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Limitations of the Safe Harbor Defense: Lessons from Amgen v. Hospira

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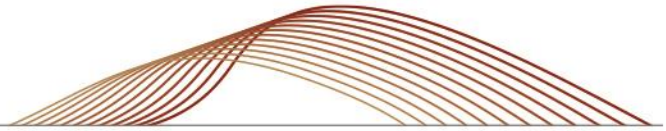
On August 27, 2018, the United States District Court for the District of Delaware denied Hospira, Inc.'s ("Hospira") motion for judgment as a matter of law and found substantial evidence supported an earlier jury verdict that certain batches of drug product manufactured by Hospira failed to qualify for the safe harbor created by 35 U.S.C. § 271(e)(1). In its decision, the court cited, *inter alia*, Hospira's communications describing batches for use as "commercial inventory" and evidence demonstrating that testing performed with certain batches was not required for U.S. Food and Drug Administration ("FDA") approval as supporting the jury's verdict.[1] Read the decision here.

I. Overview of Section 271(e)(1) "Safe Harbor"

Section 271(e)(1) creates an exception to patent infringement for activities related to obtaining approval for drug products from the FDA. Under this safe harbor, manufacturers are able to engage in otherwise-infringing activities provided that such infringing activities 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 products."[2] The statute thus permits a manufacturer to engage in FDA review activities while a drug is still covered by patent protection, and to enter the market more expeditiously once patent protection has ended. Notably, the safe harbor has been found to broadly protect "all uses of patented inventions that are reasonably related to the development and submission of *any* information" to the FDA[3] without consideration of "the underlying purposes or attendant consequences of the activity . . . as long as the use is reasonably related to FDA approval."[4]

II. Hospira's Safe Harbor Defense Denied at Summary Judgment, Trial, and Post-Trial Stages of the Litigation

The *Amgen v. Hospira* action involves Plaintiffs Amgen, Inc. and Amgen Manufacturing, Limited's (collectively, "Amgen") U.S. Patent Nos. 5,856,298 ("the '298 patent") and 5,756,349 ("the '349 patent"); both of which cover EPOGEN®, Amgen's EPO product. In December 2014, Hospira submitted Biologics License Application ("BLA") No. 125-545 to the FDA, seeking approval for a biosimilar version of EPOGEN®.[5] Allegedly in support of its BLA, Hospira manufactured 21 lots of EPO from 2013 to 2015.[6] In a motion for summary judgment filed in May 2017, Hospira alleged that the Section 271(e)(1) safe harbor applied to those batches because they were "'solely for uses reasonably related to the development and submission of information' to the FDA."[7] The court found this argument unpersuasive given the "tens of millions of doses[] of EPO in its 2013, 2014 and 2015 manufacturing campaigns."[8] Moreover, the court noted that Hospira's own submissions and statements to the FDA labeled some of these lots as "for 'commercial inventory.'"[9] Because there was



a genuine dispute of material fact as to the applicability of the safe harbor, the court denied Hospira's summary judgment motion.[10]

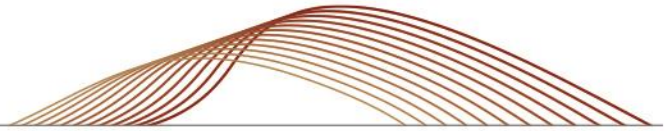
Following a five-day trial in September 2017, a jury found only seven of the 21 lots of EPO as entitled to protection under the safe harbor.[11] Moreover, although Hospira was not found to have infringed the asserted claims of the '349 patent, the jury awarded Amgen $70 million in damages for Hospira's infringement of the asserted claims of the '298 patent.[12] [13] Hospira challenged these findings, including on the issue of the safe harbor, in a motion for judgment as a matter of law or, in the alternative, remittitur or a new trial.

In its post-trial motion, Hospira alleged that no reasonable juror could find that the safe harbor defense did not apply to all 21 of its EPO lots because "each batch was used for . . . biosimilarity testing, updating product specifications, process validation, stability testing, or continued process validation."[14] Hospira further argued that the jury must have improperly "second-guessed . . . 'the subjective reason'" behind the manufacture of at least the batches identified as "for 'commercial inventory,'" and that the court failed to properly instruct the jury regarding the role of intent in a safe harbor analysis.[15] Based on "Amgen's presentation of FDA guidance documents, admissions in Hospira's internal documents, and post-litigation changes to Hospira's representations to the FDA," the court held that a reasonable juror could have concluded that not all of the 21 batches of EPO were protected under the safe harbor.[16] The court credited evidence that the batches were not used for testing actually required for FDA approval, as opposed to cleaning validation, stability, or process verification testing that could occur post-approval.[17] With respect to Hospira's additional argument that "the jury impermissibly focused on Hospira's intent," the court concluded that this could not be true because the jury found at least some of the 2015 EPO lots "designated for use as 'commercial inventory'" fell within the scope of the safe harbor.[18] Upholding its jury instruction, the court clarified that "evidence of intent can be a relevant factor in determining whether an activity is reasonably related to obtaining FDA approval," although intent or alternative uses would not bar the application of Section 271(e)(1) once that determination had been made.[19]

III. Considerations Following *Amgen v. Hospira*

The history and ultimate outcome of the *Amgen v. Hospira* district court litigation illustrate potential challenges for biosimilar manufacturers asserting safe harbor defenses under 35 U.S.C. § 271(e)(1), and opportunities for patent owners to successfully overcome such arguments. Although Hospira had argued batches it produced prior to FDA approval were entitled to the defense, the court first found there was a sufficient factual dispute to warrant a jury decision on the issue, and then held that substantial support existed to uphold the jury's finding of infringement. The court's decision on Hospira's motion for judgment as a matter of law affirming the jury's verdict suggests batches may not be entitled to this defense merely because some amount of product from each batch is used for regulatory testing.

Biosimilar makers should note that additional factors may influence the fact finder as to whether the safe harbor defense applies. As one example, the fact finder may consider whether batches are used for testing required for FDA approval as opposed to post-approval testing, such as release testing. The fact finder may also consider whether batch testing is described in the BLA. The *Amgen v. Hospira* litigation also made clear that how batches are described in communications with the FDA and in company documents can be instructive. Accordingly, biosimilar makers may want to carefully consider what will constitute a commercial batch and may want to avoid labeling batches as commercial when those batches will also be used for testing as required by the FDA. By doing so, biosimilar makers may



avoid giving their opponent additional ammunition by which to attack a safe harbor defense. Conversely, patent owners should be vigilant to identify any facts such as these that would support a challenge to a Section 271(e)(1) safe harbor defense.

In sum, it remains to be seen whether the *Amgen v. Hospira* litigation is the beginning of a trend toward significantly narrowing the safe harbor defense. Until the answer to that question becomes clear, biosimilar makers may wish to consider a conservative approach toward manufacturing batches that are not necessary to obtain regulatory approval. To the extent that the purpose of a particular batch is unclear, biosimilar makers may wish to avoid building an internal record that takes a position that may prove unhelpful to a safe harbor defense in later litigation. The *Amgen v. Hospira* decision may be appealed to the Federal Circuit, providing further clarity on these issues.

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If you have any questions concerning these developing issues, please do not hesitate to contact any of the following Paul Hastings New York lawyers:

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[1] D.I. 386 (C.A. 15-839), Op. at, 9-10, 46.

[2] § 271(e)(1).

[3] *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193, 202 (2005).

[4] *Abtox, Inc. v. Exitron Corp.*, 122 F.3d 1019, 1030 (Fed. Cir. 1997), *opinion amended on reh'g*, 131 F.3d 1009 (Fed. Cir. 1997).

[5] D.I. 386 (C.A. 15-839), Op. at 1.

[6] D.I. 295 (C.A. 15-839), Op. at 4.

[7] D.I. 200 (C.A. 15-839), Def. Hospira's Opening Br. in Support of Its Mot. for Summary Judgment of Non-Infringement at 1 (public version).

[8] D.I. 295 (C.A. 15-839), Op. at 4.

[9] *Id.*

[10] *Id.*

[11] D.I. 386 (C.A. 15-839), Op. at 1.

[12] *Id.*

[13] Notably, Hospira did not obtain approval for its biosimilar product until after the expiration date of the '298 patent. *See* D.I. 357 (C.A. 15-839), Def. Hospira Opening Br. in Supp. of Mot. for Judgment as a Matter of Law under Rule 50(b) at 14.

[14] D.I. 386 (C.A. 15-839), Op. at 5.

[15] *Id.* at 5-6, 9, 24.

[16] *Id.* at 9.

[17] *Id.* at 7-8.

[18] *Id.* at 10.

[19] *Id.* at 26.