Prometheus Patents Struck Down, 9-0: *Mayo Collaborative Services v. Prometheus Laboratories, Inc.* Analysis

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In a strong rebuke to the Federal Circuit, a unanimous U.S. Supreme Court held (pdf), on March 20, 2012, that Prometheus Laboratories' claims to methods of administering drugs to treat gastrointestinal autoimmune diseases do not meet the patentable subject matter standard of section 101 of the Patent Act. The representative claim quoted by the Court recites, "A method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder" comprising two steps: (a) administering one of a class of drugs (thiopurines) and (b) determining the level of a specified metabolite, "wherein" a level below a given threshold "indicates a need to increase the amount of said drug subsequently administered" [to improve efficacy], and a level above the threshold "indicates a need to decrease the amount of said drug subsequently administered" [to avoid toxicity].

History of the Case. Mayo originally bought and used Prometheus test kits that employed the patented method, but it then decided to sell and market its own test, which was similar, but not identical. Prometheus sued for patent infringement. The district court found that Mayo's test would infringe the Prometheus patents, but it then held the patents invalid as essentially claiming unpatentable laws of nature–in this case, the relationship between the levels of the specified metabolite and the efficacy or toxicity of the relevant drugs.

The Federal Circuit reversed this decision in 2009, finding that the claims satisfied its then-controlling machine-or-transformation test. Both the administering and determining stages, the court held, brought about a transformation of the patient's body. In the summer of 2010, while a *Prometheus* cert. petition (a request for Supreme Court review) was pending, the Supreme Court decided Bilski v. Kappos, a case involving a patent on a method of commodities hedging. In a set of murky opinions, the Court held that the machine-or-transformation test was not the exclusive test of subject matter eligibility for method claims, but that it could be helpful in appropriate cases. Immediately thereafter, the Court ordered the Federal Circuit to reconsider its *Prometheus* opinion in light of Bilski. In an opinion that might be described as perfunctory, the Federal Circuit held once more that the Prometheus patents comprised statutory subject matter, and the Supreme Court granted *cert*.

The Supreme Court's Reasoning. The Court's opinion (pdf) focuses on the difference between claims to laws of nature themselves and claims to specific applications of such laws: the former fail the section 101 subject matter test, while the latter pass. The laws of nature involved here are the "relationships between concentrations of certain metabolites in the blood and the likelihood that a dosage of a thiopurine drug will prove ineffective or cause harm." The legal question then becomes, "do the patent claims add *enough* to their statements of the correlations to allow the processes they describe to qualify as patent-eligible processes that *apply* natural laws?" For all nine members of the Court, the answer was a clear no.

The Court's analysis of the claims went through four steps. First, it observed, the administering step just defines "the relevant audience"—doctors who treat patients with thiouprine drugs. Second, "the 'wherein' clauses simply tell a doctor about the relevant natural laws." Third, the determining step does not specify any particular process, but merely invites doctors "to engage in well understood, routine, conventional activity.' And fourth, "to consider the three steps as an ordered combination adds nothing to the laws of nature that is not already present when the steps are considered separately." In sum, "the three steps simply tell doctors to gather data from which they may draw an inference in light of the correlation." They "are not sufficient to transform unpatentable natural correlations into patentable applications of those regularities." To allow such a patent could "inhibit further discovery by improperly tying up the future use of laws of nature."

What Do We Learn? The first point is that section 101 is alive and well as the first test of patentability. Some recent Federal Circuit opinions have suggested that section 101 can and should be avoided in most cases, leaving the work of evaluating patents to sections 102 (novelty), 103 (nonobviousness), and 112 (written description). The Court explicitly rejects that approach, refusing to let section 101, with its law of nature prohibition, become "a dead letter." So the Patent Office and the courts will continue to have to make an initial determination of whether an invention comprises statutory subject matter, independent of whether it satisfies the other criteria of patentability. Nonetheless, the language quoted above about "well understood, routine, conventional activity" suggests that novelty and obviousness have some relevance to subject matter eligibility, despite loud protests that this conflates section 101 with issues presumably assigned to 102 and 103.

Second, although this opinion is light years ahead of *Bilski* in terms of clarity, it is still hard to be absolutely certain of what the subject matter test for method patents is. We know—from the last paragraph of the opinion—that patents that "effectively claim the underlying laws of nature themselves" are invalid. Another version of this is that a survivable claim must "differ significantly from a claim that just said 'apply the algorithm.'" But just how to identify such a claim is a more difficult issue. We know that a claim structured just like Prometheus's is invalid: that is, a claim that involves nothing more than gathering data that may provoke an inference based on a law of nature (for example, maybe, the claims upheld by the Federal Circuit on August 31, 2011 in *Classen Immunotherapies, Inc. v. Biogen IDEC*?). Some additional *application* of the law of nature is required—but how much?

The Court rejects "simply appending conventional steps, specified at high level of generality, to laws of nature." It expresses particular concern about claims so broad as to "seek pre-empt the use" of the law of nature. But it gives little affirmative guidance about how specific the application of the law must be, declining to speculate on precisely what additional limitations might have saved the Prometheus claims before it.

Impact on *Myriad*? There have already been a lot of questions raised about the impact of *Prometheus* on the *Myriad* litigation, in which a cert petition is still pending in the Supreme Court. Does this new decision make it more or less likely that the Court will take *Myriad?* Does it suggest a likely outcome if the Court does take it?

Before speculating about these questions, it is important to remember that the Federal Circuit decision in Myriad addressed three separate sets of patent claims: (1) the court upheld (with a partial dissent) Myriad's *product* claims on cDNA and isolated DNA; (2) the court also upheld Myriad's claims to *methods* of screening potential cancer therapeutics by analyzing growth rates of cells with altered BRCA genes in the presence or absence of the treatments; but (3) the court rejected Myriad's claims to *methods* of analyzing BRCA gene sequences and comparing those with cancer-predisposing mutations to normal sequences. The cert petitions filed by both sides do not address the methods claims (only the product claims and the highly technical standing issue), but the Supreme Court could order briefing and argument on any aspect of the case.

The *Prometheus* decision says nothing about gene product claims, so is irrelevant to issue (1) in *Myriad.* But it says a lot, obviously, about method claims that bear at least some structural similarity to those in *Prometheus*. So does *Prometheus* indicate that the Court is more or less likely to review those method claims? (Warning: anyone who claims to have inside information about pending Supreme Court decisions is lying—Court security makes the old KGB look like a sieve.) Our guess (and it's little more than that) is that the issuance of *Prometheus* makes it *less* likely that the Court would review the *Myriad* method claims. It has just issued a unanimous and—by the standards of Supreme Court patent cases—relatively clear opinion on generally similar medical methods. History suggests that is unlikely to want to revisit that topic the very next year. *Prometheus* itself is an obvious exception, of course, coming right after *Bilski.* But the Court may have realized how unhelpful its fractured *Bilski* opinion was, and all of the justices apparently believed that the Federal Circuit had either failed to understand it or chosen to ignore it. And the history of *Prometheus* suggests a possible pathway for *Myriad:* that the Supreme Court would grant cert, but (with respect to the method claims) for the limited purpose of vacating the Federal Circuit's opinion and ordering reconsideration in light of *Prometheus.*

But if the Court does decide to review *Myriad* (or if the Federal Circuit is ordered to do it over), does *Prometheus* help us to predict the outcome? The method claims that the Federal Circuit rejected ((3) above) are hard to distinguish from those in *Prometheus*: doctors gather information and make a straightforward comparison, using basic genetic knowledge. Those claims are likely to be rejected once again. The drug-screening claims that were upheld ((2) above) are a closer call. If the "algorithm" is the protocol for comparing the effects of treating or not treating cell lines, then "do the patent claims add *enough* to their statements of the correlations [or algorithm] to allow the processes they describe to qualify as patent-eligible processes that *apply* natural laws?" There is a good bit of practical application going on here: cell lines must be grown and drugs applied (or not) before a judgment is made. It *looks* more like a real-world pharmaceutical process than a broad statement of an algorithm. For that reason, it seems more likely than not that this category of method claims would be upheld once again under section 101.

Conclusion. We now know considerably more about the Supreme Court's views on methods than we did after the worse-than-useless *Bilski* opinion. It is refreshing to these observers that the Court dove right back into method patents in an apparent effort to rectify the damage it did in *Bilski* (and there's also some entertainment value in the revival of the Supreme Court-Federal Circuit tension that seemed to have abated a bit). But it also seems unlikely that the Court would go back to the method issue immediately, so we doubt that it will take that part of *Myriad,* except for the limited purpose of remanding to the Federal Circuit for reconsideration.

In terms of impact on the marketplace, there is, of course, serious impact if your business model depends on patents just like these (e.g., if you are Dr. Classen). But for others, both in biotechnology and IT, the effect should be minimal. Admittedly, the mere changing of the test from one that was formerly more inclusive to one that narrows eligibility is potentially destabilizing–under the former machine-or-transformation test, "administering" and "determining" steps were generally transformative and therefore corresponded with patent eligibility. But the key word is *potentially*, since the Prometheus patents already reflected an extreme stretching of section 101's limits, and were also—as the Federal Circuit pointed out in its 2009 opinion—highly suspect under sections 102 and 103.