOR MOLECULAR PATHOLOGY; AMERICAN COLLEGE OF MEDICAL GENETICS; AMERICAN SOCIETY FOR CLINICAL PATHOLOGY; COLLEGE OF AMERICAN PATHOLOGISTS; HAIG KAZAZIAN, MD; ARUPA GANGULY, PhD; WENDY CHUNG, MD, PhD; HARRY OSTRER, MD; DAVID LEDBETTER, PhD; STEPHEN WARREN, PhD; ELLEN MATLOFF, M.S.; ELSA REICH, M.S.; BREAST CANCER ACTION; BOSTON WOMEN'S HEALTH BOOK COLLECTIVE; LISBETH CERIANI; RUNI LIMARY; GENAE GIRARD; PATRICE FORTUNE; VICKY THOMASON; KATHLEEN RAKER, Plaintiffs, v. UNITED STATES PATENT AND TRADEMARK OFFICE; MYRIAD GENETICS; LORRIS BETZ, ROGER BOYER, JACK BRITTAIN, ARNOLD B. COMBE, RAYMOND GESTELAND, JAMES U. JENSEN, JOHN KENDALL MORRIS, THOMAS PARKS, DAVID W. PERSHING, and MICHAEL K. YOUNG, in their official capacity as Directors of the University of Utah Research Foundation, Defendants.	Civil Action No. 09-4515 (RWS)

DECLARATION OF NANCY J. LINCK, J.D., Ph.D.

I, Nancy J. Linck, hereby declare that:

1. I am currently a member of Rothwell, Figg, Ernst & Manbeck, P.C., 1425 K Street, NW, Suite 800 Washington, DC 20005.

2. I specialize in intellectual property law, particularly in the biotechnology and pharmaceutical areas. I have experience in private and corporate practice, including consulting and litigation at both trial and appellate levels and inter partes matters before the U.S. Patent and Trademark Office ("USPTO"). From 1997 to the present, I have served as an adjunct professor at George Washington University and Georgetown Law Center, lecturing on current issues in intellectual property law. I have published numerous articles in the intellectual property area; these are listed in my *curriculum vitae*, attached as Exhibit 1.

3. I served as an Administrative Patent Judge on the USPTO's Board of Patent Appeals & Interferences in the Board's biotechnology practice group from May 2006 to February 2008. In this capacity, I was responsible for hearing and deciding appeals from Examiners' rejections in the pharmaceutical and biotechnology sectors.

4. Before becoming an Administrative Patent Judge, I was Deputy General Counsel, IP & Trade for the Biotechnology Industry Organization ("BIO") where I was responsible for all intellectual property and trade secret related issues.

5. During the 2002 to 2005 period, I was Senior Vice President, Intellectual Property and Regulatory Affairs, and Chief Compliance Officer for Guilford Pharmaceuticals ("Guilford"). I was a member of the executive management team at Guilford and was

responsible for all aspects of intellectual property, both domestically and internationally. While at Guilford, I also served as Senior Vice President & General Counsel and was responsible for the company's legal matters and all aspects of intellectual property.

6. I served as the Solicitor of the United States Patent and Trademark Office ("USPTO") from August 1994 until November 1998; at that time, the highest legal position in the USPTO, i.e., the Commissioner's General Counsel. As Solicitor, I represented the USPTO in patent, trademark and administrative law litigation and was heavily involved in all legal matters within the USPTO, including evaluation of proposed changes to relevant statutes, rules, and the Manual of Patent Examining Procedure ("MPEP"). In addition, I was responsible for what ultimately became known as the USPTO's "legal guidelines," and personally played a lead role in their drafting and adoption by the USPTO.

7. With respect to the USPTO's litigation, I oversaw over 100 appeals at the U.S. Court of Appeals for the Federal Circuit ("Federal Circuit") and a number of district court cases. Among these cases were *Wu v. Wang*, *Hoechst-Roussel Pharms v. Lehman*, *Merck & Co. v. Kessler*, *Astra v, Lehman*, *In re Baird*, *In re Morris*, *In re Portola Packaging Inc.*, *In re Recreative Tech. Corp.*, and *State Street Bank v. & Trust Co. v. Signature Fin. Group, Inc.*, 149 F.3d 1368 (Fed. Cir. 1998) (a case in which the Federal Circuit adopted the USPTO's legal guidelines relating to the patent-eligibility of computer-related inventions under § 101). In addition, I assisted the Department of Justice in intellectual property cases before the U.S. Supreme Court, including *Lehman v. Zurko*, *Markman v. Westview Instruments*, and *Warner-Jenkinson Co. v. Hilton Davis Chem. Co.*

8. Between 1991 and 1994, I was a partner at the intellectual property law firm, Cushman, Darby & Cushman, Washington, D.C. While at Cushman, Darby & Cushman, I represented a number of clients in prosecution and litigation matters, including *Haworth v. Steelcase*, *Perkins v. Kwon*, and *Bigham v. Godtfredsen.*

9. I received my J.D., magna cum laude, from Western New England College School of Law in 1984. In 1986 and 1987, I was a Federal Circuit law clerk for the Honorable Pauline Newman.

10. Prior to my legal education, I received my Ph.D. and M.S. in Inorganic Chemistry from University of California, San Diego (1982) where I studied transition metal complex reactions (organic molecules with metal centers). In 1973, I received a B.S., with honors, in Chemistry from University of California, Berkeley. I recently received my M.S. in Biotechnology from John Hopkins University (2009). My work toward my M.S. included an in-depth study of nucleic acid molecules (DNA and RNA) and their function and structure.

11. I reviewed the following documents: Plaintiffs' Memorandum of Law in Support of Motion for Summary Judgment; Plaintiffs' Rule 56.1 Statement of Material Facts; Declaration of Sir John E. Sulston, Ph.D. of August 17, 2009; Declaration of Myles W. Jackson of August 18, 2009; and United States Patent Nos. 5,747,282 ("the '282 patent"); 5,837,492 ("the '492 patent"); 5,693,473 ("the '473 patent"); 5,710,001 ("the '001 patent"); 5,753,441 ("the '441 patent"); and 6,033,857 ("the '857 patent"), (collectively "Myriad patents").

II. THE USPTO ADMINISTERS THE LAWS ENACTED BY CONGRESS

12. The USPTO is an administrative agency charged with examining patent applications and issuing U.S. patents, if the applications meet the statutory requirements of Title 35. The USPTO must apply the laws Congress has enacted, as interpreted by the Federal Circuit and the Supreme Court. The USPTO has no policy-making authority and, in fact, cannot even adopt substantive rules in doing its job. *In re Alappat*, 33 F.3d 1526 (Fed. Cir. 1994); *Tafas v. Kappos*, --- --, 2009 WL 3806451 (Fed. Cir. Nov. 13, 2009).

13. In the 1994 to 1995 time period, Commissioner Bruce Lehman charged me with determining whether the USPTO was following controlling law with respect to issuing patents for biotechnology inventions. As Solicitor, Commissioner Lehman asked me to study the relevant law and determine what it required the USPTO to do in examining biotechnology patent applications. As part of that effort, I reviewed the precedential cases involving patentability under § 101, particularly focusing on Federal Circuit and Supreme Court cases and those relied upon by these two courts.

14. The threshold issue we investigated was whether biotechnology inventions, such as isolated DNA and RNA molecules were eligible for patent protection under § 101. After reviewing and discussing the relevant cases, I and others working with me on the project concluded that the law dictated granting patents on such biotechnology inventions, if they satisfied the other statutory requirements, particularly that of utility under § 112.

15. In fact, we found that rejections under § 101 in cases relating to biotechnology

and pharmaceutical technology rarely had been sustained by the federal courts. Generally speaking, in those rare cases, the § 101 rejection was sustained either because the patent applicant had failed to disclose any utility for the invention or the asserted utility was not credible. As a result, we developed and issued the first version of our § 101 guidelines (hereafter "1995 Guidelines") to provide guidance to patent examiners to ensure compliance with the law. Exhibit 2; *Utility Examination Guidelines*, 60 Fed. Reg. 36263 (1995) (reproduced in MPEP § 706.03(a)(1) (July 1998)). In the 1995 Guidelines, we identified the tests set forth by the Supreme Court in *Diamond v. Chakrabarty*, 447 U.S. 303 (1980). The tests are identified in the MPEP § 2105 (July 1998):

> (A) "the laws of nature, physical phenomena and abstract ideas" are not patentable subject matter.
> (B) A "nonnaturally occurring manufacture or composition of matter – a product of human ingenuity – having a distinctive name, character, [and] use" is patentable subject matter.
> (C) '[A] new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter. Likewise, Einstein could not patent his celebrated $E=mc^2$; nor could Newton have patented the law of gravity. Such discoveries are 'manifestations of ... nature, free to all men and reserved exclusively to none.'"
> (D) "[T]he production of articles for use from raw materials prepared by giving to these materials *new forms, qualities, properties, or combinations whether by hand labor or bu machinery"* [emphasis added] is a "manufacture" under 35 U.S.C. 101.

16. In addition to identifying the above *Chakrabarty* tests, our analysis of the relevant case law led us to conclude that the Court (1) did not limit *Chakrabarty* to genetically engineered living organisms and the Court (2) had "enunciated a very broad interpretation of 'manufacture' and 'composition of matter.'" *See id. See also infra* notes 3 & 4 (quoting the Court's interpretation of these terms). I note that both these terms encompass Myriad's product claims (hereafter "DNA claims") under the Court's

definitions.

17. Finally, while recognizing the need to determine patent eligibility under § 101 on a "case-by-case basis following the tests set forth in *Chakrabarty*," we determined that the law required the USPTO to find patent eligible any "non-naturally occurring manufacture or composition of matter." *Id.*

18. An analysis of the precedential cases we considered prior to issuing the 1995 Guidelines was included in the later published *Utility Examination Guidelines*, 66 Fed. Reg. 1092 (January 5, 2001) (Exhibit 3) (hereafter the "2001 Guidelines"). My analysis of these cases, along with that of other cases discussed in the 2001 Guidelines, is given below. *See infra* at ¶¶ 29-42; 50-69; & 77.

III. THE UNITED STATES PATENT LAWS

19. We began our legal analysis by acknowledging that our founding fathers recognized the importance of fostering innovation and thus provided Congress with broad powers to "promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive right to their respective writings and Discoveries." U.S. Const, Art. 1, § 8, cl. 8.

20. Pursuant to these broad powers and its policy-making authority, Congress enacted the patent statutes. First enacted in 1790 (Act of April 10, 1790, ch. 7, 1 Stat 109) and found today in Title 35 of the United States Code, these statutes provide patent protection for a limited time period to whomever "invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof . . . , subject to the conditions and requirements of this title." 35 U.S.C. § 101.

The "conditions and requirements" referenced in § 101 are found in 35 U.S.C. §§ 102, 103 and 112, *i.e.*, the invention must be novel, not obvious and described in a way that one skilled in the relevant field can make and use it.

21. The use of the expansive term "any" in § 101 reflects Congress' intent not to place restrictions on the subject matter for which a patent may be obtained beyond those specifically recited in § 101. Indeed, the Supreme Court has acknowledged that Congress intended § 101 to extend to "anything under the sun that is made by man." *Chakrabarty*, 447 U.S. at 309 (quoting S.Rep. No. 1979, 82nd Cong., 2nd Sess., 5 (1952); H.R.Rep. No. 1923, 82nd Cong., 2nd Sess., 6 (1952)).

22. We further acknowledged that, despite the apparent sweep of § 101, the Supreme Court has held that three distinct categories of subject matter, namely "laws of nature, natural phenomena, and abstract ideas," are not entitled to patent protection. *Chakrabarty*, 447 U.S. at 309; *see also*, *Diamond v. Diehr*, 450 U.S. 175, 185 (1981).

23. However, there is no basis in law for any other category of subject matter excluded from patent eligibility. Thus, Plaintiffs improperly read in a fourth category of excluded subject matter – isolated products of nature – into the Supreme Court line of cases. Pl. Br. at 19-20. The Supreme Court has never held that isolated products of nature are *per se* not patent eligible.

24. It is improper to read into § 101 limitations as to the subject matter that may be patented where the legislative history does not indicate that Congress clearly intended such limitations. *See Chakrabarty*, 447 U.S. at 308 ("We have also cautioned that courts should not read into the patent laws limitations and conditions which the legislature has

not expressed.") (internal citations omitted).

25. As recognized by the Supreme Court, the "authority of Congress is exercised in the hope that '[t]he productive effort thereby fostered will have a positive effect on society through the introduction of new products and processes of manufacture into the economy, and the emanations by way of increased employment and better lives for our citizens.'" *Chakrabarty*, 447 U.S. at 307 (quoting *Kewanee Oil Co. v. Bicron Corp.*, 416 U.S. 470, 480 (1974)) (other citations omitted).

26. Following the Supreme Court decision in *Chakrabarty*, patent law operated exactly as Congress hoped it would by promoting science in the biotechnology area and thereby creating a new industry, along with increased employment and better lives for all of us by providing new products such as Myriad's diagnostic tools for breast and ovarian cancer, which are covered by the claims of the Myriad patents.

27. The Myriad patents generally relate to the identification of the *BRCA*1 and *BRCA*2 genes, which are associated with breast and ovarian cancer. The widespread adoption of the diagnostic tests protected by the patents suggests the tests represent a significant breakthrough for the development of cancer diagnostics and therapeutics which would not have happened but for the patent system in effect. Indeed, the discoveries of Myriad and some of the other defendants likely were a result of the post-*Chakrabarty* era which lead to the exponential growth of the biotechnology industry in the United States. Such discoveries are incentivized by the patent system's grant of an exclusivity period. But for such a reward system, investors are unwilling to invest in the costly research and development needed to make products like Myriad's available to

those who need them.

28. Plaintiffs contend that patents related to isolated DNA molecules run afoul of § 101. *MF*s ¶ 96; Pl. Br. at 20-26; Sulston Decl. ¶¶ 26-27. To support their position, Plaintiff cite the Bermuda Principles and state that"[a]ll human genomic sequence information should be freely available and in the public domain" to encourage research and development. Sulston Decl. ¶ 33. Yet, I am not aware of any therapeutic or diagnostic product that has been made available to the public as a result of such data sharing. In contrast, numerous diagnostics and therapeutic products protected by patents have entered the commercial market place.

A. NATURAL PRODUCTS THAT HAVE BEEN ISOLATED AND PURIFIED ARE ELIGIBLE FOR PATENT PROTECTION

29. In each of the following cases patentability was upheld because the compositions sought to be patented were isolated and purified. Those compositions, or compounds, did not exist in nature or the prior art in pure form, as claimed in the subject patents.

30. In a seminal case, *Parke-Davis & Co. v. H. K. Mulford Co.*, Judge Learned Hand held valid a patent on an adrenalin compound isolated and purified from the suprarenal glands of certain animals. 189 F. 95, 103 (S.D.N.Y. 1911). In *Parke-Davis,* it had been known that suprarenal gland in powdered form had "hemostatic, blood pressure raising and astringent properties" but could not be used for those purposes in gross form. The patentee isolated and purified adrenaline having the desired characteristics in pure and stable form. The new composition of matter differed from the prior art extracts "in kind" -- not merely in "degree of purity." *Id.* at 103. Further, the change in the new composition resulted in "ample practical differences." *Id.* The court held that

> "even if [the adrenaline] were merely an extracted product without change, *there is no rule that such products are not patentable.* [The Patentee] was the first to make [adrenaline] available for any use by removing it from the other gland-tissue in which it was found, and, *while it is of course possible logically to call this a purification of the principle, it became for every practical purpose a new thing commercially and therapeutically.* That was a good ground for a patent."

Parke-Davis, 189 F. 95 at 103 (emphasis added).

31. In *Merck*, at issue was a patent on "Vitamin B_{12}-Active Composition" useful for treating pernicious anemia. *Merck & Co., Inc. v. Olin Mathieson Chem. Corp.*, 253 F.2d 156, 157-158 (4th Cir. 1958), *cited with approval in In re Kratz*, 592 F.2d 1169, 1174 (C.C.P.A. 1979). Vitamin B_{12} "is produced in minute quantities in the bodies of cattle." *Id.* at 161. Such naturally occurring Vitamin B_{12} has "some therapeutic and commercial value, but the great superiority of the patented composition is clearly established." *Id.* Patentees obtained the claimed Vitamin B_{12} compositions from the microorganism, *Lactobacillus lactus*. The court held that that patented compositions satisfied the novelty and utility requirement. The Court reasoned that "[t]he active substance was *unidentified and unknown*" prior to the patentee's invention. *Id.* at 163 (emphasis added). But, the purification step from the naturally occurring product was one "from complete uselessness to great and perfected utility" and hence was "no mere advance in the degree of purity of a known product." *Id.* at 164.

32. The Court's holding in *Merck* was premised on the statutory language of the 1952 Patent Act. As the Court properly noted, "[t]here is nothing in the language of the Act which precludes the issuance of a patent upon a 'product of nature' when it is a 'new and useful composition of matter' and there is compliance with the specified conditions for patentability." *Merck*, 253 F.2d at 161.

33. *In re Bergstrom* dealt with the prostaglandins PGE2 and PGE3, extracted from human or animal prostate glands. 427 F.2d 1394, 1397 (C.C.P.A. 1970). The patent examiner had rejected the claims, reasoning that "inasmuch as the 'claimed compounds are naturally occurring' . . . they therefore 'are not 'new' within the connotation of the patent statute.'" *Id.* at 259. *Bergstrom* is precedential and binding in the instant case as it is from the Court of Customs and Patent Appeals ("CCPA") – the predecessor to the current Federal Circuit. *South Corp. v. U.S.*, 690 F.2d 1368, 1370 (Fed. Cir. 1982) (adopting CCPA body of law). The claimed compositions occurred inherently in "nature," *i.e.*, in sheep prostate glands and in previously known crude extracts of those glands. The court reversed the Patent Office and explained the error:

> "what appellants claim--pure PGE2 and PGE3--is not 'naturally occurring.' Those compounds, as far as the record establishes, do not exist in nature in pure form, and appellants have neither merely discovered, nor claimed sufficiently broadly to encompass, what has previously existed in fact in nature's storehouse, albeit unknown, *or* what has previously been known to exist."

Bergstrom, 427 F.2d. at 1401 (emphasis in original).

34. Another precedential case, *In re Kratz*, related to the naturally occurring chemical, 2-methyl-2-pentenoic acid ("2M2PA"), a chemical responsible for the characteristic flavor of strawberries. 592 F.2d 1169 (C.C.P.A. 1979). Tellingly, Plaintiffs never cite *Kratz*, in spite of its precedential value. Kratz and Strasburger were the first to establish the presence of 2M2PA in strawberries and to discover that when 2M2PA was added to foodstuffs, it imparted a strawberry flavor and aroma. Their claim to 2M2PA in "substantially pure" form was upheld even though "2M2PA is a naturally occurring constituent of strawberries and is not 'per se' novel," "since the claims do not encompass natural compositions in that 'substantially pure' 2M2PA does not apparently occur in

nature." *Id.* at 1174.[1]

B. NO CASE STANDS FOR THE PROPOSITION THAT NATURAL PRODUCTS ARE NOT PATENT-ELIGIBLE

35. On careful analysis, the kind the Solicitor's Office conducted prior to issuing the 1995 Guidelines, it becomes clear that patentability was denied in the following cases because the composition sought to be patented was known and used from time immemorial – *not* because the products were naturally occurring.

36. In *American Wood-Paper Co. v. Fibre Disintegrating Co.*, 90 U.S. 566 (1874), cellulose had been obtained from various sources, including rags, straw, wood and other vegetable substances in the paper industry. 90 U.S. at 594-95. The patent at issue related to cellulose derived from wood pulp by a new process. Patentee claimed "a pulp *suitable* for the manufacture of paper, made from wood or other vegetable substances." *Id.* at 577 (emphasis added). The pulp which had been in common public use prior to the patentee's alleged invention, was "undeniably also cellulose, *suitable for manufacturing paper*, and so far as appears, *equally suitable*." *Id.* at 594 (emphasis added). Thus, the court noted that "[t]he *substance of the products . . . , was the same, and so were their uses*." *Id.* (emphasis added). The court held that "[p]aper-pulp obtained from various vegetable substances was in common use before the original patent was granted [to patentee], and whatever may be said of their process for obtaining it, the product was in no sense new."

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[1] In a case decided with *Chakrabarty* by the lower court, *In re Bergy*, a claim to a "biologically pure culture of Streotomyces vellosus" was held not to be a "product of nature," contrary to the examiner's position, and patent eligible under § 101. 596 F.2d 952, 972, 987 (CCPA 1979). On certiorari, the Supreme Court held Chakrabarty's microorganisms patent eligible under § 101 but did not address the *Bergy* case, as it had become moot. *See Chakrabarty*, 447 U.S. at 307.

Id. at 596. Thus, the patent was "void for want of *novelty* in the manufacture patented." *Id.* (emphasis added).

37. In *Cochrane v. Badische Anilin & Soda Fabrik*, alizarine was a known compound that had been extracted from the roots of madder plant and used in the dye industry. 111 U.S. 293 (1884). The Supreme Court held that the artificial alizarine, synthetically produced was not patentable because "[i]t was an old article," *i.e.*, it was the same chemical composition as alizarine previously extracted from madder root that had been used from "time immemorial" for dyeing. *Id.* at 311-12.

38. *Ex parte Latimer* involved cellulose fibers, a "well known material" which had been used from "time immemorial" in the textile industry. 1889 Dec. Comm'r Pat. 123, 125 (1889). The patentee developed a process for isolating the fibers from pine needles. The court noted, " [f]iber, whether of plants – such as hemp, flax, cotton -- or of the leaves of trees – such as the [pine tree] -- or of the wood of trees and shrubs, is a well known material … It has been employed from time immemorial in the manufacture of threads, cordage, fabrics and textiles…" *Id.* The court found that the claimed fiber isolated from its natural matrix was the "*same* thing" having the "*same* construction" as prior art fiber used in the textile industry and no different from its naturally occurring counterpart. *Id.* (emphasis added). The Patent Commissioner held that the patentee had failed to make any "discovery" since the fibers claimed were not a "new' and useful product. *Id.* at 125-26.

39. *General Elec. Co. v. De Forest Radio Co.* related to tungsten, an "old product" which had been isolated since at least the early 1700s and had been used in metallurgy

ever since. 28 F.2d 641 (3d. Cir. 1928). The oxide of tungsten (WO_3) found in the earth, is brittle, whereas pure or substantially pure tungsten is highly ductile. The patentee developed a process to convert tungsten oxide to pure tungsten. The court found that the claimed tungsten of high ductile strength was not patentable because it was *not new* at all. *Id.* at 643.

40. *In re Marden*, 47 F.2d 957 (C.C.P.A. 1931) ("*Marden* I") related to uranium, which had been discovered in 1789 and its properties had been "well known for many years." Patentee claimed uranium as a "new article," including some of its properties. The court held there was "nothing new" or "inventive" and thus denied patent protection. *Id.* at 957-58.

41. Similarly, in *In re Marden*, 47 F.2d 958 (C.C.P.A. 1931) ("*Marden* II") pure vanadium had been known for years in the metallurgy industry. Patentee attempted to obtain patent rights to not only methods for preparing vanadium in ductile form but also pure, ductile vanadium. The court denied patent protection and held that "pure vanadium is *not new in the inventive sense*." *Id.* at 959 (emphasis added).

42. The patent at issue in *Funk Bros. Seed Co. v. Kalo Inoculant Co.* related to inoculants of the bacteria genus Rhizobium. 333 U.S. 127 (1948). These bacteria infect the roots of leguminous plants and form nodules that allow the plants to fix nitrogen from the air (*i.e.*, a fertilizer). Different species of the bacteria were effective for different types of plant crops. Prior to the patent at issue, manufacturers packaged and sold single species inoculants. *Id.* at 129. A few mixed cultures were sold but they had been "generally unsatisfactory," because different species produced an inhibitory effect on

each other. *Id.* The patentee discovered six strains of species of the bacteria that were mutually non-inhibitive, and capable of inoculating several groups of plants.[2] *Id.* at 130. The claims, however, were not limited to the six strains. Rather, they were directed to an inherent natural property of an unspecified mixture of old products. The Supreme Court recognized that the mixture covered by the claims was a new composition but denied the patent because it found the combination of bacteria to be an obvious combination of known, commercially available products. *Id.* at 131-32.

IV. MYRIAD'S COMPOSITION OF MATTER CLAIMS COMPLY WITH THE PATENT LAWS

43. I reviewed claims 1, 2, 5, 6, and 7 of the '282 patent; claim 1 of the '473 patent; and claims 1, 6, and 7 of the '492 patent. These claims all relate to isolated DNA molecules comprising either the *BRCA*1 or *BRCA*2 DNA -- molecules that fall squarely under the statutory category "composition of matter."[3] For ease of reference I will refer to such claims as the "isolated DNA" claims.

44. The term "isolated" is expressly defined in the patent specification of the Myriad patents. *See, e.g.*, '473 patent at col. 19:6-15. The patent states that an "isolated" or "substantially pure" nucleic acid (*e.g.*, an RNA, DNA or a mixed polymer) is one which is substantially separated from other cellular components which naturally accompany a native human sequence or protein, *e.g.*, ribosomes, polymerases, many other human

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[2] Jackson misstates the basic facts of the case, reflecting his lack of experience in precise legal case analysis. Funk Brothers was not denied a patent. Bond, the patentee was. Further, the bacteria disclosed in *Funk*, was not a "weed killer," rather it was a fertilizer. Jackson Decl. ¶ 32.

[3] *Chakrabarty*, 447 U.S. at 309 ("'composition of matter' has been construed consistent with its common usage to include 'all compositions of two or more substances ... and all composite articles, whether they be the results of chemical union, or of mechanical mixture, or whether they be gases, fluids, powders, or solids.'") (citations omitted).

genome sequences and proteins. The term embraces a nucleic acid sequence or protein which has been removed from its naturally occurring environment, and includes recombinant or cloned DNA isolates and chemically synthesized analogs or analogs biologically synthesized by heterologous systems. In other words, DNA molecules that have been excised and extracted from cells or chemically synthesized.

45. The claimed isolated *BRCA*1 and *BRCA*2 DNA molecules of the Myriad patents are chemical compositions that have a specific utility, *e.g.*, molecular diagnostics. These DNA molecules, like all other DNA molecules, are chemical compounds consisting of a chain or strand of four different types of nucleotides, i.e., adenine ("A"), cytosine ("C"), guanine ("G") and thymine ("T"). These bases are linked together through the sugar phosphate backbone. These four letters of the alphabet are used as a shorthand scientific notation to represent the chemical composition of the DNA molecule. Indeed, shorthand notation, such as letters of the alphabet, are frequently used to name chemical compounds and is not a practice exclusive to DNA molecules. For example, prostaglandin is designated as PGE; Vitamin B12 is designated as $C_{63}H_{87}CoN_{14}O_{14}P$; and the polymer polypropylene is designated as PPE.

46. All chemical compounds inherently carry information. DNA molecules are no different. Indeed, the information in a chemical compound is dictated by its chemical, physical and structural properties. These inherent properties mandate the functionality of the chemical entity. Like any other chemical compound, DNA molecules in general and the claimed *BRCA*1 and *BRCA*2 DNAs at issue here, may be patent eligible if all conditions for patentability are met. The mere fact that the DNA molecules of the invention inherently carry information is not a bar to patentability.

47. Under the patent statutes and case law interpretation of those statutes, "isolated and purified" DNA molecules are patent eligible subject matter on multiple grounds. First, an excised gene or synthetic DNA is eligible for patent protection either as a "composition of matter" or as "an article of manufacture" – categories of patentable subject matter specifically enumerated by § 101. Second, "isolated" DNA molecules do not occur in nature and are different from the complex naturally occurring native DNA. *See* the legal analysis in the 2001 Guidelines, discussed *supra* at ¶ 18.

48. "Isolated" DNA molecules are structurally and functionally distinct from their naturally occurring counterpart in the human body. The environment of a DNA molecule dictates not only its structure but also its function (what it does). DNA in the human body is an integral part of chromosomes. In the chromosomal structure, DNA is typically present with proteins bound and highly regulated in its native environment. When DNA is no longer in its native environment, its expression can be regulated by artificial mechanisms. In addition, complementary DNA ("cDNA") is completely artificial as admitted by Plaintiffs (MF ¶ 62; Mason Decl. ¶ 29), and is structurally distinct from chromosomal DNA in that, among other differences it contains no intronic sequences and is not associated with proteins. cDNA is also functionally distinct from chromosomal DNA in that it does not contain regulatory sequences; it can serve as a template for mRNA synthesis; and it can be used as a diagnostic tool in this "isolated" form. Additionally, functions of genes as they occur naturally are not completely understood. Plaintiffs' attempt to equate the function of isolated genes to that of their naturally occurring counterparts is simply trivializing the complexity of the scientific principles at issue in this case.

49. Myriad's isolated DNA claims are directed to compositions of matter and thereby patent eligible subject matter under 35 U.S.C. § 101. The patent eligibility of the isolated DNA claims of the Myriad patents is fully supported by binding precedent of the Supreme Court, the Federal Circuit, and the CCPA. Patenting compositions or compounds isolated from nature follows well-established legal precedence and was by no means a new practice at the USPTO. *See the discussion supra* at ¶¶ 30-34 re *Parke-Davis*, *Merck*, *Bergstrom*, and *Kratz*. In 1980, the Supreme Court held that "anything under the sun that is made by man" is patent eligible, consistent with these earlier cases. *Chakrabarty*, 447 U.S. at 309.

V. PLAINTIFFS MISINTERPRET THE CASE LAW ON THE PATENT ELIGIBILITY OF ISOLATED AND PURIFIED NATURAL PRODUCTS

50. Plaintiffs attempt to distinguish *Parke-Davis*, denigrate *Merck* and *Bergstrom* and omit any discussion of *Kratz*. *MF* ¶¶ 117, 119; Pl. Br. at 24-25 Jackson ¶¶ 26-31, 35-37. In my opinion, these cases are directly analogous to the instant case.

51. Like the purified adrenaline of *Parke-Davis*, the isolated DNA molecules of the Myriad claims are different "in kind" from naturally occurring counterparts. The isolated DNA molecules claimed in Myriad's patents are distinct functionally and structurally from the naturally occurring *BRCA* genes, allowing the claimed compositions to be used for a practical new purpose, *e.g.*, diagnostics, which can only be achieved by virtue of the isolation and purification of the molecule. The isolated DNA molecules of the Myriad patents become "a new thing commercially" and thus patentable under the rubric of *Parke-Davis*.

52. Plaintiffs contend that *Parke-Davis* is not analogous to the claims in the Myriad patents, relying on Jackson ¶¶ 26-31 (*MF* ¶ 117, Pl. Br. at 25; Jackson Decl. ¶¶ 26-31). Jackson states: "The human body does not possess a natural process for purifying adrenaline as it does for isolating and splicing together genes. Genes and their splicing occur naturally, without human intervention; purified adrenaline does not." Jackson Decl. ¶ 29. This position is factually incorrect. The human body does not have *any* natural mechanism for isolating and splicing genes. Rather, splicing to remove introns (present in DNA molecules) is a modification of RNA molecules – not DNA molecules. *See* Jackson Decl. ¶ 28. *See also, e.g.*, Lehninger, PRINCIPLES OF BIOCHEMISTRY 1008-11 (4th ed. 2005).

53. If anything, the human body possesses a natural mechanism for "isolating" adrenaline by virtue of secretion of this hormone into the blood stream. Genes are not secreted by cells in the body, nor are they naturally isolated by the body. Genes remain intact in the nucleus. The isolation of genes or any DNA through molecular biological techniques requires cell disruption and chemical cleavage to remove the DNA from the chromosome, or chemical synthesis and amplification of synthetic DNA.

54. Just as the patentee in *Parke-Davis* provided a new use for adrenaline (*i.e.*, hemostatic, blood pressure raising and astringent properties) by its isolation and removal of gland tissues, here too, Myriad has provided an entirely new utility for the isolated *BRCA*1 and *BRCA*2 DNA, *i.e.,* diagnostics, as compared to their naturally occurring counterparts which are incapable of performing this function.

55. In *Merck*, the court concluded: "No one had produced even a comparable

product" to the product at issue in the case and there was no novelty bar to the product claimed. 253 F.2d at 162. The same is true in this case. Like the situation in *Merck*, Myriad's patented compositions, *i.e.*, DNA molecules covering *BRCA*1 and *BRCA*2 nucleotides, were previously "unidentified and unknown" prior to being disclosed in the Myriad patents, and it was their very isolation from the chromosomal DNA environment which rendered them useful as a diagnostic.

56. The court in *Merck* rejected defendant's argument that "anyone skilled in the field searching for a new B vitamin would turn to the known sources of other B vitamins." 253 F.2d at 161. The court emphasized that this argument "assumes knowledge of which the scientific world was ignorant until the work of the patentee was done." *Id.* Similarly, here, just because the DNA encoding the *BRCA*1 and *BRCA*2 genes are necessarily present in chromosomal DNA does not preclude patenting the newly identified, isolated genes and their function.

57. Plaintiffs attempt to distinguish *Merck* from the instant case. *MF* ¶ 119, Pl. Br. at 24-25; Jackson Decl. ¶ 37. Yet, Plaintiffs' analysis is flawed. Like the Vitamin B_{12} compositions at issue in *Merck*, the isolated *BRCA*1/*BRCA*2 DNA molecules of the Myriad patents have "never existed before; there was nothing comparable to them." 253 F.2d at 164. Indeed, it was the inventors' discovery of the structure and function of the *BRCA1* and *BRCA2* genes that revealed their actual, practical, "real world" utility. In their "natural" form, the *BRCA*1/*BRCA*2 DNA molecules of the Myriad patents, like the "natural" Vitamin B_{12} compositions of *Merck*, are quite "useless" for the intended utility of the invention (*i.e.*, diagnostics in the instant case).

58. Like the chemical compounds at issue in *Bergstrom*, the isolated and purified *BRCA*1/*BRCA*2 DNA molecules are eligible for patent protection when isolated from their natural state and purified. As the court in *Bergstrom* noted, "pure materials necessarily differ from *less* pure or impure materials and, if the latter are the only ones existing and available as a standard of reference, ... perforce the 'pure' materials are 'new' with respect to them." 427 F.2d. at 1402 (emphasis in original). Moreover, the mere existence of *BRCA*1/*BRCA*2 DNA as part of the chromosomal DNA does not negate the novelty or patentability of the isolated and purified *BRCA*1/*BRCA*2 DNA molecules. *See id.* ("*The existence of a compound as an ingredient of another substance does not negative novelty in a claim to the pure compound*, although it may, of course, render the claim unpatentable for lack of invention [*i.e.*, the predecessor test for obviousness under Section 103]...") (quoting *In re Williams*, 171 F.2d 319 (C.C.P.A. 1948) (emphasis in original).

59. As in *Kratz*, the claimed isolated DNA molecules of the Myriad patents do not cover *natural* compositions because the isolated DNA molecules are distinct in form and kind from their naturally occurring counterparts. *Supra* ¶ 34.

60. Plaintiffs have not – because they cannot – point to a single case standing for the proposition that natural products are not patent eligible *per se*. Rather, to support their position that the isolated DNA molecules of the Myriad patents are not eligible for patent protection, Plaintiffs rely on a line of cases in which the court found known, old products or commercially available products unpatentable. *MF*s ¶¶ 115-123; Pl. Br. at 21-24; Jackson Decl. ¶¶ 7-16 (citing *Cochrane & Others v. Badische Anilin & Soda Fabrik*, 111 U.S. 293 (1884)); ¶¶ 17-25 (citing *American Wood-Paper Co. v. Fibre Disintegrating*

Co., 90 U.S. 566 (1874)); ¶¶ 38-40 (citing *General Elec. Co. v. De Forest Radio Co.*, 28 F.2d 641 (3d. Cir. 1928)); ¶¶ 32-24; ¶¶ 32-34 (citing *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948)); *see also* Pl. Br. at 31 (citing *Marden* I and *Marden* II).

61. These are the very cases I reviewed when I was the Solicitor in addressing the patent eligibility of biotechnology inventions under § 101 for Commissioner Lehman. See my discussion of these cases *supra* at ¶¶ 35-42.

62. Plaintiffs' reliance on these cases is misplaced for at least two independent reasons. First, in each case, the composition sought to be patented was old – in that it was commercially available or known in the art. These cases primarily turn on whether the products at issue met the "novelty" or non-obviousness statutory requirements. Second, these cases have marginal precedential value as they were issued pre-1952 Patent Act, which is the relevant legal standard of analysis.

63. In *Cochrane,* the court's holding of invalidity of the reissue patent was based, in part, on the fact that artificial alizarine synthetically produced was *identical* in its properties and composition to alizarine previously produced by other methods. *Cochrane*, 111 U.S. at 300-301. Similarly, the pulp product claimed in *Wood-Paper* had been in common public use and the court's holding turned on the "novelty" statutory requirement. *Wood-Paper*, 90 U.S. at 596. Finally, the Patent Commissioner's refusal to grant patentee's application was because the pine needle fibers in *Latimer* were essentially the *same* cellulose fibers that had been known and used in the manufacture of threads, cordage, fabrics and textiles. *Latimer*, 1889 Dec. Comm'r Pat. at 125. *See also*,

Marden I, 47 F.2d 957 and *Marden* II, 47 F.2d 958 (rejecting patentability where the product was not "new" or "inventive").

64. Unlike the situation in *Cochrane*, *Wood-Paper*, *Latimer*, *Marden* I and *Marden* II, it is undisputed that the isolated DNA molecules coding for the *BRCA1* and *BRCA2* genes were *not* known prior to the invention disclosed in the Myriad patents. Indeed, it was the discovery of the location, structure and function of the *BRCA1* and *BRCA2* genes that was a fundamental breakthrough for the development of cancer diagnostics and therapeutics, warranting patent protection. Additionally, as explained *supra* (¶¶ 29-34), the isolated DNA molecules covered by the patent-in-suit are by no means "identical" to their naturally occurring counterparts and are in fact distinct – chemically, structurally and functionally. Thus, application of *Cochrane*, *Wood-Paper*, *Latimer*, *Marden* I and *Marden* II to this case carries no force.

65. The same holds true for *General Electric.* In *General Electric*, the issue of patentability of tungsten turned on the "novelty" requirement. As the court properly noted, the patentee had not sought a patent for a "new" composition of matter. Rather, patentee had claimed a product that later proved to be tungsten – an old product. 28 F.2d at 641.

66. *Funk* is equally inapplicable to the instant case. The claim at issue in *Funk* was not for a true "product of nature." The claimed mixed culture did not exist in natural form and thus, contrary to Plaintiffs' representations (*MFs* ¶ 118, Pl. Br. at 21-22, 26; Jackson Decl. ¶ 32-34), *Funk* does not stand for the proposition that products of nature are not patentable. Instead, the *Funk* decision is more appropriately directed to non-

obviousness or pre-1952 Patent Act "invention" requirement and not to the statutory classes of patent eligible subject matter. The court's decision turned on obviousness of the claimed product as a combination of old, commercially available products. Each of the individual strains of each bacterial species had been commercially available prior to the patent-in-suit. The court admitted that one could patent "the application of the law of nature to a new and useful end" but held that the "aggregation of species fell short of invention ... [i.e., was obvious]... within the meaning of the patent statutes" because the mixed culture performed no new function other than that of convenient packaging. *Funk*, 333 U.S. at 130-31.

67. In his concurring opinion, Justice Frankfurter urged caution with respect to the majority's use of the phrases "works of nature" and "laws of nature":

> It only confuses the issue . . . to introduce such terms as 'the work of nature' and the 'laws of nature.' For these are vague and malleable terms infected with too much ambiguity and equivocation. Everything that happens may be deemed 'the work of nature,' and any patentable composite exemplifies in its properties 'the laws of nature.' Arguments drawn from such terms for ascertaining patentability could fairly be employed to challenge almost every patent. On the other hand, the suggestion that 'if there is to be invention from such a discovery, it must come from the application of the law of nature to a new and useful end' may readily validate [patentee's] claim. Nor can it be contended that there was no invention because the composite has no new properties other than its ingredients in isolation. [Patentee's] mixture does in fact have the new property of multi-service applicability.

333 U.S. at 134-35.

68. Further, the claims at issue in *Funk* did not define the composition (i.e., the combination of the six strains). Rather, the claims were directed to an inherent natural property of an unspecified mixture of old products. As indicated in Justice Frankfurter's concurrence, had the claims actually been directed to the strains which were mutually non-inhibitory, the outcome of the case might have been different. Indeed,

notwithstanding his objections, Justice Frankfurter, in his concurring opinion, ruled to invalidate the patent on the ground that the product claim was too broad. The claim was for any mixture of compatible strains and did not adequately identify the particular strains that the patentee had discovered. *Funk*, 333 U.S. at 133.

69. Plaintiffs' improper application of *Funk* to the present case is premised on the misunderstanding that "[p]atented genes can, and normally do serve the ends nature originally provided." Jackson Decl. ¶ 34 (relying on *Funk*, 333 U.S. at 131). But, as explained above, isolated and purified genes, such as those claimed in the Myriad patents do *not* "serve the ends nature originally provided" because they are distinct structurally and functionally by virtue of their isolation.

70. Plaintiffs' application of these cases is additionally flawed because it is premised on a fundamental misconception and misunderstanding of how to apply basic principles of patent law and policy to biotechnological inventions. *MFs* ¶ 58-59, 62-63, 65, 113-114; Pl. Br. at 20-28; Jackson Decl. ¶ 12-15, 30-34. For example, Jackson disputes the scientifically based principle that DNA and genes are chemicals and "should be analyzed for patent purposes in the same manner as other chemicals." Jackson Decl. ¶ 12. Jackson is wrong. DNA *is* a chemical composition. A DNA molecule is a chain or strand of four different types of bases, i.e., adenine, cytosine, guanine, and thymine and, these bases are linked together via a sugar-phosphate backbone. Thus, a DNA molecule is a combination of basic chemical elements, *i.e.*, oxygen, nitrogen, carbon, phosphate. By any definition, DNA falls squarely within what is considered a chemical composition.

71. A concern voiced by Plaintiffs in treating genes as chemical entities is that the

"threat of the patentee locking up a substance and all its uses is far greater with gene patents than with chemicals dues to the science of genes." Jackson Decl. ¶ 15. *See also MF* ¶ 114; Pl. Br. at 36-37. Dr. Jackson reasons that while one can readily invent around chemical molecules "by creating either a slightly different method of synthesis or a minor variation of the patented (or natural) substance," one "cannot invent around a gene, potentially allowing patents holders to enjoy a monopoly, thereby hampering further downstream diagnostic and therapeutic research." Jackson Decl. ¶ 15. Plaintiffs, in essence, imply that the grant of an exclusionary patent right is wrong. *MFs* ¶ 125-141, Pl. Br. at 6, 35, Jackson Decl. ¶ 13, 15. In fact, the right to exclude others from practicing a claimed invention is the very essence of the patent right. *See* 35 U.S.C. § 271. Thus, the ability to invent around an invention frustrates that right. If a pioneering invention, such as that covered by the Myriad claims, is properly claimed, those claims should prevent "inventing around" and allow the inventor to fully benefit from the exclusionary rights granted by the patent. By granting exclusionary rights, the patent system promotes making improvements on the claimed invention and permits others to practice the claimed invention after the patent expires. In contrast, if another party can invent around the claimed invention and reap the benefits of the patentee's discovery, the patentee's ability to recoup and benefit from its investment are frustrated.

72. Indeed, these very concerns were raised prior to the implementation of the 2001 Guidelines. *See e.g.*, Letter from R. Rodney Howell, President, Association for Molecular Pathology to Commissioner, USPTO (March 20, 2000), *available at* http://www.uspto.gov/web/offices/com/sol/comments/utilguide/acmg.pdf ; Letter from Debra G.B. Leonard, President, Association for Molecular Pathology to Commissioner,

USPTO (March 17, 2000), *available at* http://www.uspto.gov/web/offices/com/sol/comments/utilguide/amp.pdf. As the USPTO recognized such concerns are unfounded. When a patent claiming a new chemical composition issues, the patentee has the right to exclude others from making, using, offering for sale, selling, or importing the composition for a limited time. 35 U.S.C. § 154. In exchange for this limited exclusionary right, the patentee is required to disclose only one utility, that is -- teach others how to use the invention in at least one way – as long as the utility is specific, substantial and credible. *See* the 2001 Guidelines, cited *supra* at ¶ 18. The patentee is *not* required to disclose *all possible uses*. In fact, promoting the subsequent discovery of other uses – uses that can be patented if they meet the statutory requirements -- is one of the benefits of the patent system.

73. Accordingly, when patenting is made available for genes as it is for other chemical compositions, progress is promoted for at least four independent reasons. First, the claimed invention is fully disclosed to those working in the field and thus made fully available after the limited exclusionary period (here, in 2014) instead of being held as a trade secret. Second, the original inventor has the ability to obtain financial support to recoup research and development costs. Third, a new chemical composition is made available as a basis for future research. Other inventors are incentivized to develop new uses for the patented composition and have the opportunity to patent those uses, if the patent statutes are met. Last but certainly not least, a new and nonobvious invention (here, a diagnostic tool) is provided for those who need the invention (here, diagnosis of a propensity toward contracting breast and ovarian cancer).

74. Thus, Plaintiffs' concerns are unsupported by the underlying principles of patent

law and policy. Since *Chakrabarty*, the biotechnology industry has flourished at an exceptional rate in the United States by virtue of the patent system. The United States has emerged as a leader in the biotechnology industry serving as a role model for other countries striving to compete in this industry. Indeed, the post-*Chakrabarty* patent system has been critical to the growth and competitiveness of American biotechnology because, among other reasons, investors simply expect a company to have its intellectual property protected. Thus, the promise of patent protection attracts capital that the biotechnology industry requires to survive.

75. Most, if not all, of the life saving inventions available world-wide would never have been discovered, developed and commercialized but for the potential profits afforded by the exclusive rights granted by the patent system. In this case, Myriad probably would not have -- because it could not have -- spent the capital necessary for the research and development that led to the ground-breaking discoveries of the *BRCA1* and *BRCA2* genes and ultimately to their commercialization had it not been for the exclusive rights granted by the patent system. Those rights provided Myriad with the possibility of recouping its costs and reaping the benefits of its discoveries.

76. Moreover, Plaintiffs' flawed analysis of the case law is premised on a misunderstanding of basic scientific principles. *MFs* ¶ 48, 58-60, 62, 65, 114, 117; Pl. Br. at 4-5, 20, 26-27; Jackson Decl. ¶¶ 25, 29, 31. For example, like adrenaline, vitamin B12 and/or 2M2PA where patentability was upheld (*supra* ¶¶ 30-34), DNA, too, is a chemical composition (¶¶ 43-46). It thus requires application of the same patentability analysis as do other chemical compositions. Further, all chemical compositions inherently carry "information" in that the nature of the atoms in the composition, their arrangement, and

their environment dictates their function. DNA is no different. *Compare with* Jackson Decl. ¶ 20. The "information" inherent in any chemical composition is dictated by the laws of nature through its inherent chemical, physical and structural properties. These inherent properties of a chemical entity mandate its functionality, including for example, its chemical reactivity, catalytic properties, and biological interactions. The same holds true for DNA. For example, the transcription of a gene into mRNA consists merely of a series of well-orchestrated chemical reactions that are being dictated by the inherent properties of the DNA molecule.

77. Finally, *American Fruit Growers v. Brogdex Co.*, 283 U.S. 1 (1931) does not support Plaintiffs' unsubstantiated "legal principle" that "natural products" are not patentable *per se*. The Court's holding in *American Fruit Growers* was not predicated on the borax treated fruit being a "natural product." Rather, the Court used this opportunity to define what constitutes an "article of manufacture"[4] and held that the borax treated fruit was not. In contrast, the isolated DNA molecules of the Myriad patents fall squarely within the Court's definition of an "article of manufacture." The *BRCA1/BRCA2* DNA molecules are isolated from cells, *i.e.*, substantially separated from other cellular components which naturally accompany a native human sequence or protein, *e.g.*, ribosomes, polymerases, many other human genome sequences and proteins. *See*, *e.g.*, '473 patent, col. 19:6-15; '282 patent, col. 19:8-18; and '492 patent, col. 17:62 – col. 18:5 . By virtue of this "isolation" they are necessarily "transformed" under *American Fruit Growers*. In other words, the claimed DNA molecules are produced from raw materials

[4] *American Fruit Growers*, 283 U.S. 1, 11 (1931) ("manufacture' means "the production of articles for use from raw or prepared materials by giving to these materials new forms, qualities, properties, or combinations, whether by hand-labor or by machinery"), *quoted with approval in Chakrabarty*, 447 U.S. at 309.

(the naturally occurring gene or the chemical molecules that make up the claimed DNA) in a "new and different" form that does not occur in nature -- a form that provides the basis for a diagnostic tool (i.e., a new property).

VI. MYRIAD'S METHOD CLAIMS ARE PATENT ELIGIBLE UNDER *BILSKI* AND ITS PROGENY BECAUSE THEY ALL HAVE A "TRANSFORMATIVE" STEP CENTRAL TO THE PURPOSE OF THE CLAIMS

78. In addition to assessing the requirements of patentability of biotechnology inventions, Commissioner Lehman charged me with clarifying the legal requirements for statutory subject matter with regard to computer-related inventions. This initiative led to the Examination Guidelines for Computer-Related Inventions (61 Fed. Reg. 7478 (1996) (legal analysis reproduced in MPEP § 2106 (July 1998)), and involved the analysis of all the cases cited by Plaintiffs relating to such subject matter. *See* Jackson ¶¶ 43-48. *MFs* ¶ 122-124; Pl. Br. at 26-29. Specifically, these cases addressed whether the subject matter sought to be patented was an "abstract idea" precluding patentability.

79. I will discuss these cases as they pertain to the "method claims" at issue in this case. Specifically, I have reviewed claim 20 of the '282 patent; claim 1 of the '999 patent; claim 1 of the '001 patent; claim 1 of the '441 patent and claims 1 and 2 of the '857 patent. These claims are collectively referred to as the "method claims."

80. I understand that Plaintiffs contend that these claims run afoul of *Bilski* and its progeny because they purportedly cover mental steps and abstract ideas. Pl. Br. at 29-30 n.9 (citing *In re Bilski*, 545 F.3d 943, 954(Fed. Cir. 2008), *cert. granted*, 129 S. Ct. 2735 (2009)). For the reasons discussed below, I disagree.

81. Out of the at least 25,000 genes now identified, Myriad discovered that mutations in the *BRCA*1 or *BRCA*2 gene are correlated with breast and/or ovarian cancer -- a discovery Myriad scientists were first to make. Based on this discovery, Myriad invented and claimed certain diagnostic methods for detecting whether a patient has the mutation.

82. Each of Myriad's method claims requires analyzing a sequence of the *BRCA* gene from a human tissue or tumor sample. To do so, the DNA[5] must be isolated from the sample and sequenced prior to identifying variations in the DNA.

83. Whether the method is for "detecting a germline alteration" (*e.g.*, claim 1 of the '999 patent), for "screening" for an "alteration" (*e.g.*, claim 1 of the '001 patent and claim 20 of the '282 patent), "for identifying" a "mutant nucleotide sequence" (*e.g.*, claim 1 of the '857 patent), or for "diagnosing a predisposition for breast cancer" (*e.g.*, claim 2 of the '857 patent), the claimed method cannot be conducted while the DNA is in its naturally occurring state.[6]

84. Furthermore most of the method claims involve additional transformations. For example, claim 20 of the '282 patent reads:

> 20. A method for screening potential cancer therapeutics which comprises: *growing* a transformed eukaryotic host cell containing an altered BRCA1 gene causing cancer in the presence of a compound suspected of being a cancer therapeutic, *growing* said transformed eukaryotic host cell in the absence of said compound, *determining* the rate of growth of said host cell in the presence of said compound and the rate of growth of said

[5] For simplicity, I use the term "DNA" to describe what molecule is analyzed. In fact, its corresponding RNA or cDNA can be used for the analysis.
[6] For simplicity, I use the word "detecting" to include "screening," "identifying," and "diagnosing," the various terms used in the patents-in-suit.

> host cell in the absence of said compound and *comparing* the growth rate of said host cells, wherein a slower rate of growth of said host cell in the presence of said compound is indicative of a cancer therapeutic.

'282 patent at col. 156:15-27 (emphasis added).

Each of the italicized actions involves a transformation ("growing") or requires a machine to perform the claimed step ("determining" and "comparing"). These latter steps cannot be performed in the absence of a machine. *See Prometheus Labs. v. Mayo Collaborative Servs.*, 581 F.3d 1336, 1347 (Fed. Cir. 2009) ("Some form of manipulation, such as the high pressure liquid chromatography method specified ... is necessary to extract the metabolites from a bodily sample and determine their concentration.")

85. Myriad's method claims are in many ways analogous to those in *Prometheus. See, e.g., Prometheus,* 581 F.3d at 1347-50 (discussing claims 46 and 53 of the '653 patent). Prometheus discovered a correlation between metabolite levels in a patient's blood and therapeutic efficiency. It then invented a method to optimize therapeutic efficiency while minimizing side effects by determining metabolite levels and identifying a need to adjust drug dosage upward or downward based on the levels.

86. The Federal Circuit applied its recently articulated *Bilski* "machine-or-transformation" test and held that Prometheus's claimed methods satisfied the transformation prong of the test and reversed the district court's summary judgment grant of invalidity. *Id.* at 1343-48, 1350. The Court did not address the machine prong.

87. Most relevant to this case, the court held that the claimed "determining the level of 6-thioguanine" in a patient was transformative because "[s]ome form of manipulation .

. . or other modification of the substances to be measured, is necessary to extract the metabolites from a bodily sample and determine their concentration." *Id.* at 1347.

88. The Federal Circuit quoted approvingly Prometheus's expert: "'at the end of the process, the human blood sample is no longer human blood; human tissue is no longer human tissue.'" *Id.*

89. The Federal Circuit rejected Mayo's argument that such manipulation of the sample was "merely a necessary data-gathering step" and instead found that transforming the sample was "central to the purpose of the claims." *Id.* "Measuring" the metabolite levels was what enabled possible adjustments to the drug dosage to optimize efficacy or reduce toxicity. *Id.*

90. Similarly in this case, Myriad's method claims each requires the transformation of a tissue or blood sample in order to isolate the patient's DNA and thus would satisfy the *Bilski* transformation test. Further, Myriad's manipulation of the sample is "central to the purpose of the claims," just as it was to Prometheus's method. Transforming the tissue or blood sample is what enables making the comparison between the wild-type gene and the patient's gene and therefore the detection of any germline alteration.

91. In addition to the transformation of the human sample, the Myriad method claims require further manipulation of the isolated DNA fragment to perform the detecting step. For example, hybridization can be used to bind the isolated DNA in single strand format, thereby transforming the single stranded DNA into a new molecule called a "hybridization product." *See, e.g.*, claim 5 of the '999 patent ("a germline alteration is detected by hybridizing a BRCA1 gene probe . . . to genomic DNA isolated from said

sample and detecting the presence of a hybridization product").

92. Other dependent claims in each of the method patents reflect a number of manipulations of the isolated DNA encompassed by the terms "detecting," "screening," "identifying" and "diagnosing" and envisioned by the inventors. Each of these manipulations involves a transformation of isolated DNA fragment into a different, non-naturally occurring form.

93. In *Prometheus*, the Federal Circuit distinguished *In re Grams*, 888 F.2d 835 (Fed. Cir. 1989) because "the essence of the claimed process" in *Grams* was a mathematical algorithm. 581 F.3d at 1348. The court in *Prometheus* observed: "The patent and thus the court focused only on the algorithm rather than the clinical tests purported to be covered by the claims." *Id.*

94. Significantly in *Grams*, the court posed the "critical" question: "What did applicants invent?" 888 F.2d at 839. The answer in *Grams* was a mathematical algorithm, since performing the clinical tests was already in the prior art and not the focus of the specification. *Id.* at 839.

95. This case elicits a very different answer to the critical question, what did applicants invent? Myriad's invention is not a mathematical algorithm but instead is a novel diagnostic procedure based on their discovery of a correlation between mutations in the *BRCA*1 and *BRCA*2 genes and certain cancers. Thus, unlike the situation in *Grams*, the transformative steps of collecting and analyzing tissue and blood samples for the BRCA1 relevant mutations must be treated as central to the claimed invention. *See* ¶ 93 above.

96. Further, Myriad's claims are not analogous to those in *Gottschalk v. Benson*, 409 U.S. 63 (1972), or *Parker v. Flook*, 437 U.S. 584 (1978), based on similar reasoning. Each of these cases, like *Grams*, involved an attempt to patent a mathematical formula or algorithm, as part of a software program, in the absence of an inventive application.

97. Significantly, Myriad's method claims do not involve a mathematical algorithm as that term was used in *Benson* and *Flook* or a software program for performing a mathematical algorithm. Neither do they involve pure information. Rather, they involve chemical molecules that are capable of many complex reactions yet to be fully understood, including replication, transcription and translation. The fact these molecules are abbreviated with the first letters of their nucleotides does not make the abbreviated recitation purely information. *See supra* ¶ 45.

98. Even if *Benson* and *Flook* are relevant here, they are easily distinguished. Benson's claimed invention was to "a method of programming a general purpose digital computer to convert signals from binary-coded decimal form into pure binary form." 409 U.S. at 66. No new machinery was necessary and, in fact, the algorithm could be performed without a computer. *Id.* at 68. The Court concluded the claims were to the algorithm itself and thus not patentable. *Id.* at 72-73.

99. In *Benson*, the Supreme Court recognized a process could be patentable without requiring a machine: "'That a process may be patentable irrespective of the particular form of the instrumentalities used cannot be disputed. . . . A process is a mode of treatment of certain materials to produce a given result. It is an act, or a series of acts, performed upon the subject matter to be transformed and reduced to a different state or

thing.'" *Benson*, 409 U.S. at 69-70 (quoting *Cochrane v. Deener*, 94 U.S. 780, 786-87 (1876)) (a case involving a process for manufacturing flour to improve its quality)).

100. Immediately following its discussion of *Cochrane*, the Supreme Court reiterated: "Transformation and reduction of an article 'to a different state or thing' is the clue to the patentability of a process claim that does not include particular machines." *Id.* at 70. This test has become known as the "machine-or-transformation test" presently being considered by the Supreme Court in *Bilski v. Kappos*, 129 S. Ct. 2735 (2009) (argued Nov. 9 (2009)) and applied by the Federal Circuit in *Prometheus*. *See supra* at ¶¶ 85-90.

101. Again, Myriad's method claims involve several transformative manipulations of tissue or blood and the DNA to detect a genetic mutation in the *BRCA*1 or *BRCA*2 gene. Thus, the method claims involve "an act, or series of acts, performed upon the subject matter to be transformed and reduced to a different state or thing," and therefore are to statutory subject matter under *Benson*.

102. In *Parker v. Flook*, the claimed invention involved a computer program for determining when an alarm limit was reached. 437 U.S. at 585 (1978). Like the situation in *Benson*, in *Flook*, the only novel feature of the claimed method was a mathematical algorithm. *Id.* at 585-86. The Court concluded: "Respondent's process is unpatentable under § 101, not because it contains a mathematical algorithm as one component, but because once that algorithm is assumed to be within the prior art, the application, considered as a whole, contains no patentable invention." *Id.* at 594.

103. In contrast, Myriad's claimed methods are not based on a mathematical algorithm but rather on the application of their discovery that a particular DNA sequence is

associated with certain cancers to provide a diagnostic tool for such cancers. Further, even assuming the newly discovered correlation is analogous to a mathematical algorithm, the practical application of that correlation is entitled to patent protection under the *Benson* and *Flook* analyses.

104. This case is more analogous to *Diamond v. Diehr*, 450 U.S. 175 (1981) than it is to *Benson* or *Flook*. The claimed subject matter in *Diehr* was a process for curing rubber which included a mathematical algorithm and a programmed digital computer. *Id.* at 178. Respondents did not seek a patent on a mathematical algorithm but rather on a process for curing rubber. *Id.* at 188. Recognizing that "an *application* of a law of nature or mathematical algorithm to a known structure or process may well be deserving of patent protection," *id.* (emphasis in original), the Court held Diehr's claims eligible for patenting. *Id.* at 193-94.

105. Similarly, Myriad's method claims are to an application of a law of nature—a method for detecting a germline alteration linked to breast and ovarian cancer—and not to the law of nature itself.

106. Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct.

Executed on: Dec. 23, 2009

Nancy J. Linck

APPENDIX 1

EXHIBIT LIST

Exhibit No.	Title
Exhibit 1	*Curriculum vitae* of Dr. Nancy J. Linck
Exhibit 2	*Utility Examination Guidelines*, 60 Fed. Reg. 36263 (1995) (reproduced in MPEP § 706.03(a)(1) (July 1998))
Exhibit 3	*Utility Examination Guidelines*, 66 Fed. Reg. 1092 (January 5, 2001)

CERTIFICATE OF SERVICE

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

/s/ Brian M. Poissant
Brian M. Poissant