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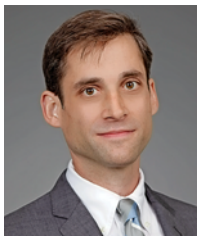
Dance Fever: A Recap of Recent BPCIA Litigation



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Introduction

The recent flurry of biosimilars litigation proceeding under the Biologics Price Competition and Innovation Act (BPCIA) has reinforced the often-repeated observation that the statute is both unwieldy in its complexity and unclear as to many of its procedural requirements. In particular, subsection 262*(l)* of the BPCIA, the complex patent infringement litigation resolution procedure known colloquially as ''the patent dance,'' has spawned many hotly contested disputes over the obligations of the parties under the statute. Reference product sponsors (RPSs) and biosimilar applicants (applicants) have wrangled energetically over key questions such as whether they are required to ''dance,'' the consequences of an applicant refusing to dance, whether courts may issue injunctions forcing an applicant to dance, and whether an applicant may walk off the floor before the dance ends.

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Given this procedural uncertainty and the high stakes in biosimilars patent infringement litigation generally, the task of setting a litigation strategy for a given biosimilar has been plagued with uncertainty. One of the key variables that applicants have had to triangulate is whether to engage in the patent dance at all, and if so, for how long. The procedure takes about six months to complete, which can represent a significant delay in commercial launch. Another variable has been when to give the 180 days of notice of commercial launch specified by the statute. This represents another six months of delay, and applicants have been attempting various methods of giving that notice as soon as possible. For their part, RPSs have had to contend with the uncertainty of whether the patent dance and all of its steps are mandatory, what disclosures are actually required under each step, and whether they have the right to seek an injunction in district court to force an applicant to comply with those steps.

As the Supreme Court considers the Federal Circuit's seminal decision in *Amgen v. Sandoz*, 794 F.3d 1347 (Fed. Cir. 2015) which held that a biosimilar applicant could choose to opt out of the patent dance and that notice of commercial launch may only be given after the U.S. Food & Drug Administration (FDA) approves the biosimilar application, it is worth pausing to consider the three main strategies that have been employed to

date, the implications of those strategies in terms of the remedy for patent infringement, and the impact of the pending Supreme Court review on future dance strategies.

Background

The BPCIA was signed into law as part of the Affordable Care Act on March 23, 2010. It is codified principally at 42 U.S.C. § 262.

Subsection 262(k) of the BPCIA created an abbreviated licensure pathway for biological products that are shown to be ''biosimilar'' to, or, if additional evidence suggests, ''interchangeable'' with, a reference product that already has been licensed by the FDA. This abbreviated biologics license application, or ''aBLA,'' permits a biosimilar applicant to obtain FDA approval on less than the full package of preclinical and clinical test data normally required for approval of a new biologic product.

Subsection 262(*l*) of the BPCIA also introduced a new scheme to resolve patent disputes involving biosimilar products. This scheme has been dubbed the ''patent dance'' because it lays out a schedule of timed steps in which both parties—the applicant and the RPS— exchange certain information and contentions concerning potential patent disputes. The patent dance is initiated by the applicant disclosing to the RPS ''a copy of the application . . . and such other information that describes the process or processes used to manufacture'' the biosimilar product. *See* § 262(*l*)(2)(A).

(Click here to request a copy of Goodwin's *Guide to the Biosimilars Patent Dance*.)

In response, the RPS provides the applicant with a list of patents it believes may be infringed, and identifies those it is willing to license. *See* § 262(*l*)(3)(A). The applicant then responds to that list and licensing offer, principally by disclosing contentions as to the invalidity, unenforceability, or non-infringement of the listed patents. *See* § 262(*l*)(3)(B)(ii)(I)-(II). The RPS then responds with contentions as to the validity, enforceability, and infringement of the listed patents. *See* § 262(*l*)(3)(C). The parties then negotiate which of the listed patents should be litigated in a ''first wave'' of litigation, and following which the RPS initiates suit. *See* § § 262(*l*)(4)-(6). The applicant must also provide the RPS with at least 180 days' notice of commercial launch of its product. *See* § 262(*l*)(8)(A). After it receives such notice, the RPS may initiate a ''second wave'' of litigation, asserting patents it included on its original patent dance list but that the parties omitted from the first wave. *See* § 262(*l*)(8)(B).

As the BPCIA has been interpreted by the Federal Circuit, a biosimilar applicant has the option of whether to engage in this complex and time-consuming patent dance, which normally takes about six months to complete. *See Amgen*, 794 F.3d at 1352. When an applicant opts out of the dance, typically by declining to disclose its aBLA or manufacturing information to the RPS, the RPS's sole remedy is to immediately initiate a declaratory judgment action for patent infringement pursuant to 35 U.S.C. § 271(e)(2)(c)(ii). *Id.* at 1356-57. The Federal Circuit also ruled that the applicant may only provide notice of commercial launch after it receives FDA approval of its product, which effectively gives the RPS an automatic six months of additional market exclusivity. *Id.* at 1358. The Supreme Court has granted the parties' petitions for review of the Federal Circuit's interpretation, and is scheduled to hear oral arguments on the issues on April 26, 2017. The Court will likely issue a decision by the end of June 2017. *See* Big Molecule Watch, *Supreme Court Announces Briefing Schedule in* Amgen v. Sandoz, available here.

Stepping on Toes: Litigation to Date Involving the Patent Dance

To date, the patent dance strategies of biosimilar applicants have fallen into three general categories: opting out of the dance entirely, allegedly only partially completing one or more of the steps, and completing all of the steps. Below are examples of each strategy, some observations about the implications of each on the available remedies for patent infringement, and the potential impact that the pending Supreme Court review of *Amgen v. Sandoz* may have on each.

1. No Dance: Amgen v. Sandoz, N.D. Cal. 3:14cv4741

Sandoz's application to market a biosimilar version of Amgen's Neupogen® (filgrastim) was the first to be accepted for FDA review under the BPCIA abbreviated pathway, on July 7, 2014. Once the FDA accepted Sandoz's application, Sandoz wrote a letter to Amgen declining to engage in the patent dance. Instead, Sandoz offered to provide Amgen its biosimilar application under certain specified confidentiality provisions. Sandoz also told Amgen that it expected FDA approval as early as March 8, 2016, and intended to launch its biosimilar product immediately upon FDA approval. In other words, Sandoz stated it would not dance, but did attempt to provide notice of commercial marketing under § 262(*l*)(8)(A) (''The subsection (k) applicant shall provide notice to the reference product sponsor not later than 180 days before the date of the first commercial marketing of the biological product licensed under subsection (k).'').

Amgen filed a complaint in the U.S. District Court for the Northern District of California seeking an order compelling Sandoz to engage in the patent dance and asserting that Sandoz could not provide notice of commercial marketing until after the FDA had approved its product. The district court ruled in favor of Sandoz on both counts, finding that the patent dance is not mandatory and that biosimilar applicants need not wait for FDA approval before providing notice. As to the notice issue, the district court found Amgen's position ''problematic'' as it ''would tack an unconditional extra six months of market exclusivity onto the twelve years reference product sponsors already enjoy under [the BPCIA].'' *Amgen v. Sandoz*, N.D. Cal., No. 14-cv-04741-RS, 3/25/15; *see also* Big Molecule Watch, *Legal Issues and Early Litigation Concerning the BPCIA:* Amgen v. Sandoz, available here.

On appeal of that ruling, a panel of the Federal Circuit split on these issues. The Federal Circuit first held that the patent dance is not mandatory, and Amgen's only remedy for Sandoz's failure to engage in the dance was to file an infringement action against Sandoz. The Federal Circuit further held that Sandoz was not permitted to provide notice of commercial marketing under the BPCIA prior to FDA approval. *See* Big Molecule Watch, *Analysis: Federal Circuit Split Decision in* Amgen v. Sandoz, available here.

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The parties have appealed the Federal Circuit's decision, which is now pending before the Supreme Court. The outcome of the Supreme Court's review will likely decide both of the statutory interpretation issues regarding the patent dance and subsection (*l*)(8)(A) notice, as well as the attendant issue whether there is a private right of action to enforce the provisions of the patent dance. Some watchers are wondering whether the Supreme Court will follow the Solicitor General's view of the BPCIA, which is (1) that the steps of the dance, including the notice-of-launch provision, are mandatory but that the only remedy available to an RPS for violation of those steps is to bring an immediate patent infringement action; and (2) an applicant is authorized to give notice of commercial marketing prior to FDA approval. *Sandoz Inc. v. Amgen Inc.*, U.S., Nos. 15-1039 and 15-1195, *Brief for the United States as Amicus Curae,* 2/22/17. Of course, the Supreme Court could endorse the Federal Circuit's view, or do something unpredictable. Thus, biosimilar applicants and RPSs must consider the possible ways that the Supreme Court's ruling, which will likely issue prior to June 2017, will change the landscape during the pendency of existing or imminent BPCIA litigation. Moreover, if the Supreme Court finds a private right of action to enforce the steps of the dance through district court injunctions (contrary to the Federal Circuit's interpretation and the approach advocated by the Solicitor General), this could pave the way for new litigation disputes. All of these possibilities should be weighed when determining a patent dance strategy, at least in the near term.

2. Alleged Partial Dance: Janssen v. Celltrion, D. Mass. 1:15cv10698, and Genentech v. Amgen, D. Del. 1:17cv00165 At issue in *Janssen v. Celltrion* is Celltrion's Inflectra® product, which is a biosimilar to Janssen's Remicade® (infliximab). In August 2014, Celltrion filed its biosimilar application with the FDA, seeking approval to market through its partner Hospira (now owned by Pfizer). The application was accepted for review by the FDA on Oct. 7, 2014. On Feb. 5, 2015, Celltrion provided notice of its intent to market upon FDA approval.

Within the 20-day window under subsection (*l*)(2), Celltrion provided Janssen with its application, which includes certain manufacturing information, but not any additional manufacturing information. Janssen asserted that Celltrion was obligated to serve additional manufacturing information beyond that found in the aBLA, and thus that Celltrion had not fully complied with the patent dance. However, Janssen served a patent list identifying six patents. In response, Celltrion provided a detailed statement and agreed that all of the patents identified by Janssen would be the subject of the first wave of litigation.

Janssen filed its complaint in March 2015 alleging infringement of the six previously-identified patents and seeking to enforce the BPCIA's patent dance provisions. The parties have since stipulated to the dismissal of four of those asserted patents, leaving two patents asserted in the litigation. On one of the asserted patents, the district court entered a partial judgment in favor Celltrion, finding that the patent was invalid for obviousness-type double patenting. Janssen has appealed that ruling while proceedings in the district court concerning the other asserted patent continue.

Most recently, the district court issued guidance as to the appropriate measure of damages in the case. In particular, the court's guidance addressed whether 35 U.S.C. § 271(e)(6) would, on the facts of the case, limit Janssen's damages to a reasonable royalty. § 271(e)(6) (where an infringement action is filed after the expiration of the 30-day period described in subsection (*l*)(6) of the BPCIA, ''the sole and exclusive remedy that may be granted by a court, upon a finding that the making, using, offering to sell, selling, or importation into the United States of the biological product that is the subject of the action infringed the patent, shall be a reasonable royalty''). The court expressed the view that the statute did not limit the available remedy in this case because ''[i]t is only the list of patents that emerge from the properly completed BPCIA procedure that are potentially subject to the reasonable royalty damages limitation.'' Memorandum and Order at 6-7, *Janssen Biotech, Inc. v. Celltrion Healthcare Co.*, D. Mass., No. 1:15-cv-10698-MLW, 3/3/17.

In a different case involving Amgen's proposed biosimilar to Genentech's Avastin® (bevacizumab), Amgen, too, provided only its aBLA to Genentech and not any additional manufacturing information. There, Genentech responded by filing a declaratory judgment action against Amgen, seeking a declaration that Amgen had violated the patent dance provisions by disclosing only its aBLA. *See* Big Molecule Watch, *Genentech Files DJ Action Against Amgen Regarding Avastin Biosimilar*, available here. Amgen moved to dismiss, arguing that, under the Federal Circuit's decision in *Amgen v. Sandoz*

, the only remedy for non-compliance with subsection (*l*) is an immediate infringement action. Genentech argued in response that *Amgen v. Sandoz* does not control because there Sandoz (the biosimilar applicant) did not participate in the BPCIA patent dance provisions at all. *See* Big Molecule Watch, *Genentech v. Amgen: Amgen Seeks Dismissal Under Amgen v. Sandoz*, available here. The district court agreed with Amgen and dismissed Genentech's claim alleging non-compliance with the patent dance, with leave for Genentech to amend its complaint within 45 days to allege patent infringement under 42 U.S.C. § 271(e).

As these cases show and as currently interpreted, the statute provides both flexibility and the possibility of litigation disputes over the issue of how much information the biosimilar applicant must disclose and when. In particular, while the courts continue to adjudicate whether subsection (*l*)(2)(A) requires an applicant to disclose any manufacturing information beyond that found in the aBLA, these disclosure decisions by applicants may have consequences in terms of the remedies available to the RPS. Biosimilar applicants should consider the potential risk of losing the benefit of the damages limitation under § 271(e)(6) when considering their patent dance strategies.

3. Full Dance: Amgen v. Apotex, S.D. Fla. 0:15cv61631 While some biosimilar applicants have chosen not to participate in the patent dance, or not to complete it, Apotex engaged in the entire statutory procedure in the litigation involving its proposed biosimilar versions of Neulasta® (pegfilgrastim) and Neupogen® (filgrastim). The parties engaged in all of the exchanges set forth in subsection (*l*) and agreed to include two patents in the litigation, which was filed on Aug. 6, 2015.

Apotex also provided early notice of commercial marketing, informing Amgen that it intended to launch

upon receiving FDA approval. Amgen brought a preliminary injunction motion seeking to prevent Apotex from giving notice until after Apotex receives FDA approval. The district court granted Amgen's motion, and declined to draw a distinction between no-dance situations and full-dance situations for purposes of interpreting the notice provision of the BPCIA: Apotex had argued that the decision in *Amgen v. Sandoz* was limited to situations where the subsection (k) applicant ''completely fails to provide its aBLA and the required manufacturing information to the RPS by the statutory deadline,'' and did not apply when the applicant had provided the full information disclosure under the patent dance. The district court rejected that distinction, as did the Federal Circuit on Apotex's appeal of the district court's ruling*Amgen Inc. v. Apotex Inc.*, 827 F.3d 1052, Fed. Cir., 2016. Meanwhile, trial proceeded on Amgen's patent infringement claims, and the district court held that Apotex did not infringe the asserted patents. (Amgen has appealed the district court's judgment of noninfringement. *See* Big Molecule Watch, *Briefing Complete in Appeal in* Amgen v. Apotex, available here.) Apotex petitioned the Supreme Court to review the Federal Circuit's ruling on the BPCIA notice provision, arguing that the notice provision served no purpose in a situation such as Apotex's, where the RPS has exhausted its patent rights, and a mandatory post-licensure notice requirement would operate only to delay the biosimilar's launch by 180 days. *Apotex Inc. v. Amgen Inc.*, U.S., 137 S. Ct. 591, *Petition for Writ of Certiorari* 2016 . The Supreme Court denied Apotex's petition for review.

Thus, even in cases where the parties engage in the full patent dance, disputes concerning whether each step has been fully or properly performed can still impact the litigation. The expected approval timeline for an aBLA, the anticipated timing of the resolution of any first-wave patent litigation, and uncertainties over when notice of commercial marketing may be provided should all be considered by biosimilar applicants in advance of filing an aBLA.

Looking Ahead

There are still many open questions in the area of biosimilars litigation. As appeals in these litigations progress, the Federal Circuit and Supreme Court will weigh in on a host of issues, including whether the patent dance is mandatory, the timing of notice of commercial marketing, and the available remedies for alleged noncompliance with various provisions of the statute. The answers to these questions--some of which the Supreme Court is expected to resolve soon--may have significant implications for biosimilar applicants going forward.

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