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Federal Circuit Patent Bulletin: *Amgen Inc. v. Apotex Inc.*

July 5, 2016

"[Under the BPCIA, a biosmilar] applicant must provide a reference product sponsor with 180 days' post-licensure notice before commercial marketing begins, regardless of whether the applicant provided the (2)(A) notice of FDA review."

On July 5, 2016, in *Amgen Inc. v. Apotex Inc.*, the U.S. Court of Appeals for the Federal Circuit (Wallach, Bryson, Taranto*) affirmed the district court's preliminary injunction in an action under Biologics Price Competition and Innovation Act of 2009 (BPCIA) enjoining Apotex from commercially marketing its pegfilgrastim biosimilar of Amgen's Neulasta® for stimulating the production of neutrophils in chemotherapy. The Federal Circuit stated:

This appeal, however, does not involve the merits of the infringement allegations. Rather, it involves Amgen's motion for a preliminary injunction concerning what will happen if and when the FDA licenses Apotex's proposed biosimilar product. . . . The Biologics Act authorizes enterprises like Apotex to gain approval, after a time, for a product sufficiently similar to the "reference product," without repeating all of the work of the pioneer, the "reference product sponsor" Under § 262(k), an applicant may obtain a license by demonstrating, among other things, that its product is "biosimilar" to a reference product. In so doing, it may use publicly available information about the reference product's safety, purity, and potency to support its application. For the purpose of "balancing innovation and consumer interests," Congress prescribed that a biosimilar-product application under § 262(k) "may not be submitted" until four years after the reference product was first licensed under § 262(a) and that a biosimilar-product license "may not be made effective" until twelve years after the reference product was first licensed.

Of particular relevance here, the Biologics Act contains a detailed, multi-part subsection, § 262(l), that is focused in various ways on potential patent disputes between the reference product sponsor and biosimilar product applicant. That subsection by its terms provides for two stages of litigation—one under paragraph (6), the other under paragraph (8). In this opinion, we will often refer to paragraphs and subparagraphs within that subsection without repeating the "§ 262(l)"; unless otherwise made clear, any such short-hand references are to that subsection. We also will usually call the § 262(k) applicant simply the "applicant." The § 262(l) provisions of principal present significance are as follows. Under (2)(A), within 20 days after the FDA notifies the applicant that its application has been accepted for review, the applicant is to give notice to the reference

product sponsor by providing the application as well as information describing the manufacturing process. Under (3)(A), within 60 days of receiving that notice, the reference product sponsor is to provide a list of patents that could reasonably be asserted against the applicant and specify which it would be prepared to license to the applicant.

Under (3)(B), within 60 days after receiving that list, the applicant is to respond with a detailed statement identifying why each patent on the reference product sponsor's list is invalid, unenforceable, or not infringed, or declaring that it does not intend to commercially market the biosimilar product before a particular patent expires, and also addressing the reference product sponsor's statement of readiness to license. The applicant, in its response, may also provide its own list of patents that it believes could reasonably be asserted against it. Under (3)(C), then, within 60 days of receiving the applicant's (3)(B) response, the reference product sponsor is to provide a detailed reply regarding those patents on its (3)(A) list as to which the applicant has asserted non-infringement, invalidity, or unenforceability. While the reference product sponsor may later supplement its (3)(A) list under paragraph (7), it is the original lists under (3) that form the basis of the next steps in the process leading to immediate litigation under paragraph (6). Those steps begin with paragraph (4), which requires that the reference product sponsor and the applicant enter into good-faith negotiations over which of the patents listed under (3) will be the subject of an immediate patent-infringement action. If the parties reach agreement, (6)(A) provides that the reference product sponsor must bring an action for infringement on all such patents within 30 days. The applicant must then notify the FDA. If the parties do not reach agreement within 15 days of starting their negotiation, (4)(B) directs the parties to paragraph (5) for the process that determines the scope of immediate litigation. That process gives the applicant a scope-limiting ability, based on an exchange of lists of patents to be litigated. The applicant tells the reference product sponsor how many patents will be on the applicant's list; that number caps how many patents the reference product sponsor may list, except that if the applicant lists none, the reference product sponsor may list one; and the two sides exchange lists. Within 30 days, under (6)(B), the reference product sponsor must sue for infringement on precisely those patents that appear on the combined lists. And the applicant must notify the FDA. Notably, the immediate litigation is limited to a single patent if the applicant lists no patents, no matter how many patents the reference product sponsor designated in (3)(A) as reasonably assertable against the making, selling, etc., of the proposed biosimilar product. Given the deadlines set in § 262(l), and the time commonly taken for FDA review, we may assume that the early litigation under paragraph (6) will be initiated before the FDA licenses the applicant's biosimilar product. But the Biologics Act—having provided for a narrowing of the scope of the paragraph (6) litigation, including by allowing the applicant to exclude potentially meritorious patents from that litigation—provides, in paragraph (8), for a second stage of patent litigation. Paragraph (8) does so by first requiring, in (8)(A), that the applicant give the reference product sponsor notice at least 180 days before commercially marketing its "licensed" product. We held in Amgen v. Sandoz that the notice starting the 180-day clock must follow, not precede, the licensure. (8)(B) then declares that, after receiving the (8)(A) post licensure notice but before the applicant's commercial marketing begins, the reference product sponsor may seek a preliminary injunction based on any patent within either of two classes. The first class, expressly described in (8)(B), consists of the patents that appeared on any of the original paragraph (3) lists, minus patents that were the subject of paragraph (6) litigation (by agreement under (4) or by the narrowing process under (5)). The second class consists of certain patents that were issued

to or exclusively licensed by the reference product sponsor after it gave the applicant its (3)(A) list. As to those patents, paragraph (7) prescribes an information exchange and states that they "shall be subject to paragraph (8)," —which evidently means that patents within (7) are to be treated as falling under (8)(B). For this second-stage litigation, (8)(C) requires that the parties reasonably cooperate to expedite new discovery needed in connection with the preliminary injunction motion. Paragraph (9) of § 262(l) reinforces the just-described channeling of litigation and provides incentives for the applicant to proceed in those channels. It does so by addressing when declaratory-judgment actions are or are not available in certain circumstances—in (9)(C), as to applicants that simply bypass the process of information exchange that begins with (2)(A); and in (9)(A) and (B), as to applicants that begin but do not complete the process. (9)(C) addresses an applicant that does not even provide the first-step notice under (2)(A). For such an applicant, the reference product sponsor, but not the applicant, may bring an action under 28 U.S.C. § 2201 for a declaratory judgment of "infringement, validity, or enforceability of any patent that claims the biological product or a use of the biological product." The subject of such action is not limited by reference to any patent lists. (9)(A) and (B) together address an applicant that does provide the (2)(A) notice. (9)(A) protects the two-stage litigation scheme under paragraphs (6) and (8): it declares that neither side may bring a declaratory-judgment action relating to any patent described in (8)(B) for the second stage litigation until after the (post-licensure) 180-day notice of commercial marketing under (8)(A) is received. Then, (9)(B) reinforces the applicant's incentives to complete the orderly process: it specifies that the (9)(A) bar on declaratory-judgment actions is lifted for the reference product sponsor, but not for the applicant, if an applicant that has given the (2)(A) notice "fails to complete an action required" of the applicant at specified steps past the (2)(A) step. The specified applicant duties are those prescribed by paragraph (3)(B)(ii) (responding to the reference product sponsor's (3)(A) list); by paragraph (5) (furnishing lists defining the first-stage litigation in the absence of agreement); by paragraph (6)(C)(i) (notifying the FDA of the first-stage litigation); by paragraph (7) (responding to the reference product sponsor's update of its (3)(A) list); and by paragraph (8)(A) (providing a 180- day notice before commercial marketing of the licensed product). A failure of the applicant at any of those stages lifts the (9)(A) bar on the reference product sponsor, allowing it to bring a declaratory-judgment action on any patent on its (3)(A) list as supplemented under (7).

Besides setting out the foregoing regime, the Biologics Act amended the infringement provision of the Patent Act, 35 U.S.C. § 271, in a way that is tied to that regime. As amended, 35 U.S.C. § 271(e)(2) provides that, in two circumstances, it is "an act of infringement" for a person "to submit" "an application seeking approval of a biological product" if the purpose is to obtain approval "to engage in the commercial manufacture, use, or sale of the biological product claimed in a patent or the use of which is claimed in a patent before the expiration of such patent." The two circumstances involve, respectively, an applicant that has launched the Biologics Act information-exchange process we have described and an applicant that has not. Specifically, one circumstance is when the patent "is identified in the list of patents described in" paragraph (3), "including as provided under" paragraph (7), of the Biologics Act's patent provisions described above. Filing the biosimilar application is an act of infringement of patents that the reference product sponsor has listed through the Biologics Act's prescribed processes, which occurs only when the applicant has provided the (2)(A) notice. The other circumstance involves an applicant that "fails to provide the application and information required" under (2)(A). In that case, filing the biosimilar application is an act of infringement as to a patent

that "could be identified pursuant to" (3)(A), i.e., a patent that the reference product sponsor could identify as one it believes "could reasonably be asserted" with respect to the biosimilar product at issue. 35 U.S.C. § 271 (e)(4) addresses remedies for such infringements. Subparagraphs (B) and (C) authorize injunctions and damages, and subparagraph (D) states that "the court shall order a permanent injunction" against infringement of a patent in certain cases decided in the Biologics Act's first-stage (paragraph (6)) litigation. Section 271(e)(4) adds that those remedies "are the only remedies which may be granted by a court for an act of infringement described in paragraph (2)," except for attorney's fees. 35 U.S.C. § 271(e)(6), however, then limits the just described remedies in two ways evidently designed to reinforce the reference product sponsor's incentives to follow the distinctive Biologics Act's patent process where the applicant has launched that process. First: If the reference product sponsor is late in bringing the first stage infringement action under § 262(l)'s paragraph (6), i.e., does so more than 30 days after the scope of that litigation has been determined under (4) or (5), the only remedy the reference product sponsor can get in that action is a reasonable royalty. Second: If a patent that the reference product sponsor should have included on its (3)(A) list or its (7) supplement "was not timely included," then the owner of that patent may not sue for infringement under 35 U.S.C. § 271 with respect to the biological product at issue. . . .

The (8)(A) requirement of 180 days' post-licensure notice before commercial marketing, we conclude, is a mandatory one enforceable by injunction whether or not a (2)(A) notice was given. Paragraph (8)(A) provides that "[t]he 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)." The word "shall" generally indicates that the directive is mandatory. . . . The language of (8)(A) is categorical in the sense relevant here. It contains no words that make the applicability of its notice rule turn on whether the applicant took the earlier step of giving the (2)(A) notice that begins the § 262(l) information-exchange process. . . . Amgen v. Sandoz likewise disposes of Apotex's argument that giving (8)(A) its plain meaning would effectively extend, by six months, the 12-year exclusivity period given to a reference product sponsor by § 262(k)(7). Notably, § 262(k)(7) by its terms establishes the 12-year date only as an earliest date, not a latest date, on which a biosimilar license can take effect. Even when entry is delayed under (8)(A) to what amounts to 12 years plus 180 days after the reference product sponsor's licensure, the result is consistent with § 262(k)(7). Moreover, it is implicit in the Biologics Act that any such delay beyond 12 years should occur less and less as time goes by. Doubtless, there will be some exclusivity periods beyond 12 years in the early years of the Biologics Act, as biosimilars are introduced for reference products licensed well before the Act was adopted in 2010. But as time passes, more and more of the reference products will be newer, and a biosimilar-product applicant, entitled to file an application a mere four years after licensure of the reference product can seek approval long before the 12-year exclusivity period is up. In such circumstances, we have been pointed to no reason that the FDA may not issue a license before the 11.5-year mark and deem the license to take effect on the 12-year date—a possibility suggested by § 262(k)(7)(A)'s language about when the FDA approval may "be made effective." And we read (8)(A) as allowing the 180-day notice of commercial marketing to be sent as soon as the license issues, even if it is not yet effective, because it is at the time of the license that "the product, its therapeutic uses, and its manufacturing processes are fixed." In any event, the established and evident purpose of (8)(A) covers applicants that file (2)(A) notices as well as those that do not. . . . Congress clearly made a categorical fixed-period judgment in (8)(A)—as it did elsewhere in the

Biologics Act—and we have explained that the "statute must be interpreted as it is enacted, not especially in light of particular, untypical facts of a given case." That litigation-focused purpose extends to applicants that launch and pursue the information-exchange process of § 262(l). . . .

Apotex's final argument is that paragraph (9) of § 262(l) makes a declaratory-judgment action, discussed in (9)(B), the exclusive remedy for violations of (8)(A). We reject that contention. Apotex has not asserted that (8)(A) creates no privately enforceable right, even when asserted as part of an infringement action concerning patent rights whose fair and unhurried adjudication (8)(A) is designed to protect. Nor has it identified any statutory commitment to a government agency of responsibility or authority to enforce or to seek to enforce the (8)(A) command. Instead, Apotex suggests that the only remedy for an applicant's unilateral denial to the reference product sponsor of the 180-day period for post-licensure litigation decision-making is a declaratory-judgment action on a patent—which (9)(B) permits if the applicant "fails to complete" any one of several steps, including the giving of the (8)(A) notice. We cannot infer such an exclusive-remedy conclusion from paragraph (9).[W]e do not find that paragraph (9) establishes that a declaratory-judgment action is the sole remedy for violating (8)(A).