Bloomberg Law Reports® Intellectual Property

Do Patents to Diagnostic, Theranostic, and Therapeutic Methods Pre-empt Nature?

Sarah A. Kagan, Banner & Witcoff, Ltd.

Ever since the U.S. Supreme Court granted and subsequently dismissed the writ of *certiorari* in *Laboratory Corp. of America Holdings v. Metabolite Laboratories, Inc.*,[1] those who depend on the patentability of clinical diagnostic methods have been waiting for the other shoe to drop. The provocative dissent to the dismissal by Justice Breyer has sown uncertainty in the diagnostics industry. However, the Supreme Court has not yet properly considered the question of subject matter patentability of clinical diagnostic methods.[2]

Subject matter patentability as an issue is now percolating up from the U.S. Court of Appeals for the Federal Circuit to the Supreme Court for resolution in one or more cases. *Prometheus Laboratories, Inc. v Mayo Collaborative Services*,[3] was recently decided by the Federal Circuit. The Federal Circuit's *Prometheus* decision relied heavily on its own prior decision in *In re Bilski*.[4]

The Supreme Court held oral arguments in the *Bilski* case, a dispute regarding subject matter patentability of a business method, on November 9, 2009. Mayo Collaborative Services petitioned the Supreme Court on October 26 to consider the subject matter patentability of diagnostic claims in *Prometheus v. Mayo*. The Supreme Court's decision in *Bilski* may directly affect diagnostic, therapeutic, and theranostic claims, obviating any need to grant *certiorari* in *Prometheus*. Alternatively, the Supreme Court may decide to hear both cases, providing even more attention and clarity to this important issue.

The Holding in Prometheus

In its October 2008 *Bilski* decision, the Federal Circuit held that a claimed process is patent eligible subject matter if "(1) it is tied to a particular machine or apparatus, or (2) it transforms a particular article into a different state or thing."[5] Whether the *Bilski* test, forged in the area of business methods, would endorse or ban medical methods, however, was unclear. The Federal Circuit has now applied the machine-or-transformation test to medical treatment and theranostic claims in *Prometheus*, and the biotechnology and pharmaceutical industries collectively exhaled. In just under a year, the Federal Circuit has applied the *Bilski* test to this distinct technological area, showing the test to be more flexible than it may have seemed.

The Federal Circuit panel held that both the Prometheus claims to methods of treating patients with drugs and the Prometheus claims to methods of analyzing a clinical sample qualified as patent-eligible subject matter under 35 U.S.C. § 101

using the machine-or-transformation test.[6] Both types of claims were found to comply with the transformation prong of the test.

Technological area of the Prometheus claims

One claim of Prometheus, in abstracted form, is directed to:

A method of treating, comprising:

a.) administering one of a certain class of drugs to a subject that has one of a certain class of disorders; and
b.) measuring a certain metabolite of the drug in the subject.

The claim recites that the measured amount of the metabolite can be used in an algorithm with which one can decide whether to modulate the dose of drug administered subsequently.[7] Another claim that the panel considered omitted step (a) but retained step (b) and retained the description of the algorithm for modulating dose.[8]

The Federal Circuit described both types of claims as therapeutic methods, even the claim which omits the step of administering drug, i.e., step (a) above. The claim without step (a) is perhaps more accurately described as a theranostic claim, as no treatment is required by the claimed method. The method helps decide how treatment should be given.

The *Prometheus* panel held that the mere recitation of an algorithm within the claims did not nullify the patentability of the claims, which must be considered as a whole. The panel referred to the algorithm as a mental step; however careful parsing of the claim language reveals that the claim requires performance of no mental steps.[9] The claim does not require that any calculation, decision, or modulation be performed.

The *Prometheus* panel broadly stated that methods of treatment "are always transformative when a defined group of drugs is administered to the body to ameliorate the effects of an undesired condition."[10] The panel described both the chemical conversion of drug to active metabolite, as well as the overall effect of drug on the subject as transformations.[11] Step (b) for performing a clinical assay was also deemed to qualify as a transformation, despite the fact that no particular assay is required. The panel concluded that the amount of the metabolite had to be determined by more than mere inspection, and thus, a transformation must be involved.

Finally, the *Prometheus* panel dismissed as irrelevant special exceptions to patentability that are invoked when a claim recites an algorithm. One special exception excludes a claim from patentability if the non-algorithm steps are considered to be mere data gathering for the algorithm itself. Another special exception excludes a claim from patentability if the non-algorithm steps are considered "insignificant, extra-solution activity." The assessment of both of these

exceptions requires a weighing of the "integral involvement" of the non-algorithm steps in the method as a whole. The *Prometheus* panel deemed the steps to be integral to the method as a whole, but provided no standards or guideposts for making such an assessment.

Yet another special exception excludes from patentability claims that wholly pre-empt use of an algorithm or a natural process. The *Prometheus* panel hastily concluded that this exception did not apply, and urged that "because the claims meet the machine-or-transformation test, they do not pre-empt a fundamental principle."[12] Thus, the *Prometheus* panel has essentially eliminated pre-emption as a special exception by subsuming it under the machine-or-transformation test.

Prior cases relied upon in Prometheus

Prometheus applied the holding in *Bilski*. *In re Bilski* arose from a Patent Office rejection of claims to a method of doing business. *Bilski* generated a huge amount of interest; a total of thirty-nine amicus curiae briefs were submitted to the Federal Circuit. Despite the particular subject matter of Bilski's claims, a method of managing risk in a commodity market, the amici included pharmaceutical giant Eli Lily and Company and trade association the Biotechnology Industry Organization, signaling the impact that the case could exert on the biotechnology and pharmaceutical sectors.[13]

The Federal Circuit sua sponte reviewed *Bilski* en banc. It was so controversial that the Federal Circuit judges issued five separate opinions (a majority, a concurring, and three dissenting opinions). The majority framed the question as whether Bilski was claiming a patent-eligible process or was merely claiming a patent-ineligible, fundamental principle or mental process. The Supreme Court had previously excluded the latter two categories from patentable processes. The majority opinion in *Bilski* relied on the Supreme Court's "machine-or-transformation" test as a definitive test for what is surely patent-eligible under 35 U.S.C. § 101: a process is patentable if it is tied to a particular machine or apparatus *or* if it transforms a particular article to a different state or thing.

The *Bilski* majority appeared to endorse the machine-or-transformation test as the only test for determining patent eligibility of processes. Even though the *Bilski* majority applied the test to business methods, it left the area of diagnostic, theranostic, and therapeutic processes largely unexplained.

The *Prometheus* panel traced the development of the machine-or-transformation test from *Benson*[14] (1972) through *Diehr*[15] (1981) to *Abele*[16] (1982) and *Grams*[17] (1989). Benson tried to obtain patent protection for a method of converting signals from binary-coded decimal form to pure binary form useful for programming computers. The Court characterized the method as a pure algorithm, a generalized formulation from which specific applications can be developed. The method could be performed with or without a computer. The Benson claims were found patent-ineligible; they were found to fail the machine-or-transformation test.

The *Diehr* Court dealt with a computer-controlled method for curing rubber which employed a mathematical formula. The Court found the curing of rubber to be transformative. The Court proscribed dissection of the claims for analysis. Rather, it held that the claims as a whole must be considered. It further proscribed intermingling of the analyses for novelty and subject matter eligibility. Despite the positive outcome for the patentee, the Court expressed wariness of patent draftsmen who might evade the prohibition against patenting algorithms per se. They warned that limiting use of a formula to a particular technological environment or adding insignificant post-solution activity were not sufficient to make an algorithm patent eligible.

Abele claimed a method of performing computerized axial tomography (CAT) scans which used a formula to produce an image. The Court grappled with the relationship of the formula to the physical steps of the method. It held one independent claim to be unpatentable as directed solely to an algorithm. It held a dependent claim of that independent claim to be patentable. The dependent claim merely added a limitation on the type of data used in the method of the independent claim. The patentable, dependent claim did not recite any additional steps. Nonetheless, the Court viewed the method as a whole to be patentable, and did not view the dependent claim as merely limiting the unpatentable independent claim to a particular technological environment.

Grams presents the closest subject matter to Prometheus' claims. Grams' claim recited first performing a plurality of undefined clinical laboratory tests on an individual to produce a set of parameters. Second, Grams recites manipulating the parameters in a specified way. The court characterized the second part as an algorithm. The *Grams* panel held that the first step was mere data gathering for the algorithm.

Consistency of Prometheus *with precedent*

The *Prometheus* panel identified *Grams* as the closest case. *Grams* came to the opposite conclusion from *Prometheus*, finding the methods patent-ineligible because the recited clinical tests were not transformative, and thus the clinical tests were merely to gather data. The *Prometheus* panel found the Grams claims to be "readily distinguished" from the Prometheus claims.

But note the similarity between the claims. Claim 7 of Prometheus' U.S. Patent No. 6,680,302 requires one physical step ("determining the level of 6-thioguanine or 6-methylmercaptopurine in a subject administered a drug providing 6-thioguanine, said subject having said immune-mediated gastrointestinal disorders") followed by an algorithm using the determined level. Claim 1 of Grams' U.S. Serial No. 625,247 recites one physical step ("performing said plurality of clinical laboratory tests on the individual to measure the value of the set of parameters") followed by an algorithm which uses the set of parameters measured.

The claims seem to be very similar, indeed. But in *Grams*, the clinical-laboratory test was held to be non-transformative, whereas in *Prometheus*, the clinical laboratory

test was found to be transformative. The two recitations of physical steps seem only to differ in specificity. *Grams* encompasses *any* clinical laboratory tests and *Prometheus* only those that measure 6-TG or 6-MP. Neither step specifies a particular assay or type of assay. Neither recites a particular chemical or physical transformation or a particular apparatus.

Thus, facing extremely similar claims head-on and comparing them, two panels of the Federal Circuit came to divergent answers.

Appropriate standards for a 35 U.S.C. § 101 analysis

The courts considering subject matter patentability have tied themselves in analytic knots because they have strayed from a fundamental principle in patent law: the claims define the invention. Rather than analyzing the claims and permitting the claims to dominate the analysis, the courts have let other considerations trump the claims. As the panel stated in *In re Grams*:

> In all instances, this critical question must be answered: "What did applicants invent?" [*In re Abele*] at 907, 214 USPQ at 687. And in answering this inquiry:
>
> > [e]ach invention must be evaluated as claimed: yet semantogenic considerations preclude a determination based solely on words appearing in the claims. In the final analysis under §101, the claimed invention, as a whole, must be evaluated for what it is.
> >
> > Hence, the analysis requires careful interpretation of each claim in light of its supporting disclosure.[18]

The statement, while in some ways unremarkable ("invention as a whole," "claim in light of its supporting disclosure") also reflects a suspicion that claims can be misleading ("preclude a determination based solely on words appearing in the claims"). Such skepticism is articulated in *Diehr*: the special exceptions to patent-eligibility are necessary to prevent "a competent draftsman to evade the recognized limitations on the type of subject matter eligible for patent protection."[19]

This skepticism has permitted the courts to move away from the claims as defining the invention and to use an indefinite test or tests which is tantamount to a gut feeling. Allowing the courts to ask the question, "What did the applicant invent?" without relying on the words of the claims for the answer is a recipe for inconsistent results and unpredictability. Moreover, it invites the improper consideration of novelty and obviousness to be intermingled with the consideration of subject matter eligibility.

Which of the many tests for patent eligibility should be retained and which are unhelpful? While the exclusion from patenting of a phenomenon of nature or a

fundamental principle is deeply embedded in the case law, it should be assessed with reference to the claim only. One who discovers such a phenomenon or principle and is able to apply it to real-life problems by using it in otherwise patent-eligible processes should be granted protection. The naked phenomenon or principle, per se, may not be protectable, but an otherwise acceptable process should not lose patentability by employing a phenomenon or principle.

The "wholly pre-empt" exclusion is not helpful. If an inventor can frame a patent eligible process that employs an algorithm, even if the algorithm has no other uses, that should be of no moment. Breadth of a claim, if a problem, should be dealt with using other parts of the patent statute. Improper breadth should be attacked if it lacks adequate written description (35 U.S.C. § 112), lacks enablement for full scope of a claim (35 U.S.C. § 112), lacks novelty (35 U.S.C. § 102), or is obvious (35 U.S.C. § 103).

The exclusions for insignificant post-solution activity or data-gathering should be set aside. These exclusions invite characterizations of claims that are subjective and, therefore, unpredictable. What type of activity is significant or insignificant? Why is performance of some tests considered transformative while performance of others is "merely data-gathering?" These exclusions are unhelpful to the analysis and should be disavowed in favor of the much clearer machine-or-transformation test.

While precedential cases state that field-of-use limitations are not sufficient to rescue an unpatentable algorithm, this exclusion again invites characterization of an invention rather than analysis of a claim's recited process steps. This exclusion should be set aside in favor of an analysis of recited claim steps using the machine-or-transformation test.

Mental processes and abstract intellectual concepts are also a special exclusion to patentability. These exclusions do not add anything to the machine-or-transformation test. Any process that meets the machine-or-transformation test will not be an abstract intellectual concept. As such, these exclusions too, should be set aside.

The *Bilski* machine-or-transformation test may not be the exclusive test for subject matter patentability. But it may be strong enough to displace and subsume numerous special exceptions to patentable subject matter which have led to inconsistent results based on subjective or non-existent criteria.

Diagnostic, theranostic, and therapeutic methods do not pre-empt nature. Nature does not perform such methods on its own. All methods and processes performed by humans and machines function according to the laws of nature, including chemistry, mechanics, and physics. If the employment of nature is the test for patent ineligibility of processes, then the set of patentable processes will be the null set.

Sarah A. Kagan is a shareholder with Banner & Witcoff, Ltd. Ms. Kagan has trained and practiced with Banner & Witcoff for over 25 years. She specializes in molecular genetics and cancer. She previously worked in medical and agricultural molecular

biology. This article is for educational and informational purposes only and should not be construed in any way as legal advice. The opinions in this article are the author's alone and are not necessarily the opinions of Banner & Witcoff, Ltd., or any of its clients. Ms. Kagan can be reached at skagan@bannerwitcoff.com.

---

[1] *Laboratory Corp. of America Holdings v. Metabolite Laboratories, Inc.*, 548 U.S. 124, 126 S. Ct. 2921 (2006) (per curiam).

[2] Subject matter patentability or patent eligibility is considered under 35 U.S.C. § 101.

[3] *Prometheus Laboratories, Inc. v. Mayo Collaborative Services*, No. 08-01403, 2009 BL 197073 (Fed. Cir. Sept. 16, 2009).

[4] *In re Bilski*, 545 F.3d 943 (Fed. Cir. 2008) (en banc), *cert. granted*, 129 S. Ct. 2735 (U.S. June 1, 2009) (No. 08-00964).

[5] *Bilski*, 545 F.3d at 954.

[6] The panel did not determine whether the claims complied with the other requirements of the patent statute.

[7] U.S. Patent No. 6,680,302, cl. 1.

[8] U.S. Patent No. 6,680,302, cl. 7.

[9] The algorithm reads: "wherein the level of 6-thioguanine less than about 230 pmol per 8 x 10^8 red blood cells indicates a need to increase the amount of said drug subsequently administered to said subject, and wherein the level of 6-thioguanine greater than about 400 pmol per 8 x 10^8 red blood cells or a level of 6-methyl-mercaptopurine greater than about 7000 pmol per 8 x 10^8 red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject wherein said decrease reduces toxicity."

[10] *Prometheus Laboratories*, 2009 BL 197073, at 15.

[11] The *per se* patentability of a treatment method under U.S. law starkly contrasts with many other countries' blanket exclusion from patentability of methods of treating an animal or human body.

[12] *Prometheus Laboratories*, 2009 BL 197073, at 22.

[13] The Supreme Court has received additional biotechnology and pharmaceutical company amici briefs.

[14] *Gottschalk v. Benson*, 409 U.S. 63 (1972).

[15] *Diamond v. Diehr*, 450 U.S. 175 (1981).

[16] *In re Abele*, 684 F.2d 902 (C.C.P.A. 1982).

[17] *In re Grams*, 888 F.2d 835 (Fed. Cir. 1989).

[18] *Grams*, 888 F.2d at 839.

[19] *Diehr*, 450 U.S. at 192.