ExecutiveCOUNSEL
THE MAGAZINE FOR THE GENERAL COUNSEL, CEO & CFO

MAJOR DNA PATENT CASE BEFORE THE FEDERAL CIRCUIT

A Myriad of Amicus Briefs

By Christopher Loh and Amy Fuetterer

ON MARCH 29, 2010, THE SOUTHERN DISTRICT OF NEW YORK RULED THAT DNA ISOLATED FROM HUMAN GENES WAS NOT PATENTABLE. THAT CONTROVERSIAL RULING WAS APPEALED TO THE FEDERAL CIRCUIT, AND IN NOVEMBER AND DECEMBER OF 2010 IT ATTRACTED NO FEWER THAN TEN AMICUS BRIEFS ARGUING FOR ITS REVERSAL.

The Federal Circuit's eventual decision in the appeal likely will have significant implications for the biotechnology and pharmaceutical industries, which are increasingly relying on DNA technology to develop new drugs and therapies. This article discusses the issues raised in the amicus briefs, which in turn may shed light on how the Federal Circuit will decide the appeal.

THE DISTRICT COURT DECISION

On May 12, 2009, the Association for Molecular Pathology and various public health groups sued the Patent and Trademark Office and Myriad Genetics in the Southern District of New York, to challenge the validity of Myriad's patents claiming DNA isolated from BRCA 1 and BRCA 2 genes. Mutations in those genes predispose patients to developing breast and ovarian cancer.

Genes are sequences of DNA units, or "nucleotides," that carry information for making proteins. When it comes time for a cell to make a protein, the information in the gene is copied from DNA onto another molecule called mRNA. The mRNA is then read by cellular mechanisms to make the needed protein. Mutations in genes such as the BRCA genes can alter these processes and lead to illnesses such as cancer.

The patents in the Myriad suit claim (i) DNA isolated from the naturally occurring BRCA genes, and having the same nucleotide sequences as those genes and (ii) cDNA, which is DNA synthesized in the laboratory by reverse-copying mRNA.

On August 26, 2009, the plaintiffs moved for summary judgment, asking the district court to find Myriad's patents invalid. The district court granted the motion on March 29, 2010, holding that the patents did not cover patentable subject matter pursuant to § 101 of the Patent Act as interpreted by Supreme Court precedent. Such precedent excludes from the ambit of patent protection "products of nature" – as opposed to "man-made" inventions.

In reaching that decision, the district court first defined the patent term "isolated DNA" to mean "a segment of DNA nucleotides existing separate from other cellular components normally associated with native DNA, including proteins and other DNA sequences comprising the remainder of the genome, and includes both DNA originating from a cell as well as DNA synthesized through chemical or heterologous biological means."

By that definition, the district court emphasized the biological, information-carrying function of DNA over its chemical characteristics. The district court also included in its definition "synthesized" DNA such as cDNA.

With that definition in hand, the district court analogized isolated DNA to purified products of nature (cellulose, dyes, tungsten) for which courts previously had denied patent protection, noting that purification alone was insufficient to render products of nature patentable.

The district court next distinguished DNA from other patentable chemicals, focusing again on its information-carrying function and noting that "the information encoded in DNA is not information about its own molecular structure incidental to its biological function ... DNA, and in particular the ordering of its nucleotides therefore serves as the physical embodiment of laws of nature – those that define the construction of the human body."

Finally, the district court found that the chemical differences between Myriad's isolated DNA and naturally occurring BRCA genes were insufficient to rendered them "markedly different" from each other in terms of the information they carried.

THE AMICUS BRIEFS

Myriad appealed the decision to the Federal Circuit on June 16, 2010. In November and December, ten other parties filed amicus briefs with the Federal Circuit:

- Department of Justice (DOJ).
- Genetic Alliance.
- Biotechnology Industry Organization and Association of University Technology Managers (BIO/AUTM).
- American Intellectual Property Law Association (AIPLA).
- Intellectual Property Owners Association (IPO).
- Christopher M. Holman and Robert Cook-Deegan.
- Gilead Sciences and Biogenerator (Gilead).
- Alnylam Pharmaceuticals (Alnylam).
- Rosetta Genomics and George Mason University (Rosetta).
- University of New Hampshire Law School (UNH).

While the amici agree that the district court erred in holding isolated DNA unpatentable, they disagree on the nature and extent of the error.

- Issue 1: Whether "isolated DNA" is man-made. DOJ seeks reversal of the district court decision only with regard to cDNA. It argues that molecules "engineered by humans, including cDNAs, vectors, recombinant plasmids, chimeric proteins, and similar fruits of the manipulation of genetic material will almost invariably be patent-eligible subject matter." Except for cDNA, however, DOJ maintains that the district court correctly held isolated DNA to be an unpatentable product of nature.

THE DISTRICT COURT ANALOGIZED ISOLATED DNA TO PURIFIED PRODUCTS OF NATURE (CELLULOSE, DYES, TUNGSTEN) FOR WHICH COURTS PREVIOUSLY HAD DENIED PATENT PROTECTION, NOTING THAT PURIFICATION ALONE WAS INSUFFICIENT TO RENDER PRODUCTS OF NATURE PATENTABLE.

Although DOJ acknowledges that laboratory processes used "to select and extract a naturally occurring segment of DNA" may be patentable, the product of those processes – isolated DNA itself – "remains, in structure and function, what it was in the human body."

The other amici disagree. They characterize both cDNA and isolated DNA as man-made, emphasizing the chemical differences between isolated DNA and naturally occurring genes. AIPLA, for example, argues that the act of excising DNA from its natural location in human chromosomes alters its structure, noting that the excised DNA segments are "much smaller and do not have the same three-dimensional structural and chemical complexity of the larger genomic DNA."

BIO/AUTM asserts that "at no point in the process of protein production – or at any other point in an organism's natural life – are genes excised or uncoupled from the rest

of the chromosome."

If the Federal Circuit agrees that isolated DNA is a patentable, man-made invention rather than a product of nature, it need not address the other issues on appeal. Alternately, the Federal Circuit could hold that whether isolated DNA is man-made remains an unresolved issue of fact and remand that issue to the district court for further consideration.

• Issue 2: Whether "purified" products of nature are patentable. Several amici argue that, even if isolated DNA is a product of nature, it nevertheless is patentable because it possesses features not shared by naturally occurring genes. Such arguments rely upon a line of decisions upholding the patentability of certain purified substances on the ground that they have uses and characteristics not shared with the products of nature from which they were derived. Those substances include drugs purified from animal glands, vitamins purified from fungal cultures, and flavoring purified from strawberries.

If the Federal Circuit classifies isolated DNA as a product of nature, its focus likely will be whether "isolation" – by analogy to "purification" – is sufficient to transform DNA into an article with new uses and characteristics.

SEVERAL AMICI ARGUE THAT, EVEN IF ISOLATED DNA IS A PRODUCT OF NATURE, IT IS PATENTABLE BECAUSE IT POSSESSES FEATURES NOT SHARED BY NATURALLY OCCURRING GENES.

On this issue, the amici again disagree. DOJ argues that "isolated genomic DNA is not rendered patentable on the theory that it is pure." Although DOJ admits purification "can in some cases transform a natural substance into a new compound sufficiently different in kind from its natural ancestry to cross the threshold of section 101," it distinguishes isolated DNA on the grounds that such DNA is not sufficiently "transformed" from its natural form. According to DOJ, "'the claimed isolated DNA retains...the identical nucleotide sequence found in native DNA,' thereby rendering it valuable for medical and diagnostic and therapeutic applications."

The other amici assert that it is precisely those medical, diagnostic and therapeutic applications that render isolated DNA patentable over naturally occurring genes. BIO/AUTM and Rosetta argue that the act of isolating DNA imparts new uses and characteristics upon such isolated DNA, including its use in developing new drugs, genetically modifying organisms, treating patients through gene therapy and – as used by Myriad itself – diagnosing a patient's predisposition to breast and ovarian cancer. In view of those new uses and characteristics, the amici argue that isolated DNA should be held patentable as a purified and transformed product of nature.

One potential obstacle to that argument is Funk Bros. v. Kalo, a 1948 Supreme Court decision holding that a mixture of bacteria that helped plants grow was not patentable because the bacteria in the mixture merely "serve the ends nature originally provided and act quite independently of any effort of the patentee." The amici distinguish Funk Bros. on the ground that Myriad's isolated DNA serves a different purpose than the naturally occurring BRCA genes: diagnosing a patient's susceptibility to cancer.

In view of Funk Bros., the Federal Circuit may need to address or remand the collateral issue of whether isolated DNA "serves the ends nature originally provided."

• Issue 3: Whether the district court erroneously applied precedent. In holding Myriad's patents invalid, the district court relied upon the landmark 1980 Supreme Court decision Diamond v. Chakrabarty – which upheld the patentability of a genetically modified bacterium used to break down oil spills – to assert that an invention derived from a product of nature must be "markedly different" from its natural form to be patentable.

The district court used that standard in rejecting Myriad's argument that the chemical differences between isolated DNA and naturally occurring genes render them "markedly different." The district court instead focused on the "essential characteristic" shared by both isolated DNA and naturally occurring genes – their information-carrying function – to conclude that isolated DNA is not "markedly different" from naturally occurring genes.

Gilead, AIPLA and UNH take issue with the district court's use of the term "markedly different." Gilead argues that the district court misconstrued the import of the term in Chakrabarty, asserting that the Supreme Court used that language not to promulgate a new patentability standard, but to distinguish Funk Bros. on the ground that Chakrabarty (unlike Funk Bros.) had produced a bacterium "with markedly different characteristics from any found in nature."

Gilead contends that the "markedly different" language describes a "sufficient condition for a substance to be man-made," but that the standard for patentability under § 101 is whether there exists sufficient human intervention to render an invention "man-made."

By contrast, AIPLA and UNH do not dispute that Chakrabarty imposes the condition that an invention must be "markedly different" from its natural form to be patentable. Instead, they challenge the district court's application of that condition. AIPLA contends that the district court's application was too narrow because it ignored the chemical differences between isolated DNA and naturally occurring genes and instead focused on a "shared essential characteristic" between the two. AIPLA asserts that "[n]o legal basis exists for arbitrarily and categorically excluding such DNA-derived inventions from the scope of § 101 on the ground that they share a characteristic with the native, naturally occurring DNA."

AIPLA further asserts that such exclusion would be untenable, since biotechnology inventions unavoidably share "essential characteristics" with the products of nature from which they are derived.

UNH contends that the district court's application of the "markedly different" condition was too broad because it led the district court to conclude that "a physical embodiment of the laws of nature" – a description applicable not just to DNA, but to any invention that works by the laws of physics or chemistry – is unpatentable. UNH) argues there is no precedent for such exclusion under § 101, and it urges the Federal Circuit to follow the guidance of Chakrabarty not to create exceptions to patentability unless set forth in the Patent Act.

THE CLAIM THAT PATENTS OF ISOLATED DNA IMPEDE SCIENTIFIC COLLABORATION, ACCORDING TO SOME AMICI, CAN BE ADDRESSED BY OTHER MEANS THAN CATEGORICALLY DENYING PATENT PROTECTION.

- Issue 4: Whether Congress intended DNA to be patentable. The intent of Congress in drafting the Patent Act may be an important factor in the Federal Circuit's decision, as it was for the Supreme Court in Chakrabarty. On that subject, Gilead makes the argument that the intent of Congress was to ensure that "any useful subject matter 'made-by-man'... satisfies the statutory requirement of §101."

Genetic Alliance argues that "Congress has acted specifically to facilitate patents involving isolated DNA molecules" and marshals supporting evidence from the Patent Act itself. Genetic Alliance asserts that provisions of the Act are based upon Congress's understanding that isolated DNA is patentable, and argues that "holding that isolated DNA molecules are not patentable would render portions of [those provisions] meaningless."

In view of such arguments, the Federal Circuit may need to address whether Congress intended isolated DNA to be patentable, and whether the district court interpreted § 101 consistently with Congressional intent.

- Issue 5: Whether public policy favors patenting DNA. Several amici raise policy arguments in favor of patenting isolated DNA. Rosetta comments on the "astronomical costs and inherent large risks associated with ... going from laboratory to market" with DNA-based therapies, and warn that such therapies may not reach the public absent patent protection to offset the costs and risks of their development. IPO cautions that a ban on isolated DNA patents would discourage research not only on human genes, but on genes from other organisms, noting the thousands of patents claiming useful plant, bacterial and viral DNA, while BIO/AUTM provides examples of isolated DNA patents that have contributed to advances in drugs and vaccines, genetic testing, agriculture, and industrial and environmental biotechnology.

Some amici advance the idea that the criticisms of isolated DNA patents – that they impede collaboration within the scientific community and limit public access to new technology – can be addressed by means other than categorically denying patent protection for isolated DNA. Those amici note that isolated DNA patents can still be attacked and invalidated as anticipated by, or obvious in view of, prior work in the field. Genetic Alliance further notes that, for any government-funded DNA inventions, the government can exercise its "march-in rights" and force a patentee to license its invention as necessary to safeguard public health and safety.

Finally, Alnylam argues that holding isolated DNA unpatentable would go against the international Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS), under which "the United States promised to grant 'patent rights enjoyable without discrimination as to...the field of technology.'" Alnylam notes the role of the United States as an advocate of uniform global standards for patent protection, and contends that excluding isolated DNA from patent protection in the United States would undermine that goal.

The Federal Circuit faces a number of issues in deciding the appeal. It could base a decision on whether or not isolated DNA is man-made; whether or not isolated DNA is a "purified" product of nature; whether or not the district court properly applied precedent in finding isolated DNA not "markedly different" from naturally occurring genes; whether or not Congress intended for DNA to be patentable; and whether or not policy considerations favor patents for isolated DNA.

Regardless of the precise contours of the Federal Circuit's eventual decision, the issues raised in the amicus briefs make clear that the decision likely will have significant implications for the biotechnology and pharmaceutical industries.

CHRISTOPHER LOH *is a partner at Fitzpatrick, Cella, Harper & Scinto. He practices general intellectual property law, with an emphasis on biotechnology and Hatch-Waxman pharmaceutical patent litigation. He has litigated patent cases involving diverse technologies, and has significant experience in drafting licensing agreements, preparing non-infringement and freedom-to-operate opinions, and advising clients on complex intellectual property transactions.*
cloh@fchs.com

AMY FUETTERER *is an associate at Fitzpatrick, Cella, Harper & Scinto. She practices intellectual property law with an emphasis on complex patent and Hatch Waxman litigation in the pharmaceutical, biotechnology and chemical arts.*
afuetterer@fchs.com