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 Case

BRIEF OF *AMICUS CURIAE* GENETIC ALLIANCE IN OPPOSITION TO CERTAIN POSITIONS OF THE PLAINTIFFS

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ABBREVIATIONS

ACLU Br.	Plaintiffs' Memorandum of Law in Support of Motion for Summary Judgment
ACLU S.M.F.	Plaintiffs' Rule 56.1 Statement of Material Facts
Myriad Br.	Myriad Defendants' Memorandum of Law (1) in Support of Their Motion for Summary Judgment and (2) in Opposition for Plaintiffs' Motion for Summary Judgment
Myriad S.M.F.	Defendants' Rule 56.2 Statement of Material Facts
PTO	United States Patent & Trademark Office
PTO Utility Guidelines	Utility Examination Guidelines, 66 Fed. Reg. 1092-1099 (Jan. 5, 2001).
PTO Written Description Guidelines	Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, "Written Description" Requirement, 66 Fed. Reg. 1099-1111 (Jan. 5, 2001).
Alberts	BRUCE ALBERTS ET AL., MOLECULAR BIOLOGY OF THE CELL (3d ed. 1994) Garland Publishing, Inc..
Bold italicized text	All emphasis in this brief has been added unless otherwise noted.

I. INTRODUCTION

Amicus Curiae Genetic Alliance is a not-for-profit, tax-exempt health advocacy organization founded in 1986 (as the Alliance for Genetic Support Groups). It brings together diverse stakeholders that create novel partnerships in advocacy. By integrating individual, family, and community perspectives to improve health systems, Genetic Alliance seeks to revolutionize access to information to enable translation of research into services and individualized decision-making. Genetic Alliance here seeks to provide this court with insight into the importance of so-called "gene patents" not only for genetic testing, but also for the development and manufacture of potential treatments for genetic diseases.

Despite plaintiffs' contention that various harms are caused by patents claiming isolated DNA molecules, Genetic Alliance believes that under appropriate conditions such patents can play a valuable and essential role in making diagnostic tests for genetic disease available. An example is U.S. Patent No. 6,780,587, which claims methods of detecting the mutations responsible for the genetic disease pseudoxanthoma elasticum (PXE).[1] PXE International, a non-profit organization (*see* http://www.pxe.org.), is a co-assignee and licensing agent of that patent. The patent is licensed for a token fee in order to ensure wide availability of the tests for PXE from a quality provider, and the testing results are added to a mutation database hosted by the National Institutes of Health. Another example of the positive use of such a patent is the licensing of the patent for the CFTR gene that is involved in cystic fibrosis. (Ex. 1.)

[1] Sharon Terry, the President and CEO of Genetic Alliance, is an inventor on this patent. She has two children with PXE. She participated in the research to isolate and purify the PXE gene in hopes that its invention would lead to the development of diagnostic tests and therapies to benefit her children and other similarly situated patients. She receives no income from the patent.

Genetic Alliance wants to see not only diagnostic tests developed and made available to the public, but also the development of effective treatments. It recognizes the importance of patents to provide incentives and protections for investment in the discovery and commercialization of diagnostics, drugs, and other treatment modalities. The wholesale invalidation sought by plaintiffs of all patents on isolated DNA molecules (and on all compounds isolated and purified from natural sources) would impede the necessary investment, committed development, and commercialization of effective products and treatments for a whole range of genetic and other diseases. Genetic Alliance believes that invalidating all such patents is an inappropriate vehicle for remedying the problems alleged by the plaintiffs, and that less extreme remedies may be available for the problems that the plaintiffs allege.

II. ISOLATED DNA MOLECULES CLAIMED IN PATENTS ARE NOT "PRODUCTS OF NATURE"

A. "Gene" Patents Actually Claim Isolated DNA Molecules, Which Are Chemical Compounds

Plaintiffs mischaracterize what a so-called "gene" patent claim actually encompasses.[2] While plaintiffs argue that "gene" patents claim the "information" in a gene, and by extension the gene's function, the claims at issue here cover specific *molecules*, i.e., isolated DNA molecules.[3] They are chemical compounds. *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991) ("A gene is a chemical compound, albeit a complex one . . . ."). Like any other chemical entity, isolated and purified DNA molecules can be patented as compositions of matter if they meet all other requirements defined in the patent statute.

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[2] For explanations of the scientific concepts discussed in this brief, amicus refers the court to Defendants' Rule 56.2 Statement of Material Facts, and to the Factual Background section of the Brief for Amicus Curiae Biotechnology Industry Organization.

[3] For simplicity we focus on isolated DNA molecules, but most of the statements herein apply equally to patent claims involving RNA.

B. Isolated DNA Molecules Claimed in "Gene" Patents Are Not Found In Nature

Plaintiffs argue that isolated DNA molecules are not patentable subject matter because they are "products of nature." (ACLU Br. at 20-26.) ***Isolated DNA molecules, however, are not found in nature***. They are made by scientists, and their chemical composition is significantly different from DNA existing in genes inside a living organism. The molecules defined by the claims require substantial human intervention to prepare them. (*E.g.*, U.S. Patent No. 5,709,999, col. 9 line 44-col. 17 line 13 (outlining laboratory techniques for isolating, sequencing, and comparing DNA).) These molecules have properties and characteristics which differ in kind from genes in the body. They can be used for innovative purposes that genes found in nature cannot (for example, as diagnostic reagents). To paraphrase *In re Bergy*, 596 F.2d 952, 972 (C.C.P.A. 1979), the claimed isolated DNA molecules are "a product of a [scientist] and not a product of nature." Simply put, without the inventors, the claimed isolated DNA molecules would not exist.

A ***gene*** is defined in a leading textbook as a "[r]egion of DNA that controls a discrete hereditary characteristic, usually corresponding to a single protein or RNA. This definition includes the entire functional unit, encompassing coding DNA sequences, noncoding regulatory DNA sequences, and introns." (*Alberts* at G-10 (Ex.2).) In contrast, a cDNA is a "DNA molecule made as a copy of mRNA and therefore ***lacking the introns*** that are present in genomic DNA." (*Alberts* at G-6) Therefore, a cDNA is ***not*** a gene and does not exist in nature, as plaintiffs admit. (ACLU Br. at 5; ACLU S.M.F. ¶¶ 62-63; D. Mason ¶ 29.) Indeed, none of the DNA in a cDNA molecule is from the body–it was made in a laboratory. Most of the *BRCA* claims involve cDNA molecules, or short segments of cDNA molecules, none of which exist in nature.

In addition to not being found in nature, isolated DNA molecules may be chemically modified differently than genomic DNA in the body and these differences may further affect their function.[4] Plaintiffs repeatedly assert that cDNA is "functionally" or "informationally" the same as DNA in a gene. (*E.g.,* ACLU Br. at 11, 12.) Those arguments are efforts to gloss over the admitted fact that the claimed cDNA molecules are ***chemically different*** from DNA in a gene, and are ***not found in nature***. (ACLU S.M.F at ¶ 62 ("Complementary DNA does not exist in the body . . ."); ACLU Br. at 46 ("there are certain structural differences, such as removal of the regions that are not used in creating the protein. . .).) Similarly, the plaintiffs' anthropomorphic references to DNA such as "created by nature" (*e.g.*, ACLU S.M.F. at ¶¶ 81, 93; ACLU Br. at 9) should not obscure the fact that the claimed isolated DNA molecules are novel chemicals made by human endeavor.

C. Isolated DNA Has Different Functions (Uses) Than DNA in Genes

Isolated DNA molecules are not, in fact, functionally identical to a gene in the body. For example, many isolated DNA molecules lack promoter regions or regulatory control sequences, some of which are found in ***introns*** (non-coding regions missing in cDNA). DNA sequences within introns can regulate the amount of protein produced from a gene or determine which version of a protein is produced. (*See, e.g.*, Guang-Ji Wang et al., *Gene Variants in Noncoding Regions and Their Possible Consequences*, PHARMACOGENOMICS, Mar. 2006, at 203, 205 (2006)

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[4] For example, the DNA of genes in the body may be methylated (*see* Myriad S.M.F. at ¶¶ 12, 35.) to various extents and this affects the expression of these genes (and ultimately how much protein is made). (*See, e.g.*, Guang-Ji Wang et al., Gene Variants in Noncoding Regions and Their Possible Consequences, PHARMACOGENOMICS, Mar. 2006, at 203, 205 (2006) (Ex. 3).) For example, in normal ovary cells, *BRCA2* is methylated in a way that keeps expression of the gene (and protein levels) low. (Kelvin Y.K. Chan et al., *Epigenetic Factors Controlling the BRCA1 and BRCA2 Genes in Sporadic Ovarian Cancer*, 62 CANCER RES. 4151, 4151 (2002) (Ex. 4).) In cancerous cells, *BRCA2* becomes less methylated, resulting in too much BRCA2 protein being made. *Id.* at 4151, 4155. Isolated DNA (particularly cDNA that has undergone rounds of copying) is not methylated like genomic DNA.

(Ex. 3).) For example, the *BRCA1* gene contains regulatory elements in intron 1 that help . (Ting-Chung Suen & Paul E. Goss, *Identification of a Novel Transcriptional Repressor Element Located in the First Intron of the Human BRCA1 Gene*, 20 ONCOGENE 440, 440 (2001)orchestrate the proper amount of protein produced (Ex. 5).) Isolated cDNA molecules lacking these elements certainly cannot "function identically" to a gene in the body.

Furthermore, small DNA molecules such as those in claim 6 of the '282 patent, claiming an isolated DNA having at least 15 nucleotides of the cDNA of *BRCA1*, do not exist in nature and most do not code for any protein (only a string of amino acids, if anything at all) and therefore cannot function identically to a gene in the body.[5] However, they are useful as chemical reagents, research tools, and as diagnostic and biological probes.

Finally, isolated DNA molecules can have new uses for research, diagnosis, discovery of therapeutics, clinical studies, and manufacture of proteins in microorganisms. A leading textbook describes cDNA as "[u]sed to ***determine the amino acid sequence of a protein by DNA sequencing or to make the protein in large quantities*** by cloning followed by expression." (*Alberts* at G-6 (Ex. 2).) Isolated and copied DNA molecules can be sequenced for diagnosis. Isolated human DNA molecules can be copied and cloned into plasmids to produce proteins in entirely different species, such as yeast or bacteria. Isolated DNA molecules can be used in gene therapy. DNA in genes inside the body simply cannot directly be used in these ways.

[5] This fact is reflected in plaintiffs' admission that "a partial amino acid sequence can—and usually does—function much differently than the complete sequence from which it is taken." (ACLU Br. at 11.)

D. The "Information," "Code," or "Function" of Isolated DNA Molecules Is Irrelevant to Whether They Are Excluded from 35 U.S.C. § 101 as "Products of Nature"

While admitting that the isolated DNA molecules claimed in patents are not chemically identical to the DNA in genes, plaintiffs argue that this "does not matter" because the molecules have the same "function" and "information" as DNA in genes and thus fall into the "product of nature" exception to patentability. (*E.g.*, ACLU Br. at 4-5, 20; ACLU S.M.F. ¶¶ 64-65.). But what is interesting and exciting to scientists in their research is quite different from what is required by the patent law. Claims to "isolated DNA molecules" are ***not*** claims to "information," "code," or "function." While such biological properties of an isolated DNA molecule may be relevant to issues of utility, anticipation under § 102, and nonobviousness under § 103, it is irrelevant to whether the molecule is patentable subject matter under § 101. The PTO has recognized this key distinction between "descriptive information" and patentable DNA molecules, stating that "[w]hile descriptive sequence information ***alone*** is not patentable subject matter, a new and useful purified and isolated DNA ***compound*** described by the sequence is eligible for patenting, subject to satisfying the other criteria for patentability." PTO Utility Guidelines, 66 Fed. Reg. 1092, 1093 (Jan. 5, 2001).

E. Isolated DNA Molecules Are Not "Manifestations of Laws of Nature"

Plaintiffs argue that "[t]he gene's instructions to the body are laws of nature. Because the gene sequence claims embody a law of nature, they encompass natural phenomena and cannot be patentable subject matter under section 101." (ACLU Br. at 27.) But this is irrelevant because claims to isolated DNA molecules do not claim "the gene's instructions to the body," or any law of nature. The composition claims at issue cover artificially isolated DNA molecules, not "the genes themselves" or "all of the information for all of its uses." (ACLU Br. at 28.)

F. Cases Cited by Plaintiffs Regarding the Unpatentability of a "Law of Nature" Are Not Relevant Here[6]

In *O'Reilly v. Morse*, 56 U.S. (15 How.) 62 (1853), the Supreme Court invalidated a claim to any use of electromagnetism to send signals over distance. Contrary to the plaintiffs' characterization of *Morse*, (ACLU Br. at 27), that claim was not invalidated because it was directed to a law of nature. The Court invalidated the claim because it was not supported by the description in Morse's patent (a failure of what is now called the "written description requirement" of § 112). The Court noted that "[i]n fine [Morse] claims an exclusive right to use a manner and process ***which he has not described and indeed had not invented***, and therefore could not describe when he obtained his patent." *Morse,* 56 U.S. at 113; *see also id.* at 120 ("[H]e claims what he has ***not described in the manner required by law***."). The Court, therefore, held that the claim fails the written description requirement ("he claims what he has not described"), not that it is drawn to unpatentable subject matter (i.e., he claims a law of nature). The Federal Circuit has repeatedly explained that *Morse* is a case about written description, not § 101. *See Ariad Pharm., Inc. v. Eli Lilly and Co.*, 560 F.3d 1366, 1371 (Fed. Cir. 2009) (citing *Morse* as supporting a separate written description requirement to ensure the inventors have actually invented or conceived of claimed subject matter).[7]

Other cases cited by plaintiffs for the proposition that laws of nature are not patentable (*Gottschalk v. Benson*, 409 U.S. 63 (1972), *Parker v. Flook*, 437 U.S. 584 (1978), *Diamond v. Diehr*, 450 U.S. 175 (1981), and *Nippon Elec. Glass Co.v. Sheldon*, 539 F. Supp. 542 (S.D.N.Y.

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[6] The alleged statement of "facts" about the cases cited by plaintiffs at ACLU S.M.F. ¶¶ 114-124 are not facts at all, but rather legal opinions of a declarant who is not a lawyer and is admittedly not qualified to give legal opinions. (D. Jackson ¶ 6.)

[7] *See also Carnegie Mellon Univ. v. Hoffmann-La Roche, Inc.*, 541 F.3d 1115, 1122 (Fed. Cir. 2008) (same holding); *LizardTech, Inc. v. Earth Res. Mapping, Inc.*, 424 F.3d 1336, 1345 (Fed. Cir. 2005) (same holding); *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 929 n.9 (Fed. Cir. 2004) (same holding).

1982) are inapposite because claims to isolated DNA molecules are not directed to a law of nature, an idea, a phenomenon of nature, an equation, or a mathematical formula. Claims to isolated DNA molecules fall in none of those exceptions to § 101. They are directed to novel, man-made chemical reagents.

G. PTO Guidelines Expressly Authorize Patenting Isolated DNA Molecules Because They Are Not Natural Products

In its 2001 Utility Examination Guidelines, the PTO confirmed that isolated and purified DNA molecules can be patented. The PTO distinguished these molecules from natural products, stating that an "isolated and purified DNA molecule that has the same sequence as a naturally occurring gene is eligible for a patent because (1) an excised 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***, or (2) synthetic DNA preparations are eligible for patents because ***their purified state is different from the naturally occurring compound***." PTO Utility Guidelines, 66 Fed. Reg. at 1093. The PTO thus equates isolated DNA molecules not with products of nature, but with man-made chemical compositions, stating that "[l]ike other chemical compounds, ***DNA molecules are eligible for patents when isolated from their natural state and purified or when synthesized in a laboratory from chemical starting materials***." *Id.*[8]

The PTO also endorsed the patentability of isolated DNA molecules by addressing what written description would be adequate to claim such molecules in its Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, "Written Description" Requirement, 66 Fed. Reg. 1099, 1108 n.13 (Jan. 5, 2001). For example, a claim to "[a] ***gene*** comprising SEQ ID NO:1" may have inadequate written description because it would not clearly disclose whether

[8] Virtually every other industrialized nation also permit patenting of these isolated DNA molecules. (Myriad Br. at 29 n.10)

"the claim as a whole covers . . . specific structures such as a promoter, a coding region, or other elements." *Id.* The PTO recognizes that ***isolated DNA molecules differ from genes*** in nature based on the presence or lack of such structures. The Federal Circuit has endorsed the PTO Guidelines as "an accurate description of the law by the agency responsible for examining patent applications, and thus persuasive authority." *See Carnegie Mellon University v. Hoffmann-La Roche Inc.*, 541 F.3d 1115, 1124 (Fed. Cir. 2008).

III. CONGRESS HAS ACTED TO SPECIFICALLY FACILITATE "GENE PATENTS"

A. Rather Than Forbidding Patents Involving Isolated DNA Molecules, Congress Has Acted to Facilitate Such Patents

The PTO has granted thousands of patents claiming isolated DNA sequences and their use, and the courts have upheld those patents. In addition, the PTO has granted and the courts have upheld many patents on other chemicals found in nature when isolated and purified. *See* section IV.B. This court should not change these almost universally accepted interpretations of the patent statute without a clear and certain signal from Congress. *See Deepsouth Packing Co., Inc. v. Laitram Corp.*, 406 U.S. 518, 531 (1972). In both *Warner-Jenkinson Co., Inc. v. Hilton Davis Chem. Co.*, 520 U.S. 17, 28 (1997), and *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 535 U.S. 722, 739 (2002), the Supreme Court explicitly admonished that courts should not upset the settled expectations of the patent community. If the law should be changed, it should be done by Congress.

Congress has the Constitutional power to modify the patent law. Congress has amended the patent statute several times since the major codification of the Patent Act in 1952, and has had opportunities to change the current law regarding eligibility for patents. Instead of eliminating "gene patents," Congress has amended the patent law several times to facilitate obtaining such patents and to enhance their enforceability.

1. 35 U.S.C. § 103(b)

For a time in the 1980s the patenting of biotechnological processes was practically foreclosed by *In re Durden*, 763 F.2d 1406 (Fed. Cir. 1985), which held that even if a process used a novel starting material or produced a novel product, it was nevertheless unpatentable as obvious under 35 U.S.C. § 103 if the process steps that were applied were old. That decision hit patenting of biotechnological inventions hard, because many important inventions used newly invented isolated DNA molecules and known biotechnology processes to make, for the first time, useful quantities of important proteins that were known (and thus not themselves patentable). Such processes were unpatentable under *Durden*. To remedy this problem, Congress amended 35 U.S.C. § 103(b) expressly to overrule *Durden* and facilitate the patenting of biotechnological processes, including those that used or produced isolated DNA molecules.[9]

Section 103(b) provides that "a ***biotechnological process*** using or resulting in ***a composition of matter*** [which would include isolated DNA molecules] that is novel under section 102 and nonobvious under subsection (a) of this section shall be considered nonobvious" if certain conditions are met. "Biotechnological processes" are defined in § 103(b)(3) to include "a process of genetically altering or otherwise inducing a single- or multi-celled organism to- (i) express ***an exogenous nucleotide sequence*** [which includes isolated DNA molecules from other species], (ii) inhibit, eliminate, augment, or alter expression of an ***endogenous nucleotide sequence*** [which includes isolated DNA molecules from the same species]." Thus, § 103(b)

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[9] *See* Biotechnological Process Patents Act, Pub. L. No. 104-41, 109 Stat. 351 (1995); 141 CONG. REC. S15220, S15222 (daily ed. Oct. 17, 1995) (statement of Sen. Hatch) ("S. 1111 resolves the *In re Durden* problem in our patent law by providing that a biotechnological process of making or using a product may be considered nonobvious if the starting material or resulting product is patentable. This change will provide a degree of certainty to the protection of biotechnology inventions . . . .").

shows Congressional approval of the patenting of isolated DNA molecules and their use in biotechnological processes.

2. 35 U.S.C. § 271(e)(1)

Another provision of the patent law, 35 U.S.C. § 271(e)(1), permits generic drug makers and others to freely use patented materials and processes to obtain information needed to apply for FDA approval. *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193, 202 (2005) (explaining that "§ 271(e)(1)'s exemption from infringement extends to all uses of patented inventions that are reasonably related to the development and submission of any information" to the FDA). Congress, however, carved out an exception in § 271(e)(1) to protect certain patents claiming isolated DNA molecules. "It shall not be an act of infringement to make, use, offer to sell, or sell . . . a patented invention (***other than a new animal drug or veterinary biological product . . . which is primarily manufactured using recombinant DNA***, ***recombinant RNA***, . . . or other processes involving site specific genetic manipulation techniques) . . . ." Thus, unlike all other patented products and processes used to gather information to submit to the FDA, if the drug is an animal drug or veterinary biological product made using recombinant DNA, then making that product will nevertheless infringe patents claiming the recombinant DNA or its use. Again, Congress recognized that some patents would include claims to isolated DNA molecules, and provided special protection for a certain class of such patents.

3. 35 U.S.C. § 271(g)

Congress added 35 U.S.C § 271(g) to the Patent Act in 1988 to deal with infringement of processes patented in the United States but practiced abroad.[10] It states in part

[10] *See* Process Patent Amendments Act of 1988, Pub. L. No. 100-418, § 9003, 102 Stat. 1107, 1564 (1988).

> Whoever without authority imports into the United States or offers to sell, sells, or uses within the United States a product which is made by a process patented in the United States shall be liable as an infringer . . . . A product which is made by a patented process will, for purposes of this title, not be considered to be so made after -
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> (1) it is materially changed by subsequent processes . . . .

The legislative debate reflected Congress's concern that U.S. patents on processes of using isolated DNA to make valuable unpatented proteins would be used abroad, and the proteins then imported back into the U.S. Addressing this concern, the legislative history made clear that this fact pattern would constitute infringement. *See* H.R. REP. NO. 100-576, at 1086-87 (1988) (Conf. Rep.) (stating that the statute provides a remedy when a foreign manufacturer uses a patented "process of preparing a DNA molecule comprising a specific genetic sequence" and then uses that DNA molecule to produce and sell a protein.) This legislative intent was the reason that human growth hormone (a protein) made abroad using a patented process to make a plasmid (DNA coding for the protein plus control sequences) infringed under § 271(g) when it was imported into the U.S. *Bio-Technology General Corp. v. Genentech, Inc.*, 80 F.3d 1553, 1561 (Fed. Cir. 1996). Thus, Congress expressly facilitated and endorsed patents covering processes that use isolated DNA sequences.

IV. NATURAL SUBSTANCES CAN BE PATENTABLE WHEN THEY ARE ISOLATED AND PURIFIED

Plaintiffs' argument that isolated DNA molecules such as the *BRCA* patents are unpatentable relies on contending that ***all*** isolated or purified natural substances are unpatentable under § 101. That contention is irrelevant because, as shown above, the isolated DNA molecules claimed in "gene" patents are man-made molecules that do not occur in nature. Nevertheless, even molecules that are chemically identical to those that occur in nature may be patentable when they are isolated and purified.

A. Old Supreme Court Cases Relied on by Plaintiffs Do Not Support Their Contention that Isolated, Purified Chemicals Are Excluded from Patentability

Two Supreme Court cases from the 1800s cited by plaintiffs, *American Wood Paper Co. v. Fibre Disintegrating Co.*, 90 U.S. 566 (1874) and *Cochrane v. Badische Anilin & Soda Fabrik*, 111 U.S. 293 (1884), fail to support plaintiffs' assertion that purification cannot transform a composition that occurs in nature in an impure state into a patentable composition. (ACLU Br. at 22-23.) In both cases the Supreme Court invalidated the product claims for reasons unrelated to whether purified natural products could be patented. The Court in *American Wood* held invalid a patent to "a pulp suitable for the manufacture of paper, made from wood or other vegetable substances" because the claimed pulp was ***not a new*** composition of matter (***lacked novelty***), not because it was extracted from a natural product. 90 U.S. at 577, 593, 596. Pulp had been produced from wood and other sources and used in the manufacture of paper long before the patent was filed. *Id*. at 594. The Court explained that an extract "cannot be called a new manufacture" when"[i]t may have been in existence and in common use before . . . it was known that it could be extracted." *Id.* at 593-94.

Similarly, *Cochrane* did not hold that the claimed dye was unpatentable because it occurs in nature. (ACLU Br. at 23.) Instead, the *Cochrane* Court held invalid a reissue patent to alizarine because, despite the patentability of the new process for producing the dye, the product as claimed was an old, well-known substance. 111 U.S. at 311-12. In addition, the Court also held that the specification of the original patent did not support a scope wide enough to cover the defendant's product. *Id*. at 313.

B. Courts and the PTO Have Stated that Isolated and Purified Natural Substances Are Patentable

Several courts of appeals and district courts have concluded that a natural substance can be patentable when isolated and purified. Plaintiffs have either misinterpreted those holdings or ignored the passages that expressly support the patentability of isolated and purified natural substances under § 101.

In *Merck & Co. v. Olin Mathieson Chemical Corp.*, 253 F.2d 156 (4th Cir. 1958), for example, the court held that an isolated and purified form of B-12 vitamin was patentable despite allegations that it was a "product of nature." 253 F.2d at 162. The court considered the patentability of natural substances under § 101 and found "nothing in the language of the [Patent] Act which precludes the issuance of a patent upon a 'product of nature' when it is a 'new and useful composition of matter'" and complies with other statutory requirements. *Id*. at 161-62. The court added that "[t]he fact . . . that a new and useful product is the result of processes of extraction, concentration and purification of natural materials does not defeat its patentability." *Id.* at 163.

In fact, the *Merck* court distinguished the very cases that plaintiffs cite, (ACLU Br. at 23-24), to support their contention that purified natural products are not patentable (*i.e., General Elec. Co. v. De Forest Radio Co*., 28 F.2d 641 (3d Cir. 1928), *In re Marden*, 47 F.2d 957 (C.C.P.A. 1931) (*Marden I*), and *In re Marden*, 47 F.2d 958 (C.C.P.A. 1931)(*Marden II*)). 253 F.2d at 162. When distinguishing these cases, the *Merck* court noted that useful products that are unpatentable under § 103 are sometimes improperly referred to as "products of nature." *Id.* The court clarified that such products are unpatentable because they are obvious, not because they are derived from nature, and that "where the requirements of the [Patent] Act are met, patents upon products of nature are granted and their validity sustained." *Id*. In *General Elec.* and *Marden I*

and *II*, purified tungsten, uranium, and vanadium were unpatentable because the purified elements were not sufficiently different from those found in nature or were well-known substances (*i.e.*, not novel). *General Elec.*, 28 F.2d at 642; *Marden I*, 47 F.2d at 957 ("Uranium was discovered in 1789 . . . [and] [i]ts qualities have been well known for many years."); *Marden II*, 47 F.2d at 959 ("But pure vanadium is not new in the inventive sense . . . [p]ure vanadium has been known to the metal art for many years"). In contrast, in *In re Seaborg*, 328 F.2d 996, 999 (C.C.P.A. 1964), the court found the chemical element Americium to be patentable over the prior art.

In re Merz, 97 F.2d 599 (C.C.P.A. 1938), another case cited by plaintiffs, (ACLU Br. at 24), is distinguishable in a similar manner. In *Merz*, the court agreed with the patent examiner that purified ultramarine was unpatentable because it was well-known long before applicant's application was filed. 97 F.2d at 600. The court noted, however, that claims to products purified from previously known materials, where the products obtained had properties and characteristics different from those of the known products, have been upheld. *Id*. at 601.

In *Parke-Davis*, Judge Learned Hand held that a claimed isolated and purified substance was a new composition of matter, noting that "no one had ever isolated a substance which was not in salt form, and which was anything like" the claimed composition. *Parke-Davis & Co. v. H.K. Mulford Co.*, 189 F. 95, 103 (S.D.N.Y. 1911). Plaintiffs ignore Judge Hand's explicit recognition that after isolation and purification, the claimed composition "became for every practical purpose a new thing commercially ***and therapeutically***." *Id.* Thus, isolating the

purified composition differentiated it chemically and functionally from a natural product (not just its commercial value) and made it patentable.[11]

Contrary to plaintiffs' assertions, *In re Bergstrom*, 427 F.2d 1394 (C.C.P.A. 1970) also supports patentability of isolated and purified natural substances. The court addressed § 101 arguments by distinguishing the facts in *Bergstrom* from those in *Funk Bros.* Whereas the bacteria in *Funk Bros.* were held to be discovered from nature, the *Bergstrom* court found that isolating and purifying prostaglandins, which are chemicals, made them a patentable invention. The court held that "[the claimed] compounds . . . do not exist in nature in pure form . . . ." 427 F.2d at 1401.[12]

Patent practitioners in the field of biotechnology have long understood the need to exclude naturally-occurring products and processes from the scope of their patent claims. The words used to do so are well known to patent drafters. *See, e.g.*, *Amgen Inc. v. Hoechst Marion*

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[11] Plaintiffs misconstrue *Parke-Davis* by arguing that Judge Hand erred by citing two cases involving patents on purified man-made compositions. (ACLU Br. at 25.) He cited *Kuehmsted v. Farbenfabriken*, 179 F. 701 (7th Cir. 1910) and *Union Carbide Co. v. American. Carbide Co.*, 181 F. 104 (2d Cir. 1910) for the proposition that ***whether or not a composition is derived from a natural product***, it may be patentable if purification renders it a new composition of matter. *Parke-Davis*, 189 F. at 103.

[12] Although not directed to isolated molecules, the Plant Patent Act, 35 U.S.C. §§ 161-164 (1954), is entirely consistent with the principle that isolated things that exist in nature can be patentable. The express purpose of the Plant Patent Act was to give agriculture "the ***same*** opportunity to participate in the benefits of the patent system as has been given industry." *In re Bergy*, 596 F.2d 952, 982 (C.C.P.A. 1979) (citing S. REP. NO. 71-315, at 1 (1930) and H.R. REP. NO. 71-1129, at 1 (1930)). The Plant Patent Act did not change the scope of patentable subject matter under Title 35. *See Diamond v. Chakrabarty*, 447 U.S. 303, 313 (1980) (rejecting the argument that the Plant Patent Act was enacted "because § 101 did not include living things."). Instead, it relaxed the description requirements in view of the fact that new plants were hard to describe under the rigid requirements of § 112, first paragraph. *Chakrabarty*, 447 U.S. at 312; s*ee also Bergy*, 596 F.2d at 984; 35 U.S.C. § 162 (1952). Patents granted under the Plant Patent Act still must comply with all other "conditions and requirements" of Title 35, including §§ 102 and 103. *See* 35 U.S.C. § 161 (1953). The Plant Patent Act serves as an example where Congress has explicitly allowed applicants to patent "products of nature." *See also In re* Bergy, 596 F.2d at 976 (isolated and pure culture of a microorganism found in nature is patentable subject matter under § 101).

Roussel, 314 F.3d 1313, 1329 (Fed. Cir. 2003) (claiming "non-naturally occurring" erythropoietin (EPO)). In *Amgen,* the Federal Circuit was called upon to interpret the words "non-naturally occurring" in claims that were asserted to be infringed. The Federal Circuit held that the "'non-naturally occurring' limitation in claims 3 and 4 merely prevents Amgen from claiming the human EPO produced in the natural course." *Id*. The Federal Circuit further explained that "[b]y limiting its claims in this way[,] Amgen simply avoids claiming specific subject matter that would be unpatentable under § 101. This court has endorsed this approach, recognizing that patentees can use negative limitations such as 'non-human' and 'non-natural' to avoid rejection under § 101." *Id*. Here, the claims in question, reciting an isolated DNA molecule, clearly constitute the sort of non-natural subject matter that can be patentable under § 101.

The PTO has followed these holdings, and stated unequivocally that isolated and purified DNA molecules may be patented as compositions of matter. *See* Utility Examination Guidelines, 66 Fed. Reg. at 1093. According to PTO utility guidelines, isolated and purified DNA molecules, like any other chemical compounds, are "eligible for patents when isolated from their natural state and purified or when synthesized in a laboratory from chemical starting materials." *Id.* Plaintiffs incorrectly argue that the guidelines fail to distinguish between "mere purification" and instances where isolation and purification creates a composition "different in kind" from known products. (ACLU Br. at 24.) On the contrary, the PTO guidelines state that isolated DNA molecules with credible utility are patentable precisely ***because*** they differ chemically and functionally from known compounds. *See Id*.[13]

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[13] The PTO utility guidelines also cite both historic patent practice and case law to support the patentability of isolated DNA molecules as isolated and purified compositions. Utility Guidelines, 66 Fed. Reg. at 1093. For example, the guidelines trace patents on isolated

V. DIAGNOSTIC METHOD CLAIMS USING ISOLATED DNA ARE PATENTABLE UNDER 35 U.S.C. § 101 BECAUSE THEY NECESSARILY INVOLVE TRANSFORMATION OF MATTER

Under current Federal Circuit law, the "machine-or-transformation" test determines whether a method is patentable under § 101. *See Bilski v. Kappos*, 545 F.3d 943 (Fed. Cir. 2008) (en banc), *cert. granted*, 129 S.Ct. 2735 (2009).[14] Method claims for screening a sample for genetic alterations are patentable under 35 U.S.C. § 101 ***because*** isolating and sequencing DNA necessarily involves a transformation of matter.

The Federal Circuit clarified what constitutes a "transformation" in the medical and diagnostic context in *Prometheus Laboratories, Inc. v. Mayo Collaborative Services*, 581 F.3d 1336 (Fed. Cir. 2009). In that case, decided just after the plaintiffs in this case filed their summary judgment motion, the Federal Circuit found that determining levels of certain metabolites in the human body and using that information to guide therapy was patentable under § 101 because it involved a transformation. Even though the independent claim did not specify using a particular machine or laboratory technique to determine metabolite levels, the court said that "[d]etermining the levels . . . in a subject necessarily involves a transformation, for those

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and purified compositions at least as far back as Louis Pasteur's article of manufacture patent on "[y]east, free from organic germs of disease." *Id.* The PTO also finds support for its position in the holdings of both *Parke-Davis* and *In re Bergstrom*. *Id.*

[14] As shown here, diagnostic method claims using isolated DNA molecules clearly satisfy the "machine-or-transformation" test of *Bilski* and *Prometheus*, so the court should deny plaintiffs' motion for summary judgment or grant the defendants' motion for summary judgment. Amicus brings to the attention of the court that the Supreme Court granted certiorari in *Bilski*, which was argued November 9, 2009. In *Bilski*, numerous amicus briefs specifically addressed the patentability of biotechnology and medical methods under § 101. Further, two cases addressing § 101 patentability in the context of medical methods, decided recently in the Federal Circuit, are before the U.S. Supreme Court on petition for certiorari. *See Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, 581 F.3d 1336 (Fed. Cir. 2009), *petition for cert. filed*, (U.S. Oct. 22, 2009) (No. 09-490); *Classen Immunotherapies, Inc. v. Biogen IDEC*, 304 Fed. App'x 866 (Fed. Cir. Dec. 19, 2008), *petition for cert. filed*, (U.S. May 11, 2009) (No. 08-1509). These petitions were distributed for conference, but the U.S. Supreme Court has neither granted nor denied certiorari.

levels cannot be determined by mere inspection." *Prometheus*, 581 F.3d at 1347. The court stated that some form of manipulation, such as the standard laboratory techniques claimed in the dependent claims, are "necessary to extract the metabolites from a bodily sample and determine their concentration." *Id.*

Plaintiffs, citing the now reversed *Prometheus* district court opinion, argue that diagnostic methods using isolated DNA molecules require "no physical steps and no human intervention involved in triggering the correlation."[15] (ACLU Br. at 31 n.11.) They are wrong. As in *Prometheus*, diagnostic methods using isolated DNA molecules necessarily involve chemical transformations because one cannot determine the sequence of a gene merely by inspecting a biological sample. In order to compare gene sequences, substantial human manipulation and chemical transformation of a sample outside the body is necessary. *See, e.g.*, U.S. Patent No. 5,709,999 col. 9 line 44-col. 17 line 13 (describing laboratory methods for isolating, sequencing, and comparing DNA). Therefore, claims to diagnostic methods based on isolated DNA satisfy the requirements of § 101 under *Bilski* because, as in *Prometheus*, such claims necessitate human intervention to transform DNA sequences physically and functionally.[16]

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[15] This position squarely contradicts plaintiffs' own admissions that "to sequence, or read a gene, one has to remove it from the cell of an organism and place it in a form so that it can be replicated outside the body," (ACLU S.M.F. at ¶ 55), or that isolating and purifying a gene requires "removing it from the body and placing it in a form so that it can be sequenced and possibly used in other ways." (ACLU S.M.F. at ¶ 65.)

[16] This transformation is more evident where, as in the '999 patent, the dependent claims disclose possible laboratory techniques to accomplish these ends. For example, claim 3 of the '999 patent specifies detection by hybridizing a *BRCA1* gene probe and detecting the presence of a hybridization product, while claim 6 recites amplifying all or part of a *BRCA1* gene in the tumor sample to produce nucleic acids, which are then sequenced. U.S. Patent No. 5,709,999 at col. 161, ll. 37-50, 59-63. These methods necessarily require a transformation that is central to the claimed method, and thus fall within § 101 as set out in *Prometheus*.

Contrary to plaintiffs' assertions, claims to isolated DNA molecules bear little similarity to the algorithm in *In re Grams*. The applicant in *Grams* claimed use of a mathematical algorithm to troubleshoot "any complex system, whether it be electrical, mechanical, chemical or biological, or combinations thereof." *In re Grams*, 888 F.2d 835, 840 (Fed. Cir. 1999). The Federal Circuit held this invention to be unpatentable because it claimed no more than the mathematical algorithm. *Id.* The *Prometheus* court "readily distinguished" *Grams*, finding that the integral involvement of transformative steps such as determining metabolite levels was in stark contrast to the claim in *Grams* to a mathematical algorithm. *Prometheus*, 581 F.3d at 1348. As in *Prometheus*, DNA-based diagnostic methods for detecting genetic diseases require manipulation and transformation of chemical substances extracted from biological samples, not a mathematical algorithm. Such claims are thus patentable under § 101 under the *Bilski* test.

VI. ARTICLE I, SECTION 8, CL. 8 OF THE CONSTITUTION DOES NOT GIVE THIS COURT THE POWER TO PROHIBIT PATENTS ON ISOLATED DNA MOLECULES

Plaintiffs additionally contend that the patent claims in suit are invalid as unconstitutional under Article I, § 8, Clause 8, of the Constitution ("The Patent and Copyright Clause"), which provides: "That Congress shall have the power . . . [t]o 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[.]" Citing only to copyright cases, plaintiffs suggest that because courts have held that the fair use doctrine codified in Copyright Act furthers the purpose of the Copyright Clause, "the patent claims in this case can be held as a matter of law to impede rather than promote the progress of science." (ACLU Br. at 37-38 (citing *Attia v. Society of the NY Hosp.*, 201 F.3d 50, 50 (2d Cir. 1999); *Salinger v. Colting*, 641 F. Supp. 2d 250, 255 (S.D.N.Y. 2009).) Plaintiffs provide no legal basis for applying these copyright decisions to patent law. There is no doctrine in patent law that is analogous to copyright's fair use doctrine.

Most importantly, this argument fails because the Supreme Court has interpreted the "progress of science and useful arts" preamble of the Patent and Copyright clause to be a limit on ***Congressional authority to legislate***, not a requirement of individual patent claims. The Court has examined the text of the preamble "to promote the progress of science" in the context of the Copyright Term Extension Act ("CTEA"). *Eldred v. Ashcroft*, 537 U.S. 186, 213 (2003) (applying a rational basis test to hold that Congress's CTEA legislation was rationally related to the objective of promoting the progress of science). The Court rejected petitioners' argument that the CTEA's extension of existing copyright terms failed to "promote the Progress of Science," and was therefore unconstitutional. *Id.* at 211-12. The Court held that "it is generally "for Congress, not the courts, to decide how best to pursue the Copyright Clause's objectives." *Id.* at 213.

When it addressed the same Constitutional passage in the context of the patent system, the Federal Circuit followed the Supreme Court's interpretation of the preamble in *Eldred* to hold that the preamble in the Patent Clause is a limitation on ***Congress's*** legislative authority. *Figueroa v. United States*, 466 F.3d 1023, 1030-32 (Fed. Cir. 2006) ("[J]udicial review of legislation enacted pursuant to Article I authorization is limited to determining whether Congress's actions were a rational exercise of the legislative authority conferred by the Patent Clause."). Promoting the progress of the useful arts is the Constitutional mandate of Congress when legislating under the Patent and Copyright Clause. It is ***not*** a test of the validity of individual patent claims. Therefore, there is no legal basis for declaring individual patent claims or specific types of patents invalid under the Patent and Copyright Clause.

VII. ABOLITION OF "GENE" PATENTS IS NOT AN APPROPRIATE VEHICLE FOR REMEDYING THE PROBLEMS OF WHICH PLAINTIFFS COMPLAIN

A. The Problems of Which the Plaintiffs Complain Do Not Warrant the Abolition of Patents on Isolated DNA Molecules

Plaintiffs insist that the harms they attribute to "gene patents" require nothing less than a profound and disruptive shift in patent law. If plaintiffs' wishes were realized, the consequences would be far-reaching and disproportionate to the purported harms. The alleged problems plaintiffs identify simply do not warrant the full-scale abolition of specific types of patents as suggested by plaintiffs.

1. The Problems of Which the Plaintiffs Complain Are Not Caused by the Patents at Issue in this Case or Patent Law in General

Many of the problems plaintiffs allege cannot be remedied by a change in § 101 and are therefore not germane to the patentable subject matter question at issue here. For example, plaintiffs complain that many women cannot afford the *BRCA* diagnostic tests. (ACLU Br. at 6.) This is not an issue of patent law. Millions of Americans lack health insurance, a problem Congress is seeking to address. Even among patients with insurance it is not unusual for either private or public insurers to decline to pay for tests or treatments. Plaintiffs have not established, and indeed there is no conclusive evidence, that such access problems are uniquely or disproportionately caused by patents.

2. Patents on Isolated DNA Do Not Stifle Academic Research, but Instead They Incentivize Important Research and Commercialization Activities

Plaintiffs contend that isolated DNA patents stifle research and go as far as to say that the claims at issue here could essentially preclude research into any gene. (ACLU Br. at 5-6, 28, 37-38.) The claims at issue, however, recite "isolated DNA molecules" and do not encompass genes

other than the specific ones claimed (here, *BRCA1* and *BRCA2*), nor do they encompass "the entire genome." Therefore, plaintiffs' assertion that the claims essentially preclude research into any gene is untenable, as shown by the large number of peer-reviewed journal articles reporting research on genes. (*See* Myriad Br. at 46 and evidence cited therein.)

While it may be true that the potential for obtaining patents on isolated DNA molecules plays a minor role in motivating some individual academic researchers, such patents can serve as a crucial incentive for developing that research into commercial applications. Biotechnology ventures are highly speculative and risky investments. Without the promise of temporary exclusivity for successfully commercialized products, far less investment would occur. *See Biotechnology Indus. Org. v. District of Columbia*, 496 F.3d 1362, 1372-73 (Fed. Cir. 2007). Put simply, individuals very much need the new drugs and diagnostics that the biotechnology and personalized genomics revolution can be expected to yield–***if*** investors can continue to expect stability in patent law.

B. Serious Harms Would Result From Abolishing Patents on Isolated DNA Molecules

In addition, plaintiffs' attacks against "gene" patents (and against all patents on isolated purified naturally occurring chemicals) are so broad that they would affect a multitude of inventions unrelated to patents on DNA-based tests for genetic mutations. Areas affected would include, for example, antibiotics and other pharmaceuticals isolated from natural sources, and new lifesaving vaccines and protein drugs made using isolated DNA molecules. Proteins coded by isolated DNA molecules are also used as targets for screening assays directed to new pharmaceuticals that affect those proteins. *See, e.g.*, *Univ. of Rochester v. G. D. Searle & Co.*, 358 F.3d 916 (Fed. Cir. 2004).

In addition to their vital importance in the pharmaceutical industry, patented isolated DNA molecules are important in many other contexts. For example, they are used to make industrial enzymes that have diverse uses, such as making ethanol for fuel. *See, e.g.*, *Novozymes A/S v. Genencor Intern., Inc.*, 446 F.Supp.2d 297 (D.Del. 2006). They are used in diagnostic tests for HIV (AIDS) and other viruses. (Ex. 6.) Isolated nucleic acids are being used in agricultural research in attempts to improve food production. Abolishing all so-called "gene" patents would negatively affect these and many other important industrial and scientific activities.

C. There Are Alternative Remedies for the Harms that Plaintiffs Allege

There is no need for the radical disruption of the patent law urged by plaintiffs and the attendant damage to numerous industries, the economy, and the public. Alternative remedies are potentially available to the plaintiffs for the harms they allege, which would be more appropriate to their complaints about specific patents or types of patents. For example, Congress could fashion appropriate remedies directly tailored to specific problems. *See, e.g.*, 35 U.S.C. §§ 271(e)(1), 272, 273, 287(c). Furthermore, there are multiple defenses under established patent law for holding specific patent claims to be invalid in litigation. 35 U.S.C. § 282. Claims in a patent may also be invalidated or narrowed in reexamination, which can be initiated by members of the public. 35 U.S.C. §§ 301-319. If the invention was partly financed by government funds, the Bayh-Dole Act, 18 U.S.C. § 200 *et seq*., provides for "march-in rights." March-in rights give the federal agency under whose funding agreement an invention was made the right to grant a license to a responsible new applicant if, among other things, the current manufacturer has failed to make the product available to the public on reasonable terms, 18 U.S.C. §§ 201(f), 203(1)(a), or if action is necessary to alleviate health or safety needs which are not reasonably satisfied by the current manufacturer. 18 U.S.C. § 203(1)(b). There is no need for

the wholesale disruption of the patent law requested by plaintiffs in pursuit of their specific objectives.

VIII. CONCLUSION

Genetic Alliance is committed to promoting research on genetic diseases and to making testing and therapies widely available. However, the specific remedies proposed by plaintiffs are both legally untenable and undesirable as public policy, because they would diminish the promise of genetic research for patients and negatively affect other areas of medicine. Therefore, Genetic Alliance opposes the wholesale abolition of patents on isolated DNA molecules and isolated purified natural substances proposed by the plaintiffs.

Respectfully Submitted,

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CERTIFICATE OF SERVICE

I hereby 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.

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