

Biotech Roundup

By Crissa Cook

Think that biotechnology only applies to you if you are a scientist, researcher, or pharmaceutical company? Think again. Several current events in biotechnology will have ramifications beyond the biotech and even patent world.

The Written Description Requirement Could Be “No More”

This past spring, the Federal Circuit, in *Ariad Pharmaceuticals, Inc. v. Eli Lilly & Co.*, invalidated claims broadly reciting methods of repressing the activity of NF-kB, an important regulator of gene transcription. The Federal Circuit held that the disclosure was insufficient to “bear the weight of the vast scope of these generic claims.” In other words, the claims were invalidated based upon the written description requirement for being overly broad as compared to the specification, such that Ariad had not demonstrated “possession” of the invention at the time of filing.

Judge Linn, in his concurrence, criticized the majority for relying on written description to invalidate the claims and not addressing the important enablement issues in the case.^[1] He would have decided the case based upon the fact that Ariad had not enabled the full scope of its claims.

Ariad petitioned for, and was granted, an *en banc* rehearing of the case. In its *en banc* order, the Federal Circuit posed the following question:

Whether 35 U.S.C. § 112, first paragraph, contains a written description requirement separate from an enablement requirement, and if so, what the scope and purpose of that requirement is?

Oral arguments were heard December 7, 2009, and a decision is expected by next May. Thus, depending upon how the *en banc* court rules, written description may no longer be a separate requirement for patentability.

Numerous *amicus* briefs were filed in this case, some arguing that there is no separate written description requirement; and others arguing that written description should only be used to police new matter added to the claims after the original filing date, but not used to determine sufficiency of the disclosure. The latter argument may have some merit, since it seems that Ariad, at least in theory, had “possession” of the general concept recited in the claims at issue. However, the real problem was that it had not enabled the full scope of what it was purporting to claim. Thus, as Judge Linn advocated, the claims would still have been invalidated, but based on lack of enablement.

What *is* clear is that the court’s written description jurisprudence to date has created substantial ambiguity for patentees, especially in the biotech and chemical fields. Thus, regardless of how the Federal Circuit decides, this decision will hopefully provide clarification on the role of written description in assessing patentability, and will have a significant impact on the patent community.

Patentable Subject Matter - *Bilski* and Biotech at the Supreme Court

Mayo v. Prometheus: Medical Treatment and Diagnostic Claims

In *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, the Supreme Court will once again take up the issue of patentable subject matter. Aside from its ramifications for the patent world, many believe this case is important for the future of personalized healthcare, as it deals with medical treatment and diagnostic-type claims. In general these types of claims deal with administering a drug or assaying a metabolite, obtaining test results measuring some variable in the patient, and correlating those results with a diagnosis for further treatment. In theory, this should permit the physician to not only personalize the treatment for that particular patient, but also optimize the efficiency of that treatment, based upon the correlated results.

The representative claim is copied below:

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 8×10^8 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 8×10^8 red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.

The lower court found this claim invalid as being directed towards patent-ineligible subject matter. The Federal Circuit reversed after applying the “machine of transformation” test of *In re Bilski*. According to the Federal Circuit, “the administering and determining steps are part of a treatment protocol, and they are transformative.”

The Supreme Court granted *certiorari* this fall. Many expect this case to be decided in tandem with *Bilski*, which was also taken up by the Court and argued last month. One issue expected to be addressed is whether *Bilski*'s “machine of transformation” test is sufficient to deal with biotechnology, or whether a different standard for patentable subject matter needs to be applied. This case will also decide the fate of medical method and diagnostic-type claims, and whether such claims qualify as patentable subject matter altogether.

A similar case, *Laboratories Corp. of America Holdings v. Metabolite Laboratories, Inc.* (“*LabCorp*”), went up to the Supreme Court a few years ago, but was dismissed in 2006 as “improvidently granted.” The claim at issue was similar to the claim in *Prometheus* and involved assaying a body fluid and correlating the level of a metabolite with a specific medical condition. Three Justices (Breyer, Stevens, and Souter), who would have heard the case, dissented from the dismissal. The dissent made it clear they would have found the claim invalid as being directed towards unpatentable subject matter. Of course, Justice Souter has since retired, and it is unclear how Justice Sotomayor will rule on this issue in *Prometheus*.

There are some key differences between the *Prometheus* and *LabCorp* claims, and the Federal Circuit's opinion seemed to zero in on these differences when discussing the patentable aspects of the *Prometheus* claim.^[2] For example, unlike the claim in *LabCorp*, the *Prometheus* claim requires administering a drug, and according to the Federal Circuit, there is a transformation

after administration of a drug, including all of the various physical and chemical transformations of the drug inside the body. The human body itself also undergoes a transformation. The court stressed that the fact that the transformation relies on the natural processes of the body does not disqualify the administering step as patentable subject matter. The determining step was also deemed to be “transformative,” since it is necessary to first collect the patient samples and then modify the samples so that the metabolite levels can be measured using high pressure liquid chromatography or other detection methods. Finally, the Federal Circuit explained that the administering and determining steps are both central to the purpose of the method, and not “merely assaying or correlating,” as in *LabCorp*. Accordingly, under *Bilski*, the Federal Circuit concluded that the claims fell within the realm of patentable subject matter.

Generic Drugs and Legislation Prohibiting Reverse Payment Settlements

Under Hatch-Waxman,^[3] generic drug makers can obtain FDA approval for a generic drug by relying on the clinical trial data of the original brand name drug. Thus, generic drug makers can enter the market using an Abbreviated New Drug Application (ANDA) by showing among other things, bioequivalence of the generic product to the brand name product, and do not have to perform their own clinical trials to obtain FDA approval. Hatch-Waxman also includes an exemption from patent infringement, allowing generic drug makers to manufacture and test their drugs despite the existence of the brand name drug maker’s patent(s).

As part of filing an ANDA, the generic drug maker must file a certification that either there are no patent issues (i.e., that there is no patent, or that the patent has expired, or will expire), or that the patent is invalid or will not be infringed by the generic drug (termed a “paragraph IV” certification). Under the Act, the filing of a paragraph IV certification is, in and of itself, an act of infringement. Thus, the ultimate result of this process is generally litigation between the generic manufacturer and the patent owner.

Importantly, at the time of the paragraph IV certification, the generic drug maker will have made no infringing sales (because no FDA approval). Thus, the patent owner ends up being a plaintiff in a lawsuit from which it will receive no damages. As a result, many brand name companies involved in Hatch-Waxman litigation ultimately enter into settlement agreements with the generic drug makers, paying them to delay entry of the generic drug into the marketplace.

On one hand, settlement negotiations and agreements in general are favored in litigation and viewed as beneficial from a public policy standpoint. However, many consumer groups, academics, and even the Federal Trade Commission believe this practice with regard to Hatch-Waxman litigation to be inherently anticompetitive and have called for these types of reverse payment agreements to be considered presumptively illegal under the antitrust laws.

On October 15, 2009, the Senate Judiciary Committee voted to send to the Senate floor a bill prohibiting these “reverse payments” by brand name drug manufacturers to generic drug companies.^[4] The bill provides that reverse payment agreements “shall be presumed to have anticompetitive effects and be unlawful if” the generic drug company receives anything of value and agrees to limit or forgo “research, development, manufacturing, marketing, or sales” of the generic drug for “any period of time.” The bill further provides that this presumption can be overcome if the parties can demonstrate by clear and convincing evidence that the procompetitive benefits of the agreement outweigh the anticompetitive effects. The bill also vests enforcement of these provisions in the Federal Trade Commission. A vote is expected sometime next year.

Follow-On Biologics Legislation and Health Care Reform

Biologics are drugs isolated from natural sources and/or produced from biological processes and biotechnology methods.^[5] They are often the drugs responsible for cutting edge cancer treatments, etc. “Follow-on” biologics are like generic versions of the brand name biologic (i.e., the innovator). However, unlike conventional small molecule drugs, follow-on biologics are *similar* to, but not the *same* as “generic” versions of the innovator biologic. They are also not “manufactured” in the traditional sense of the term. Biologics, in general, are also much more complex and the existing generic drug approval pathway with the FDA is not appropriate for their approval.

As a result, legislation has been proposed by both the House and the Senate in an attempt to provide a regulatory pathway for follow-on biologics. However, the molecular complexity of biologics makes it nearly impossible to make a “generic” biologic drug without the initial data from the maker of the innovator biologic. Thus, access to this data is critical, and a key issue in this legislation has been the length of time the innovator company should be permitted to retain exclusive rights in its non-patent data. It seems that everyone from pharmaceutical companies and trade organizations to legislators and even *Time* magazine have weighed in on the length of the period of exclusivity.

After much debate, both the House and Senate Healthcare Reform bills contain provisions setting a 12-year non-patent data exclusivity period for brand name biologic drugs before follow-on biologics can enter the market. That is, the maker of a follow-on biologic cannot rely on the FDA’s prior approval of innovator biologics to support approval of their own products for a period of 12 years after the innovator biologic is approved. This is more than twice the period of exclusivity in non-patent data that traditional drug manufacturers enjoy under the current regulatory scheme.

The result for consumers if this provision makes it to law will be a much longer period before generic biologic drugs (and the cutting edge treatments they represent) are available to patients.

Crissa Cook is an associate at Hovey Williams. Crissa recently served as a panelist for “The Cutting Edge of Biotechnology Patent Law,” Biolaw 3.0: Law at the Frontiers of Biology, The University of Kansas Annual Biolaw Symposium, November 6, 2009. You can contact Crissa at ccook@hoveywilliams.com.

[1] i.e., That one “must describe the manner and process of making and using the invention so as to enable a person of skill in the art to making use the full scope of the invention without undue experimentation.” 35 U.S.C. 112

[2] Interestingly, the Federal Circuit made a point in *Prometheus* to stress that the *LabCorp* dissent was not controlling law.

[3] The 1984 Hatch-Waxman Amendments to the Food, Drug, and Cosmetic Act.

[4] S. 369 (2009). A similar bill (S. 316) was introduced back in January 2007, but did not reach the Senate floor.

[5] They are the drugs often responsible for cutting edge treatments for various conditions, such as cancers, for which no other treatments are available.