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REPORT

FEDERAL CIRCUIT ADDRESSES PATENT ELIGIBILITY OF ISOLATED DNA AND RELATED DIAGNOSTIC METHODS

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On July 29, the U.S. Court of Appeals for the Federal Circuit issued a decision addressing patent eligibility under 35 U.S.C. §101 in the context of biotechnology, and in particular, diagnostic technology, in *Association for Molecular Pathology v. USPTO*, also known as the *Myriad* case because the patents at issue are owned by Myriad Genetics, Inc.[1] In three separate opinions, a three-judge panel of the Court held that (1) certain composition claims directed to engineered or isolated DNA define patent eligible subject matter, and (2) some diagnostic method claims define patent eligible subject matter while others do not. While there are inconsistencies among the three opinions, substantial guidance for drafting and/or challenging such patent claims can be gleaned from the case.

I. The Claims

The Court addressed six representative claims from the seven patents at issue: three composition claims and three method claims. The three composition claims were respectively directed to: (1) an isolated DNA coding for a polypeptide having a specified amino acid sequence; (2) an isolated DNA coding for a polypeptide having a specified amino acid sequence and having a specified cDNA nucleotide sequence; and (3) an isolated DNA having at least 15 nucleotides of the isolated DNA coding for a polypeptide having a specified amino acid sequence. The three method claims were respectively directed to: (1) a method for detecting an alteration in a gene, comprising *analyzing* a specified sample gene, sample RNA, or cDNA made from sample mRNA; (2) a method for screening a tumor sample for a genetic alteration, comprising *comparing* a first sequence of a specified tumor sample gene, tumor sample RNA, or cDNA made from tumor sample mRNA with a corresponding second sequence from a nontumor sample wherein a difference indicates an alteration in the tumor sample gene; and (3) a method for screening potential cancer therapeutics, comprising *growing* host cells containing a specific altered gene in the presence of a candidate therapeutic compound, *growing* the same type of host cells in the absence of the candidate therapeutic compound, *determining* the respective growth rates of those cells, and comparing the growth rates. The *italics* above indicate the method step limitations on which the court focused.

[1] Appeal No. 2010-1406 (Fed. Cir. July 29, 2011).

II. The Opinions of the Three-Judge Panel

Judge Lourie wrote the primary decision of the Court. Judge Moore wrote a decision concurring in the result, but disagreeing with some of the reasoning underlying that result. Judge Bryson wrote a decision concurring in part (as to the method claims) and dissenting in part (as to the composition claims). In addressing the claims at issue, all three opinions also addressed other hypothetical claims, thus providing insight into the Court's positions on patent eligibility of a wide range of types of claims.

A. The Diagnostic Method Claims

All three judges agreed that two of the representative diagnostic method claims are not directed to patent eligible subject matter under §101, while the third representative diagnostic method claim is directed to patent eligible subject matter. In particular, the judges found that the method claims in which the only active steps were "comparing" or "analyzing" sequences are not directed to patent eligible subject matter. On the other hand, they found that the method claim in which active steps included "growing a … host cell" and "determining the rate of growth of the host cell" is directed to patent eligible subject matter.

The Court found the first two representative method claims to be directed to a patent ineligible abstract mental process of "comparing" or "analyzing" information, and to fail the "machine-or-transformation" test. The Court refused to read into the claims any physical steps of extracting DNA, sequencing DNA (determining the sequence of nucleotides in DNA), or otherwise processing a sample. It further found that the "comparing" and "analyzing" steps were directed to comparison of sequence information, rather than of physical molecules, and thus could be accomplished "by mere inspection." The Court distinguished claims that had been held patentable in the *Prometheus v. Mayo* case that is now under review by the U.S. Supreme Court.[2] The *Prometheus* claims included steps of "administering" a drug and "determining" the drug's metabolite levels in a subject. The Court noted that the latter steps are transformative in that they implicitly require manipulation to extract the metabolites from a sample and determine their concentration, and could not be achieved by mere inspection.

The Court found the third representative method claim to be directed to patent eligible subject matter because it includes transformative steps. The Court found that the "growing" and "determining" steps include more than the abstract mental step of comparing two sets of data, but involve manipulating cells and their growth medium. The Court specifically held that the step of "determining" the cells' growth rates necessarily involves physical manipulation of the cells. To complete its analysis, the Court found that these steps are "central to the purpose of the claimed process" rather than "mere data gathering," and that the claim is not so "manifestly abstract" as to claim an entire scientific principle, because it is tied to specific host cells, specific genes and specific types of therapeutics, and "thus presents 'functional and palpable applications' in the field of biotechnology."

B. The Composition Claims

In the primary opinion authored by Judge Lourie, the Court focused on the U.S. Supreme

[2] *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, 628 F.3d 1347 (Fed. Cir. 2010), *cert. granted*, 2011 WL 973139 (June 20, 2011).

Court's decisions in *Chakrabarty*[3] and *Funk Brothers*[4] as setting out "the framework for deciding the patent eligibility of isolated DNA molecules." All three judges agreed that in those cases, "the Supreme Court has drawn a line between [1] compositions that, even if combined or altered in a manner not found in nature, have similar characteristics as in nature, and [2] compositions that human intervention has given 'markedly different,' or 'distinctive,' characteristics." The Court held that: "the distinction, therefore, between a product of nature and a human-made invention for purposes of §101 turns on a change in the claimed composition's identity compared with what exists in nature." In *Chakrabarty*, the patent eligible claims were directed to a genetically engineered microorganism, while in *Funk Brothers*, the patent ineligible claims were directed to a non-naturally occurring mixed culture of naturally occurring bacteria.

In response to arguments that isolated DNA claims cover unpatentable "products of nature," the Court held (with Judge Moore's concurrence) that the claims to isolated DNAs, whether limited to cDNAs or not, and whether limited by length or not, are directed to patent-eligible subject matter under 35 U.S.C. §101.[5]

In the primary opinion authored by Judge Lourie, the Court emphasized that isolated DNA as claimed has been cleaved from a larger molecule by breaking covalent bonds, or has been synthesized, and thus "has a markedly different chemical nature than the native DNA." The Court distinguished isolated elements such as minerals found in the earth or a leaf separated from a tree, on the basis that the claimed composition has "a distinctive chemical identity from that of the native element, molecule, or structure." The Court declined to decide whether other isolated forms may or may not be sufficiently "markedly different from the one that exists in nature." The Court also focused on the fact that the PTO has issued patents directed to DNA molecules for almost 30 years without Congressional intervention, stating that the resulting settled expectations of the inventing community should not be lightly ignored.

Judge Moore concurred with this result, but advocated for a "more flexible" test. Under that test, she recommended that courts "analyze the isolated DNA claims …, to determine whether they have markedly different characteristics with the potential for significant utility, e.g., an 'enlargement of the range of … utility' as compared to nature."

Like Judge Lourie, Judge Moore focused on the creation of a distinct molecule resulting from changes in chemical bonds and separation of the isolated DNA from a much larger molecule. She further argued that isolated DNA, separated from "confounding sequences that are naturally present in the larger chromosomal polymer," … "has important practical consequences and leads to additional utility, particularly for the smaller isolated fragments." Thus, she stated that mere differences in chemical structure should not be sufficient, but that those differences should "impart a new utility which makes the molecules markedly different from nature."

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[3] *Diamond v. Chakrabarty*, 447 U.S. 303 (1980).
[4] *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948).
[5] Judges Moore and Bryson both agreed that the cDNA claims are patent-eligible because cDNA does not occur in nature. Judge Bryson also suggested that claims to labeled ("tagged") sequences may be patentable because they, too, do not occur in nature.

For claims directed to isolated segments of naturally occurring DNA, Judge Moore therefore distinguished between different lengths of isolated segments. Particularly with reference to claims limited to short sequences that could be used as probes or primers, she found that "the ability to use isolated DNA molecules as the basis for diagnostic genetic testing is clearly an 'enlargement of the range of … utility' as compared to nature." She thus considered claims limited to such short sequences to be clearly patent eligible. She considered claims directed to larger strands of isolated DNA, particularly those that include most or all of the entire gene, to present a much closer case because they do not present an enlargement of the range of utility as compared to nature. She compared such longer-sequence claims to patent claims directed to purified natural materials, such as purified adrenaline and purified vitamin B-12, which had both previously been upheld by federal courts.

Nevertheless, Judge Moore concurred in the holding of the Court because of the long-settled expectations that had been established by many years of issuance of such patents and many court decisions in which they had been upheld. She noted that the courts have "allowed patents on purified natural products for centuries." In that context, she commented that regardless of the sequence length encompassed by the claims, fundamentally altering the scope of patent-eligible subject matter by adopting such a test would be improper in the face of long acceptance of such claims by the Patent Office and the courts and Congressional inaction on the subject.[6]

Judge Bryson dissented from the Court's holdings regarding isolated DNA fragment claims. He argued that: "the only material change made to those genes from their natural state is the change that is necessarily incidental to the extraction of the genes from the environment in which they are found in nature." He further argued that such mere extraction from a natural location, making the alterations attendant to such extraction, does not give the extractor the right to patent the products themselves. Judge Bryson argued that the breaking of covalent bonds emphasized in Judge Lourie's decision is conceptually no different from the breaking of weaker bonds involved in washing dirt off of a diamond.

Judge Bryson argued that the more important distinction is whether or not the extraction of a product results in the product retaining the "character and function" of the product as found in nature. He referred to prior case law holding that merely purifying a naturally occurring substance does not render the substance patentable unless it results in a marked change in functionality. Thus, he focused on analyzing "(1) the similarity in structure between what is claimed and what is found in nature and (2) the similarity in utility between what is claimed and what is found in nature." He suggested that he would agree with Judge Moore's concurring opinion that claims to shorter sequences that may be used as probes or primers may satisfy the patent eligibility test, while claims to longer sequences would not satisfy that test. He

[6] Judge Lourie's opinion for the Court also addressed claims to purified materials, but did so more ambiguously. In *dicta* in that opinion, the Court distinguished "isolated" DNA from "purified" DNA. While the Court did not explicitly so hold, it appeared to suggest that a claim to a merely purified natural genetic material, as opposed to a cleaved or engineered material, may not be patentable, while mentioning in a footnote several cases in which purified materials had previously been held patentable.

disagreed with her that the Court should be bound by a prior history of Patent Office grant of such claims. Furthermore, he found all of the composition claims in question to be too broad to satisfy that test.

III. Analysis

The *Myriad* decision was unfortunately fragmented, in that the three judges on the panel wrote three different opinions. Thus, there is a significant possibility that the case may be taken up *en banc* by the full Federal Circuit, and/or on a petition for *certiorari* by the U.S. Supreme Court. Accordingly, the holding may not be permanent.

On the other hand, the decision was unanimous as to a number of issues. For example, all three judges agreed regarding: (1) patent ineligibility of method claims with only mental steps ("comparing" or "analyzing" sequences); (2) patent eligibility of method claims with explicit or implicit manipulative steps ("growing" and "determining … rate of growth"); (3) patent eligibility of cDNA composition claims; (4) patent eligibility of claims limited to isolated short segments of naturally occurring DNA with defined utility; and (5) patent eligibility of claims limited to isolated segments of naturally occurring DNA with a new utility or functionality relative to naturally occurring DNA.

In addition, Judge Lourie analyzed patent eligibility of claims to isolated DNA solely based on differences in chemical structure from naturally occurring DNA, while questioning similar claims directed to purified naturally occurring materials. Judge Moore reluctantly went along with this analysis without ultimately distinguishing similar claims directed to purified naturally occurring materials, to avoid radically changing settled expectations of the inventing community. Judge Bryson dissented because he considered this analysis inadequate. However, Judges Moore and Bryson apparently both agreed that such an analysis, coupled with a requirement for new utility or functionality of the claimed subject matter relative to the utility of naturally occurring DNA, would provide a satisfactory basis for analyzing patent eligibility of claims directed to either isolated DNA or purified naturally occurring materials.

IV. Recommendations

The decision was fragmented, and may well be reviewed and revised in the future (including perhaps by the Supreme Court's forthcoming decision in *Prometheus*). Nevertheless, we believe that the following recommendations are appropriate for drafting claims, and that the absence of the recommended features may provide bases for challenging patents that have not been drafted with the *Myriad* issues in mind.

When appropriate in drafting claims directed to DNA-based compositions:

1. consider including cDNA claims;
2. consider including labeled DNA claims;
3. consider including claims directed to limited-length sequences and short sequences (claims "comprising" a sequence, or including "at least" a sequence or stated number of nucleotides of a sequence leave the length of the sequence effectively unlimited);
4. consider including claims reciting a new functionality of the composition that is not possessed by naturally occurring products; and
5. consider including claims that recite additional components that contribute to a new functionality of the subject composition that is not possessed by naturally occurring products (e.g., in composition and/or kit format).

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When appropriate in drafting claims directed to diagnostic methods:

1. include affirmative manipulative steps in the claims; and

2. consider including machine-implementation steps in the claims.

Of course, the specification should also be drafted to support such claims (or may be challenged for failing to include such support).

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