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Searching For Patent Drafting Pointers In Prometheus

Law360, New York (March 29, 2012, 1:49 PM ET) -- There is little doubt that the U.S. Supreme Court's recent decision in Mayo v. Prometheus will have an impact on the type and scope of claims that will be awarded by the U.S. Patent and Trademark Office (and upheld by the courts). Mayo Collaborative Servs. v. Prometheus Labs. Inc., 566 U.S. ___ (2012). While the full scope of the case's impact will likely take several years to play out in the courts, life sciences companies are left to consider how they can adapt their patent drafting strategies in order to protect inventions that involve "laws of nature."

What are some of the more encouraging statements made by the court? How might these be used to implement strategies that will maximize the likelihood of differentiating future claims from the claims that were invalidated in Prometheus?

Before tackling these questions, consider the facts of the case. The patents-in-suit (U.S. Patent Nos. 6,355,623 and 6,680,302) relate to methods of optimizing therapeutic efficacy and reducing toxicity when using thiopurine drugs to treat immune-mediated gastrointestinal disorders such as Crohn's disease. When ingested, the body metabolizes these drugs to produce metabolites in the bloodstream. Claim 1 of the '623 patent was used by the court to exemplify the patented methods and is concerned with optimizing therapeutic efficacy based on levels of the metabolite 6-thioguanine (6-TG):

> 1. A method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder, comprising: (a) administering a drug providing 6-thioguanine to a subject having said immune-mediated gastrointestinal disorder; and (b) determining the level of 6-thioguanine in said subject having said immune-mediated gastrointestinal disorder, wherein the level of 6-thioguanine less than about 230 pmol per 8x108 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 8x108 red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.

The court held that claims such as this one are not patentable under 35 U.S.C. §101 because they do not do enough to transform "unpatentable natural laws" (specifically "relationships between the concentration in the blood of certain thiopurine metabolites and the likelihood that the drug dosage will be ineffective or induce harmful side-effects") into "patent eligible applications of those laws". Mayo, slip op. at 3.

Did Prometheus Claim the Wrong Type of Invention?

Prometheus chose to claim its invention from a diagnostic perspective — the steps of the methods are all geared toward diagnosing whether a particular patient should receive a higher or lower dose of the drug by giving the drug to the patient, waiting for the patient's body to metabolize the drug, determining metabolite levels and using these levels to come up with a diagnosis.

In general, this particular type of diagnostic claim is always going to be harder to distinguish from the "natural laws" that underlie the diagnosis because the diagnosis is based on a result (metabolite levels) that is driven entirely by how the patient's body metabolizes the drug (a "natural law" according to the court). While the claimed methods involve steps of administering the drug to the patient and determining the metabolite levels, these were dismissed by the court as necessary but insignificant "pre-solution activity" that simply serves to observe the "natural laws" at work: "Anyone who wants to make use of these laws must first administer a thiopurine drug and measure the resulting metabolite concentrations.." Id. at 10.

Instead of claiming its invention from a diagnostic perspective, Prometheus could have claimed it from a therapeutic perspective. For example, the invention could have been presented as a method of treating a patient with a particular dose of drug that was optimized for that patient based on a prior diagnostic test. Another approach might have been to claim a method of treating a patient where the dose is lower or higher than a standard (prior art) dose and yet produces a level of metabolites within a desired range. While such therapeutic claims would need to consider joint and indirect infringement issues, they would have the advantage of applying the diagnostic information instead of simply gathering it.

The court makes it clear that merely adding the words "apply it" after "an unpatentable law of nature" will not transform it into a "patent-eligible application of such a law." However, the court also makes a point of recognizing that patents on "a new way of using an existing drug" are more likely to be patent eligible because they "confine their reach to particular applications of [natural laws]." Id. at 3 and 18.

Some may take the position that this statement was meant to cover traditional second medical use claims where the "new way" involves using an existing drug to treat a new disease. However, the statement seems broad enough to also encompass personalized medicine methods where an existing drug is used to treat an old disease in a "new way," e.g., using a different dose for a particular population as in Prometheus, treating a population that overexpresses a particular biomarker, etc.

Until this is fully tested, drafters should consider describing and claiming diagnostic inventions as both diagnostic and therapeutic methods.

Should the "Inventive Concept" Be Embraced?

One of the themes that runs throughout the court's decision is that patent eligible claims must include an "inventive concept" that goes beyond the natural law itself: "a process that focuses upon the use of a natural law [must] also contain other elements or a combination of elements, sometimes referred to as an 'inventive concept,' sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the natural law itself." Id. at 3 citing from Parker v. Flook, 437 U.S. 584, 594 (1978).

Thus, in finding that the Prometheus claims were not patent eligible, the court stated that, "the steps in the claimed processes (apart from the natural laws themselves) involved well-understood, routine, conventional activity previously engaged in by researchers in the field." Id. at 4. In contrast, the court noted that in Diehr (where the claims were held to be patent eligible), "[the court] nowhere suggested that all [the] steps, or at least the combination of those steps, were in context obvious, already in use, or purely conventional." Id. at 12 discussing Diamond v. Diehr, 450 U.S. 175, 177-179 (1981).

Similarly, in discussing Neilson (where the claims were also held to be patent eligible) the court noted that: "[T]he claimed process included not only a law of nature but also several unconventional steps (such as inserting the receptacle, applying heat to the receptacle externally, and blowing the air into the furnace) that confined the claims to a particular, useful application of the principle." Id. at 15 discussing Neilson v. Harford, Webster's Patent Cases 295, 371 (1841).

The court explicitly acknowledged that this approach to patent eligibility could sometimes lead to an overlap with criteria such as novelty: "We recognize that, in evaluating the significance of additional steps, the §101 patent-eligibility inquiry and, say, the §102 novelty inquiry might sometimes overlap." Id. at 21.

While this reliance on concepts of novelty and obviousness when assessing eligibility under §101 creates a confusing standard, it may provide another approach for differentiating future claims from the Prometheus claims.

Early in the opinion, the court makes a point of noting that at the time the Prometheus patents were filed it was already known in the art that levels of metabolites (including 6-TG which forms the basis for exemplary claim 1 of the '623 patent) were somehow correlated with the likelihood that a particular dosage of a thiopurine drug would be effective or toxic: "At the time the discoveries embodied in the patents were made, scientists already understood that the levels in a patient's blood of certain metabolites, including, in particular, 6-thioguanine and its nucleotides (6–TG) and 6-methyl-mercaptopurine (6–MMP), were correlated with the likelihood that a particular dosage of a thiopurine drug could cause harm or prove ineffective." Id. at 4.

This may be a significant fact because it allowed the court to characterize the "administering" and "determining" steps (i.e., the steps that went beyond the "natural law" itself) as steps that were "well-understood, routine, conventional activity already engaged in by the scientific community." Id. at 11.

In contrast to the Prometheus patents, many existing diagnostic method patents were filed at a time when a particular diagnostic marker was not already being assessed, or at least not in the claimed context. Will that make a difference, or will the courts treat any step of assessing a diagnostic marker as "insignificant pre-solution activity" irrespective of novelty? Will it make a difference if the claims involve assessing a panel of markers that have never been tested as a group? What if the methods employ an artificial algorithm to combine results generated by the panel?

These are hard questions to answer at this stage, but they identify the fact that the Prometheus claims were on the weaker end of the scale and can therefore potentially be distinguished. As long as the courts rely on concepts of "inventiveness" to analyze patent eligibility, drafters may want to consider including (and emphasizing) novel steps and novel combinations of steps in their methods. As discussed above, the novelty could result from the nature of the marker or markers but it could also result from the nature of the sample, the nature of the technique used to assess the marker, etc.

In certain situations it may also be beneficial to claim some of these features more narrowly than one might have done before the Prometheus decision. Indeed, some of the comments made by the court imply that the breadth of Prometheus' "determining" step was a factor in its decision: "the 'determining' step tells the doctor to determine the level of the relevant metabolites in the blood through whatever process the doctor or the laboratory wishes to use" and "the claim simply tells doctors to: (1) measure (somehow) the current level of the relevant metabolite." Id. at 10 and 13. See also: "The 'determining' step too is set forth in highly general language covering all processes that make use of the correlations after measuring metabolites, including later discovered processes that measure metabolite levels in new ways." Id. at 18.

Therefore, if the “inventive concept” results in part from the nature of the sample (e.g., the test works unexpectedly better with saliva samples than blood samples) or the nature of the technique used to assess the marker (e.g., protein detection is unexpectedly superior to nucleic acid detection) then these more specific aspects of the invention should be emphasized and claimed.

Finally, it is also worth noting that the Prometheus claims involved a relatively simple and direct correlation, especially when viewed in light of the prior art. Indeed, there is a direct link and therefore correlation between the two “variables” in the method (i.e., the drug dose and the level of metabolites that are produced by metabolizing the drug). In contrast, many diagnostic and prognostic methods involve correlations that are much less direct.

For example, a method of identifying a suitable therapeutic by measuring expression levels of a biomarker is likely to be much less obvious than a method of adjusting drug dose based on how extensively the drug is metabolized. While these differences may arguably relate to the “natural law” itself instead of its application they may well provide other ways of differentiating these types of claims from those in Prometheus and be another reason to embrace rather than reject the “inventive concept.”

Moving Forward

While the full impact of the Mayo v. Prometheus decision remains to be seen, there are clearly some new “useful clues” in the decision that could provide avenues for protecting inventions that involve “laws of nature.” Patent applicants should consider these carefully and try to incorporate them into drafting and claiming strategies going forward in order to maximize the likelihood of obtaining patent eligible claims.

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