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THE SAFE HARBOR FOR FDA SUBMISSIONS EXPANDS: DID THE FEDERAL CIRCUIT REVERSE COURSE?

Section 271(e)(1) of the patent code, known as the "safe harbor" provision, immunizes from infringement suits various acts that are undertaken in order to submit information to the Food and Drug Administration ("FDA"). The scope of these various acts and thus of the safe harbor remains in flux. Last year, in *Classen*,[1] the Federal Circuit held that the safe-harbor clause does not shelter acts undertaken to gather "information that may be routinely reported to the FDA, long after marketing approval has been obtained." This August, however, the Federal Circuit held that Section 271(e)(1) *does* apply to post-approval "submissions that are required to maintain FDA approval." *Momenta Pharmaceuticals, Inc. v. Amphastar Pharmaceuticals, Inc.* Judge Moore, who had dissented in *Classen*, wrote the majority opinion in *Momenta*. Chief Judge Rader, who was part of the majority in *Classen*, wrote a fierce dissent in *Momenta*, arguing that the majority opinion conflicts with *Classen* and "will render worthless manufacturing test method patents."[2]

SAFE HARBOR FOR FDA SUBMISSIONS

Under the FDA safe-harbor clause:[3]

> It shall not be an act of infringement to make, use, ... or sell ... a patented invention ... 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.

Congress enacted this provision as part of the 1984 Hatch-Waxman Act. According to the Supreme Court, in enacting Section 271(e)(1), Congress was responding to case law[4] holding that the manufacture and use of a patented invention constituted an act of infringement, "even if it was for the sole purpose of conducting tests and developing information necessary to apply for regulatory approval."[5] The Federal Circuit expanded on this theme in 2008, writing that "[t]he basic idea behind this provision was to allow

competitors to begin the regulatory approval process while the patent was still in force, followed by market entry immediately upon patent expiration."[6]

Controversy arises over whether the safe harbor protects acts that go beyond those required for seeking regulatory approval for generic drugs. Appellate cases have therefore focused on whether Section 271(e)(1) shelters otherwise-infringing activity performed while testing a medical device to obtain premarket approval,[7] performing preclinical research on a drug for which no new drug application was ever filed,[8] selling machinery used in the development of regulatory submissions,[9] testing after submission of a Biologics License Application,[10] analyzing the effect of the scheduling of immunization,[11] and most recently in *Momenta*, testing the purity of commercial batches.

Knowing the outer limits of the safe harbor is important to manufacturers, since they have continuing regulatory obligations. These obligations include filing submissions to the FDA regarding changes or deviations from the approved manufacturing process, labeling changes, adverse events, and investigations of adverse events.[12] Manufacturers sometimes must also perform and report upon post-approval studies and clinical trials, or submit a risk evaluation and mitigation strategy.[13] A manufacturer may also want to supplement an NDA to obtain approval for additional indications. Furthermore, as became critical in *Momenta*, manufacturers must continually test their commercial batches to ensure that their products conform to approved specifications.[14]

THE *MOMENTA* DECISION

Both parties in *Momenta* are generic manufacturers of enoxaparin (the generic of Lovenox®, which is marketed by Sanofi-Aventis). Enoxaparin is a drug used to prevent and treat deep vein thrombosis. Plaintiff Momenta received FDA approval to market enoxaparin in July 2010 and thereafter obtained revenues of $260 million per quarter from sales of that drug. Slip. Op. at 6. Momenta also holds a patent that claims a method of testing the purity of a sample of enoxaparin. *Id.* Defendant Amphastar received FDA approval for its generic product on September 19, 2011. Momenta filed suit two days later, alleging that Amphastar infringed Momenta's patent, and that Amphastar has chosen to satisfy ongoing FDA testing regulations through an infringing method. The district court enjoined Amphastar from launching its product through a TRO issued on October 7, 2011 and a preliminary injunction issued on October 28. The Federal Circuit stayed the injunction on January 25, 2012, and vacated it in its recent opinion.

Judge Moore wrote the majority opinion, joined by Judge Dyk. The panel held that under the "plain language" of the safe-harbor clause, that statute "is not restricted to pre-approval activities." Slip. Op. at 19-20. "As long as the use of the patented invention is done to generate information that will be submitted pursuant to a relevant federal law, that use falls within the safe harbor." Slip Op. at 22. The majority held that Amphastar was not required to use a non-infringing testing method, whether or not such a method was available. Slip. Op. at 21. *Classen* was distinguished on the ground that Amphastar's submissions "are not 'routine submissions' to the FDA, but instead are submissions that are required to maintain FDA approval." Slip Op. at 18.

The majority also took an expansive view of when a document qualifies as a "submission" within the meaning of the safe-harbor clause. Testing results are not, in most instances, sent to the FDA. Rather, FDA regulations require manufacturers to maintain batch records that are subject to FDA inspection.[15] The majority held that using an invention to develop such records "satisfies the requirement that the uses be reasonably related to the development and submission of information to the FDA." Slip. Op. at 16. Furthermore, "the safe harbor is not limited to acts which only produce information for the FDA but protects *all* acts, even interim research steps and acts that might produce other useful data, as long as there is a reasonable basis for believing that the act will produce the types of information that are relevant to a submission to the FDA." Slip. Op. at 22 n.2.

THE *MOMENTA* DISSENT

Chief Judge Rader responded with a lengthy and sharply worded dissent. He relied heavily on the policy underlying Section 271(e)(1), as shown by its legislative history. (Chief Judge Rader is no doubt very familiar with that legislative

history, having served as counsel to Senator Hatch while the Hatch-Waxman Amendments were being debated.) In Chief Judge Rader's view, "§ 271(e)(1) won approval because it was limited in time, quantity, and type." Dissent Op. at 8. The safe-harbor clause "only applies to **pre-**marketing approval," "only applies to experimentation," and does "not apply to commercial sales." Dissent Op. at 8, 9, 10. The dissent argued that the distinction between pre-approval and post-approval uses was the core of the *Classen* decision; the majority's decision, applying the safe-harbor clause to post-approval conduct, "cannot be genuinely reconciled with *Classen* … [and] should instead request the entire court to resolve the issue *en banc*." Dissent Op. at 16.

The dissent notes that "Amphastar uses Momenta's patented method in the manufacture of each commercial batch it sells." Dissent Op. at 14. The dissent views such uses as being neither preapproval, nor limited, nor experimental. *Id.* In Chief Judge Rader's view, affording safe harbor to such uses "repeals the incentives and protections of the patent act in this area" and "does violence to patent law and future research incentives in this field." Dissent Op. at 17.

CONCLUSION

The debates in the *Classen* and *Momenta* opinions underscore a division regarding what policy underlies the safe-harbor clause. Is the clause's protection limited to efforts to gain marketing approval, or does the language of the statute indicate a broader purpose? *Momenta* is unlikely to be the last word on this issue. A petition for certiorari in the *Classen* case is pending before the Supreme Court. The Court has already expressed interest in the case, having invited the Solicitor General to submit a brief. Although the safe-harbor clause is applicable only to a specialized area of the law, the *Momenta* decision can only increase the likelihood that the Supreme Court will address the safe-harbor clause for a third time.[16]

Drug manufacturers, and others who hold patents relevant to the manufacture of drugs, should monitor developments closely.

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ENDNOTES

1 *Classen Immunotherapies, Inc. v. Biogen Idec*, 659 F.3d 1057 (Fed. Cir. 2011).

2 Dissent Op. at 2, 16.

3 35 U.S.C. § 271(e)(1).

4 *Roche Products Inc. v. Bolar Pharmaceutical Co.*, 733 F.2d 858 (Fed. Cir. 1984).

5 *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 670 (1990).

6 *Proveris Scientific Corp. v. Innova Systems, Inc.*, 536 F.3d 1256, 1261 (Fed. Cir. 2008).

7 *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661 (1990) (applying safe harbor).

8 *Merck KGAA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193 (2005) (applying safe harbor).

9 *Proveris Scientific Corp. v. Innovasystems, Inc.*, 536 F.3d 1256 (Fed. Cir. 2008) (rejecting safe-harbor defense).

10 *Amgen, Inc. v. International Trade Comm'n*, 565 F.3d 846 (Fed. Cir. 2009) (remanded for further fact-finding; uses would be exempt if "supplemental to the BLA and intended for submission to the FDA").

11 *Classen Immunotherapies, Inc. v. Biogen Idec*, 659 F.3d 1057 (Fed. Cir. 2011) (rejecting safe-harbor defense).

12 FD&C Act § 506A; 21 C.F.R. §§ 314.70, 314.80.

13 FD&C Act §§ 505(o)(3)(A), 505-1(a), 506B.

14 21 C.F.R. § 211.165(a).

15 21 C.F.R. §§ 211.180, 211.188.

16 The previous two Supreme Court cases were *Merck KGAA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193 (2005) (addressing how early in the drug discovery process the safe harbor reaches) and *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661 (1990) (addressing whether the safe harbor applies when seeking pre-marketing approval for a medical device).