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

July 21, 2015

"[A biosimilar] applicant may only give effective notice of commercial marketing after the FDA has licensed its product [and where the biosimilar applicant] completely fails to provide its [abbreviated biologics license application] and the required manufacturing information to the [reference product sponsor (RPS)] by the statutory deadline, the requirement [that the biosimilar applicant provide notice of commercial marketing to the RPS no later than 180 days before commercial marketing of the licensed product] is mandatory."

On July 21, 2015, in *Amgen Inc. v. Sandoz Inc.*, the U.S. Court of Appeals for the Federal Circuit (Newman, Lourie,* Chen) affirmed-in-part, vacated-in-part, and remanded the district court's judgment, inter alia, that the Biologics Price Competition and Innovation Act of 2009 (BPCIA) provided no remedy for Sandoz's refusal, as the applicant for Zarxio—a filgrastim biosimilar to Neupogen, to provide the reference product sponsor Amgen with Sandoz's biosimilar application and manufacturing information, and that Sandoz could market Zarxio as of March 6, 2015. The Federal Circuit stated:

In 2010, as part of the Patient Protection and Affordable Care Act, Congress enacted the BPCIA, which established an abbreviated pathway for regulatory approval of follow-on biological products that are "highly similar" to a previously approved product ("reference product"). Congress established such "a biosimilar pathway balancing innovation and consumer interests." . . . Traditionally, the Food and Drug Administration ("FDA") approves a biological product for commercial marketing by granting a biologics license under 42 U.S. C. § 262(a). An applicant filing a biologics license application ("BLA") typically provides clinical data to demonstrate the safety and efficacy of its product. In contrast, under the abbreviated pathway created by the BPCIA, codified at 42 U.S.C. § 262(k), an applicant filing an abbreviated biologics license application ("aBLA" or "subsection (k) application") instead submits information to demonstrate that its product is "biosimilar" to or "interchangeable" with a previously approved reference product, together with "publicly-available information regarding the [FDA]'s previous determination that the reference product is safe, pure, and potent. The BPCIA thus permits a biosimilar applicant to rely in part on the approved license of a reference product.

To balance innovation and price competition, Congress enacted the BPCIA to provide a four-year and a twelve-year exclusivity period to a reference product, both beginning on the date of first licensure of the reference product. Specifically, a subsection (k) application "may not be submitted to the Secretary until the date that is 4 years after the date on which the reference product was first licensed under subsection (a),"

and approval of a subsection (k) application "may not be made effective by the Secretary until the date that is 12 years after the date on which the reference product was first licensed under subsection (a)." Thus, a sponsor of an approved reference product (the "reference product sponsor" or "RPS") receives up to twelve years of exclusivity against follow-on products, regardless of patent protection.

Moreover, the BPCIA established a patent-disputeresolution regime by amending Titles 28, 35, and 42 of the United States Code. The BPCIA amended the Patent Act to create an artificial "act of infringement" and to allow infringement suits based on a biosimilar application prior to FDA approval and prior to marketing of the biological product. The BPCIA also established a unique and elaborate process for information exchange between the biosimilar applicant and the RPS to resolve patent disputes. Under that process, codified at 42 U.S.C. § 262(l), the biosimilar applicant grants the RPS confidential access to its aBLA and the manufacturing information regarding the biosimilar product no later than 20 days after the FDA accepts its application for review. The parties then exchange lists of patents for which they believe a claim of patent infringement could reasonably be asserted by the RPS, as well as their respective positions on infringement, validity, and enforceability of those patents. Following that exchange, which could take up to six months, the parties negotiate to formulate a list of patents ("listed patents") that would be the subject of an immediate infringement action, and the RPS then sues the biosimilar applicant within 30 days. That information exchange and negotiation thus contemplates an immediate infringement action brought by the RPS based only on listed patents.

Subsection 262(l) also provides that the applicant give notice of commercial marketing to the RPS at least 180 days prior to commercial marketing of its product licensed under subsection (k), which then allows the RPS a period of time to seek a preliminary injunction based on patents that the parties initially identified during information exchange but were not selected for the immediate infringement action, as well as any newly issued or licensed patents (collectively, "non-listed patents"). Subsection 262(l) additionally provides, in paragraph (l)(9)(A), that if the applicant discloses the information "required under paragraph (2)(A)," then neither the RPS nor the applicant may bring a declaratory judgment action based on the non-listed patents prior to the date on which the RPS receives the notice of commercial marketing under paragraph (l)(8)(A). Paragraphs (l)(9)(B) and (l)(9)(C), however, permit the RPS, but not the applicant, to seek declaratory relief in the event that the applicant fails to comply with certain provisions of subsection (l). . . .

We first consider whether the district court erred in concluding that a subsection (k) applicant may elect not to disclose its aBLA and the manufacturing information under 42 U.S.C. § 262(l)(2)(A), subject only to the consequences set forth in § 262(l)(9)(C). Paragraph (l)(2)(A) provides that: Not later than 20 days after the Secretary notifies the subsection (k) applicant that the application has been accepted for review, the subsection (k)applicant shall provide to the reference product sponsor a copy of the application submitted to the Secretary under subsection (k), and such other information that describes the process or processes used to manufacture the biological product that is the subject of such application . . . . Paragraph (l)(9)(C) provides that: If a subsection (k) applicant fails to provide the application and information required under paragraph (2)(A), the reference product sponsor, but not the subsection (k) applicant, may bring an action under section 2201 of Title 28, for a declaration of infringement, validity, or enforceability of any patent that claims the

biological product or a use of the biological product. Additionally, 35 U.S.C. § 271(e)(2)(C)(ii), as amended by the BPCIA, provides that: It shall be an act of infringement to submit . . . if the applicant for the application fails to provide the application and information required under section 351(l)(2)(A) of such Act, an application seeking approval of a biological product for a patent that could be identified pursuant to section 351(l)(3)(A)(i) of such Act . . . .

We conclude that, read in isolation, the "shall" provision in paragraph (l)(2)(A) appears to mean that a subsection (k) applicant is required to disclose its aBLA and manufacturing information to the RPS by the deadline specified in the statute. . . . However, the "shall" provision in paragraph (l)(2)(A) cannot be read in isolation. In other provisions, the BPCIA explicitly contemplates that a subsection (k) applicant might fail to disclose the required information by the statutory deadline. It specifically sets forth the consequence for such failure: the RPS may bring an infringement action under 42 U.S.C. § 262(l)(9)(C) and 35 U.S.C. § 271(e)(2)(C)(ii). Those latter provisions indicate that "shall" in paragraph (l)(2)(A) does not mean "must." And the BPCIA has no other provision that grants a procedural right to compel compliance with the disclosure requirement of paragraph (l)(2)(A). . . . Notably, both 42 U.S.C. § 262(l)(9)(C) and 35 U.S.C.§ 271(e)(2)(C)(ii) are premised on a claim of patent infringement, and the BPCIA does not specify any nonpatent-based remedies for a failure to comply with paragraph (l)(2)(A). Once the RPS brings an infringement suit under those two provisions, it can access the required information through discovery.

Importantly, mandating compliance with paragraph (l)(2)(A) in all circumstances would render paragraph (l)(9)(C) and 35 U.S.C. § 271(e)(2)(C)(ii) superfluous, and statutes are to be interpreted if possible to avoid rendering any provision superfluous. . . . Here, Amgen alleged that Sandoz violated the BPCIA, but the alleged violation is precisely an act of infringement under § 271(e)(2)(C)(ii), for which § 271(e)(4)provides the "only remedies." We therefore conclude that, even though under paragraph (l)(2)(A), when read in isolation, a subsection (k) applicant would be required to disclose its aBLA and the manufacturing information to the RPS by the statutory deadline, we ultimately conclude that when a subsection (k) applicant fails the disclosure requirement, 42 U.S.C.§ 262(l)(9)(C) and 35 U.S.C. § 271(e) expressly provide the only remedies as those being based on a claim of patent infringement. Because Sandoz took a path expressly contemplated by the BPCIA, it did not violate the BPCIA by not disclosing its aBLA and the manufacturing information by the statutory deadline.

We next consider whether the district court erred in concluding that a subsection (k) applicant may satisfy its obligation to give notice of commercial marketing under 42 U.S.C. § 262(l)(8)(A) by doing so before the FDA licenses its product. Paragraph (l)(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)." [U]nder paragraph (l)(8)(A), a subsection (k) applicant may only give effective notice of commercial marketing after the FDA has licensed its product. The statutory language compels such an interpretation. It means that notice, to be effective under this statute, must be given only after the product is licensed by the FDA. . . .

While it is true that only a licensed product may be commercially marketed, it does not follow that whenever the future commercial marketing of a yet-to-be licensed product is discussed, it is the "licensed" product. It is not yet "the licensed product." Congress could have used the phrase "the biological product that is the subject of" the application in paragraph (l)(8)(A), as it did in other provisions, but it did not do so. We believe that Congress intended the notice to follow licensure, at which time the product, its therapeutic uses, and its manufacturing processes are fixed. When a subsection (k) applicant files its aBLA, it likely does not know for certain when, or if, it will obtain FDA licensure. The FDA could request changes to the product during the review process, or it could approve some but not all sought-for uses. Giving notice after FDA licensure, once the scope of the approved license is known and the marketing of the proposed biosimilar product is imminent, allows the RPS to effectively determine whether, and on which patents, to seek a preliminary injunction from the court.

Requiring that a product be licensed before notice of commercial marketing ensures the existence of a fully crystallized controversy regarding the need for injunctive relief. It provides a defined statutory window during which the court and the parties can fairly assess the parties' rights prior to the launch of the biosimilar product. If a notice of commercial marketing could be given at any time before FDA licensure, the RPS would be left to guess the scope of the approved license and when commercial marketing would actually begin. Indeed, filing an aBLA only suggests that a subsection (k) applicant intends to commercially market its product someday in the future.

Furthermore, requiring FDA licensure before notice of commercial marketing does not necessarily conflict with the twelve-year exclusivity period of § 262(k)(7)(A). It is true that in this case, as we decide infra, Amgen will have an additional 180 days of market exclusion after Sandoz's effective notice date; that is because Sandoz only filed its aBLA 23 years after Amgen obtained FDA approval of its Neupogen product. Amgen had more than an "extra" 180 days, but that is apparently the way the law, business, and the science evolved. That extra 180 days will not likely be the usual case, as aBLAs will often be filed during the 12-year exclusivity period for other products. A statute must be interpreted as it is enacted, not especially in light of particular, untypical facts of a given case. Finally, it is counterintuitive to provide that notice of commercial marketing be given at a time before one knows when, or if, the product will be approved, or licensed.

We therefore conclude that, under paragraph (l)(8)(A),a subsection (k) applicant may only give effective notice of commercial marketing after the FDA has licensed its product. The district court thus erred in holding that a notice of commercial marketing under paragraph (l)(8)(A) may effectively be given before the biological product is licensed, and we therefore reverse its conclusion relating to its interpretation of § 262(l)(8)(A) and the date when Sandoz may market its product. . . . Here, Sandoz's notice in July 2014, the day after the FDA accepted its application for review, was premature and ineffective. However, the FDA approved Sandoz's aBLA on March 6, 2015, and Sandoz gave a "further" notice of commercial marketing on that day. These facts are uncontested. That notice in March 2015 thus serves as the operative and effective notice of commercial marketing in this case.

A question exists, however, concerning whether the "shall" provision in paragraph (l)(8)(A) is mandatory. We conclude that it is. Both paragraph (l)(2)(A) and (l)(8)(A) use the word "shall," which presumptively signals a statutory requirement. As we have noted with respect to paragraph (l)(2)(A), however, the BPCIA explicitly contemplates that a subsection (k) applicant might fail to comply with the requirement of paragraph (l)(2)(A) and further specifies the consequence for such failure in 42 U.S.C. § 262(l)(9)(C) and 35 U.S.C. § 271(e)(2)(C)(ii). Because of those explicit statutory provisions, and to avoid construing the statute so as to render them superfluous, we have interpreted the BPCIA as allowing noncompliance with paragraph (l)(2)(A), subject to the consequence specified in those other provisions.

In contrast, with respect to paragraph (l)(8)(A), we do not find any provision in the BPCIA that contemplates, or specifies the consequence for, noncompliance with paragraph (l)(8)(A) here, which would be the case if Sandoz attempts to launch in disregard of the requirement of paragraph (l)(8)(A), as we have interpreted it. . . . While it is true that paragraph (l)(9)(B) specifies the consequence for a subsequent failure to comply with paragraph (l)(8)(A) after the applicant has complied with paragraph (l)(2)(A), it does not apply in this case, where Sandoz did not comply with paragraph (l)(2)(A) to begin with. Indeed, the consequence specified in paragraph (l)(9)(B) is a declaratory judgment action brought by the RPS based on "any patent included in the list described in paragraph (3)(A), including as provided under paragraph(7)." 42 U.S.C. § 262(l)(9)(B). Here, however, because Sandoz did not provide the required information to Amgen under paragraph (l)(2)(A), Amgen was unable to compile a patent list as described in paragraph (l)(3)(A) or paragraph (l)(7).

Paragraph (l)(8)(A) is a standalone notice provision in subsection (l), and Sandoz concedes as much. Unlike the actions described in paragraphs (l)(3) through (l)(7), which all depend on, or are triggered by, the disclosure under paragraph (l)(2)(A), nothing in paragraph (l)(8)(A) conditions the notice requirement on paragraph (l)(2)(A) or other provisions of subsection (l). Moreover, nothing in subsection (l) excuses the applicant from its obligation to give notice of commercial marketing to the RPS after it has chosen not to comply with paragraph(l)(2)(A). The purpose of paragraph (l)(8)(A) is clear: requiring notice of commercial marketing be given to allow the RPS a period of time to assess and act upon its patent rights. We therefore conclude that, where, as here, a subsection (k) applicant completely fails to provide its aBLA and the required manufacturing information to the RPS by the statutory deadline, the requirement of paragraph (l)(8)(A) is mandatory. Sandoz therefore may not market Zarxio before 180 days from March 6, 2015, i.e., September 2, 2015.