The BRCA battle continues

Myriad has failed to obtain a rare preliminary injunction to stop Ambry offering genetic tests using the BRCA1 or BRCA2 genes as Ambry raised a substantial question about the validity of the claims of Myriad's patents. MaryAnne Armstrong reports.

University of Utah Research Foundation et al v Ambry Genetics Corporation

On June 13, 2013, the US Supreme Court handed down a seminal decision for the biopharma industry in *Association for Molecular Pathology v Myriad Genetics*, Inc, 133 S. Ct. 2107 (2013) (*Myriad*). In the *Myriad* decision the court held that naturally occurring nucleic acid sequences are not patent-eligible subject matter because they are products of nature.

In addition, claiming nucleic acids as being "isolated" will not render the nucleic acids patent-eligible. The court, however, left open the question of whether claims directed to methods of using the nucleic acids may be patentable.

Following the *Myriad* decision, Ambry Genetics announced that it would offer screening of the BRCA1 and BRCA2 genes, the subject of the Myriad patents. Myriad filed for a preliminary injunction to prevent Ambry from offering genetic tests using the BRCA1 or BRCA2 genes.

This decision from the US District Court Utah, Central Division is in response to that request for a preliminary injunction.

It should be noted at the outset that a "preliminary injunction is a drastic and extraordinary remedy that is not to be routinely granted"—*National Steel Car Ltd v Canadian Pacific Railway, Ltd* 357 F.3d 1319 (Federal Circuit 2004). To obtain a preliminary injunction the plaintiff must show the following:

1) Irreparable harm in the absence of the preliminary injunction;
2) That the plaintiff is likely to succeed on the merits of the case;
3) That the balance of equities is in favour of the plaintiff; and
4) That a preliminary injunction would be in the public interest.

The court considered each of these factors in its decision. This article considers the decision by the court with regard to factor 2), ie, whether the plaintiff was likely to succeed on the merits. The court concluded that Myriad was unlikely to be successful because Ambry had raised a substantial question about the validity of the claims of the patents at issue.

The claims involved in the suit can be essentially grouped as either "primer" claims, which were directed to various DNA primers, or "method" claims, which were directed to screening and diagnostic methods using the BRCA1 and/or BRCA2 genes.

With regard to the primer claims, Myriad argued that the Supreme Court held in *Myriad* that claims directed to 'synthetic' nucleic acids are patent-eligible and the

claims to nucleic acids are patent-ineligible under 35 USC§101 only if they are directed to 'naturally occurring' nucleic acid molecules.

Thus, Myriad argued that the reason that the Supreme Court found complementary DNA (cDNA, used by Myriad in its tests for the BRCA genes) to be patentable subject matter was because cDNA is synthetic. The court in following the more commonly accepted interpretation of the *Myriad* decision held that whether or not the nucleic acid is synthetic is not the determining feature in finding whether a nucleic acid is patent-eligible subject matter.

Rather, a nucleic acid is patent-eligible only if the sequence of the nucleic acid does not occur in nature. Thus, the court stated that "this court interprets *AMP [Myriad]* to stand for the proposition that even synthetic, non-cDNA, isolated DNA is patent-ineligible where it reflects the same nucleotide sequence as the genomic DNA."

The primers recited in the Myriad claims may have been synthetic, but the sequences of the primers were the same sequences found in the natural BRCA1 and BRAC2 genes. This is likely to be the case with many claims directed to primers because the length of primers is short. Unless a primer has been somehow modified with an artificial nucleic acid residue, the sequences of the primers are typically the same as a naturally occurring sequence and therefore subject to the same analysis used in the *Utah* decision.

Method claims

More noteworthy was the court's treatment of the method claims. As mentioned above, the Supreme Court left open the question of patent-eligibility of method claims because only nucleic acid claims were considered by the court. The court stated: "It is important to note what is not implicated by this decision. First, there are no method claims before this court. Had Myriad created an innovative method of manipulating genes while searching for the BRCA1 and BRCA2 genes, it could possibly have sought a method patent." *Association for Molecular Pathology v Myriad Genetics, Inc,* 133 S. Ct. 2107, 2119 (2013).

In considering the method claims, the court in *Utah* found that "the only 'inventive concepts' in their method claims are the patent-ineligible naturally occurring BRCA1 and BRCA2 sequences themselves. The claims contain no otherwise new process for designing or using probes, primers or arrays beyond the use of BRCA1 or BRCA2 sequences in those processes." The court further found that the method claims improperly "preempt a law of nature" and concluded that "the defendant [Ambry] has raised a substantial question concerning the method claims' subject matter eligibility for patent."

> "The USPTO states that such a claim is patentable because 'the claim as a whole recites something significantly different from the natural products'."

The finding by the court with regard to the method claims is particularly important because, as noted, the Supreme Court had left this question open in the *Myriad* decision. In addition, the position taken by the court appears to be going in a different direction from that adopted by the USPTO. On March 4 this year, the USPTO issued a guidance memorandum to US patent examiners to implement procedures for examiners to determine patent-eligible subject matter in view of *Myriad and Mayo Collaborative Services v Prometheus Laboratories, Inc,* 566 US 132 S. Ct. 1289, 101 USPQ2d 1961 (2012).

The memorandum presents various examples of claims. Example E has the following two claims.

- Claim 1. A pair of primers, the first primer having the sequence of SEQ ID NO: 1 and the second primer having the sequence of SEQ ID NO: 2.
- Claim 2. A method of amplifying a target DNA sequence comprising:
  - (a) Providing a reaction mixture comprising a double-stranded target DNA, the pair of primers of Claim 1, Taq polymerase, and a plurality of free nucleotides comprising adenine, thymine, cytosine and guanine;
  - (b) Heating the reaction mixture to a first predetermined temperature for a first predetermined time to separate the strands of the target DNA from each other;
  - (c) Cooling the reaction mixture to a second predetermined temperature for a second predetermined time under conditions to allow the first and second primers to hybridise with their complementary sequences on the first and second strands of the target DNA, and to allow the Taq polymerase to extend the primers; and
  - (d) Repeating steps (b) and (c) at least 20 times.

The memorandum states that Claim 1 is not directed to patent-eligible subject matter because, similar to the analysis used in *Utah*, the sequences of the primers are the same sequences that occur in nature and the primers' molecules are not "markedly different" from the nucleic acid occurring in nature.

However, the memorandum states that method Claim 2 is claiming patent-eligible subject matter. Claim 2, like the *Utah* claims, recites primers that are products of nature being used with conventional and known process steps and reagents. However, the USPTO states that such a claim is patentable because "the claim as a whole recites something significantly different from the natural products, ie, the claim includes elements in addition to the judicial exceptions that amount to a practical application of the natural products."

It should be noted that the *Utah* decision is for a request for a preliminary injunction, which is difficult to obtain in a patent infringement case, and the case is still to be heard fully on its merits. However, the decision does present an important indication of the direction in which some US district courts are leaning with regard to the patent-eligibility of the types of method claims in *Myriad*. The decision is particularly important because it appears to be in the opposite direction from the position being taken by the USPTO. ■

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