CASE COMMENTS

US SUPREME COURT PROVIDES LIMITED GUIDANCE REGARDING BIOSIMILAR PATENT LITIGATION

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Over 30 years ago, in an attempt to balance disparate interests in competition and innovation with small molecule pharmaceuticals, the Drug Price Competition & Patent Term Restoration Act was signed into US law. Commonly known as the Hatch-Waxman Act, this legislation established the concept of an Abbreviated New Drug Application (commonly, an 'ANDA'), enabling generic manufacturers to gain regulatory approval without needing to prove safety and efficacy. Although a watershed moment for the generics industry, the Hatch-Waxman Act did not encompass biologic drugs, such as monoclonal antibodies, which are of a molecular size and complexity far greater than small molecule pharmaceuticals. Biologic drugs, such as Humira™, Enbrel™, Rituximab™, Avastin™ and Herceptin™ now dominate lists of the largest selling drugs globally.

The Biologics Price Competition and Innovation Act ('BPCIA') was enacted in 2010 to provide an abbreviated pathway for regulatory approval of biologics ('biosimilars') by filing an abbreviated Biologic License Application ('aBLA'). Similar to the Hatch-Waxman procedure, the counterweight to this abbreviated (but much more complex) pathway is the BPCIA's amendment to the Patent Act,[1] creating an artificial act of infringement that allows reference product sponsors ('RPSs') to bring infringement suits based on the mere filing of biosimilar applications. To facilitate these infringement suits, however, the BPCIA provides for a complex set of information exchanges, commonly dubbed the 'patent dance'.

Seven years after the enactment of the BPCIA, the Supreme Court of the United States in *Sandoz Inc. v Amgen Inc.* ('*Sandoz*'),[2] interpreted two key provisions of the statute. Biologic and biosimilar manufacturers were hoping that the Supreme Court would clarify: (1) whether the 'patent dance' is mandatory and enforceable, and (2) whether the required 180-day notice of commercial marking can be given *before* FDA approval of the biosimilar application.

In a unanimous decision penned by Justice Thomas, the Supreme Court answered only the second question definitively: the required 180-day notice of commercialisation *prior* to FDA approval is effective and, as such, a biosimilar applicant need not await FDA approval before providing the notice. However, the court held it was not required to answer the first question, that is, whether the patent dance (or, more specifically, §262(l)(2)(A) under which the biosimilar applicant 'must' provide its aBLA to the RPS, starting the patent dance) is mandatory. Rather, the court framed the question as 'whether §262(l)(2)(A)'s requirement – that the applicant provide its application and manufacturing information to the sponsor – is itself enforceable by injunction'.[3] The court held that an injunction is not available under federal law to force this exchange. Thus, an RPS's only remedy is to file a declaratory judgment action under §262(l)(9)(C) asserting its patents, even though it may lack critical information regarding possible infringement, particularly as to process patents. The court remanded the case to the Federal Circuit to determine whether an injunction forcing the biosimilar applicant to provide its aBLA and

1) 35 USC §271.

2) 137 S. Ct 1664 (2017).

3) Ibid. at 1671.

manufacturing details to the RPS was available via state law, in this instance California law.

Background of the Case

Amgen markets Neupogen®, a filgrastim product used to treat neutropenia – a lack of certain white blood cells caused by cancer, bone marrow transplant, receiving chemotherapy, or by other conditions. Amgen holds patents on methods of manufacturing and using the drug. Sandoz sought FDA approval to market a biosimilar filgrastim product under the brand name Zarxio®, identifying Neupogen® as the reference product. The day after the FDA accepted its application for review, Sandoz provided its 180-day notice of commercialisation to Amgen. In other words, Sandoz notified Amgen that it had submitted an aBLA and that it intended to market Zarxio® immediately upon receiving FDA approval. Sandoz also informed Amgen that it did not intend to provide its aBLA and the manufacturing information 'required' by §262(l)(2)(A) and that Amgen could sue immediately for infringement under §262(l)(9)(C).

Shortly thereafter, Amgen sued Sandoz for infringement of a method of treatment patent, but also asserted that Sandoz had engaged in 'unlawful' conduct in violation of California's unfair competition law by violating two provisions of the BPCIA: (i) Sandoz's failure to provide its aBLA and related manufacturing information under §262(l)(2)(A); and (ii) by providing its 180-day notice of commercial marketing *prior* to obtaining FDA approval. Amgen sought injunctions to enforce Sandoz to comply with both BPCIA requirements, that is, provide its aBLA and give its 180-day notice *after* FDA approval. As relevant here, Sandoz argued that it had not violated the BPCIA by either action. In March 2016, while the case was pending, the FDA approved Zarxio®, and Sandoz provided Amgen with a second 180-day notice of commercialisation, indicating it would not market its drug until September 2016, more than 180 days after the second notice.

The district court subsequently granted judgment to Sandoz on its BPCIA counterclaims and dismissed Amgen's two unfair competition claims.[4] Amgen appealed.

In July 2015, the Federal Circuit affirmed the dismissal of Amgen's state law claims. It first held that Sandoz did not violate the BPCIA by failing to disclose its aBLA and manufacturing information, because such disclosure is not mandatory, but optional.[5] On the second issue, the court agreed with Amgen and held that under §262(l)(8)(A), the applicant must provide the 180-day notice of commercial marketing only *after* it receives FDA approval. It thus enjoined Sandoz from marketing Zarxio® until 180 days after the date of its second 180-day notice. After the expiration of that period, Sandoz began marketing Zarxio® in the United States.

No Injunctive Relief under Federal Law for Failure to Disclose the aBLA, but State Law Remedies may be Possible

The Supreme Court agreed with one part of the Federal Circuit's decision and held that an injunction is unavailable to force a biosimilar applicant to provide an RPS with its aBLA and related manufacturing information under federal law. The Federal Circuit had interpreted §271(e)(2)(C)(ii) of the patent statute to make the failure to provide an aBLA one element of the artificial act of infringement. As a result, the Federal Circuit reasoned that the available remedies were limited to those articulated in §271(e)(4), and those remedies do not include an injunction forcing the applicant to provide its aBLA. The Supreme Court disagreed. According to the Supreme Court, only the submission of an aBLA constitutes an act of artificial infringement; thus, failing to disclose an aBLA and manufacturing details under §262(l)(2)(A) is not an element of the artificial act of infringement. Accordingly, the only remedy under the statute is that the RPS may file a declaratory judgment action under §262(l)(9)(C) asserting its patents.

At the same time, the court remanded the case to the Federal Circuit to determine whether California law would treat non-compliance with §262(*l*)(2)(A) as 'unlawful', and, if so, 'whether the BPCIA pre-empts any additional remedy available under state law for an applicant's failure to comply with §262(*l*)(2)(A)'.[6] The Federal Circuit is therefore left to answer what remedies, if any, are available under California state law to force Sandoz to provide Amgen with its aBLA and related manufacturing details.

4) *Amgen Inc. v Sandoz, Inc.*, 2015 WL 1264756, *7–*9 (N.D. Cal., Mar. 19, 2015).

5) *Sandoz Inc. v Amgen Inc.*, 794 F.3d 1347 (Fed Cir. 2015).

6) Ibid. at 1676.

Although an injunction compelling disclosure is not available under federal law, the Supreme Court expressed confidence that biosimilar applicants had significant incentives to participate in the patent dance. In this regard, the court noted that by participating in the dance, biosimilars 'will have the opportunity to litigate the relevant patents before the biosimilar is marketed'.[7] In contrast, by failing to provide its aBLA and other manufacturing information, a biosimilar applicant vests in the RPS 'the control that the applicant would otherwise have exercised over the scope and timing of the patent litigation' and 'depriv[ing] the applicant of the certainty it could have obtained by bringing a declaratory-judgment action prior to marketing its product'.[8]

Notice of Commercialisation is Effective Prior to FDA Approval

The Supreme Court reversed the Federal Circuit's holding on the timing of the 180-day notice of commercial marketing. As noted above, the Federal Circuit held that an applicant must provide the 180-day notice of commercial marketing to the RPS only *after* FDA approval. The Supreme Court rejected this interpretation, holding that under §262(l)(8)(A), the 180-day notice may be provided *before* FDA approval. While acknowledging the numerous practical ramifications of its interpretation, the court apparently did not give them much weight. As such, these policy considerations 'could not overcome the statute's plain language' and, in any event, 'are appropriately addressed to Congress, not the courts'.[9]

Justice Breyer Invites the FDA to Weigh In

In a one paragraph concurring opinion, Justice Breyer noted that the FDA could modify the court's interpretation of the BPCIA. In Justice Breyer's view, Congress implicitly delegated authority to the FDA to interpret the terms of the BPCIA. Thus, if the FDA, after greater experience administering this statute, determines that a different interpretation would better serve the statute's objectives, it could depart from, or modify, the court's interpretation.

Implications for Biologic and Biosimilar Manufacturers

The Supreme Court's opinion answered some questions – generally siding with biosimilar applicants – but it left many issues uncertain. For example, although the court held that under §262(l), a biosimilar applicant '*must*' provide its aBLA and related manufacturing information to the RPS, it held there is no federal remedy for failing to do so.[10] Thus, questions remain as to whether this 'required' disclosure can be enforced under state law. And if so, does the ability to enforce this provision vary from state to state? For biosimilar applicants, the uncertainty of concurrent state law claims seeking disclosure will factor into their decision to dance or not dance, at least until the Federal Circuit (or possibly a state court) resolves the issue.

On a related note, biosimilar applicants should be aware that a decision not to dance could be used as a factor favouring injunctive relief. In a footnote, the court expressed no view on whether a district court could consider an applicant's violation of §262(l)(2)(A) (or any other BPCIA procedural requirement) in deciding whether to grant a preliminary injunction under 35 USC §271(e)(4)(B) or §283, which would prohibit marketing of the biosimilar.[11]

While the importance of the above footnote in preliminary injunction practice has not yet been analysed, RPSs will likely highlight a biosimilar applicant's refusal to 'dance' as part of their injunction arguments. Indeed, district courts may well consider the biosimilar's failure to dance as a negative factor in balancing the equities in considering injunctive relief. Thus, failure to comply with the information exchange provision of §262(l)(2)(A) may have significant ramifications beyond those at issue in this one case.

Other questions remain regarding how an RPS can enforce its process patents. Rule 11 of the Federal Rules of Civil Procedure requires parties to have a good faith basis when filing suit; indeed, violations of this rule can result in sanctions. Without the biosimilar's manufacturing information, which usually

7) Ibid. at 1672.

8) Ibid. at 1675.

9) Ibid. at 1678.

10) Ibid. at 1670 (emphasis added).

11) Ibid. at 1678 n.2.

details the processes used to prepare the biosimilar drug, an RPS will have difficulty analysing which, if any, of its process patents cover the biosimilar's manufacturing process. And future discovery in lawsuits on other patents, including process patents, covering the biologic may not be available, as confirmed by the Federal Circuit in *Amgen, Inc. v Hospira, Inc*.[12]

Lastly, the 180-day notice provision envisioned two distinct phases of patent litigation – before and after the notice. Now, however, since the patent dance is optional, the two phases of litigation can be collapsed into one, allowing an RPS to institute suit on *all* its patents immediately after notice is given in instances where the applicant does not dance.

While this decision marks the first Supreme Court guidance on what the Federal Circuit once called the 'riddle wrapped in a mystery inside an enigma', which is the BPCIA, many questions remain as the United States' biosimilar industry continues to develop.

12) No. 2016–2179 (Fed. Cir.).