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Myriad Ruling Vs. Biotech Patent Eligibility In Europe

Law360, New York (June 21, 2013, 12:35 PM ET) -- Companies investing in biotechnology understand that while returns can be enormous, the path toward approval of new biotechnological products is long, arduous and, most of all, expensive. With aging populations and decreases in the governmental resources set aside for their care, reimbursement for health services is becoming more difficult to obtain. Moreover, the implementation of pharmaceutical price controls in many developed nations is on the rise. In a difficult financial environment, these factors are increasingly impacting the biotechnology investment formula and business model.

Recent high-profile decisions from the U.S. Supreme Court relating to defining the scope of biotechnology patent subject matter eligibility may further strongly impact the overall investment climate. As such, we summarize the U.S. Supreme Court decision in Myriad and contrast the issues it raises with the legal framework existing in Europe.

The Myriad Case

On June 13, 2013, the United States Supreme Court decided Association for Molecular Pathology et al. v. Myriad Genetics Inc. et al. This case has also been referred to as “the Myriad case" and has been watched closely by the biotechnology industry given that it relates to fundamental issues of patent eligibility regarding biological molecules.
Under the U.S. Patent Act, “[w]hoever 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.” 35 U.S.C. § 101.

The Supreme Court has construed § 101 broadly, explaining that “[i]n choosing such expansive terms ... modified by the comprehensive ‘any,’ Congress plainly contemplated that the patent laws would be given wide scope.” Bilski v. Kappos, 130 S.Ct. 3218, 3225 (2010).

The U.S. Supreme Court, however, has also held that § 101 is not unlimited. With respect to the patent eligibility of naturally occurring things, the court indicated that patent protection strikes a delicate balance between creating “incentives that lead to creation, invention, and discovery” and “imped[ing] the flow of information that might permit, indeed spur, invention.” The court applied this standard in determining whether Myriad’s patents claim a “new and useful ... composition of matter,” §101, or claim naturally occurring phenomena.

The petitioners in the Myriad case are a collection of medical organizations, researchers, genetic counselors and patients. They initially sued respondent Myriad Genetics Inc. and the Directors of the University of Utah Research Foundation (collectively, “Myriad”) in the U.S. Federal District Court for the Southern District of New York for declaratory judgment that certain Myriad patents were invalid for encompassing subject matter which was not eligible for patent protection. The claims at issue are exemplified below in condensed form:

- Claim 1: An isolated DNA coding for a BRCA1 poly-peptide, said polypeptide having the amino acid sequence set forth in SEQ ID NO:2 (i.e., the BRCA1 protein sequence).

- Claim 2: The isolated DNA of claim 1 wherein the DNA has the sequence set forth in SEQ ID NO: 1 (i.e., the BRCA1 coding cDNA).

It should be noted that claim 1 above encompasses any nucleotide sequence encoding the BRCA1 proteins. As such the claim reads on genomic DNA. Alternatively, Claim 2 is limited to a specific cDNA sequence encoding the BRCA1 protein.

The SDNY agreed with the plaintiffs and held that the claims exemplified above were invalid under 35 U.S.C. § 101 for reading on patent ineligible subject matter. Assoc. for Molecular Pathology v. U.S. Patent & Trademark Office, 702 F.Supp.2d 181 (S.D.N.Y.2010).

Specifically, the district court held that the composition claims were invalid because isolated DNA molecules fall within the judicially created "products of nature" exception to § 101 because such isolated DNAs are not "markedly different" from native DNAs in nature. The district court relied on the fact that, unlike other biological molecules, DNAs are the "physical embodiment of information," and that this information is not only preserved in the claimed isolated DNA molecules, but also essential to their utility as molecular tools. In view of this emphasis on "information" carried by protein encoding DNA, the court did not recognize a patentable distinction between genomic and cDNA.

The Court of Appeals for the Federal Circuit reversed the SDNY as to the patentability of the composition claims in an initial opinion that issued in July 2011. Assoc. for Molecular Pathology v. U.S. Patent & Trademark Office, 653 F. 3d 1329 (2011) ("AMP I"). That decision was appealed to the Supreme Court which remanded AMP I to the Federal Circuit in view of its decision in Mayo Collaborative Services v. Prometheus Laboratories, Inc., 566 U. S. ___ (2012) ("Prometheus") involving patent eligibility of methods of medical diagnoses.

In Prometheus, the Supreme Court held that the patent eligibility of diagnostic claims will likely depend on clear and convincing evidence: (1) whether they recite and monopolize a law of nature; and (2) whether any additional claim steps are merely conventional steps specified at a high level of generality appended thereto. The Supreme Court stated that "[w]e recognize that, in evaluating the significance of additional steps, the §101 patent-eligibility inquiry and, say, the §102 novelty inquiry might sometimes overlap." Id.

Nevertheless, the court, "decline[d] the Government's invitation to substitute §§102, 103, and 112 inquiries for the better established inquiry under §101." Id. Unfortunately and to the potential detriment of the personalized medicine industry, how one actually determines whether additional method steps are "conventional," remains unclear.

The Federal Circuit decided in the Myriad case on remand in Assoc. for Molecular Pathology v. U.S. Patent & Trademark Office, 689 F. 3d 1303 (Fed. Cir. 2012) ("AMP II") and again upheld the patent eligibility of the claims directed to "isolated" DNA.

In AMP II, Judge Alan Lourie opined that the distinction between a product of nature and a human-made invention for purposes of § 101 depends on a change in the claimed composition's identity compared with what exists in nature. Specifically, the Federal Circuit argued that the Supreme Court drew a line between compositions that, even if combined or altered in a manner not found in nature, have similar characteristics as in nature, and compositions that human intervention has given "markedly different," or "distinctive," characteristics.
In using this test with respect to the claims directed to isolated DNA, the Federal Circuit concluded they

were directed to patentable subject matter because the claims cover molecules that are markedly different — have a distinctive chemical identity and nature — from molecules that exist in nature.

It is unsurprising that Judge Lourie focused on the chemical/structural elements of the claimed DNAs at issue in the Myriad case. The Written Description Requirement ("WDR") set forth in 35 U.S.C. § 112, first paragraph, is meant to effectively curtail attempts to claim inventions involving nucleic acid and polypeptides in purely functional terms, i.e., as simple conveyors of information. The WDR requires that a patent specification objectively demonstrate that an applicant actually invented and was in possession of a claimed genus of nucleic acids. A demonstration of such possession generally requires sufficient chemical/structural/sequence description to describe what a claimed genus of nucleic acids is as opposed to what it does. Ariad Pharmaceuticals v. Eli Lilly 598 F.3d 1336 (Fed. Cir. 2010)(en banc.)

In AMP II, the Federal Circuit discussed the differences between naturally occurring chromosomes, genomic DNA encompassing the BRCA1/2 genes and the exon-only cDNAs encompassed by the claims at issue to hold that BRCA1 and BRCA2 in their isolated states are not the same as DNA as it exists in the body. The Federal Circuit asserted that human intervention in cleaving or synthesizing a portion of a native chromosomal DNA imparts on that isolated DNA a distinctive chemical identity from that possessed by native DNA.

The Federal Circuit dismissed AMD's arguments that isolated DNA was not markedly different than what occurred in nature because both forms included the same protein coding information. The Federal Circuit stated, "[w]e recognize that biologists may think of molecules in terms of their uses, but genes are in fact materials having a chemical nature and, as such, are best described in patents by their structures rather than their functions."

Thus, Judge Lourie's opinion in AMP II is consistent with the Federal Circuit's track record of discounting the information-transmitting aspects of DNA while overemphasizing its chemical/structural features.

The Federal Circuit also pointed out that the USPTO has issued patents directed to DNA molecules for almost thirty years resulting in 2,645 patents claiming "isolated DNA." The Federal Circuit stated that, "if the law is to be changed, and DNA inventions excluded from the broad scope of § 101 contrary to the settled expectation of the inventing community, the decision must come not from the courts, but from Congress."

In a unanimous 9-0 decision, the Supreme Court has now rejected the Federal Circuit's logic with respect to the patent eligibility of claims to isolated DNA and partially affirmed and reversed its decision in AMP II. The court in effect, held genomic DNA not patent eligible whereas synthetic cDNA is deemed to be patent eligible.

As indicated above, claim 1 reads on genomic DNA whereas claim 2 is specific to cDNA. With respect to genomic DNA, the court noted that, "[i]t is undisputed that Myriad did not create or alter any of the genetic information encoded in the BRCA1 and BRCA2 genes." The court characterized, Myriad's "principal contribution" to be "uncovering the precise location and genetic sequence of the BRCA1 and BRCA2 genes within chromosomes 17 and 13."

The court then asked itself as to whether the efforts associated with such localization "renders the genes patentable." The court distinguished the claimed DNA genomic sequences from the patentable bacterial strain of the landmark Diamond v. Charkarbarty case of 1980, by stating that it was new "with markedly different characteristics from any found in nature," which were "due to the additional plasmids and resultant capacity for degrading oil."

In contrast, the court stated that Myriad, "did not create anything." Indeed, the court held that, "separating that gene from its surrounding genetic material is not an act of invention." Furthermore, the

court dismissed Myriad's work in isolating the BRCA1/2 genes asserting that, "extensive effort alone is insufficient to satisfy the demands of §101."

Moreover, the Supreme Court disregarded the AMP II opinion's focus on the chemical attributes of the claimed genomic sequences by stating that Myriad's "claims [are not] saved by the fact that isolating DNA from the human genome severs chemical bonds and thereby creates a non-naturally occurring molecule."

In view of claim 1's generic recitation of any isolated nucleic acid encoding the BRCA1 protein, the court stated that claims "understandably focus on the genetic information encoded." Ignoring the Doctrine of Equivalents, the court then implied that if the claim were focused on chemical features, it would be easy for a potential infringer to design around the claim by merely including "an additional nucleotide pair." The court assets that such an outcome would not be beneficial to Myriad and so that is why it is, "concerned primarily with the information contained in the genetic sequence, not with the specific chemical composition of a particular molecule."

The court also declined to give any weight to the USPTO's long-standing practice of granting patents on "isolated" DNA relying on the U.S. government's position as set forth in its amicus brief, that the "PTO's practice was not 'a sufficient reason to hold that isolated DNA is patent-eligible.'"

The court, however, upheld the patent eligibility of the claimed cDNAs because, "creation of a cDNA sequence from mRNA results in an exons-only molecule that is not naturally occurring." The court stated that cDNA is not a "product of nature" and is patent eligible under §101, "except insofar as very short series of DNA may have no intervening introns to remove when creating cDNA." Under those circumstances, "cDNA may be indistinguishable from natural DNA."

With a view toward its decision in Prometheus, the court explicitly stated that method claims are "not implicated by this decision." Additionally, the court stated that the claiming of the applications of these genes or altered genetic sequences would not be impacted by the decision.

In Europe, the Situation Is Different

Chemical compounds were excluded from patentability in various European countries until the Strasbourg Patent Convention came into force in 1963.

The German Federal Supreme Court decision "Imidazoline" of 1972 (GRUR 1972, 541 — Imidazoline) made clear that synthetically produced chemical compounds are patent eligible, including absolute compound protection.
Subsequently, the German Federal Patent Court decided in "Antamanid" (BPatG, GRUR 1978, 238) that synthetically produced chemical compounds, which also occur in nature, are patent eligible, including absolute compound protection, provided for the invention related to an invention and not a discovery.

The German Federal Supreme Court decision "IFN-γ" of 1996 (BGHZ 130, 259) confirmed the principle previously applied to various chemical entities then for human DNA.

In the meantime in 1998, after nearly 10 years of heated debate, the European Parliament and the Council passed Directive 98/44/EC related to the legal protection of biotechnological inventions.

Although planned for the future, at present there is no existing regional patent system that is solely governed by the laws of the European Union. The European patent system is based on an independent international treaty, the European Patent Convention ("EPC"). A European patent is granted by the European Patent Office. It represents a bundle of national patents. In parallel there are the national patent systems in each country.

The main provisions of Directive 98/44/EC were quickly incorporated into the Implementing Regulations ("IR") to the EPC by a decision of the Administrative Council of the European Patent Organization of June 16, 1999. Thus, the patentability of biotechnological inventions is assessed by the EPO based on a one-to-one implementation of the directive, i.e., European Community law.

Hence, now one could have had the impression that decision T 272/95 Relaxin/HOWARD FLOREY INSTITUTE concerning a DNA fragment encoding human H2-preprorelaxin, said H2-preprorelaxin having a certain amino-acid sequence finally, laid the issue to rest. Although, it was argued by the opponent that the essence of the invention was the elucidation of the genetic sequence of the H2-relaxin gene, in simple terms, the proprietor had obtained a code book from the donors (the genetic material) and "cracked the code" (discovered the number and sequence of human relaxin genes) which was no more than a discovery of the characteristics of a substance which had existed in nature probably for many thousand years, the EPO decided otherwise. Rule 23(e)(2) of the IR defines which biological material originating from the human body may be patented. It states that:

(2) An element isolated from the human body or otherwise produced by means of a technical process including the sequence or partial sequence of a gene may constitute a patentable invention, even if the structure of that element is identical to that of a natural element.

Consequently, the EPO will, provided the patentability requirements are met, grant a patent on a human gene, the corresponding cDNA and the respective protein with full compound protection.

However, the governments of France, Germany and Austria were among the countries that most heavily debated certain aspects of the directive. Ethical questions and the boundaries of patentability played an important role in these debates. Hotly debated for example, was the question of the extent to which inventors could claim elements isolated from the human body. Critics of composition of matter protection for (human) gene sequences argued that biotech inventions were not comparable to "traditional" chemical inventions due to additional "information" contained in the gene sequences which goes beyond the chemical composition of the sequence itself.

Notwithstanding the fact that Germany was already acknowledging, accepting and validating patents granted by the EPO (which was operating in compliance with the directive); France and Germany, as well as other continental European member states, were sued by the European Commission for their national non-implementation of the directive.

Finally, in 2005 Germany reluctantly implemented the directive at the national level. However, legal implementation of the directive into German national was not seemless. For example, the German government amended the German Patent Act in a manner which differs substantially from the directive. The amendment provided that the scope of patent protection conferred for a sequence or a partial sequence of a gene whose structure is concordant to the structure of a natural sequence or partial sequence of a human gene must be limited in the patent claim to the use disclosed in the patent application ("purpose-limited compound protection").

A gene per se is, however, patentable both before the EPO and the German patent office as neither office distinguishes between a gene and a corresponding cDNA. Hence, in contrast to the United States it is not considered non-patent eligible subject matter.

However, while an applicant can obtain a patent on a human gene from the European Patent Office with full composition of matter protection, this is not the case if the same applicant applies for a patent in Germany where the scope of protection will be limited to those uses disclosed in the specification.

Thoughts in Conclusion

While the biotech industry appears to have shrugged its collective shoulders following the Myriad decision, it is important to note that many types of biotechnologies may run into hurdles with respect to patentability in the U.S. These include novel and nonobvious:

- prokaryotic genes (which do not include introns) derived from industrially valuable microorganisms
- genomic biomarker sequences, e.g., short tandem repeats associated with disease outcomes or treatment success
- therapeutic ribosomal RNAs
- genomic sequences differentially regulated by epigenetic mechanisms associated with disease

While it does not appear that such issues would arise in patent applications before the European Patent Office, there are many steps that experienced patent practitioners need to take to ensure that clients' patent applications are drafted and prosecuted in a way that valuable claims are still obtained in the U.S. while also taking into account the nuances of European biotech patent law.

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