BIOSIMILAR DEVELOPMENT

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A Biosimilar Applicant's (Illusory?) Right To Declaratory Relief

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The Declaratory Judgment Act allows federal courts to "declare the rights and other legal relations of any interested party" in a case of "actual controversy." Declaratory judgment (DJ) actions are intended to resolve uncertainty with respect to such rights and legal relations before actual harm occurs to either side. For example, a biosimilar maker may want to seek declaratory relief of noninfringement or patent invalidity, as opposed to waiting to be sued by the reference product sponsor (RPS), to remove the cloud of uncertainty and insecurity before launch and/or to control the time and place of the lawsuit.

Suits brought by biosimilar makers *before* submission of an abbreviated biologics license application (aBLA) have been dismissed by courts as lacking actual "case or controversy." Courts found that in the *pre-application* context, the purported harm — potential infringement liability — was too remote and speculative to create DJ jurisdiction. The Federal Circuit expressly declined to address, however, whether the Biologics Price Competition and Innovation Act of 2009 (BPCIA) forecloses a DJ action by the biosimilar applicant once an aBLA is filed.

This article explains why having the right and option to seek declaratory relief is still important to a biosimilar applicant despite the patent resolution mechanism provided by BPCIA, examines the limitations on DJ actions imposed by BPCIA, and discusses recent court cases addressing biosimilar applicants' rights to declaratory relief.

BPCIA's Patent Dance Does Not Obviate The Need For Declaratory Relief

BPCIA provides for an elaborate mechanism of pre-suit disclosures and negotiations between the biosimilar applicant and the RPS, known as the "patent dance," intended to resolve potential patent disputes in an orderly and expeditious fashion. The "dance" starts within 20 days of the FDA's acceptance of the aBLA for review. It takes about six and a half months, and unless a settlement is reached, leads to a "first phase" patent infringement action on a certain number of patents to be filed within 30 days of conclusion of the dance. Failure to timely prosecute will limit the RPS's remedy to a reasonable royalty upon a finding of infringement. Under the statute, the RPS may seek preliminary injunction in a "second phase" on patents not included in the final list but identified in the earlier exchanged lists when the biosimilar applicant gives notice of commercial marketing, which must be given "not later than 180 days before the date of the first commercial marketing" of the licensed biosimilar product.

Despite its laudable goals, the dispute resolution scheme envisioned by BPCIA may not be as orderly or as expeditious as it intended. Unless a settlement is reached, it adds another seven and a half months to the already protracted district court litigation, typically two and a half years to trial for a patent case. (In comparison, in Hatch-Waxman litigations, the brand must file suit within 45 days of receipt of the Paragraph IV certification.) Being able to bring a DJ action to avoid delay and/or to control the venue of the suit would still be a good option to have for a biosimilar applicant.

BPCIA's Limitations On Declaratory Relief

On its face, Section (*l*)(9) of BPCIA puts three limitations on DJ actions based on the conduct of a biosimilar applicant:

A. If the biosimilar applicant timely provides the RPS with a copy of the aBLA and relevant manufacturing information, then neither party may bring a DJ action on "second phase" patents before the notice of commercial marketing is given;
B. If the biosimilar applicant starts the dance but fails to complete a subsequent action required under certain paragraphs — including paragraph (3)(B)(ii) (provide disclosure of noninfringement, invalidity, and/or unenforceability contentions) and paragraph (5) (if no agreement is reached after negotiation, give notice as to the

number of patents to be litigated in phase 1 and exchange patent list accordingly) — the RPS, *but not the biosimilar applicant*, may bring a DJ action on any patents included in the initial patent list provided by the RPS; and

C. If the biosimilar applicant fails to provide the aBLA and relevant manufacturing information, the RPS, *but not the biosimilar applicant*, may bring a DJ action on any patent that claims the biological product or a use of the biological product.

Notably, there is no parallel penalty against an RPS who fails to meet the disclosure or negotiation requirements of BPCIA. While BPCIA does not categorically ban all DJ actions by biosimilar applicants outright, whether any meaningful declaratory relief is still possible for a biosimilar applicant under BPCIA is unclear.

Recent DJ Actions By Biosimilar Applicants

In its *Sandoz v. Amgen* decision issued in June 2017, the U.S Supreme Court indicated, albeit implicitly, that BPCIA does not bar all DJ actions by a biosimilar applicant. The court held, among other things, that the requisite commercial marketing notice, which opens the gate for the second phase of litigation, can be provided by a biosimilar applicant before FDA approval. According to the Court, "[i]n this second phase of litigation, *either* party may sue for declaratory relief." (Emphasis in original.)

Following the Supreme Court's decision, biosimilar applicants have renewed their efforts to take control of the patent resolution process via declaratory relief. So far, such efforts have failed.

Amgen v. Genentech

Amgen initiated the patent dance for Mvasi, its biosimilar to Genentech's Avastin, in January 2017. After a tumultuous exchange of information where both sides alleged deficiencies in disclosures, the parties started patent resolution negotiation on Sept. 14, 2017, the same day the FDA approved Mvasi. The parties were unable to agree on a final list of patents for litigation when the statutory period for negotiation expired on Sept. 29, 2017.

On Oct. 6, 2017, Amgen provided notice of commercial marketing and filed a DJ action in the Central District of California (where Amgen is headquartered) for non-infringement and invalidity of all 27 patents initially identified by Genentech "to remove the cloud of uncertainty flowing from Genentech's inconsistent and changing positions during the BPCIA exchange and negotiations." On the same day, Amgen started the final stage of the patent dance – identifying the patents to be litigated in phase 1.

Hours after Amgen's DJ action, Genentech filed a competing lawsuit in the District of Delaware. Genentech later filed a second lawsuit in the same court to bring its "first phase" litigation after the parties officially completed the patent dance, alleging infringement of 25 of the 27 patents. (In both actions, Genentech later added another newly issued patent.)

Genentech moved to dismiss the California action based on Amgen's alleged violations of BPCIA. Amgen moved to transfer the Delaware actions to California.

"[N]ot persuaded that either party is fully adhering to the letter or the spirit of the BPCIA," the California court chose to "exercise its discretion" in declining to hear Amgen's case without addressing the issue of whether BPCIA constituted a jurisdictional bar against the declaratory relief sought by Amgen. The court rejected Amgen's argument that it was entitled to bring suit after providing its notice of commercial marketing even though it had not yet completed the dance under BPCIA. According to the court, BPCIA envisions two phases of litigation, and the Supreme Court in the *Sandoz v. Amgen* decision "expressed an expectation that the parties finish the exchanges and negotiations contemplated by the BPCIA, allow the product sponsor the first opportunity to file suit on those first phase patents, and only then allow either party to file suit on any remaining patents after the applicant brought its notice of commercial marketing. . . . Allowing an applicant to side-step the BPCIA's exchange and negotiation requirements and bring suit on any patent simply by filing its notice of commercial marketing would effectively vitiate the BPCIA's provisions." (Interestingly, in another BPCIA litigation concerning Herceptin, Genentech cut short the patent dance and sued Pfizer in the District Court of Delaware for patent infringement the same day Pfizer provided its notice of commercial marketing, nearly two months before Pfizer's Section 3(B) statement was due.)

While the California court's final ruling was pending, the Delaware court denied Amgen's motion to transfer. Among other things, the court found that Amgen's California action, although filed first, was anticipatory in nature, thus weighing against giving it priority status.

Celltrion v. Genentech

Celltrion initiated the patent dance for Truxima, its biosimilar to Genentech's Rituxan, in July 2017. On Jan. 11, 2018, as part of the patent resolution negotiation, Celltrion indicated that it wished to litigate all 40 patents identified in Genentech's paragraph 3(A) list. On the same day, Celltrion served its notice of commercial marketing and filed a DJ action in the Northern District of California (where Genentech is headquartered). Genentech filed a counter suit in the District of New Jersey the following day.

Celltrion took a similar approach with Herzuma, its biosimilar to Genentech's Herceptin, cutting short the negotiations and bypassing the final stage of the patent dance by serving a notice of commercial marketing of Herzuma. This also resulted in dueling lawsuits in two courts: Celltrion's DJ action in the Northern District of California, filed on Jan. 11, 2018, and Genentech's counter lawsuit in the District of Delaware, filed the following day.

The California court granted Genentech's motions to dismiss. While finding that BPCIA does not create a jurisdictional bar against declaratory relief sought by a biosimilar applicant, the court held that BPCIA's patent dance provisions do impose "a series of statutory conditions an applicant must satisfy before bringing an action for declaratory judgment." The court concluded that under Section (*l*)(9)(B) of BPCIA, Celltrion may not file DJ actions with respect to the patents at issue because it "did not complete its obligations under Section (*l*)(5)," the requirement that absent an agreement, the biosimilar applicant give notice of the number of patents to be litigated in phase 1 and then exchange lists of patents with the RPS.

The court was unpersuaded by Celltrion's argument that its statement to Genentech that it wished to litigate all the patents in Genentech's initial list satisfied its obligations to engage in good faith negotiations and made the subsequent steps of identifying the number and list of patents for phase 1 litigation redundant. The court held that these are separate requirements provided sequentially in separate subsections of the statute, and they cannot be streamlined and satisfied simultaneously with a single statement or gesture. Nor can a biosimilar applicant sidestep the requirements to provide paragraph 5 number or exchange paragraph 5 lists simply by bringing a DJ action before the expiration of the 15-day negotiation period.

The court also rejected Celltrion's argument that the notices of commercial marketing it served for Truxima and Herzuma enabled it to file the DJ actions, regardless of other provisions of BPCIA. The court reasoned that BPCIA imposes three separate, independent statutory bars, and serving a notice of commercial marketing only lifts one of the three bans on DJ actions.

Following the California court's ruling, and apparently over Genentech's objections, Celltrion resumed the final stage of the patent dance for both biosimilar drugs on June 6, which concluded on June 11, 2018 with the parties' exchange of their patent lists for litigation. On July 11, Genentech filed new lawsuits relating to Herceptin and Rituxan in Delaware and New Jersey federal courts, respectively, alleging infringement of the same 40 patents already being litigated in the same courts — as it did in the Avastin suit against Amgen. In its complaints, Genentech stated that it filed the lawsuits "out of an abundance

of caution ... to avoid the burdens associated with resolving any arguments Defendants may attempt to make suggesting that the BPCIA's reasonable royalty provision limits Plaintiffs' rights."

So much for BPCIA's grand vision of order and efficiency.

Whether the lower courts correctly interpreted BPCIA's limitations on a biosimilar applicant's right to seek declaratory relief remains to be seen. After the entries of final judgments in the Herceptin and Rituxan suits in California, Celltrion filed notices of appeal to the Federal Circuit. Celltrion's opening briefs are due Sept. 14, 2018.

Should the lower courts' interpretations stand, a biosimilar applicant would not be able to use declaratory relief to expedite the patent resolution process prescribed by BPCIA, and the RPS would always have the right of first refusal to bring suit against the biosimilar applicant on "first phase" patents. Although the biosimilar applicant and the RPS would have equal opportunity in seeking declaratory relief with respect to "second phase" patents, a DJ action on these patents by the biosimilar applicant would most likely be deemed "anticipatory" and not be given priority status even if filed before the RPS's competing DJ action.

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