

GENE PATENTS SURVIVE IN THE U.S....FOR NOW

The mid-summer ruling by the Federal Circuit Court of Appeals in *Association for Molecular Pathology, et al. v. United States Patent and Trademark Office, et al.* ("Myriad Genetics") has helped calm some of the ripples in the biotech industry created by the District Court ruling the prior year. In a split decision (2-1), the appellate court panel determined that isolated genes were not "products of nature" and thus could be patented. However, the majority of the method claims directed to ways to use genes were rejected.

The rock was first tossed into the biotech pond in March 2010, when the District Court issued a 156-page opinion holding that the purification of a natural product (in this case, human BRCA1 and BRCA2 genes), without more, could not transform it into patentable subject matter. He relied on U.S. Supreme Court precedent, including the often-cited case of *Diamond v. Chakrabarty*, to determine that the appropriate test was whether the invention had "markedly different characteristics" from the natural product (i.e., had a new or distinctive form, quality or property). The court then examined the isolated DNA for the BRCA1 and BRCA2 genes as claimed in the patents, and held that it was unpatentable as it was not markedly different from native DNA as it exists in the human body.

The suit had been brought by the American Civil Liberties Union (ACLU) and the Public Patent Foundation, a not-for-profit organization, on behalf of numerous medical professionals and others in the United States District Court for the Southern District of New York. They asserted that several patents on two human genes associated with breast and ovarian cancer (BRCA1 and BRCA2) are unconstitutional and invalid. Plaintiffs included medical professionals, patients, and an assortment of healthcare organizations, including the Association for Molecular Pathology, the American College of Medical Genetics, the American Society for

Clinical Pathology, the College of American Pathologists, Breast Cancer Action, and the Boston Women's Health Book Collective. Defendants include Myriad Genetics and the University of Utah Research Foundation (UURF), who exclusively license or own the patents in question, and the United States Patent and Trademark Office itself. The circumstances indicated that this was a case that the plaintiffs intend to pursue as an attack on gene patents in general.

THE BRCA PATENTS

The plaintiffs chose a sympathetic vehicle to challenge the patentability of human genes. More than 40,000 women a year die from breast cancer in the United States, and about 1 in 8 women here will develop it at some point. Mutations in the BRCA1 and BRCA2 genes are associated with an increased risk of breast cancer, as well as ovarian cancer. Myriad Genetics owns the patents, and is the only laboratory in the United States where diagnostic testing can be performed. The patents prevent others from testing these genes or developing alternative tests, which makes it impossible for women to use other tests or get an outside second opinion about test results. Moreover, the tests are expensive—Myriad charges a relatively high rate (overly \$3000) for the tests, which place them out of the reach of many.

The plaintiffs included a number of very sympathetic individuals, including patients and medical professionals. Based upon court pleadings, one patient was unable to get a second opinion on her test, while another could not get coverage of the test by Medicaid. Another patient submitted a blood sample to Myriad that her insurance informed her it would pay for, but Myriad allegedly would not accept that particular insurance coverage.

The suit attacks both the patentability of human genetic sequences, and at least some form of diagnostic method claims. With regard to the first, it asserts that the BRCA1 and

BRCA2 genes, and their naturally-occurring mutations, are natural phenomena, products of nature, and manifestations of laws of nature, and thus are not patentable subject matter under 35 USC § 101. With regard to the second, it asserts that claims for any method of looking for naturally-occurring mutations in human genes that does not specify any particular method of analysis is invalid due to indefiniteness under 35 USC § 101, as well as being directed to an unpatentable abstract mental process.

STANDING

One of the initial hurdles was the procedural question of standing. None of the plaintiffs had themselves been sued for infringement by Myriad, although several asserted that they have received “cease-and-desist” letters and have a reasonable fear of being sued. The case is a declaratory judgment action, and thus at least one plaintiff must meet the constitutional requirement of “standing.”

In fact, the defendants initially had moved to dismiss all of the claims for lack of standing, but the District Court denied the request, finding that there was standing. The issue was raised again on appeal, and the appellate panel affirmed that there was at least one plaintiff that did have standing. While the question most likely will continue to remain an issue as the case continues the appellate process, it is secondary to the primary issue of patentability.

PATENTABILITY OF ISOLATED GENES

There is no question that isolated human genes fall within the broad category of patentable subject matter as "composition of matter." The issue is whether they fall within the judicially-created exception that excludes "products of nature" from patent-eligibility.

As a first step, the appellate panel agreed with the lower court's determination that the U.S. Supreme Court's decision in *Diamond v. Chakrabarty* established the proper framework. In *Chakrabarty*, the Court had determined that genetically-engineered bacteria modified to break down crude oil were patentable subject matter because the patent claims were directed to "a non-naturally occurring manufacture or composition of matter—a product of human ingenuity 'having a distinctive name, character [and] use.'" More specifically, the key is whether the patent claims cover something that human intervention has given "markedly different" or "distinctive" characteristics.

Applying this test, the appellate panel held that the isolated DNAs were patentable because isolated DNAs were "markedly different" from native DNAs in the human body. Isolated DNA is not simply purified DNA. Instead, human intervention in cleaving or synthesizing a portion of the native DNA imparts on the resulting isolated DNA a distinctive chemical identity. In nature, DNAs are covalently bonded to other materials (the covalent bond is the defining boundary between one molecule and another). When cleaved, an isolated DNA molecule is now a distinct chemical entity. Similarly, complementary DNA sequences (cDNA) also are patentable, as they are even more markedly different from native DNA.

The nomenclature used may be of importance, as prior cases had referred to unpatentable natural substances being merely "purified" or "isolated." The appellate panel clearly distinguished between "isolated" DNA and "purified" DNA. Purification, the court said, makes pure what was the same material, but was previously impure. A natural substance is not purified by being isolated. On the conceptual spectrum of manipulation for determining patentability, then, isolating a substance falls further toward the patentability end than purification. Of course, this should depend on what "isolating a substance" actually requires in the way of manipulation.

For DNA, isolation requires cleaving the covalent bond, thereby creating a distinct chemical entity (in the eyes of the appellate panel, at least).

A possible concern was the panel's apparent deference to PTO policy. It observed that the PTO had issued gene patents for almost thirty years, and stated that if gene patents should be excluded from the broad scope of Section 101 patentable subject matter "contrary to the settled expectation of the inventing community, the decision must come not from the courts, but from Congress." Interpreted broadly, this appears to give the PTO law-making authority that it does not possess, and may be a weak point on further appeal.

Interestingly, the US federal government had filed a brief that went against the long-standing PTO policy cited by the Court. The government had argued instead for application of a "magic microscope" test. That is, if an imaginary microscope could focus in on and observe the claimed DNA molecule as it exists in nature (i.e., in the human body), then the claim would be unpatentable. The government, in fact, argued on this basis that the claimed isolated BRCA1 and BRCA2 sequences were not patent eligible, as they exist in the human body. The appellate panel rejected this argument.

METHOD CLAIMS NOT PATENTABLE

The challenged method claims did not fare as well as well as the isolated DNA claims. The appellate court upheld the District Court's finding that five of the six challenged claims did not meet the current "machine-or-transformation" test applied to method claims in the U.S. The machine-or-transformation test requires a claimed process or method to be tied to a particular machine or apparatus, or transform a particular article into a different state or thing. There were several variations of method claims (including, for example, a claim directed towards comparing

two gene sequences to see if any differences exist). The appellate court held that the Myriad patent claims were directed to "abstract mental processes" and did not described a specific method of transforming material.

The method claim that did survive was a method for screening potential cancer therapeutics via changes in cell growth rates. The appellate panel found that the claim included a transformative step in "growing" host cells transformed with an altered BRCA1 gene, as well as a step involving physical manipulation of the cells. These steps were central to the purpose of the claimed process, and thus the machine-or-transformation test was satisfied.

NEXT ROUND

There has been an inordinate amount of attention paid to the decisions, and there undoubtedly will continue to be until there is a final resolution. The request for rehearing by the panel was rejected, and there was no rehearing *en banc*. The plaintiffs have stated that they will seek review by SCOTUS, and as the justices have shown some desire to hear Section 101 patentability issues in the past (and in the current term), there is a good chance of certiorari being granted. As there does not appear to be much dispute about the applicability of the *Chakrabarty* test, the focus is apt to be very technical: i.e., are isolated DNA fragments truly "markedly different" from native DNA?

It should be kept in mind that only *some* of the claims in the Myriad patents were challenged and thus potentially at risk. Claims directed to a kit for detecting mutations in the BRCA1 gene, for example, were unchallenged. Thus, even if all of the challenged claims are rejected on further appeal, the Myriad patents themselves will survive, albeit with a few holes

where certain claims used to be. It also should be kept in mind that the oldest of the Myriad patents begin expiring in a couple of years, possibly even before this case is finally resolved.

So, what's a biotech company supposed to do in the meantime? Patents will still need to be filed and prosecuted. And the delay in obtaining a patent is so long already, no one would want to put their patent program on hold, even if they could.

The best approach is to assume that the "markedly different" characteristic test will continue to apply. Applicants will still be able to get patents directed to genetic material, but would have to show that their claimed invention had "markedly different characteristics" from native DNA. Thus, any patent application of this sort should include some claims that at least arguably cross over the "markedly different" characteristics line. Broader "pre-Myriad" claims should be included, of course, to maximize possible protection should the line between patentable and unpatentable subject matter ultimately be drawn closer to the natural product. But this approach increases the likelihood that at least some of the claims in a resulting patent would survive a subject matter challenge.

Flexibility is key. If a final determination is made during the pendency of the application, claims may be amended or canceled as appropriate. If a patent has already issued, at least some of the claims would pass challenge. Alternatively, reissue may be an option. And continuation practice is recommended. Continuation practice not only allows a patent owner to respond to changes in the market, it allows the owner to respond to changes or modifications in the law, such as has been seen in *In re Bilski* and are likely to be seen on appeal in *Myriad Genetics*.

DISCUSSION TOPICS:

1. Should human genes, or parts thereof, be patentable as a matter of law? Of policy?
2. Did the Federal Circuit use the right test ("markedly different characteristics")? Is there another test that should be applied?
3. Did the Federal Circuit apply the markedly different characteristics test correctly? Is there a distinct line of patentability along the continuum between *Chakrabarty* and true products of nature?
4. Is there any real difference between "purified" and "isolated"? If so, is it enough to make something patentable subject matter?
5. Should the Federal Circuit have avoided all of the above issues by finding lack of standing? Is there standing, in fact?
6. Did the Federal Circuit get it right in rejecting the method claims it did?
7. What do you think the Supreme Court will do?