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U.S. Court Issues Broad Interpretation Of FDA-Related Safe Harbor

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In a 2-1 decision issued August 3, 2012 in *Momenta Pharmaceuticals, Inc. v. Amphastar Pharmaceuticals, Inc.*, the U.S. Court of Appeals for the Federal Circuit held that the safe harbor provisions of 35 USC § 271(e)(1) can shield the defendants from liability for patent infringement arising out of their use of patented methods to satisfy post-approval FDA testing requirements. The decision is in tension with the court's August 2011 decision in ***Classen Immunotherapies, Inc. v. Biogen Idec,*** where the court found that the safe harbor applies only to pre-approval activities. Although Judge Moore, writing for the majority in *Momenta*, attempts to distinguish *Classen*, Chief Judge Rader sees a clear conflict between the two decisions, which he explains in his dissenting opinion. A petition for certiorari in *Classen* is pending at the U.S. Supreme Court, and it is likely that the Supreme Court will have to resolve these conflicting views of the safe harbor.

The Products At Issue

The products at issue are generic versions of Lovenox®, which is used to treat and prevent blood clots. Lovenox® is obtained from a form of heparin obtained from porcine intestinal mucosa. As explained in the Federal Circuit opinion heparin is a heterogenous polymer, and heparin molecules "have considerable diversity in (1) the length of the polysaccharide chain and (2) in the component disaccharide units and the corresponding distribution of disaccharide unit sequences in the polysaccharide chains." The generic products ("enoxaparin") are synthetically prepared, low molecular weight versions of heparin.

The FDA Approval Process

In a separate proceeding, the manufacturer of Lovenox®, Aventis Pharmaceuticals, Inc., had argued that generic versions of enoxaparin should not be able to use the Abbreviated New Drug Application (ANDA) process because of the inherent heterogeneity of the products. The FDA disagreed, and identified five criteria that it would use to evaluate generic products. These "standards for identity" included "[e]quivalence in disaccharide building blocks, fragment mapping, and sequence of oligosaccharide species." According to the FDA, such equivalence could be proven by "exhaustive digestion of enoxaparin with purified heparin digesting enzymes (heparinases I, II, III) and nitrous acid, among other means, to yield the constituent disaccharide building blocks comprising enoxaparin," and separation, quantification, and identification of the disaccharides by a number of different techniques.

Amphastar was the first company to file an ANDA for a generic version of enoxaparin, but Momenta Pharmaceuticals, Inc. and Sandoz, Inc. (in collaboration) were the first to bring a product to market. When Amphastar's product was approved, Momenta commenced the patent infringement litigation at issue.

The Patent At Issue

The patent at issue is Momenta's U.S. Patent 7,575,886. As characterized in the Federal Circuit opinion, the '886 patent "relates 'to methods for analyzing heterogeneous populations of sulfated polysaccharides, e.g. heparin [and] . . . LMWH [e.g., enoxaparin.]"

Momenta alleged that Amphastar's manufacturing method included the method(s) claimed in the '886 patent. Indeed, Momenta asserted that "this infringing testing was necessary because the 'FDA requires a generic manufacture to include in its manufacturing process the analysis of each batch of its enoxaparin drug substance to confirm that . . . [it] includes a 1,6-anhydro ring structure.'"

The District Court Decision

At the district court, Momenta obtained a temporary restraining order and then a preliminary injunction to keep Amphastar's product off the market. In deciding in favor of Momenta, the district court rejected Amphastar's argument that its allegedly infringing activities fall under the safe harbor of 35 USC § 271(e)(1), which excludes from infringement activities that are "solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products."

The district court cited the Federal Circuit's August 2011 decision in ***Classen Immunotherapies, Inc. v. Biogen Idec***, and noted that "the alleged infringing activity involves the use of plaintiffs' patented quality control testing methods on each commercial batch of enoxaparin that will be sold after FDA approval." The district court acknowledged that "Amphastar's use of the patented method was for the purpose of developing information to submit to the FDA," but "concluded that the safe harbor does not apply" because the safe harbor "does not permit a generic manufacturer to continue in … otherwise infringing activity after obtaining … approval."

The Federal Circuit Decision

Amphastar appealed the preliminary injunction to the Federal Circuit, which stayed the preliminary injunction after hearing oral argument. The court's August 3, 2012 decision represents its "final decision on the merits of Amphastar's appeal."

In the opinion for the court, Judge Moore began the analysis with the plain language of the statute, and found no basis for limiting the reach of the safe harbor to "activities reasonably related to development of information submitted in an ANDA." Focusing on the broad language of the statute, Judge Moore wrote:

> Instead, the safe harbor applies "to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs or veterinary biological products." As long as the allegedly infringing use is "for uses reasonably related" to the development and submission of that information it is not an act of infringement, regardless of where that requirement resides in the law.

The opinion cites Supreme Court cases that also adopted an "expansive view" of the statute based on its plain language, including the 1990 Supreme Court decision in *Eli Lilly & Co. v. Medtronic, Inc.*, and the 2005 Supreme Court decision in *Merck KGaA v. Integra Lifesciences I, Ltd.*

Having addressed this threshold question, the court then considered whether Amphastar's activities could fall under the safe harbor, and found that they could.

> It is not disputed by the parties that these records are produced in order to develop and submit to the FDA proof that the Amphastar products comply with a Federal law. The fact that the FDA does not in most cases actually inspect the records does not change the fact that they are for the "development and submission of information under a Federal law." … Thus, we consider this information "submitted" for purposes of the statute.

The court characterized *Classen* as holding that "the scope of the safe harbor provision does not extend to 'information that may be routinely reported to the FDA, long after marketing approval has been obtained.'"

However, as Chief Judge Rader points out in his dissent, this narrow characterization of *Classen* conflicts with Judge Moore's own characterization of the *Classen* decision in her dissenting opinion in that case:

> The majority concludes that the district court incorrectly interpreted the safe harbor of § 271(e)(1) because, according to the majority, § 271(e)(1) is limited to pre-approval activities.

But now in *Momenta*, Judge Moore rejects such an interpretation of *Classen*:

> While Momenta urges us to adopt the pre-/post-approval distinction used by the district court, we cannot: *Classen* did not turn on this artificial distinction, and the plain language of the statute is not restricted to pre-approval activities.

Judge Moore summarizes the court's current interpretation of the safe harbor by quoting from the statute:

> We therefore hold that post-approval studies that are "reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs" fall within the scope of the § 271(e)(1) safe harbor.

The court rejected Momenta's argument that the safe harbor should not apply "because there are FDA endorsed non-infringing alternatives." The court explained:

> The safe harbor … does not mandate the use of a non-infringing alternative when one exists. … The safe harbor's protection is not limited to the dire situation where the patented invention is the only way to develop and submit the information. Instead, the safe harbor expressly allows the submitter the freedom to use an otherwise patented means to develop the necessary information demanded by the "Federal law." This makes good sense because it eliminates liability for infringement when that act of infringement is, in effect, required by the federal government as part of the continuing safety and efficacy monitoring of an approved drug. It also avoids the situation here, where a drug has received approval, but is nevertheless kept from the market based on an FDA mandated testing requirement.

Turning back to the preliminary injunction before it, the court note that "Momenta's admission that Amphastar's testing is carried out to 'satisfy the FDA's requirements,' … makes it unlikely that Momenta will succeed on the merits of its infringement claim." Because the other district court findings "were all, to some extent, predicated on its erroneous conclusion that Momenta's patent was likely infringed by Amphastar's product," the Federal Circuit vacated the preliminary injunction, and suggested that on remand the district court may be able to grant summary judgment of non-infringement in favor of Amphastar.

Chief Judge Rader's Dissent

Chief Judge Rader joined the majority opinion in *Classen* (which was authored by Judge Newman), so it is not surprising that he dissented from the decision in *Momenta*. What is somewhat surprising is that he took 29 pages to do so! Some of his main points include:

- Amphastar is freeloading on Momenta's invention:
  "Amphastar has not developed its own method, but instead delights in trespassing and refuses to pay a reasonable royalty to make the trespass lawful."
- Interpreting § 271(e)(1) in light of its legislative history is consistent with Supreme Court precedent (including *Eli Lilly & Co. v. Medtronic, Inc.*), and demonstrates that the safe harbor was intended to apply "only in limited situations, namely pre-approval experiments to obtain FDA approval."
- *Classen* indeed turned on a pre-/post-approval distinction; instead of issuing an inconsistent decision here, the issue should have been resolved *en banc*.
- The court's decision could eviscerate method of manufacturing patents in the pharmaceutical space.
- "Too often patent law is misunderstood as impeding more than promoting innovation." To the contrary, the patent system "encourages publication and sharing of research results." "Without this promise of exclusivity, researchers at corporations would be forced to turn to secrecy as the best protection for their inventions."

Will The U.S. Supreme Court Resolve This Dispute?

As noted above, a petition for certiorari is pending at the Supreme Court in *Classen*. This conflicting decision from the Federal Circuit may give the Supreme Court a further reason to take up the case for review, and once again interpret the difficult language of § 271(e)(1). If the *Momenta* interpretation stands, it may indeed undermine the value of research tool patents and method patents that are useful for satisfying post-approval FDA testing requirements, as Chief Judge Rader warns in his dissent.

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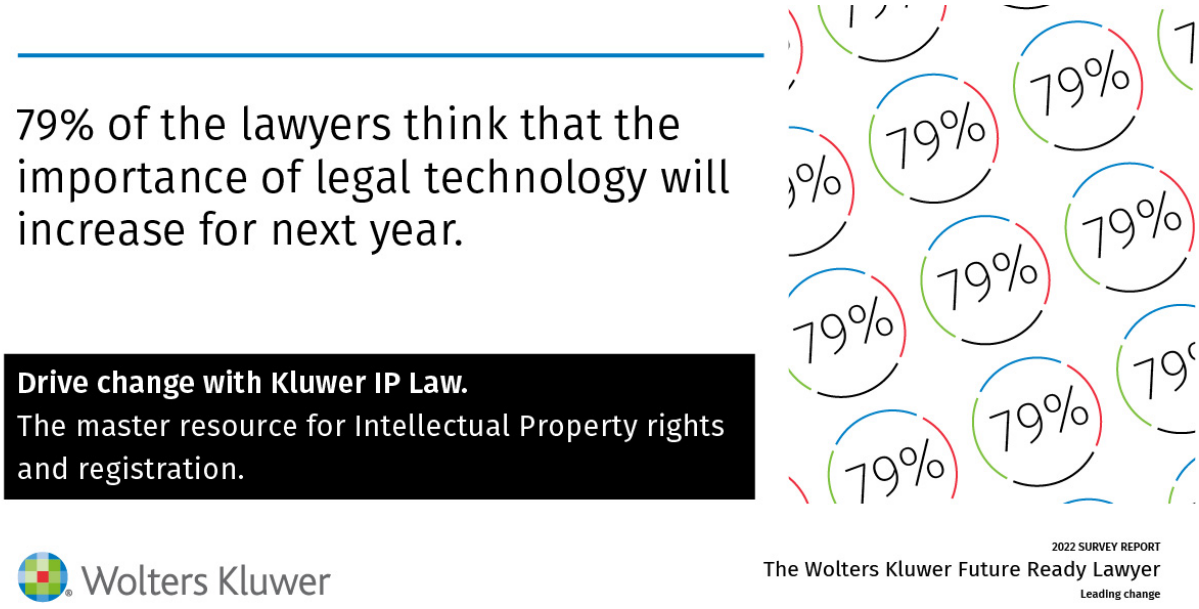

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