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Fed. Circ. Amgen Biosimilar Ruling Raises IP Damages Risk

By **Paul Ainsworth and Michael Bruns** (February 26, 2020, 4:53 PM EST)

Paul Ainsworth

Michael Bruns

The U.S. Court of Appeals for the Federal Circuit recently affirmed a $70 million jury award for infringement of a manufacturing process patent for a biosimilar product without any infringing sales. The damages award in this case was particularly notable because the patentee did not practice the claimed technology.

This decision highlights a real risk facing drug companies developing a biosimilar product: The reference sponsor's patent portfolio may include dozens of patents that surround every step and variable in the manufacturing process, including alternatives that the reference sponsor itself does not use. This decision also highlights the benefits to innovator companies who invest in a comprehensive patent strategy that protects not only the commercialized product and process but viable alternatives that a competitor might employ.

The manufacture of biologic drug products is complex, particularly in comparison to the production of small molecule drug products. The typical biologic manufacturing process will involve a number of steps and components relating to cell culture conditions and media, harvesting, purification, filtration and formulation of the final product. This complexity provides an opportunity for reference sponsors to pursue patent protection on a range of potential innovations, large and small, that surround not only their manufacturing process but also alternative manufacturing processes that potential competitor might employ.

Process patents constitute a significant portion of the patents that a biosimilar manufacturer must address in preparing for potential litigation under the Biologics Price Competition and Innovation Act. In nearly every BPCIA case filed to date, more than half of the asserted patents have been patents relating to manufacturing processes.

Because there is no patent listing requirement under the BPCIA, relevant process patents can be difficult to identify, particularly if they are not specific to the molecule under development. As such, these process patents can impose an enormous liability to the unwary biosimilar maker. Although legislative proposals have suggested changes to the BPCIA that could address this issue, the proposals have not recognized this problem. There are, however, steps biosimilar manufacturers can take to mitigate liability.

Amgen v. Hospira

In Amgen Inc. v. Hospira Inc., the Federal Circuit considered an appeal of a BPCIA case from the U.S. District Court for the District of Delaware.[1] The case arose in connection with Hospira's seeking approval to market a biosimilar to Amgen's Epogen product. Epogen contains a glyco-protein hormone (erythropoietin or EPO), which is useful for the treatment anemia.

Amgen argued that 21 batches manufactured by Hospira infringed two Amgen process patents. Hospira alleged multiple defenses, including that the 21 batches were manufactured in connection with obtaining U.S. Food and Drug Administration approval and, therefore, subject to the safe harbor under Title 35 U.S. Code Section 271(e)(1).

The jury found, among other things, that Hospira infringed U.S. Patent No. 5,856,298, which claimed methods of producing EPO isoforms having certain properties using an ion exchange column. The '298 patent issued in 1999 but claimed priority to an application first filed in 1989. The record indicated that Amgen did not use the claimed invention to produce its Epogen product.

The jury also rejected Hospira's safe harbor defense in part, finding that only seven of the accused batches were reasonably related to the development and submission of information to the FDA. While Hospira alleged that the remaining 14 batches had been used to conduct testing related to FDA approval, and in response to a complete response letter received from the FDA, there was also evidence that Hospira had initially designated these batches as commercial inventory and only redesignated them as continued process verification batches after litigation had begun.

The jury ultimately awarded $70 million in damages even though Hospira's biosimilar product had not yet received FDA approval and, therefore, was not yet on the market.

Hospira and Amgen each appealed a number of issues arising from the district court case. However, it is the Federal Circuit's conclusions relating to safe harbor issues and damages that may have the largest ramifications for biologic and biosimilar manufacturers.

Hospira's Appeal of the Safe Harbor Jury Instruction

Biosimilar manufacturers generally can avoid damages liability for patent infringement so long as they do not manufacture commercial batches before patent expiry. This is because the safe harbor exempts from infringement liability those uses of a patented invention 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."[2]

In Amgen v. Hospira, the jury received the following instruction as to the applicability of the safe harbor defense:

> If Hospira has proved that the manufacture of a particular batch was reasonably related to developing and submitting information to the FDA in order to obtain FDA approval, Hospira's additional underlying purposes for the manufacture and use of that batch do not remove that batch from the Safe Harbor defense.

Hospira criticized this instruction as placing undue emphasis on the subjective intent of the biosimilar manufacturer. Instead, Hospira argued that there should be a brighter line focused on whether the biosimilar manufacturer ultimately used the batch for purposes of submitting information to the FDA.

The Federal Circuit rejected this interpretation of the safe harbor and instead said the inquiry focuses on the use of the claimed manufacturing process, which the jury instruction properly outlined.[3]

Hospira's Appeal of the Jury Finding

Hospira also appealed the jury's finding that some of its batches were not protected by the safe harbor defense even under the challenged jury instruction. The jury found that only seven of the 21 batches at issue were made solely for uses reasonably related to the development and submission of information to the FDA.

The Federal Circuit found that substantial evidence supported the jury's finding. This evidence included testimony from Amgen's experts and an admission from a Hospira witness that certain batches would have been required for continued testing of commercial batches, but not for FDA approval. Another Hospira witness admitted that the response to an FDA complete response letter did not require manufacture of additional batches.

Additionally, Hospira documents showed that Hospira planned to use much of the material from its batches as commercial inventory before later redesignating that material for continued process validation after the onset of litigation.

Although the Federal Circuit stated that Hospira's decision to manufacture EPO as commercial inventory was not dispositive of the safe harbor defense, it was "probative of whether Hospira's use of Amgen's patented process was reasonably related to seeking FDA approval."[4]

The Federal Circuit concluded that a jury could weigh this evidence to reasonably conclude that some of these commercial inventory batches fell within the safe harbor while others did not.

Hospira's Appeal of the Damages Award

Hospira also appealed the damages award. Hospira argued that the damage award did not reflect a reasonable royalty. Hospira challenged both the damages model — a lump sum royalty — as well as the amount of awarded damages.

Amgen contended that a hypothetical negotiation for a license between Amgen and Hospira in 2015 would have resulted in a lump sum royalty. Hospira challenged the damages model on the basis that it unduly shifted the risk to the licensee and resulted in a windfall to the licensor because it was not tied to whether Hospira ever commercialized the product. It also challenged the damages model because it did not account for the fact that Amgen did not itself use the '298 patent technology.

The Federal Circuit rejected these arguments and found no error in the district court permitting the jury to hear Amgen's damages theories. It also affirmed the jury's $70 million award on the basis that it was reasonable for the jury to select a damages amount that was between the amounts proposed by the each side's damages expert.

Ramifications of the Federal Circuit's Decision

The Federal Circuit's decision in Amgen v. Hospira should serve as a cautionary note for biosimilar manufacturers.

First, biosimilar manufacturers should take care to ensure they have adequately searched for process patents and published patent applications that might present a risk to their manufacturing program.

Second, biosimilar manufacturers should be aware that the safe harbor may not insulate their manufacturing activities from precommercialization liability if there is conflicting evidence on the motivations behind those manufacturing activities. This presents a greater risk to U.S. based manufacturing operations where damages may accrue in the absence of commercial importation or domestic sales.

Third, biosimilar manufacturers should be aware that the damages awards on precommercial activities can be significant. Although Amgen sought damages between $154 million to $170 million, the jury award of $70 million is a significant hit against a product that had not even received FDA approval.

Conclusion

Amgen v. Hospira highlights the importance of process patents in BPCIA litigation. Reference sponsors can significantly enhance their exclusivity protections by developing patent strategies and portfolios that cover alternative processes to make patented products.

Biosimilar manufacturers should be aware that they could incur significant liability if they infringe a process patent, even if no drug is ever sold. Biosimilar manufacturers can mitigate this liability by conducting thorough patent searches, narrowly construing the safe harbor provision and making the minimum number of batches for FDA approval.

Paul Ainsworth is a director and Michael Bruns is an associate at Sterne Kessler Goldstein & Fox PLLC.

[1] Amgen Inc. v. Hospira Inc., 944 F.3d 1327 (Fed. Cir. 2019).

[2] 35 U.SC. § 271(e)(1).

[3] Amgen, 944 F.3d at 1338-39.

[4] Amgen, 944 F.3d at 1340.