



Global Strategies for Protecting Inventions in the Biotechnology Sector

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As the biotechnology sector continues to expand worldwide, global pharma sales are predicted to reach 1.4 trillion by 2019.¹ Pharmaceutical companies devote significant costs to research and development. For example, the average cost to develop and gain marketing approval for a new drug can be as high as \$2.558 billion.² The ability to protect intellectual property (IP)

rights is vital for biotechnology companies to protect their investments and develop new medicines, fight diseases and create new agricultural products.

Protecting IP, however, may be a major challenge for companies operating in more than one market, due to regional differences in the legal standards. These differences require thorough analysis and development of global strategies for protecting IP.

Because patent protection can be a highly valuable asset to

a biotechnology company, there is a growing need to coordinate strategies for patent protection in major markets. This article will focus on coordinating strategies for patent protection in the U.S. and Europe.

U.S.: Patent Eligibility of the Biotechnology Inventions

In the U.S., under the current legal framework for obtaining biotechnology patents, the answer to the question on whether biotech inventions are patentable is “maybe,” or “it depends.” Often, inventions that are patentable in Europe have been found ineligible for patent protection in the U.S.

Differences in patent eligibility standards are particularly problematic for biotechnology companies in view of the recent decisions of the United States Supreme Court that significantly narrowed the subject matter eligible for patent protection and clarified the scope of the ‘law of nature’ exception to patentability. The trend is especially troubling for the biotechnology sector where innovations rely on properties of naturally existing substances or components of living beings, which may be deemed ‘natural phenomena’ ineligible for patenting.

Patent eligibility is governed by Section 101 of the Patent Act.³ Under this section, “whoever invents or discovers any new and useful process, machine, manufacture, or composition of a matter, or any new and useful improvements thereof, may obtain a patent thereof, subject to the condition and requirements of this title.”⁴ However, laws of nature, physical phenomena, and abstract ideas, as well as newly discovered naturally occurring plants and minerals, are excluded from patent protection.

The prevailing doctrine on patent eligibility was formulated by the Supreme Court in 1980, in *Diamond v. Chakrabarty*.⁵ According to this doctrine,

“[a]nything under the sun that is made by man” was considered patentable.⁶

Previously, the United States Patent and Trademark Office (USPTO) routinely issued patents claiming isolated and recombinant DNA molecules used for making genetically modified organisms, along with probes, diagnostic kits and drugs including or based on isolated DNA. However, this practice changed drastically after the Supreme Court’s decision in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*⁷ In *Mayo*, the Court set forth a two-part test for determining patent eligibility of inventive subject matter. First, the court determines whether the claims are directed to a patent-ineligible concept, such as a law of nature, physical phenomena, or abstract idea. If the answer is yes, it must be determined whether other elements of the claim ‘transform’ it into patent-eligible subject matter. The second step of the analysis is described by the Supreme Court as a search for an inventive concept (*i.e.*, an element or combination of elements sufficient to ensure the patent in practice amounts to significantly more than the ineligible concept itself).

Following *Mayo*, the Supreme Court decided another case that had a profound impact on patent eligibility of biotechnology inventions. In *Ass’n for Molecular Pathology v. Myriad Genetics, Inc.*, the Court considered patent eligibility of patents covering diagnostic methods and compositions based on discovery of the precise chromosomal location of the Breast Cancer 1 (BRCA 1) gene.⁸ Myriad Genetics, Inc., the owner of the patents, used the technology for diagnosing breast and ovarian cancer. The Court determined that “separating that gene from its surrounding genetic material is not an act of invention,” and cannot be patented.⁹

Although the Court found that the mere act of isolating DNA sequence does not merit patent protection, cDNA, a

complementary DNA sequence derived from the gene but not having introns, was upheld by the Court as patentable subject matter. In *Myriad*, the Court stated “[g]roundbreaking, innovative, or even brilliant discovery does not by itself satisfy the Section 101 inquiry.”¹⁰

Many decisions restricting patent eligibility for the biotechnology inventions followed after *Mayo* and *Myriad*. For instance, the *Mayo* test was used to invalidate claims directed to methods of optimizing dosage levels,¹¹ naturally occurring DNA sequences,¹² methods for detecting a coding region of DNA based on its relationship to non-coding regions,¹³ methods of analysing and comparing DNA, primers,¹⁴ and nucleic acid probes.¹⁵

The standard of finding patent eligibility of diagnostic methods was further restricted in the decision of *Ariosa Diagnostics v. Sequenom, Inc.*¹⁶ On June 27, 2016, the United States Supreme Court issued an order denying *certiorari* in *Sequenom, Inc. v. Ariosa Diagnostics, Inc.*,¹⁷ and, thus, let stand a decision of the United States Court of Appeals for the Federal Circuit, holding a groundbreaking medical test developed by Sequenom to be ineligible for patenting.

In *Ariosa*, the invention was a method of testing for fetal abnormalities.¹⁸ The method was based on identification of cell-free fetal DNA (cffDNA) in maternal plasma and serum, which was previously discarded, but that was used in the test for detecting the small fraction of paternally inherited cffDNA to determine fetal characteristics, such as gender. The method is a simple blood test that avoids risks associated with invasive amniocentesis (performed by inserting a needle into the amniotic sac of a pregnant woman).

Claim 1 of the Sequenom U.S. patent recites:

A method for detecting a paternally inherited nucleic acid of foetal origin per-

formed on a maternal serum or plasma sample from a pregnant female, which method comprises amplifying a paternally inherited nucleic acid from the serum or plasma sample and detecting the presence of paternally inherited nucleic acid of foetal origin in the sample.¹⁹

The Federal Circuit affirmed the district court's decision that this and other claims were not patentable under Section 101 of the Patent Act.²⁰ In its analysis, the Federal Circuit applied the two-step *Mayo* test to review the claims. First, the court determined the claims at issue "are generally directed to detecting the presence of a naturally occurring thing or a natural phenomenon, cffDNA in maternal plasma or serum," that are not eligible for patent protection.²¹ In the second step of the framework, the court examined "the elements of the claim to determine whether the claim contains an inventive concept sufficient to 'transform' the claimed naturally occurring phenomenon into a patent-eligible application."²² The court concluded the practice of the method claims did not add enough to the natural phenomenon of cffDNA to transform it into a patentable invention. The court stated the preparation and amplification of DNA sequences in plasma or serum used in the methods were "well-understood, routine, conventional activities."²³

On Dec. 2, 2015, the Federal Circuit denied Sequenom's petition for rehearing *en banc*.²⁴ On March 21, 2016, Sequenom filed a petition for *writ of certiorari* in the Supreme Court.²⁵ The issue for consideration was "[w]hether a novel method is patent eligible where: (1) a researcher is the first to discover a natural phenomenon; (2) the unique knowledge motivates him to apply a new combination of known techniques to that discovery; and (3) he thereby achieves a previously

impossible result without preempting other uses of the discovery?"²⁶ The petitioner argued the *Mayo* test is overbroad, invalidates inventions that have been found patentable in the past and threatens future research. The petitioner provided examples showing that many products that were traditionally included in the subject matter eligible for patent protection would not be patented under the *Mayo* test.²⁷

For instance, vaccines combine natural phenomenon of immune response with known methods of drug administration. The Nobel-winning invention PCR combines DNA polymerase isolated from naturally occurring heat-resistant bacteria, chemical reagents with sequences of a gene and primers, and repeated heating, cooling and starting over the process to amplify the sequence of the gene. These and many other inventions would not be found patent-eligible based on the application of the *Mayo* test.

Sequenom's petition was supported by 22 *amici* briefs. In its brief, the Institute of Professional Representatives before the European Patent Office (EPO) submitted that *Myriad/Mayo* framework breaches internationally accepted norms for patent eligibility and EPO practice.²⁸ Despite the gathered support, Sequenom's petition was denied, and standards for patent eligibility in the U.S. further diverged from those applied in other countries and the EPO.

Despite the trend following the *Mayo* and *Myriad* decisions, it has been determined that some biotechnology patents directed to or based on naturally occurring substances or components are directed to patent-eligible subject matter. For example, claims directed to a process of preservation of hepatocytes involving multiple freeze-thaw cycles have been determined to be eligible for patent protection because "a new combination of steps in a process may be patentable even though all the con-

stituents of the combination were well known and in common use before the combination was made."²⁹

Europe: Patent Eligibility of Biotechnology Inventions

In Europe, biotechnology inventions are generally patentable if they satisfy the patentability requirements of Article 52 of the European Patent Convention (EPC).³⁰ Under this article, European patents are granted for inventions that are new, involve an inventive step and are susceptible to industrial application.

EPC Article 52(2) excludes claims that are abstract in nature (discoveries) or non-technical in nature (scientific theories) if they are claimed "as such."³¹ EPC Article 53(c) excludes "methods for treatment of the human or animal body by surgery or therapy and diagnostic methods practiced on the human or animal body."³² However, the provision of the article is not applicable "to products, in particular substances or compositions for use in any of these methods." Opinion G 1/04 of the Enlarged Board of Appeal further defines proper constructions of the terms "diagnostic methods" and "practised on the human or animal body."³³ The opinion defines "diagnostic methods practised on the human body" as "those methods containing all the procedural steps to be carried out when making a medical diagnosis, i.e. the examination phase involving the collection of relevant data, the comparison of the examination data thus obtained with the standard values, the finding of any significant deviation (a symptom) during that comparison and, finally, the attribution of the deviation to a particular clinical picture (the deductive medical decision phase)."³⁴

The opinion explains that because the diagnostic methods referred to in Article 53(c) are inventions, these methods must include preceding steps of a technical nature, because steps related

to deductive medical decisions are excluded from patentability as mental steps.³⁵ The opinion further specifies that the criterion “practiced on the human or animal body” is only applicable to method steps of a technical nature.³⁶ Diagnostic methods, including steps of a technical nature that are not practiced on the human body, are not excluded from patent protection.³⁷

It follows that the genetic diagnostic methods, if performed *in vitro*, may be afforded patent protection. DNA sequences may also be patented. Article 5(1) of the Biotech Directive 98/44/EC provides that “[t]he human body, at the various stages of its formation and development, and the simple discovery of one of its elements, including the sequence or partial sequence of a gene, cannot constitute patentable inventions.”³⁸ However, under Article 5 (2)-(3) of the Biotech Directive 98/44/EC, genes and other elements isolated from the human body are patentable if industrial application of the sequence is disclosed.³⁹

In line with the above reasoning, the EPO granted patents to Myriad for using the genes BRCA1 and BRCA2 to diagnose women’s predisposition to breast and ovarian cancers.⁴⁰ Similarly, the European counterpart (Sequenom EP patent) of Sequenom’s now-invalid U.S. patent was granted by the EPO.⁴¹

Diverging decisions between the EPO and the USPTO on patenting biotechnology inventions based on the DNA technology and diagnostic methods require development of adequate strategies for protecting IP assets.

Developing a Strategy

Biotech companies facing constant changes in patent eligibility in different countries have to develop global strategies for protecting biotechnology innovations.

A recommended strategy is to file patent applications tailored to the legal

standards of the countries of interest. For example, an international patent application can be filed under the Patent Cooperation Treaty (PCT), which is an international patent law treaty that provides a unified procedure for filing patent applications to protect inventions in each of its member states. An application filed under the PCT can be submitted in each country of interest as a national or regional application to obtain national or regional patents. Careful consideration should be accorded to the description and claims of the inventive products or technologies disclosed in these applications. When filing national or regional patents, the claims of the application can be modified, as necessary, to comply with the individual countries’ patent requirements.

For example, claims directed to methods of treatment of the human or animal body can be modified to recite products (*i.e.*, substances or compositions) when filing with the EPO. To satisfy the requirements of the USPTO, applications disclosing isolated and/or purified natural products should also describe structural and/or functional differences of these products from their naturally occurring forms. Process claims in such applications should explicitly recite active physically transformative steps associated with the process, include uses of machines or laboratory equipment, or include steps for adjusting a dosage or treatment protocol.

Another option is to file claims directed to methods of treatments that are patentable in the United States. Patents that cover product and method of treatments form core patent portfolios. However, biotechnology companies should not neglect applications directed to manufacturing processes, screening methods or dosage forms.⁴² These applications may be eligible for patent protection in many jurisdictions.

Patenting is not the only way to pro-

tect biomedical innovations. Biotech companies can protect innovative processes or products by keeping secret. For example, tailoring treatments based on different characteristics of individual patients, also referred to as personalized medicine, can be protected as trade secrets.⁴³ Databases and datasets also can be kept secret. For instance, Myriad’s gene-testing process identifies combinations of allelic gene variations in patients. After its loss in the Supreme Court, the company has sought to keep other information about genetic variations secret.⁴⁴

When making a decision to patent a company’s innovation or to maintain it as a trade secret, consider various factors, such as the type of invention, budget, longevity of the technology, intent to license, need to communicate information to third parties, ease of reverse engineering and ability to keep it confidential. For example, if the invention is a process, it may be easy for a competitor to circumvent steps of the method, and design procedures around the claimed processes. In this case, consider if inventive processes are amenable for protection by trade secrets. Advantageously, trade secrets do not have expiration dates as long as the secret is not revealed to the public, and typically do not require large budgets. However, there are concrete disadvantages of protecting confidential information as a trade secret. Intent to license, or disclose inventions to third parties would weigh in favor of patenting. Inventive products or compositions would be better protected by patenting in view of danger of being reverse engineered.

There is evidence that some companies, particularly diagnostic testing firms, are able to rely upon both patents and trade secrets for protection.⁴⁵ Due to the changes in life sciences patent landscape, this strategy may be followed by other companies. ☞

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ENDNOTES

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