UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF NEW YORK

ASSOCIATION FOR MOLECULAR PATHOLOGY, et al., Plaintiffs, v. UNITED STATES PATENT AND TRADEMARK OFFICE, et al., Defendants.	09 Civ. 4515 (RWS) ECF

BRIEF FOR AMICUS CURIAE

Biotechnology Industry Organization

IN SUPPORT OF DEFENDANTS' OPPOSITION TO PLAINTIFFS' MOTION FOR SUMMARY JUDGMENT

Of Counsel:

Hans Sauer
Biotechnology Industry Organization
1201 Maryland Ave. S.W., Suite 900
Washington, D.C. 20024

Counsel of Record for Amicus Curiae:

Jennifer Gordon
Steven P. Lendaris
Jennifer C. Tempesta
Baker Botts L.L.P.
30 Rockefeller Center
New York, NY 10112-4498
(212) 408-2500

TABLE OF CONTENTS

Page

TABLE OF AUTHORITIES

Page(s)

CASES

STATUTES

OTHER AUTHORITIES

STATEMENT OF INTEREST OF AMICUS CURIAE

The Biotechnology Industry Organization ("BIO") is the country's largest biotechnology trade association, representing over 1200 companies, academic institutions, and biotechnology centers in all 50 States. BIO members are involved in the research and development of biotechnological healthcare, agricultural, environmental and industrial products. BIO member companies range from start-up businesses and university spin-offs to large Fortune 500 corporations. The vast majority of BIO's members are small companies that have yet to bring products to market and attain profitability. In many cases, gene-based patents are critical for a biotech company's ability to attract the capital and investment necessary for the development of innovative diagnostic, therapeutic, agricultural and environmental products. Thus, the issues raised in this case are of great importance to the U.S. biotechnology industry. BIO has no commercial interest in the parties to this action.

Neither Myriad Genetics nor the University of Utah Research Foundation are members of BIO.

I. INTRODUCTION

Plaintiffs' unprecedented constitutional and statutory challenges to the patenting of isolated DNA molecules go far beyond the *BRCA1* and *BRCA2* genes at issue in this case; consequently, they are of tremendous concern to the Biotechnology Industry Organization and its membership (hereafter, collectively, "BIO").[1] For almost a century, jurisprudence originating in this Court has recognized the patent-eligibility of isolated substances that differ in kind, and not merely in degree of purity, from their natural counterparts. *Parke-Davis & Co. v. H. K. Mulford Co.*, 189 F. 95 (S.D.N.Y. 1911). For more than two decades, our courts and the United States Patent and Trademark Office ("USPTO") have extended the wisdom of Judge Learned Hand to isolated nucleic acids and have approved the granting of thousands of patent claims to isolated DNA molecules comprising sequences derived from human, animal, plant and bacterial sources. From the mass production of life-saving medicines by cell cultures to the screening of our blood supply for life-threatening viruses, patented isolated DNA molecules have been put to countless uses that have benefited society − uses not possible with the sequences as they exist in nature. Such uses distinguish isolated DNA molecules in kind from their counterpart naturally occurring sequences, and compel their patent-eligibility.

As discussed herein, the claimed isolated DNA molecules differ in kind from the natural *BRCA1* and *BRCA2* genes. Thus, Plaintiffs' motion to invalidate such claims should be denied in view of long-standing legal precedent.

BIO further urges this court to deny Plaintiffs' motion on policy grounds. Patents claiming isolated DNA molecules are among the cornerstones of the intellectual property portfolios of many, if not most, BIO members. A decision that the patenting of isolated DNA

[1] BIO has expressed its view on method claims involving biological correlations in *Prometheus v. Mayo*, 581 F.3d 1336 (Fed. Cir. 2009) and *Bilski v. Kappos*, No. 08-964, (U.S. 2009), and focuses herein on claims directed to isolated DNA molecules, which, to BIO's knowledge, have not previously been challenged on constitutional grounds or under 35 U.S.C. § 101.

molecules is unconstitutional, or that isolated DNA molecules fall outside the statutory classes of patent-eligible subject matter articulated in 35 U.S.C. § 101, would frustrate decades of investments in research and development undertaken in reliance on DNA patents and established legal precedent relating thereto, and, going forward, would destroy perhaps the most important incentive for investing in DNA-based inventions.

Whether the goal is to identify a DNA molecule that can be used to develop a test that will predict if someone will have a dangerous reaction to a specific drug, or to create a vaccine for the prevention of, e.g., cervical cancer, or to recombinantly produce a life-saving therapeutic protein, the prospect of obtaining patents on isolated nucleic acid molecules provides an important incentive to expend the time, energy, and investment needed to translate basic scientific discoveries into real-world products that benefit patients, physicians, and consumers. The U.S. biotechnology industry dwarfs that of the rest of the world in large part because the U.S. patent system encourages investment in biotechnology research and development, and the DNA patenting incentives of the past 25 years have significantly contributed to making the United States the global leader in biotechnology innovation that it is today. Certainly, the constitutional objective of advancing the progress of science and the useful arts will not be served if important gene-based discoveries lie barren and are not developed for public use because patents on them will not be granted. For these and the other reasons discussed herein, Plaintiffs' motion should be denied.

II. FACTUAL BACKGROUND

A. DNA Claims At Issue

The DNA claims at issue in this case are Claims 1, 2, 5, 6 and 7 of U.S. Patent No. 5,747,282 ("the '282 patent"); Claim 1 of U.S. Patent No. 5,693,473 ("the '473 patent"); and Claims 1, 6 and 7 of U.S. Patent No. 5,837,492 ("the '492 patent"). Claims 1 and 2 of the '282 patent are exemplary:

> 1. An isolated DNA coding for a *BRCA1* polypeptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO: 2.
>
> 2. The isolated DNA of claim 1, wherein said DNA has the nucleotide sequence set forth in SEQ ID NO:1.

These and the other DNA claims cover compositions of matter, i.e., actual deoxyribonucleic acid (DNA) molecules, and not merely the information encoded by the nucleotide sequences within these molecules. Claim 1 of the '282 patent is a "genus" claim; it encompasses multiple distinct DNA molecules that share the ability to code for the specified protein molecule. These molecules include genomic DNA fragments (discussed *infra*), cDNA molecules that are manufactured from mRNA (also discussed *infra*), as well as synthetic DNA molecules that, through the inherent degeneracy of the genetic code,[2] encode the specified protein. Claim 2, on the other hand, is a "species" claim; it covers a DNA molecule having a sequence identical to the cDNA specified by SEQ ID NO:1.

Significantly, each DNA claim at issue is limited to "isolated" DNA, a key term defined in, e.g., the '282 patent (Exh. 1[3]) at col. 19, ll. 8-18, as follows:

> 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…, e.g., … many other human genome sequences and proteins. The term embraces a nucleic acid sequence…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.

---

[2] DNA is a double-stranded molecule (the so-called "double helix"), each strand of which is made up of the nucleotide bases A, C, G and T, strung together like beads on a necklace. Combinations of three nucleotide bases (which form a "codon") dictate the identity of the amino acids that will get placed in series, in a growing polypeptide (or protein) chain. Because certain amino acids are encoded by more than one codon, the genetic code is called "degenerate" and, thus, multiple DNA molecules having different sequences of codons can code for the same protein.

[3] Citations to "Exh. __" refer to the Exhibits attached to the Declaration of Jennifer C. Tempesta in Support of Defendants' Opposition to Plaintiffs' Motion for Summary Judgment, submitted contemporaneously herewith.

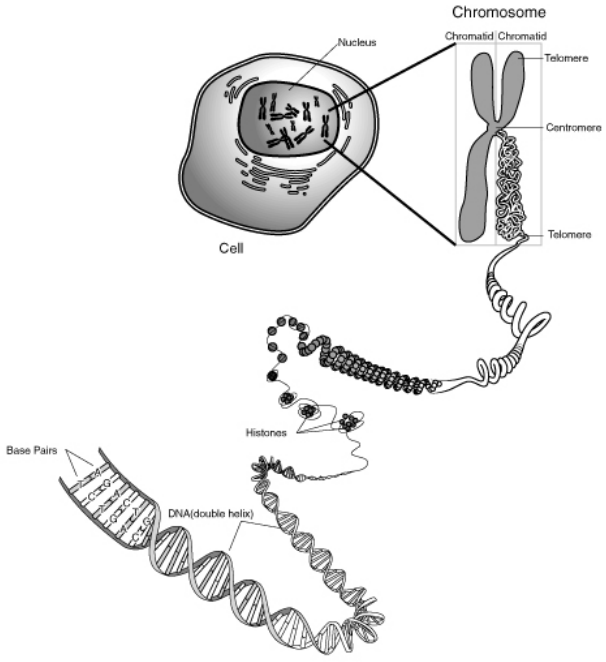
It is the term "isolated" that distinguishes the claimed molecules from anything that exists in nature. The substantial separation from other human genomic sequences and other cellular components impart utilities (discussed *infra*) to the claimed DNA molecules that simply do not exist for the counterpart natural sequences.

B. Molecular Biology Primer: Genes, mRNA, cDNA And The Proteins They Encode

1. Genomic DNA

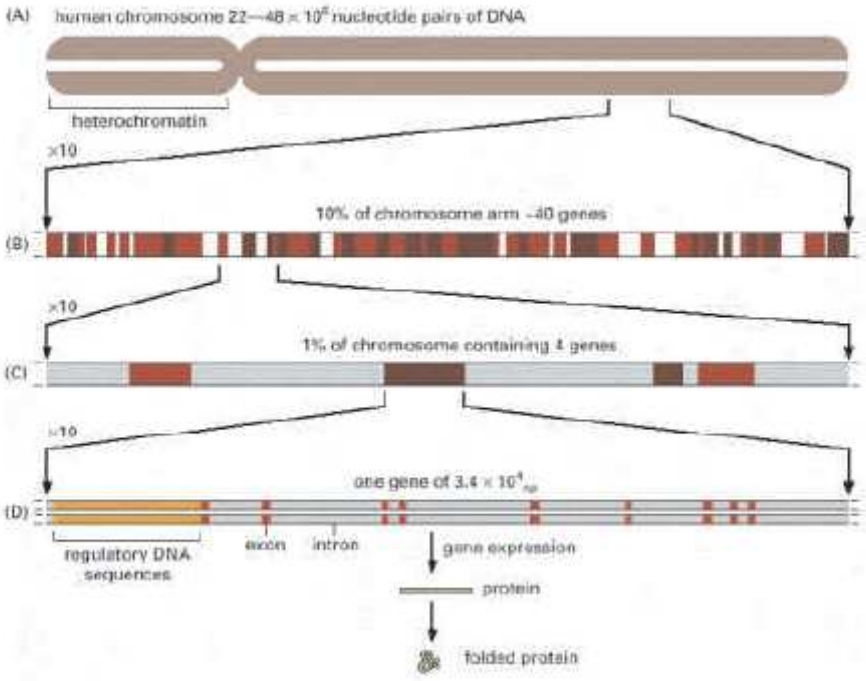
Human genes are made of DNA and comprise specific sequences of nucleotides (the "building blocks" of DNA) that encode particular proteins. They do not exist in nature as isolated DNA molecules, but rather as segments of extremely long DNA molecules called chromosomes, 23 pairs of which are carried within human cells. As illustrated in Figure 1A (Exh. 2), chromosomes reside within the sub-cellular compartment called the nucleus which, in turn, is located within the cellular cytoplasm, a complex mix of organelles (e.g. mitochondria), proteins and other cellular substances.

Figure 1A. Chromosome Structure



Human chromosomes differ in the number of genes they carry. Chromosome 1, for example, is estimated to carry more than 4,000 genes; chromosome 17 (site of the *BRCA1* gene) carries between 1,300 – 1,500 genes, and the male sex chromosome Y only about 86. The genes on any given chromosome are chemically connected, but are generally not arranged directly next to each other on the chromosomal DNA. As illustrated in Figure 1B (Exh. 3, *Molecular Biology of the Cell*, Alberts, Bruce et al. (4th ed. 2002) at Fig. 4-15), interspersed among genes are vast sequences of DNA that are not known to have any protein-encoding capability at all. In addition, there are regulatory sequences (responsive to chemical cues from the cellular environment) that control the timing and amount of the encoded protein that gets produced (or "expressed") by the gene. There are no physical landmarks on chromosomes that demarcate the genes from the non-coding and regulatory regions. Consequently, the identification, location and isolation of biologically significant genes is no small feat, as is amply set forth the in the '282 patent at col. 7, l. 33 - col. 11, l. 58 for the *BRCA1* gene.

Figure 1B. Chromosome & Gene Structure

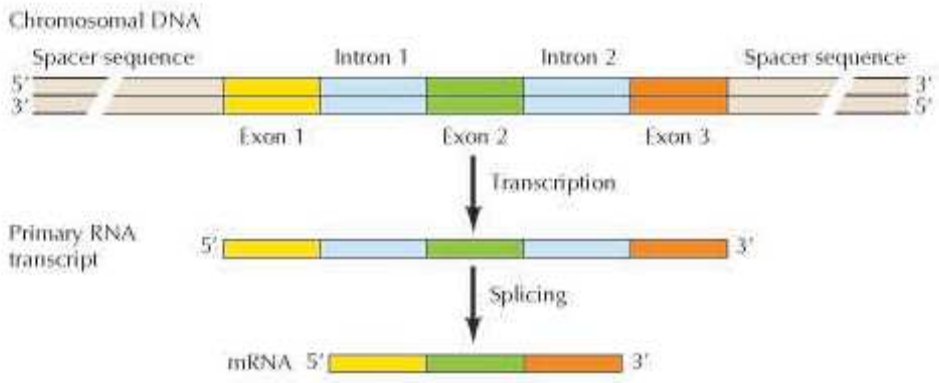


As also illustrated in Figure 1B(D), an individual human gene is made up of "exons" and "introns." Within an exon is a sequence of nucleotides that encode a stretch of amino acids that make up part of the protein encoded by the gene. Introns are DNA that is interspersed among the exons but do not code for proteins. Together, the nucleotides within the exons and introns make up the DNA sequence of the gene, or "genomic" DNA sequence.

2. mRNA

Genes reside in chromosomes within the cell's nucleus. The proteins they encode, however, are made in the cytoplasm of the cell. Therefore, another type of nucleic acid, known as messenger RNA or mRNA[4], exists that serves as an intermediary in the process of gene expression. As illustrated in Figure 2 (Exh. 4), chromosomal (genomic) DNA is "transcribed" into a primary RNA transcript that contains both exons and introns. By a process called "splicing", the introns are excised resulting in an mRNA molecule containing only protein-encoding exons.

Figure 2. mRNA Structure



The mRNA travels out of the nucleus of the cell into the cytoplasm where it is "translated", i.e., serves as a template that dictates the sequence of amino acids that are connected to make the protein encoded by the genomic DNA.

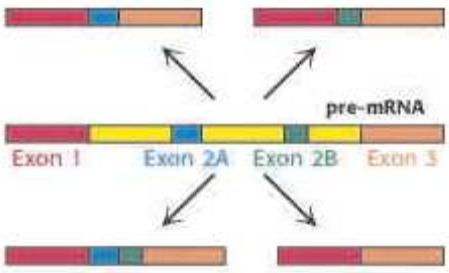
[4] RNA stands for "ribonucleic acid", a different chemical compound than DNA and one that is far more susceptible to degradation by cellular enzymes than is DNA.

Neither transcription nor splicing results in an isolated or purified nucleic acid of any sort. The mRNA molecules so made exist in the complex cytoplasmic milieu, and only for a short time before they are completely degraded by cellular enzymes.

3. Alternative Splicing

When a primary RNA transcript is spliced, the resulting mRNA does not necessarily contain a full complement of exons. Through "alternative splicing", not only are the introns of the primary transcript excised, but one or more of the exons may be excised as well. This is illustrated in Figure 3 (Exh. 5).

Figure 3. Alternative Splicing Patterns



As shown, the primary RNA transcript (or "pre-mRNA") copied from a gene with Exons 1, 2A, 2B and 3 can be alternatively spliced to yield mRNAs containing all or less than all of the possible exons. All of these mRNAs can serve as templates for protein production. Thus, a single genomic sequence can potentially generate multiple mRNA templates, which, in turn, will direct the production of multiple distinct proteins. In this respect, a genomic sequence subject to alternative splicing has greater informational content than any mRNA transcript made from it.

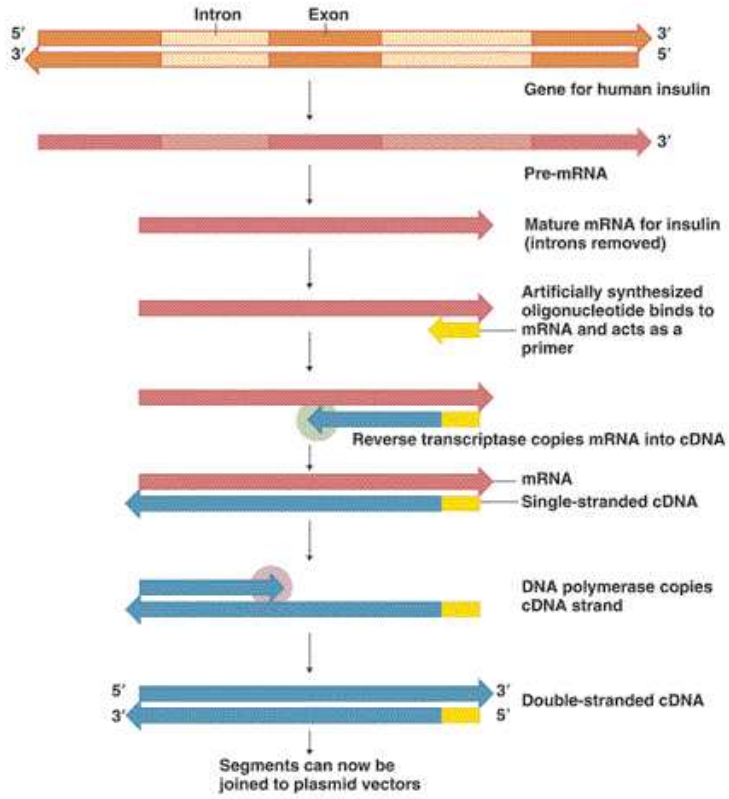
The *BRCA1* gene is known to code for more than 30 different splice variants. (*See* Exh. 6, Miao Lixia et al., *Alternative Splicing of Breast Cancer Associated Gene BRCA1 from Breast Cancer Cell Line*, J. Biochem. and Molecular Bio. 15-21 (2006)). The *BRCA2* pre-mRNA sequence is also alternatively spliced, and thus produces multiple distinct protein

products as well. (*See* Exh. 7, Ivan Bieche et al., *Increased Level of Exon 12 Alternatively Spliced BRCA2 Transcripts in Tumor Breast Tissue Compared with Normal Tissue*, J. Cancer Research 2546-2550 (June 1, 1999)).

4. cDNA

"Copy DNA" or "cDNA" does not exist in nature. It is made in the laboratory. Starting with a sample containing mRNA, a scientist adds an artificially synthesized "primer", a small piece of DNA (or "oligonucleotide") that binds to one end of the mRNA molecule, as well as a non-human enzyme called "reverse transcriptase" that extends the primer along the mRNA, making a cDNA sequence complementary to that of the mRNA. The mRNA/cDNA hybrid is dissociated and DNA polymerase is used to copy the cDNA strand, creating a double-stranded cDNA molecule. This is illustrated in Figure 4 (Exh. 8).[5]

Figure 4. Production of a cDNA Molecule



[5] In this illustration, cDNA encoding insulin is used as the example, but what is shown is the general methodology for making cDNA.

Researchers and medical professionals overwhelmingly use cDNA for most applications because of its stability (compared to mRNA), its ability to encode a single protein (compared to alternatively spliceable genomic DNA) and its greater manipulability (compared to both mRNA and genomic DNA).

III. ARGUMENT

A. The Claimed DNA Molecules Fall Within One or More of the Statutory Classes of Patent-Eligible Subject Matter

Section 101 of the Patent Act defines patent-eligible subject matter as "any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof . . . ." 35 U.S.C. §101.[6] There are notable exceptions to the statutory classes. In interpreting Section 101, the Supreme Court has repeatedly held that a hitherto unknown "phenomenon of nature . . . mental processes, and abstract intellectual concepts are not patentable . . . ." *See e.g., Parker v. Flook,* 437 U.S. 584, 589 (1978).

However, the ease with which the natural phenomena exception can be twisted, as here, to attack the patent-eligibility of biological compositions of matter has long been recognized:

> It only confuses the issue, however, 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 . . . *Arguments drawn from such terms for ascertaining patentability could fairly be employed to challenge almost every patent*.

Funk Bros. Seed Co. v. Kalo Inoculant Co., 333 U.S. 127, 134-35 (1948) (Frankfurter, J. concurring) (emphasis added).[7]

---

[6] 35 U.S.C. § 101 states in its entirety: Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

[7] Plaintiffs incorrectly characterize *Funk* as holding that the mixtures of bacterial strains at issue were patent-ineligible "works of nature". (Pl. Mem. at 21). On the contrary, the Supreme Court accepted that a product embodying the patentee's discovery represented subject matter eligible for patent protection if the other applicable tests for patentability were met. They were not. The holding in *Funk* specifically turned on lack of "invention"; a

continued …

Consequently, the Supreme Court has "cautioned that courts 'should not read into the patent laws limitations and conditions which the legislature has not expressed.'" *Diamond v. Chakrabarty*, 447 U.S. 303, 308 (1980) (citation omitted). Congress intended § 101 to be interpreted broadly and include "anything under the sun that is made by man" *Id*. at 309 (citations omitted).

All DNA molecules within the scope of the claims at issue are man-made. No DNA claim reads on a DNA molecule that exists in nature. Each claimed DNA molecule is a tangible man-made thing; it is neither an abstraction nor a thought process. Despite Plaintiffs' efforts to equate the claimed subject matter with 'information,' it is self-evident that each and every claimed DNA molecule is a chemical compound, falling indisputably within the "composition of matter" statutory class.

Furthermore, many of the DNA molecules within the scope of the claims also qualify as "manufactures." For example, a common way of obtaining DNA molecules within, e.g., the scope of Claim 1 of the '282 patent, is by the widely-used polymerase chain reaction (PCR). (Exh. 1, '282 patent at col. 17, ll. 15-27). Using the natural sequence as a template, copies of the DNA are enzymatically synthesized using DNA polymerase and small synthetic pieces of DNA that serve to "prime" the synthesis. The resulting DNA molecules are man-made "manufactures." Similarly, chemical synthesis techniques can be used to make the claimed DNAs, once again generating completely man-made "manufactures".

Even in instances where genomic sequences are isolated from cellular materials, this requires the hand of man. Plaintiffs attempt to minimize the importance of the word "isolated" in the claims as meaning "nothing more than a gene that has been removed from the body and separated from surrounding material." (Pl. Mem. at 4). Plaintiffs overlook that the specific

---

judicially developed criterion that was superseded not by 35 U.S.C. § 101 but by *35 U.S.C. §103*, which requires an invention be "non-obvious."

removal of such DNA requires nothing less than its targeted separation from thousands of other cellular components through a series of sophisticated identification and purification steps. The *BRCA1* gene, for example, consists of 84,000 DNA building blocks – "base pairs" – which occupy only a fraction of a percent of the 81 million DNA base pairs of chromosome 17, which, in turn, represents less than 3% of the human genome. In order to be isolated, the *BRCA1* DNA must be identified among the 1,300 other genes that occupy that vast length of chromosome 17 and the 25,000 other genes that comprise the human genome. The precise DNA sequence must be enzymatically excised from the rest of the chromosomal DNA, and physically separated by a technique such as gel electrophoresis. Such isolation is not a natural process and unquestionably results in a statutorily sanctioned, patent-eligible composition of matter, if not a manufacture, as well.

Lastly, the claims that are limited to DNA molecules having the sequence of a particular cDNA, e.g., Claim 2 of the '282 patent, necessarily are directed to patent-eligible compositions of matter, or indeed, manufactures. This is because cDNA molecules are man-made and do not exist in nature and thus, cannot possible be excluded from 35 U.S.C. § 101 as a "natural phenomenon" or "work of nature."

B. Courts Have Long Upheld The Patent-Eligibility of Isolated and Purified Natural Substances That Possess New Qualities And Utilities

In a case that is often cited as the first to acknowledge that isolated and purified products of nature are patent-eligible, Judge Learned Hand determined that purified adrenaline, extracted from adrenal glands, was indeed patentable. *Parke-Davis & Co. v. H.K. Mulford Co.*, 189 F. 95, 103 (S.D.N.Y. 1911).[8] Judge Hand reasoned that the new utility of the purified product conferred patent-eligibility:

[8] As discussed *infra* Plaintiffs' attempt to distinguish *Parke Davis* (Pl. Mem. at 25) is unavailing, as it is based on the fallacy that the human body possesses "a natural process for isolating and purifying genes."

> [E]ven if it were merely an extracted product without change, there is no rule that such products are not patentable. [The inventor] was the first to make it 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.

Id. *See also Scripps Clinic and Research Foundation v. Genentech, Inc.*, 666 F. Supp. 1379, 1389 n.6 (N.D. Cal. 1987) (purified Factor VIII:C, an important natural blood clotting protein, found patent-eligible under 35 U.S.C. § 101); *In re Kratz*, 592 F.2d 1169 (C.C.P.A. 1979) (isolated naturally occurring constituent of strawberries responsible for fragrance found patent-eligible); *In re Bergstrom*, 427 F.2d 1394 (C.C.P.A. 1970) (USPTO rejection of claims to substantially pure prostaglandin compounds under 35 U.S.C. § 101 reversed).

Another famous case that advances the *Parke Davis* concept that purified or isolated natural compounds are "new and useful", and hence patent-eligible under 35 U.S.C. § 101, is *Merck & Co. v. Olin Mathieson Chem. Corp.*, 253 F.2d 156 (4th Cir. 1958). In finding the claimed vitamin B12 compositions patentable, that court stated:

> The compositions of the patent here have all of the novelty and utility required by the Act for patentability. They never existed before; there was nothing comparable to them. If we regard them as a purification of the active principle in natural fermentates, the natural fermentates are quite useless, while the patented compositions are of great medicinal and commercial value. The *step from complete uselessness to great and perfected utility is a long one. That step is no mere advance in the degree of purity of a known product*. From the natural fermentates, which, for this purpose, were wholly useless and were not known to contain the desired activity in even the slightest degree, products of great therapeutic and commercial worth have been developed. *The new products are not the same as the old, but new and useful compositions entitled to the protection of the patent*.

Id. at 164-165. (emphasis added).

In re Merz, 25 C.C.P.A. 1314 (C.C.P.A. 1935), cited by Plaintiffs[9], perhaps most succinctly states the concept that patent eligibility of a purified or isolated natural product flows from its serving purposes that the natural product cannot:

> [I]f the process produces an article of such purity that it differs *not only in degree but in kind, it may be patentable*. If it differs in kind, it may have a *new utility* in which invention may rest.

Id. at 1314 (emphasis added).

More recent case law has implicitly extended the *Parke-Davis, Merck* and *Merz* concept of patent eligibility to isolated and purified DNA molecules. For example, it is well settled that prior to undertaking an analysis of whether a claim meets the requirements of 35 U.S.C. §§ 102, 103, and 112, reviewing courts are required to *first* determine whether the claimed subject matter is eligible for patent protection under 35 U.S.C. § 101. As stated by the Supreme Court: "[t]he obligation to determine what type of discovery is sought to be patented must precede the determination of whether that discovery is, in fact, new or obvious." *Parker v. Flook*, 437 U.S. 584, 593 (1978). This pronouncement is strictly followed by district courts. *See, e.g., Ariad Pharms., Inc. v. Eli Lilly & Co.* 529 F. Supp. 2d 106, 116 -117 (D. Mass. 2007) ("The court must examine what is sought to be patented . . . *before* any consideration whether that discovery meets the requirements for patentability under 35 U.S.C. §§ 102, 103 and 112.") (emphasis in original).

---

[9] Cases cited by Plaintiffs to support their position that isolated and purified natural substances are patent-ineligible are inapposite. To the extent the subject matter discussed in the following cases was deemed not patentable, it was not because the subject matter was patent-ineligible within the meaning of § 101 of the 1952 Patent Act - it was because the subject matter was not novel (in the sense of 35 U.S.C. § 102) or was obvious or not inventive (in the sense of 35 U.S.C. § 103). These cases include *Funk Bros. Seed Co. v. Kalo Inculcant Co.*, 333 U.S. 127 (1948) (composition of nitrogen fixing bacteria not inventive); *In re Merz*, 25 C.C.P.A. 1314 (C.C.P.A. 1935) (aquamarine not inventive); *In re Marden*, 18 C.C.P.A. 1046 (C.C.P.A. 1931) (uranium not novel); *In re Marden*, 18 C.C.P.A. 1057 (C.C.P.A. 1931) (vanadium not novel); *General Elec. Co. v. De Forest Radio Co.*, 28 F.2d 641 (1928) (tungsten not novel); *Cochrane v. Badische Anilon & Soda Fabrik*, 111 U.S. 293 (1884) (alizarine not novel);and *Am. Wood Paper Co. v. Fibre Disintegrating Co.*, 90 U.S. 566 (1874) (cellulose not novel). In *Am. Fruit Growers, Inc. v. Brogex Co.*, 283 U.S. 1 (1931) borax-treated citrus fruit was not considered a "manufacture" under the old statute, 35 U.S.C. § 31, because fruit so-treated did not take on a patentably distinctive use.

Thus, the cases addressing whether purified and isolated DNA molecules are patentable under sections of the patent statute other than § 101 implicitly recognize that those DNA molecules are subject to patent protection under § 101. *See, e.g., In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009) (claim to DNA encoding the p38 protein affirmed as unpatentable under 35 U.S.C. § 103; patent-eligibility not questioned); *In re Deuel*, 51 F.3d 1552, 1560 (Fed. Cir. 1995) (reversing PTO decision rejecting claims directed to a "purified and isolated DNA sequence consisting of a sequence encoding human heparin binding growth factor of 168 amino acids having the following amino acid sequence . . ."); *Amgen, Inc. v. Chugai Pharm. Co., Ltd.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991), *cert. denied*, 502 U.S. 856 (affirming patentability of claims directed to, *inter alia*, a "purified and isolated DNA sequence consisting essentially of a DNA sequence encoding human erythropoietin."); *Fiers v. Revel*, 984 F.2d 1164 (Fed. Cir. 1993) (affirming priority of invention to party that met enablement requirement of § 112, ¶ 1 for a claim directed to a "DNA which consists essentially of a DNA which codes for a human fibroblast interferon-beta polypeptide").

BIO agrees with Plaintiffs that our Supreme Court has never squarely addressed the patent-eligibility of isolated and purified DNA molecules. However, BIO submits that the failure of the parties to the foregoing cases to raise the 35 U.S.C. § 101 issue (or for that matter, constitutional issues) as well as the Supreme Court's denial of certiorari in the Amgen case, amply illustrates the wide acceptance of isolated DNA molecules as patent-eligible subject matter in accord with Parke-Davis and its progeny. Respectfully, this Court should refrain from altering the status quo.

C. The Claimed DNA Molecules Differ In Kind From Natural Sequences

Despite Plaintiffs' arguments to the contrary, the claimed isolated DNA molecules differ in structure, function, utility, and information content from natural *BRCA1* and *BRCA2* sequences. So significant are these differences that the claimed DNAs have qualities that make

them differ in kind from native sequences and are more than sufficient to confer patent-eligibility.

1. Isolated *BRCA* DNA Molecules Can Be Put To Uses That Natural *BRCA* DNA Sequences Cannot

BRCA DNA sequences within their native setting, i.e., within a large and complex chromosome, in the midst of other chromosomes and all the hundreds of other components of a cell, are essentially inaccessible and under the control of the physiology of the human in which they reside. They serve whatever their natural purpose is within a cell but can be put to virtually no practical diagnostic or therapeutic applications.

Isolating a DNA molecule imparts new utility, structure and function that does not exist in nature. Isolation of DNA creates discrete molecules that can be manipulated by molecular biological techniques. Isolation of DNA removes it from other cellular substances (such as other nucleic acids and proteins) that can contaminate or otherwise interfere with techniques, apparatus, and assays, involved in the new uses to which DNA is put.

As noted previously, all DNA claims at issue are limited to isolated DNA molecules. The patents-in-suit contemplate putting the claimed isolated DNA molecules to important diagnostic and therapeutic uses that make them functionally distinct from the natural sequences. For example, the ’282 patent discloses the DNA molecules of the invention can be subjected to direct DNA sequencing to detect DNA sequence variations of diagnostic and prognostic importance. (Exh. 1, ’282 patent at col. 12, ll. 26-28; col. 13, ll. 10-16). In such a diagnostic setting, the isolated DNA molecule is not serving the natural function of protein production. Its sequence is providing a diagnosis or prognosis of a particular disease state.

Furthermore, gene therapy with wild-type *BRCA* sequences is contemplated, whereby the claimed wild-type DNA molecules are put into vectors, which, in turn, can be introduced into cells in need of the wild-type sequences. (*See, e.g.*, Exh. 1, ’282 patent at col. 32, l. 34 - col. 33,

l. 20). In addition, introduction of the claimed cDNA molecules into bacteria for the production of tumor suppressing proteins that may be used therapeutically is also contemplated. (*Id*. at col. 34, ll. 39-63). Neither of these important utilities could be served without first isolating the desired DNA molecule from its natural setting. Moreover, unlike a natural wild-type sequence within a healthy woman, the isolated wild-type DNA molecules can be copied many times over and serve the functions of preventing or curing breast cancers in sick (or potentially sick) women who lack the wild-type genes, either by way of gene therapy or recombinant production of a therapeutic protein. Surely these uses make the claimed molecules functionally, and patentably, distinct from the natural sequences, in accordance with the holdings of *Parke-Davis* and *Merck*.

2. The Claimed Isolated cDNA Molecules Are Not Only Functionally Distinct, They Are Structurally And Informationally Distinct From Natural Sequences

Several of the challenged claims, e.g., Claim 2 of the '282 patent, claim a non-natural cDNA sequence that is structurally different from the DNA sequence of a natural *BRCA* gene. For example, the natural genomic *BRCA1* sequence has a length of approximately 84 kilobases (84,000 base pairs), making it a relatively large gene by human standards. However, the claimed cDNA comprises only 5.9 kb less than 1/10th the length of the natural gene. This disparity arises because the sections that actually encode the *BRCA1* gene product within the natural gene (exons) are interrupted by 23 long regions (introns) − together comprising more than 90% of the gene's length - which encode no protein. As explained in more detail *supra*, the claimed cDNA is therefore an artificial DNA construct from which natural, non-coding regions have been eliminated and in which the rest of the gene has been reconfigured to form one contiguous protein-coding DNA sequence that does not exist in nature. Thus, in terms of structure, the claimed isolated cDNA molecules differ significantly in kind from the natural *BRCA* sequences.

Moreover, the claimed isolated cDNA molecules have a function and information content that differs from natural *BRCA* genes. The natural *BRCA1* and *BRCA2* sequences are subject to

alternative splicing (discussed *supra*) and thus encode multiple proteins. On the other hand, cDNA encodes a single protein. The cDNA claims at issue, such as Claim 2 of the '282 patent, recite a sequence that encodes only one protein. Thus, contrary to Plaintiffs' position, the claimed cDNAs are informationally distinct; they are incapable of coding for the full range of proteins the natural sequences encode. Surely, such specific, man-made molecules, capable of serving all the new utilities described in the preceding section, in no way mimic nor usurp nature such that their patentability should be denied on Section 101 grounds.

3. Plaintiff's Scientific Reasons For Distinguishing *Parke-Davis* And Its Progeny Are Factually Incorrect

Attempting to avoid well-reasoned and controlling precedent, Plaintiffs incorrectly distinguish *Parke-Davis* as:

> [u]npersuasive in the gene patent context for scientific reasons. Whereas the human body does not possess a natural process for purifying adrenaline, the human body does possess a natural process for isolating and purifying genes. D. Jackson ¶¶ 26-29, D. Mason ¶¶ 11-12.

(Pl. Mem. at 25).

Through their experts, Jackson and Mason, Plaintiffs suggest that the natural process of transcribing genomic DNA into mRNA is the body's method to isolate and purify genes. This assertion is scientifically incorrect. As noted above, the process of transcribing a genomic DNA sequence into an mRNA molecule does not result in the isolation or purification of the genomic sequence, but rather the production of a chemically and structurally distinct mRNA copy of only a portion of the information carried in that genomic sequence. Furthermore, the production of an mRNA molecule occurs within the context of the cellular milieu and the resulting mRNA, therefore, is neither isolated nor purified. Given that the end-product of transcription is an mRNA molecule that: (1) is composed of RNA nucleotides and not DNA nucleotides; (2) includes less information than the genomic sequence and (3) exists in an unisolated,

unpurified state within the cellular milieu, it is untenable to argue that such a molecule corresponds to an isolated or purified copy of the genomic DNA sequence. Moreover, for reasons including its inherent chemical instability, mRNA cannot be put to the uses an isolated and purified DNA molecule can, such as those claimed in the patents in suit. Thus, the holdings of *Parke-Davis* and its progeny unquestionably support the patent eligibility of the claimed isolated DNA molecules.

D. The USPTO Finds Isolated and Purified DNA Molecules Patent-Eligible in Accord with "Well-Established Principles"

The USPTO has analyzed the issue of whether isolated and purified natural substances are patent-eligible in view of the relevant case law and comments received from the public. *See generally* USPTO Utility Examination Guidelines, 66 Fed. Reg. 1092 (2001). This analysis is highly instructive and confirms that isolated and purified DNA molecules are indeed entitled to patent protection:

> An isolated and purified DNA molecule that has the same sequence as a naturally occurring gene . . . is eligible for a patent as a composition of matter or as an article of manufacture because that DNA molecule does not occur in that isolated form in nature . . . *Patenting compositions or compounds isolated from nature follows well-established principles, and is not a new practice.* For example, Louis Pasteur received U.S. Patent 141,072 in 1873, claiming "[y]east, free from organic germs of disease, as an article of manufacture."
>
> ***
>
> Like other chemical compounds, DNA molecules are eligible for patents when isolated from their natural state and purified . . . .

Id. (emphasis added).

E. The Patent Eligibility of Isolated DNA Molecules Provides Incentives That Lead To Life-Enhancing Diagnostics and Therapeutics

Claims like those of the patents-in-suit have been a key foundation supporting the massive investment of time and capital that is necessary to bring life-enhancing DNA-based

diagnostics and therapeutics to the public. In the United States alone, more than $30 billion was invested in biotechnology-related research and development in 2008. (Exh. 9, Ernst & Young, Beyond Borders, Global Biotechnology Report 2009 at 34). The average capitalized cost of bringing a single biotechnology-related therapeutic to market exceeds $1.2 billion once the basic research, clinical trials, and post-approval testing is combined. (Exh. 10, Henry Grabowski, *Follow-On Biologics: Data Exclusivity and the Balance Between Innovation and Competition*, Nature Reviews Drug Discovery at 4 (May 12, 2008)). New therapeutics typically take eight years of clinical development, not to mention what often amounts to years of pre-clinical research. (*Id*. at 3).

Investing in biotechnology is not only expensive, it is also fraught with risk. (*Id*. at 3). For every successful therapeutic, numerous candidate therapeutics are dropped, often only after large investments of time and capital have been made. (*Id*.). Even with a vigilant strategy of eliminating all but the most successful candidates, only a minority of the therapeutics that begin human clinical trials ultimately obtain FDA approval. (*Id*.). In light of the clear risk to an investor's resources, raising the necessary funds to support biotechnology research and development requires the expectation that reasonable financial returns will flow from those therapeutics that do indeed make it to market. *Currently, that expectation relies primarily on the short term exclusivity afforded to patented products*. (Exh. 11, Henry Grabowski et al., *The Market for Follow-On Biologics: How Will It Evolve*, Health Affairs, 25(5): 1291-1301, 1299 (2006)).

Patents on isolated DNA molecules have featured prominently in biotechnology success stories. Amgen, for example, was awarded U.S. Patent No. 4,703,008 ("the '008 patent"), which includes claims to isolated DNA molecules encoding the human protein erythropoietin. (Exh. 12, the '008 patent). Amgen was awarded this patent for its pioneering work with isolated

erythropoietin-encoding DNA that would ultimately change the face of anemia treatment around the world. For example, a lack of sufficient erythropoietin is the primary cause of anemia associated with renal failure and, prior to Amgen's development of their DNA-encoded erythropoietin therapeutic, "Epogen®", a full 25% of renal patients on dialysis required regular blood transfusions. (Exh. 13, Wolfgang Jelkmann, *Molecular Biology of Erythropoietin*, Internal Medicine, 43(8):649-659 (August 2004)). However, once Epogen® became available, the need for such blood transfusions was virtually eliminated. (Exh. 14, Amgen Press Release entitled "FDA Clears Epogen For Treatment Of Anemia In Children On Dialysis" (Nov. 4, 1999)). The use of patented, isolated DNA encoding erythropoietin created a supply of this vital therapeutic protein that never existed before.

Amgen's erythropoietin patent estate has also been a significant factor in the overall value investors have attributed to the company. On Monday, January 22, 2001, when the District Court for the District of Massachusetts upheld the validity of certain of Amgen's erythropoietin patents, Amgen's stock value increased more than 10% in a single day. *Amgen v. Hoechst Marion Roussel, Inc.*, 126 F. Supp. 2d 69 (D. Mass. 2001); (Exh. 15, New York Times, *Technology Briefing: Biotech; Amgen Shares Rise On Rulings* (Jan. 23, 2001)). Further illustrating the point that patents relating to human genes improve and save lives, Amgen's market capitalization has allowed the company to continue to make significant investments in developing new applications for Epogen®, including for treatment of chemotherapy-related anemia, as well as developing entirely new therapeutics for diseases such as rheumatoid arthritis and colon cancer.

Another particularly well known example of how patents to isolated DNA molecules can lead to significant medical breakthroughs involves the former Chiron Corporation, which now operates as Novartis Vaccines & Diagnostics. After engaging in a near decade long struggle to

identify the causative agent of a deadly form of Hepatitis formerly known as "Non-A, Non-B Hepatitis", researchers at Chiron were able to identify, isolate, characterize and clone the Hepatitis C Virus (HCV) genome. (Exh. 16, Harvey J. Alter et al., *Hepatitis C Virus and Eliminating Post-Transfusion Hepatitis*, Nature Medicine, 6(1): 1082-1084 (2000)). Chiron's cloning of the HCV genome also led to the patenting of certain HCV genes in the late 1980's and early 1990's. Chiron's tremendous contribution to the public's understanding of Hepatitis C was recognized around the world and the company was ultimately awarded more than 100 HCV-related patents in 20 countries for its efforts. This patent estate attracted the investment dollars and license revenues that made possible dramatic changes in how the world's blood supply is tested. By screening for HCV nucleic acids, the incidence of contracting Hepatitis C during a blood transfusion dropped from an alarming 1 in 25 chance to near zero. (*Id*. at 1083).

F. Claims to DNA Molecules, Such As Those At Issue, Do Not Impede The Progress of Science

When evaluating Plaintiffs' charge that gene patents stifle scientific inquiry, it is important, as an initial matter, to draw a distinction between evaluative research on the one hand, and the provision of clinical diagnostic testing services on the other. This distinction is not always apparent, especially when, as here, an unlicensed would-be infringer is affiliated with an academic institution. For example, a clinical test provider may wish to provide unlicensed patented testing on a fee-for-service basis, provide test results to patients, and enter the results in a scientific database to conduct population genetic studies. The fees generated from such testing might allow the test provider to supplement her or his academic research grants, to train graduate students, to travel to scientific meetings, to conduct further research, and the like. Under such circumstances a patentee might rightfully take the position that unlicensed fee-for-service testing would constitute nothing less than patent infringement, undertaken in direct competition with the patentee's own commercial activities. The unlicensed test provider, on the other hand, might be

quick to claim that patent enforcement would stifle scientific research, interfere with scholarly discourse, disrupt the training of young scientists, and prevent any number of other worthwhile endeavors.

The foregoing hypothetical is meant to illustrate that certain allegations, forcefully proclaimed as if based on a position of moral high ground, deserve careful scrutiny in patent cases just like in any other civil litigation. In asserting that the claims of the patents-in-suit have impeded the progress of science, Plaintiffs contend that "[t]he effect of the patents is to give control of all knowledge of those genes and the functions dictated by nature to the defendants." (Pl. Mem. at 35). Plaintiffs are mistaken on several levels. For one, the patent system inherently operates to disseminate rather than sequester knowledge (*see* PTO Brief at 13-16). Second, under Plaintiffs' flawed reasoning, any patent could be said to give its owner control "of all knowledge" of the invention and its function. This patents do not do. A patent only gives its owner control an exclusive rights, i.e., the right to exclude others from making, using, selling, offering for sale, or importing the patented invention, 35 U.S.C. § 271(a) – "knowing" is not an act of patent infringement. Third, Plaintiffs' claim is perplexing in view of the vast body of *BRCA*-related clinical and experimental research that has been conducted and published by U.S. laboratories and clinical centers since the disputed patents were issued. (*See* Bissonnette Decl.). Fourth, several empirical studies have found no persuasive evidence that gene patents in fact interfere with basic genomic research. For example, a 2006 report by the National Research Council on the effects of genomic and proteomic patenting and licensing practices on research and innovation found

> that the number of projects abandoned or delayed as a result of difficulties in technology access is reported to be small, as is the number of occasions in which investigators revise their protocols to avoid intellectual property issues or in which they pay high costs to obtain intellectual property. Thus, for the time being, it appears that access to patented inventions or information inputs into

> biomedical research rarely imposes a significant burden for biomedical researchers.

(Exh. 17, Reaping the Benefits of Genomic and Proteomic Research: Intellectual Property Rights, Innovation, and Public Health at 134 (2006)).

A survey of academic researchers conducted by Walsh, Cho and Cohen in 2005 concluded that "patenting does not seem to limit research activity significantly, particularly among those doing basic research," with only 1% of their random sample of 398 academic respondents reporting a project delay of more than a month due to patents on knowledge inputs necessary for their research, and none reporting abandoning of a research project due to the existence of patents.[10] Murdoch and Caulfield, in a recent Canadian report on researcher perspectives on commercialization and patenting of genomic research similarly find that there is little evidence that the progress of research itself is in fact being seriously hindered or that gene patents are being aggressively enforced.[11] Holman concluded that gene patents are not litigated frequently compared to other biotechnology patents, and when they are, they settle early.

As a practical matter, research into gene sequences, expression profiles, and mutations, commonly referred to as "genomics", has exploded in the time since the USTPO began issuing gene patents. In the past two decades the field has matured to such an extent that researchers have coined new terms such as "medical genomics" and "systems medicine" to describe the advances in genomics that they anticipate "will provide a foundation for a prospective medicine

---

[10] Exh. 18, John P. Walsh et. al., *Final Report to the National Academy of Sciences' Committee Intellectual Property Rights in Genomic and Protein-Related Inventions: Patents, Material Transfers and Access to Research Inputs in Biomedical Research* (Sept. 20, 2005).

[11] *See* Exh. 19, CJ Murdoch et al., *Commercialization, Patenting and Genomics: Researcher Perspectives*, Genome Medicine 1:22 (2009) available at http://genomemedicine.com/content/pdf/gm22.pdf (last accessed December 29, 2009); Exh. 20, Christopher M. Holman, *Trends in Human Gene Patent Litigation*, Science 32, 198-200 (2008); Exh. 21, Ann E. Mills et al., *DNA-Based Patents: An Empirical Analysis*, Nature Biotechnology 26(9) 993-995 (2008).

that will be predictive, personalized, preventive and participatory . . . ."[12] Such advances in the progress of science would be impossible if entire bodies of knowledge were being turned over to private control by the USPTO as asserted by the Plaintiffs. (Pl. Mem. at 37).

In April 2009, the USPTO issued its 50,000th patent with at least one claim to a nucleic acid sequence.[13] Even with this rapid increase in the number of patents claiming nucleic acids, recent empirical research into 22 of the most common genetic diagnostic tests has shown that gene patents have not produced so-called "patent thickets", which are collections of patents that have the effect of impeding research.[14] Similarly, in a study comparing the level of secrecy in science prior to and after the advent of gene patenting, the researchers were unable to establish a significant relationship between patenting and scientific secrecy, particularly in the field of experimental biology.[15] Thus, any arguments that suggest gene patents are functioning to stifle research or are causing investigators to be more secretive about their work are simply unsupported by the empirical data.

To be sure, previous policy studies by the National Research Council (see above), the OECD[16], The Australian Law Reform Commission[17] and the Federal Trade Commission[18] have identified concerns with the operation of the patent system as it relates to genetic technology or biotechnology innovation more generally. While generally concluding that the intellectual

---

[12] Exh. 22, Charles Auffray et al., *Systems Medicine: the Future of Medical Genomics and Healthcare*, Genome Med. 1(2): doi:10.1186/gm2 (2009).

[13] Exh. 23, Chandrasekharan et al., *Gene patents and personalized medicine - what lies ahead?*, Genome Med. 1:92 (2009).

[14] Exh. 24, Isabelle Huys et al., *Legal uncertainty in the area of genetic diagnostic testing*, Nature Biotechnology, 27(10): 903, 909 (2009) ("In conclusion, the present analysis and accompanying observations do not point to the existence of a wide patent thicket in genetic diagnostic testing.").

[15] Exh. 25, Wei Hong et al., *For Money or Glory? Commercialization, Competition, and Secrecy in the Entrepeneurial University*, Sociological Quarterly, 50:145-171 (2009).

[16] *See* Genetic Inventions, Intellectual Property Rights, and Licensing Practices (2002); available at http://www.oecd.org/dataoecd/42/21/2491084.pdf.

[17] *See* Genes and ingenuity: Gene Patents and Human Health, ALRC 99, 2004, available at: http://www.austlii.edu.au/au/other/alrc/publications/reports/99/_4.html.

[18] *See* To Promote Innovation: The Proper Balance of Competition and Patent law and Policy, 2003, available at: http://www.ftc.gov/os/2003/10/innovationrpt.pdf.

property system is functioning as intended, these groups' recommendations included a strengthening of the legal standards for obviousness, raising the bar for utility, and guidelines for best licensing practices for genomic inventions.[19] Notably, none of these groups has recommended the wholesale exclusion of gene-based inventions from patent-eligibility, as Plaintiffs now propose.

G. There Is No Persuasive Evidence That Gene Patents Impair Patient Access To Genetic Diagnostic Tests

The mere fact that certain genetic tests are covered by patents, such as the tests covered by the claims of the patents-in-suit, does not mean that patients will be forced to pay inflated prices to access those tests. For example, the U.S. Secretary of Health and Human Services' Advisory Committee on Genetics, Health, and Society has released a draft report that compares the pricing of patented genetic diagnostic tests, including the *BRCA* tests covered by the patents-in-suit, to the pricing of a equivalent non-proprietary genetic tests. The Committee found that "the per-unit price of the full-sequence BRCA test, which often is cited as being priced very high, was actually quite comparable to the price of other full-sequence tests done by [ ] (PCR), at nonprofit and for-profit testing laboratories," and concluded more generally that despite public perception, evidence from its own studies did not reveal a pattern of overpricing for genetic diagnostic tests that were patented and exclusively licensed relative to tests that were either unpatented or non-exclusively licensed. (Exh. 26, SACGHS Report at 102).

Having no data to support a claim that the patents-in-suit are causing patients to pay a "patent premium" for access to *BRCA* testing, Plaintiffs have asserted that the exclusivity provided by the patents-in-suit has delayed the introduction of more advanced screening tests, including tests that detect deletions and rearrangements. (Pl. Mem. at Page 38). However, when

[19] Without endorsing any particular recommendation, BIO notes that, at least in the United States, recent judicial developments have addressed several of these concerns. *In re Fisher*, 421 F.3d 1365 (Fed. Cir. 2005) (utility); *In re Kubin*, 561 F.3d 1351 (Fed. Cir. 2009) (obviousness).

the Advisory Committee on Genetics, Health, and Society reviewed this very issue, they reported:

> The general trend for all diagnostic genetic testing has been to move toward more comprehensive analyses that detect deletions and rearrangements, and Myriad's actions have been consistent with the general trend. Indeed, in areas where there is no sole provider, there has been a similar lag in detecting deletions and rearrangements.

(Exh. 26, SACGHS Report at 74). Given that patented and non-patented tests encounter similar lags in the development of new and more accurate tests, the Plaintiffs' contentions that the delay was caused by a lack of competition are without merit.

H. A Decision That Isolated DNA Molecules Are Patent-Ineligible Would Have Far-Reaching Negative Consequences

By virtually any measure, the United States is the global leader in biotechnology. However, in order to maintain our leadership position in this field, we must continue to encourage investment into costly, and risky, research and development. As discussed, *supra*, such investments are made in significant part due to the availability of patent protection and the short term exclusivity afforded by such protection. All developed countries, including all of our major trading partners in Europe, UK, Japan, Korea, Australia, India, and China currently allow the patenting of isolated human DNA molecules. If companies cannot patent isolated DNAs domestically while other countries allow such protection, our industry will be put at a specific disadvantage and the available investment dollars will quickly be directed to other jurisdictions. Accordingly, any deviation from international norms such as the one now proposed by Plaintiffs would require a strong justification. No such justification is advanced by Plaintiffs and, as demonstrated herein, no such justification exists.

In addition to undermining the viability of the domestic biotechnology industry, a determination that isolated nucleic acids somehow represent patent-ineligible subject matter would put at risk the validity of a whole host of patents on isolated natural substances of great

medical, industrial, and agricultural value. For example, U.S. Patent No. 7,341,750 has claims directed to a compound isolated from the bark of *Ginkgo biloba* that has useful anti-platelet activity and thus may prove to be an important medicine in vascular diseases, and U.S. Patent No. 7,307,057 has claims directed to an antibiotic isolated from a particular microorganism that has shown to be effective against even some of the most dangerous multi-drug resistant bacteria in existence today. (*See* Exhs. 27-28). Taking the Plaintiffs' arguments to their natural conclusion would result in medically important inventions, like these, losing patent-eligibility.

In light of the foregoing, it is clear that striking down patents on isolated nucleic acids will not only do immeasurable harm to patients and our domestic biotechnology industry, but will have dramatic repercussions throughout the medical field and put at risk the patent-eligibility of all purified biological substances.

IV. CONCLUSION

BIO appreciates this opportunity to aid the Court in understanding the critical issues concerning the patent-eligibility of isolated DNA molecules raised in this case. For the reasons set out herein, BIO respectfully submits that Plaintiffs' Motion for Summary Judgment be denied so that the key genuine issues of material fact discussed *supra* can receive the full consideration that they deserve.

Dated: December 30, 2009

Respectfully Submitted:

By: */s/ Jennifer C. Tempesta*

Jennifer Gordon
Steven P. Lendaris
Jennifer C. Tempesta (JT4841)
Baker Botts L.L.P.
30 Rockefeller Center
New York, NY 10112
(212) 408-2500
jennifer.gordon@bakerbotts.com
steven.lendaris@bakerbotts.com
jennifer.tempesta@bakerbotts.com

Counsel of Record for Amicus Curiae, the Biotechnology Industry Organization

CERTIFICATE OF SERVICE

This is to certify that on December 30, 2009 a true and correct copy of the foregoing document has been served on registered counsel of record via the Court's ECF system.

Dated: December 30, 2009

By: */s/ Jennifer C. Tempesta*

Jennifer C. Tempesta (JT4841)
Baker Botts L.L.P.
30 Rockefeller Center
New York, NY 10112
(212) 408-2500
jennifer.tempesta@bakerbotts.com