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Biosimilar Product Approval and the Implications of *Sandoz v. Amgen*

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The U.S. Supreme Court's much-awaited decision in *Sandoz Inc. v. Amgen Inc.*, 2017 BL 198127, U.S., No. 15-1039, 6/12/17 is favorable to biosimilar applicants on two key sections of biosimilars law but many questions remain that will need to be addressed through litigation or regulation under this complex new regulatory regime.

On June 12, 2017, in a unanimous decision authored by Justice Clarence Thomas, the Court addressed two critical questions in the biosimilar approval mechanisms adopted in the Biologics Price Competition and Innovation Act of 2009 (''BPCIA'' or ''Biosimilars Act''). Specifically, the Court considered: (1) whether a federal injunction is available to enforce the BPCIA provision that a biosimilar applicant (''applicant,'' *i.e.*, a company seeking approval to market a biosimilar) engage in the ''patent dance'' by providing the reference product sponsor (''sponsor,'' *i.e.*, the company that markets the original biologic drug) a copy of its biologics license application and certain related manufacturing information, and (2) whether the BPCIA's 180 days' pre-marketing notice provision must be satisfied after the U.S. Food & Drug Administration (''FDA'') has approved the applicant's biosimilar application. The short answer to both is no. However, other BPCIA-related questions and new questions raised by this decision still need to be resolved. Some strategic implications arising from this decision are considered below.

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Question #1: The Availability of Injunctive Relief to Enforce the Provision That the Applicant Provide a Copy of the Biosimilar Application The BPCIA provides an abbreviated pathway for an applicant to obtain FDA approval of a biologic drug that is biosimilar or interchangeable to an already licensed biological drug (*i.e.*, reference product). 42 U.S.C. § 262(k). The BPCIA also provides procedures for resolving patent disputes between the applicant and the sponsor. 42 U.S.C. § 262(l). Under the BPCIA, within 20 days after the FDA accepts an applicant's biosimilar application for review, the applicant ''shall provide'' the sponsor with a copy of the application and information about how the biosimilar is manufactured. 42 U.S.C. § 262(l)(2)(A).

On the first question, *i.e.*, whether a federal injunction is available to enforce the provision that an applicant provide the sponsor a copy of the applicant's biologics license application and certain related manufacturing information, the U.S. Court of Appeals for the Federal Circuit had relied on 35 U.S.C. § 271(e)(4), which provides remedies for an act of artificial infringement, to determine that no federal injunctive relief was available. The Supreme Court affirmed the result but noted that the Federal Circuit's reasoning was incorrect. Specifically, the Supreme Court held that the act of filing the biosimilar application is the artificial act of infringement, not the applicant's failure to disclose its application and manufacturing information, and, thus, no remedy for failure to comply exists under 35 U.S.C. § 271(e)(4). Rather, the Court held that 42 U.S.C. § 262(l)(9)(C) provided the remedy for an applicant's failure to disclose its application and manufacturing information. The Court reasoned that 42 U.S.C. § 262(l)(9)(C), by authorizing the sponsor but not the applicant to bring an immediate declaratory-judgment action for artificial infringement as defined in 42 U.S.C. § 271(e)(2)(C)(ii), ''vests in the sponsor the control that the applicant would otherwise have exercised over the scope and timing of the patent litigation [and] deprives the applicant of the certainty that it could have obtained by bringing a declaratory-judgment action prior to mar-

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keting its product.'' Slip op. at 12. The Court held that ''[t]he remedy provided by § 262(l)(9)(C) excludes all other federal remedies, including injunctive relief.'' *Id*.

Although holding that a federal injunction is not available to enforce the provisions of 42 U.S.C. § 262(l)(2)(A) that an applicant ''shall provide'' the sponsor with a copy of the biosimilar application and manufacturing information, the Court did not expressly decide if this provision was a ''mandatory'' requirement (as advocated by Amgen) or a ''condition precedent'' to participation in the patent dance (as advocated by Sandoz). Slip op. at 13-15. Whether the provision is mandatory is relevant in considering whether Amgen could be entitled to injunctive relief under California's unfair competition law, as pled by Amgen, because California's unfair competition law requires there be ''unlawful'' conduct for there to be a remedy. If providing the application and information is mandatory, then Sandoz's failure to provide it could be ''unlawful'' conduct entitling Amgen to state-law injunctive relief. If providing the application and information is optional, Amgen would likely not be entitled to state-law injunctive relief.

The Court did not address the issue of whether California's unfair competition law provided for injunctive relief because that issue did not present a question of federal law. Slip op. at 14. Rather, the Court remanded this issue to the Federal Circuit for reconsideration because its earlier ruling, holding that California's unfair competition law did not provide a remedy, was decided on an incorrect interpretation of the available remedies for failing to comply with provisions of the BPCIA. Thus, the availability of injunctive relief for Amgen under California's unfair competition law will need to be reconsidered by the Federal Circuit. Amgen, however, will not be entitled to injunctive relief under California's unfair competition law if the Federal Circuit holds, as it did in its earlier ruling, that California's unfair competition law only provides a state-law remedy when the underlying statute does not specify an ''expressly exclusive'' remedy and holds further that the BPCIA provides the only remedy for an applicant failing to disclose its biosimilar application and manufacturing information. Of course, the availability of state-law injunctive relief, under any state law, will be moot if the Federal Circuit holds on remand that the BPCIA preempts any state-law remedy.

A holding by the Federal Circuit that the provisions of 42 U.S.C. § 262(l)(2)(A) are mandatory could have other implications. For example, in its rule-making capacity, the FDA could require that applicants submit a statement with a biosimilar application confirming that they have met the provisions of 42 U.S.C. § 262(l)(2)(A) before the FDA will consider (or make a final decision on) the biosimilar application. Such a rule, mandating that an applicant provide the sponsor with a copy of the biosimilar application and manufacturing information to have the application considered (or approved) by the FDA, could effectively render irrelevant the Supreme Court's holding that the BPCIA does not provide a mechanism for a sponsor to force an applicant to disclose its application and manufacturing information under 42 U.S.C. § 262(l)(2)(A). Indeed, Justice Stephen Breyer's concurrence asserted that deference should be given to the FDA's interpretation of the BPCIA. Concurrence at 1.

Additionally, the Supreme Court suggested in a footnote that an applicant's failure to provide the sponsor with a copy of the biosimilar application and manufacturing information could be a factor considered by a district court in deciding whether to grant a preliminary injunction against marketing a biosimilar in view of a sponsor's patent rights. Slip op. at footnote 2 (stating ''we express no view on whether a district court could take into account 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 U. S. C. § 271(e)(4)(B) or § 283 against marketing the biosimilar'').

Thus, although the Court held that federal injunctive relief is unavailable to sponsors as a mechanism to force an applicant to provide the sponsor with a copy of the biosimilar application and manufacturing information, several issues remain that will need to be addressed on remand to the Federal Circuit or in future litigation—or that may be affected by future FDA rulemaking relating to the biosimilar approval process under the BPCIA.

Question #2: Timing of the Notice of Commercial Marketing Following an applicant's disclosure of its application and manufacturing information, the BPCIA provides that the parties exchange information in the so-called patent dance to identify relevant patents and legal arguments that might be raised in future litigation. 42 U.S.C. § 262(l)(3). Following this exchange, the BPCIA channels the parties into two phases of patent litigation. In the first phase, the parties identify patents that they would like to litigate immediately. The second phase involves patents on the parties' § 262(l)(3) lists that were not litigated in the first phase, and is triggered when the applicant gives the sponsor notice, pursuant to 42 U.S.C. § 262(l)(8)(A), at least 180 days prior to commercially marketing the biosimilar.

Concerning the second question, *i.e.*, whether the applicant may provide its 180-day pre-marketing notice *before* the applicant has obtained FDA approval, the Supreme Court held that the applicant can provide notice *before or after* receiving FDA approval. The Court held that this construction is consistent with the plain language of 42 U.S.C. § 262(l)(8)(A) and the statutory context. In particular, the Court noted that if Congress had intended to impose *two* timing requirements on providing notice, *i.e.*, providing notice after FDA approval *and* at least 180 days before the marketing of the biosimilar, it would have used different language, such as was used in another section of the statute where a dual-timing requirement is specified. Slip op. at 16, citing 42 U.S.C. § 262(l)(8)(B).

In coming to this holding, the Court rejected Amgen's textual arguments for requiring FDA approval before effective notice. Slip op. at 17. According to the Court, Congress' use of the phrase ''biological product licensed under subsection (k)'' in the notice provision did not distinguish from its use of the phrase ''the biological product that is the subject of'' the application elsewhere in the BPCIA. The Court also dismissed Amgen's policy arguments, suggesting that policy issues should be addressed by Congress. The Court found the plain language of the statute clear and, therefore, did not see a need to address any policy considerations. Slip op. at 18. The Court thus held that an applicant need not wait for the FDA to approve its application before providing its commercial marketing notice. *Id*.

  LSLR ISSN 1935-7257

Applicants can now take comfort knowing that a notice of commercial marketing is effective whenever it is given at least 180 days before launch, regardless of whether the biosimilar application has been approved. The Court's decision on this issue is helpful to applicants not only for providing a measure of certainty but also for allowing biosimilar drugs to potentially be sold 12 years after the reference product was approved. By contrast, the Federal Circuit's interpretation of the notice provision had effectively given the reference product an additional 180 days of market exclusivity beyond the 12 years of protection during which the FDA could not approve a biosimilar application.

The Federal Circuit ruled that the applicant must provide notice of commercial marketing. *Amgen Inc. v. Apotex, Inc.*, 827 F.3d 1052, 1054 (Fed. Cir. 2016), *cert denied*, 137 S. Ct. 591 (2016). The implications of whether an applicant provides notice of commercial marketing before FDA approval differ depending on whether the applicant chooses to participate in the patent dance and how many steps of the dance it completes. *See* slip op. at 4-7 (describing the steps in the patent dance).

If an applicant opts to skip the patent dance entirely, it gives up control over the timing of subsequent litigation. *See* slip op. at 7-8; 42 U.S.C. § 262(*l*)(9)(C). In this case, there seems to be no apparent adverse consequence to providing early notice. Regardless of when the applicant provides notice of commercial marketing, it cannot initiate a declaratory judgment lawsuit to resolve issues of infringement and validity—only the sponsor can sue, and may do so at any time and on any patents claiming the biologic product or a method of using the biologic product. *See* slip op. at 7-8; 42 U.S.C. § 262(*l*)(9)(C). Similarly, if the applicant starts the patent dance but quits early, the sponsor may bring a declaratory judgment action on any of the patents on its original list plus any later-acquired patents. *See* slip op. at 7-8; 42 U.S.C. § 262(*l*)(9)(B). If the applicant gives early notice under these circumstances, it may potentially begin selling its biosimilar product immediately after FDA approval, although it risks having to pay damages if the sponsor sues and wins. The Supreme Court did not address whether the sponsor would be able to obtain a preliminary injunction preventing the applicant from selling its product. Although the statute only addresses a preliminary injunction in the context of the patent dance, a sponsor would likely seek to enjoin marketing of the biosimilar product in the same way any patent holder might enforce its patent rights.

On the other hand, if an applicant elects to provide the sponsor with a copy of its application and manufacturing information and then completes the patent dance, early notice could lead to overlap of the two phases of biosimilar litigation. The first phase will occur after the application is filed, the lists of patents are exchanged, and the patents to be litigated are identified. 42 U.S.C. § § 262(*l*)(6)(A), (B). Once the applicant provides its notice of commercial marketing, then either party may commence the second phase by bringing a declaratory judgment suit relating to infringement, validity, or enforceability of any patents on either party's list but not part of the phase-one litigation, including any newly issued or in-licensed patents. *See* 42 U.S.C. § § 262(*l*)(7), (8), (9)(A).

Because the second phase of litigation is triggered by the applicant's notice of commercial marketing, the applicant who participates in the patent dance controls the timing of initiation of the second phase. 42 U.S.C. § 262(*l*)(9)(A). One area where this may be used to the applicant's advantage is for newly issued or licensed patents, which were not available for litigation in phase one. Once the applicant has provided its notice of commercial marketing, it may sue for declaratory judgment relating to these newly issued or licensed patents. Being able to provide early notice of commercial marketing, as allowed under the Supreme Court's decision, provides the applicant the ability to time the second phase such that these additional patents are litigated before the biosimilar application is approved, allowing the applicant to market its product earlier and closer to the expiration of the 12-year regulatory exclusivity than it would otherwise be able to do, without risk, if litigation could not commence until after the application was approved.

The clearest outcome of the decision is that the sponsor is not entitled to an additional 180-day exclusivity after the 12 years granted by the statute. An additional result of the decision is that an applicant who participates in the patent dance can advantageously initiate litigation on newly issued or in-licensed patents of the sponsor before obtaining FDA approval, allowing earlier resolution of potential patent issues and, thus, earlier possible market launch of its biosimilar product.

One potential unresolved issue with early notice of commercial marketing is what constitutes effective notice. This issue is currently being disputed in *Amgen Inc. v. Hospira, Inc.*, No. 1:15-cv-839-RGA (D. Del.). Amgen contends that Hospira's notice of commercial marketing provided in April 2015 was not legally effective because, after that notice, the FDA issued a complete response letter to Hospira stating that its biosimilar application could not be approved in its current form, after which Hospira re-submitted its application. *See* Amgen's Amended Opening Brief in Support of its May 26, 2017, Motion for a Preliminary Injunction (Dkt. No. 277) in *Amgen Inc. v. Hospira, Inc.*, No. 1:15-cv-839-RGA (D. Del. June 29, 2017) at 10-11. The question remains: How effective is notice of commercial marketing if the product as approved differs from that described in the application referenced in the original biosimilar application?

Conclusions The Supreme Court held that federal injunctive relief is not a remedy for an applicant's failure to provide a sponsor with a copy of its biosimilar application and related manufacturing information. This holding is favorable to biosimilar applicants, as it permits them to elect to not fully engage in the patent dance. Likewise, the Court's holding that an applicant can provide notice of commercial marketing even before receiving FDA approval is favorable to biosimilar applicants as it provides additional control over the start of the second phase of litigation.

Although the Court answered questions about two key sections of the BPCIA, various issues are still unresolved. The consequences of the decision, even as to these two sections, remain uncertain pending remand and later district court interpretation of the ruling. In addition, potential FDA rule-making could influence how parts of the BPCIA are interpreted. Thus, we foresee more questions to be litigated, as would be expected with any complex new regulatory regime. We look for-

ward to further judicial decisions answering these and other questions in the coming months and years.

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