United States Court of Appeals for the Federal Circuit

SANDOZ INC.,
Plaintiff-Appellant,

v.

AMGEN INC. AND HOFFMANN-LA ROCHE INC.,
Defendants-Appellees.

2014-1693

Appeal from the United States District Court for the Northern District of California in No. 3:13-cv-02904 MMC, Judge Maxine M. Chesney.

Decided: December 5, 2014

JAMES F. HURST, Winston & Strawn LLP, of Chicago, Illinois, argued for plaintiff-appellant. With him on the brief were MAUREEN L. RURKA and JAMES M. HILMERT.

DAVID T. PRITIKIN, Sidley Austin LLP, of Chicago, Illinois, argued for defendants-appellees. With him on the brief were VERNON M. WINTERS, of San Francisco, California, and JEFFREY P. KUSHAN, of Washington, DC. Of counsel on the brief were WENDY A. WHITEFORD, J. DREW DIAMOND, and GAIL A. KATZ, Amgen, Inc., of Thousand Oaks, California, for Amgen Inc. Of counsel were JAMES A. HIGH, JR., of Washington, DC, M. PATRICIA THAYER, of

San Francisco, California, and SAMUEL N. TIU, of Los Angeles, California.

Before DYK, TARANTO, and CHEN, *Circuit Judges*.

TARANTO, *Circuit Judge*.

Sandoz Inc. sued Amgen Inc. and Hoffman-La Roche Inc. to obtain a declaratory judgment that two patents, owned by Hoffman-La Roche and exclusively licensed to Amgen, are invalid and unenforceable and will not be infringed if Sandoz uses, offers to sell or sells, or imports a drug product "biosimilar" to Amgen's Enbrel®. At the time it brought suit, Sandoz had not (as it still has not) filed an application for approval of its contemplated product by the Food and Drug Administration (FDA) and had only just begun certain testing required for its contemplated FDA filing. The district court dismissed the case, determining that no Article III controversy (yet) existed between the parties and also that the suit was barred by the Biologics Price Competition and Innovation Act of 2009 (BPCIA), Pub. L. No. 111-148, §§ 7001–7003, 124 Stat. 119, 804–21 (2010) (codified principally at 42 U.S.C. § 262). *Sandoz Inc. v. Amgen Inc.*, No. CV-13-2904 MMC, 2013 WL 6000069, at *2–3 (N.D. Cal. Nov. 12, 2013). We affirm, concluding that Sandoz did not allege an injury of sufficient immediacy and reality to create subject matter jurisdiction. We do not address the district court's interpretation of the BPCIA.

BACKGROUND

Amgen markets Enbrel®, a "biological product" under 42 U.S.C. § 262(i), as a therapy for rheumatoid arthritis. The active ingredient in Enbrel® is the protein etaner-

cept.[1] Amgen's predecessor, Immunex, received an FDA Biologics License for Enbrel®, under 42 U.S.C. § 262(a) and 21 C.F.R. pt. 601, in 1998. Sandoz began developing its own etanercept product in 2004.

In late 2011 and early 2012, the Patent and Trademark Office issued Patent Nos. 8,063,182 and 8,163,522 to Hoffman-LaRoche. The '182 patent claims specified proteins and related pharmaceutical compositions. The '522 patent claims certain methods of using host cells that include specified polynucleotides that encode certain proteins, specified polynucleotides themselves, and vectors and cells containing specified polynucleotides. Amgen has identified those two patents as among four patents "for etanercept." J.A. 3146; *see* J.A. 3129 (press release stating that the '182 patent is "related to Enbrel®"). Sandoz alleges in its complaint that, "[a]ccording to Amgen, the patents cover . . . 'etanercept,'" J.A. 2002; *see Sandoz,* 2013 WL 6000069, at *1, although Sandoz alleges that Amgen is wrong, J.A. 2010.

Sandoz needs FDA approval to enter the market with its own etanercept drug, and in 2010 Sandoz began a series of meetings with the FDA to plan for an application based on biosimilarity to Enbrel®. That year, Congress enacted the BPCIA, borrowing from (though not copying) the Hatch-Waxman Act's process for use of an Abbreviated New Drug Application (ANDA), rather than a full New Drug Application, to obtain approval of generic versions of previously approved drugs. *E.g.*, 21 U.S.C. § 355(j). The BPCIA establishes an FDA regulatory-approval process—

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[1] Etanercept is a dimeric fusion protein, *i.e.*, a protein composed of two subunits, each of which itself is a combination of portions of two different proteins. Specifically, each etanercept subunit consists of a portion of the human tumor necrosis factor receptor joined with a portion of the human antibody IgG1.

more abbreviated than the full Biologics License Application process—for biological products that are shown to be "biosimilar" to a "reference product" already approved by the FDA. *See* 42 U.S.C. § 262(k).[2] On June 24, 2013, after close consultation with the FDA, Sandoz announced a large-scale human (Phase III) trial for its contemplated etanercept product. *See* 21 C.F.R. § 312.21 (Phase III trials "usually include from several hundred to several thousand subjects"). This trial, expected to run into 2015, was to be completed before Sandoz filed any application for FDA approval.

The same day that Sandoz began its Phase III trial, Sandoz filed a complaint against Amgen and Hoffman-LaRoche (hereafter collectively "Amgen"). Sandoz sought a declaratory judgment that "the manufacture, use, sale, offering for sale, or importation of its etanercept product will not infringe, directly or indirectly, any valid claim of" either the '182 or the '522 patent, that both patents are unenforceable due to prosecution laches, and that both patents are invalid. J.A. 2015–18. Sandoz had not—and

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[2] Under the BPCIA, "biosimilar" means "(A) that the biological product is highly similar to the reference product notwithstanding minor differences in clinically inactive components; and (B) there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product." 42 U.S.C. § 262(i)(2). In contrast, an ANDA requires a showing of "bioequivalen[ce]." 21 U.S.C. § 355(j)(2)(A)(iv); 21 C.F.R. § 320.1.

The BPCIA also provides for approval based on "interchangeability," which confers certain benefits on the applicant and which the FDA may find if it finds biosimilarity and additional facts. 42 U.S.C. § 262(i)(3), (k)(2)(B), (k)(4), (k)(6).

still has not—filed an application for FDA approval to market an etanercept product.

Amgen moved to dismiss the complaint, arguing, among other things, that the court lacked jurisdiction because no immediate, real controversy between the parties yet existed. The district court granted the motion. It agreed with Amgen that Sandoz had not "established a 'real and immediate injury or threat of future injury'" caused by Amgen and so had not established a case or controversy. *Sandoz*, 2013 WL 6000069, at *2 (quoting *Prasco, LLC v. Medicis Pharm. Corp.*, 537 F.3d 1329, 1339 (Fed. Cir. 2008)).

The district court also relied on a separate ground for dismissal—that the BPCIA prohibited Sandoz's suit. Among its provisions, the BPCIA establishes procedures for the narrowing and resolution of patent disputes between biosimilarity applicants and reference-product sponsors. *See* 42 U.S.C. § 262(*l*). The district court concluded that Sandoz could not obtain a declaratory judgment before filing an FDA biosimilarity application. The court reasoned that, because Sandoz planned to enter the market by the biosimilarity route, it had to follow the BPCIA's patent-related procedures applicable to biosimilarity applicants—which it had not done. *Sandoz*, 2013 WL 6000069, at *1–2.

Sandoz timely appealed. We have jurisdiction under 28 U.S.C. § 1295(a)(1).

DISCUSSION

We review de novo the dismissal of a declaratory-judgment action for lack of subject-matter jurisdiction. *3M Co. v. Avery Dennison Corp.*, 673 F.3d 1372, 1377 (Fed. Cir. 2012). Sandoz bears the burden of establishing jurisdiction. *McNutt v. Gen. Motors Acceptance Corp. of Ind.*, 298 U.S. 178, 189 (1936).

A

Under the Declaratory Judgment Act, "[i]n a case of actual controversy within its jurisdiction . . . any court of the United States . . . may declare the rights and other legal relations of any interested party seeking such declaration, whether or not further relief is or could be sought." 28 U.S.C. § 2201. The Act creates a remedy, not an independent source of subject-matter jurisdiction. *Skelly Oil Co. v. Phillips Petroleum Co.*, 339 U.S. 667, 671 (1950). Indeed, "the phrase 'case of actual controversy' in the Act refers to the type of 'Cases' and 'Controversies' that are justiciable under Article III." *MedImmune, Inc. v. Genentech, Inc.*, 549 U.S. 118, 127 (2007).

To answer the underlying case-or-controversy question in this context, we ask "whether the facts alleged, under all the circumstances, show that there is a substantial controversy, between parties having adverse legal interests, of sufficient immediacy and reality to warrant the issuance of a declaratory judgment." *Id.* (internal quotation marks omitted). The inquiry, focused on the combination of immediacy and reality, involves no bright-line test. *See id.* The required distinction is between a suit involving a "real and substantial" dispute that "admit[s] of specific relief through a decree of a conclusive character" and a suit that calls for "an opinion advising what the law would be upon a hypothetical state of facts." *Id.* (internal quotation marks omitted).

We have frequently applied *MedImmune*'s "all the circumstances" standard to determine, in the patent context, whether a declaratory-judgment plaintiff has presented a case of sufficient "immediacy and reality." *See, e.g.*, *Arkema Inc. v. Honeywell Int'l, Inc.*, 706 F.3d 1351, 1356–60 (Fed. Cir. 2013); *Matthews Int'l Corp. v. Biosafe Eng'g, LLC*, 695 F.3d 1322, 1328–31 (Fed. Cir. 2012); *Cat Tech LLC v. TubeMaster, Inc.*, 528 F.3d 871, 878–83 (Fed. Cir. 2008); *Benitec Austl., Ltd. v. Nucleonics, Inc.*, 495 F.3d

1340, 1343–49 (Fed. Cir. 2007). The immediacy requirement is not concerned in the abstract with the amount of time that will occur between the filing of the declaratory judgment action and the liability-creating event. An event that is several years in the future may be an appropriate subject for a declaratory judgment. The immediacy requirement is concerned with whether there is an immediate impact on the plaintiff and whether the lapse of time creates uncertainty. The two issues—immediacy and reality—are thus related.

We have assessed "immediacy" by considering how far in the future the potential infringement is, whether the passage of time might eliminate or change any dispute, and how much if any harm the potential infringer is experiencing, at the time of suit, that an adjudication might redress. *See Matthews*, 695 F.3d at 1329–30 (citing cases). We have assessed "reality" by examining any uncertainties about whether the plaintiff will take an action that will expose it to potential infringement liability and, if so, exactly what action. *Arkema*, 706 F.3d at 1360 (noting absence of "uncertainty about whether the supplier's product is going to be used in a way that might or might not infringe the patentee's rights"); *Matthews*, 695 F.3d at 1330–31 (discussing cases requiring that plaintiff's conduct be "substantially fixed"). In short, we have focused on related questions of timing and contingency regarding the existence and content of any needed patent adjudication, as well as current concrete harms to the declaratory-judgment plaintiff from delaying an adjudication.

Reflecting *MedImmune*'s suggestion that "justiciability problem[s]" can be described in terms of standing and ripeness, 549 U.S. at 128 n.8, we have said that standing and ripeness, as well as mootness, serve as "helpful guide[s] in applying the all-the-circumstances test" because "satisfying these doctrines represents the absolute constitutional minimum for a justiciable controversy"

under Article III. *Prasco*, 537 F.3d at 1336; *see also Caraco Pharm. Labs., Ltd. v. Forest Labs., Inc.*, 527 F.3d 1278, 1291 (Fed. Cir. 2008). Here, ripeness principles in particular reinforce the importance of contingency in the analysis. "A claim is not ripe for adjudication if it rests upon contingent future events that may not occur as anticipated, or indeed may not occur at all." *Texas v. United States*, 523 U.S. 296, 300 (1998) (internal quotation marks omitted). More broadly, a ripeness analysis considers whether "further factual development would significantly advance [the court's] ability to deal with the legal issues presented," *Nat'l Park Hospitality Ass'n v. Dep't of Interior*, 538 U.S. 803, 812 (2003) (internal quotation marks omitted), and whether "the complained-of conduct has an 'immediate and substantial impact' on the plaintiff," *Caraco*, 527 F.3d at 1295 (quoting *Gardner v. Toilet Goods Ass'n*, 387 U.S. 167, 171 (1967)).

B

We conclude that Sandoz's complaint does not present a case or controversy. We reach this conclusion on the particular facts before us. *See Matthews*, 695 F.3d at 1328 ("[I]n determining whether a justiciable controversy is present, the analysis must be calibrated to the particular facts of each case . . . ."). We do not address distinct questions that may arise as Sandoz continues its efforts to develop and obtain approval to market an etanercept product. In particular, we do not address Sandoz's ability to seek a declaratory judgment if and when it files an FDA application under the BPCIA.

The Supreme Court has not had occasion to address the justiciability requirements in the context presented by Sandoz's complaint. In *MedImmune* and, more recently, in *Medtronic, Inc. v. Mirowski Family Ventures, LLC*, 134 S. Ct. 843 (2014), there was no dispute that the challenger was ready to engage in commercial activities immediately and with a specific, fixed product, without any suggestion

that regulatory hurdles still had to be cleared for the activities to begin. *MedImmune*, 549 U.S. 118 (licensed seller of FDA-approved product challenged the licensed patent's validity, wishing to continue its sales free of royalties); *Medtronic*, 134 S. Ct. 843 (factually similar situation involving medical-device manufacturer). Sandoz's position is quite different. Amgen has not suggested that anything Sandoz is currently doing exposes it to infringement liability,[3] and there is no dispute that Sandoz cannot engage in the only liability-exposing conduct at issue without FDA approval of an application precisely defining the products it may market. Sandoz has not even filed such an application.

Unlike the Supreme Court, our court has addressed justiciability in contexts similar to the one before us. In *Telectronics Pacing Sys., Inc. v. Ventritex, Inc.*, 982 F.2d 1520 (Fed. Cir. 1992), we concluded that the district court could have found no case or controversy where the accused medical device—at the relevant time being used only under an Investigational Device Exemption, in a way protected against infringement charges by 35 U.S.C. § 271(e)(1), *see* 982 F.2d at 1521, 1525—"had only recently begun clinical trials, and was years away from potential FDA approval," 982 F.2d at 1527. In *Benitec*, decided after *MedImmune*, the court held that the potentially infringing future activity of Nucleonics did not meet the immediacy and reality requirements, explaining: "The

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[3] Sandoz is conducting its clinical trial outside the United States. Moreover, 35 U.S.C. § 271(e)(1) provides a "safe harbor" that "exempt[s] from infringement *all* uses of patented compounds 'reasonably related' to the process of developing information for submission under *any* federal law regulating the manufacture, use, or distribution of drugs." *Merck KGaA v. Integra Lifesciences I, Ltd.*, 545 U.S. 193, 206 (2005) (emphasis in original).

fact that Nucleonics may file [a New Drug Application] in a few years does not provide the immediacy and reality required for a declaratory judgment." 495 F.3d at 1346. We are aware of no decision in which we have found a case or controversy when the only activity that would create exposure to potential infringement liability was a future activity requiring an FDA approval that had not yet been sought.[4]

Without adopting a categorical rule, we conclude that the present case does not meet the requirements of immediacy and reality. We begin with the immediacy requirement, noting again that contingency plays a role in applying this requirement as it does in applying the reality requirement. When Sandoz filed its suit, it was conducting a Phase III trial of a drug it hopes to make the subject of an FDA application. It told the National Institutes of Health that its trial would last until April 2015. Even that date, let alone any FDA approval, was several years away when Sandoz brought this suit. And if the Phase III trial uncovers material problems, Sandoz may, at a minimum, need to delay any FDA application considerably longer.

In considering what may occur during this period, as in assessing contingencies directly, we can hardly proceed

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[4] *Amgen Inc. v. F. Hoffman-LaRoche Ltd.*, 580 F.3d 1340 (Fed. Cir. 2009), cited to us by Sandoz, involved a declaratory-judgment action by a patent holder asserting that the defendant would infringe if it imported a product into the United States. *Id.* at 1346. We did not discuss any case-or-controversy issue. The district court ultimately granted both declaratory and injunctive relief, *id.*, and it found jurisdiction based on an amended complaint reciting that the defendant had sought FDA approval for its product, *Amgen, Inc. v. F. Hoffman-LaRoche Ltd.*, 456 F. Supp. 2d 267, 271 & n.1 (D. Mass. 2006).

by simply assuming that the Phase III trial will wholly succeed. Sandoz undertook the costly and time-consuming Phase III trial in close consultation with the FDA, even after completing other extensive studies. As those circumstances suggest, we may assume on the record here (and Sandoz does not deny) that the FDA effectively required the trial. Perhaps, like many studies, the trial's purpose was "*confirmation*" of what earlier studies had already strongly indicated. *See* Sandoz Opening Br. at 13 (emphasis in original). Even accepting that characterization, we cannot assume that there was no meaningful uncertainty to resolve. The biosimilarity approval standard is new; indeed, the FDA has not yet applied the new standard to complete its review of and approve any product under the BPCIA. *See* FDA, *Purple Book: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations*, www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/Biosimilars/ucm411418.htm (as of October 2014). Perhaps the FDA is exercising a caution that will prove excessive over time. But we have no basis for saying so.

Any dispute about patent infringement is at present subject to significant uncertainties—concerning whether it will actually arise and if so what specific issues will require decision. Sandoz's Phase III trial may fail in material ways. If so, perhaps Sandoz will not file for approval, thereby eliminating altogether the patent dispute it has asked the district court to adjudicate. Perhaps, if the trial materially fails, *i.e.*, uncovers significant problems, Sandoz will instead modify its proposed product and ultimately file for FDA approval of the modified product. At a minimum, that scenario could alter the content of any patent dispute: notably, infringement of the specific claims of the specific patents—which cover, *e.g.*, particular proteins, pharmaceutical compositions,

polynucleotides, and methods—could present different questions depending on the precise product. In fact, modifying the product now being tested might even eliminate a genuine patent dispute. Sandoz already asserts in its complaint that "the '182 and '522 patents do not cover" the "etanercept product" it seeks to market in the United States—or Amgen's product. J.A. 2010. Conceivably, some modifications would put non-infringement beyond reasonable dispute, even while allowing FDA approval under the agency's still-evolving approach to applying the biosimilarity standard. *See generally* J.A. 1575–93, 3846–60 (draft FDA guidance documents).

Sandoz has not demonstrated that these possibilities for changing or eliminating the patent dispute are so unlikely to arise that they should play no significant role in the Article III determination. Sandoz's complaint says nothing about the specific patent claims and how they do or do not map onto the product Sandoz contemplates or is currently testing (except for denying that the claims cover the product). The complaint relies on the assertions that Amgen has said that the patents cover Enbrel® (which the complaint denies), that Amgen intends to invoke its patents against products that compete with Enbrel®, and that Sandoz seeks to market a competitive product. Neither those allegations nor anything Sandoz has demonstrated about the new FDA biosimilarity standard (or the role of Phase III trials in applying that standard) enables us, on this record, to discount the potential for elimination or alteration of any needed adjudication.

In the pre-application context presented here, we conclude that the events exposing Sandoz to infringement liability "may not occur as anticipated, or indeed may not occur at all," *Texas*, 523 U.S. at 300 (internal quotation marks omitted), and that "further factual development would significantly advance" a court's ability to identify and define the issues for resolution, *Nat'l Park Hospitality Ass'n*, 538 U.S. at 812 (internal quotation marks omitted).

In these respects, this case is unlike *Arkema*, which involved no needed regulatory approvals and no meaningful contingencies affecting the reality or content of the patent dispute. 706 F.3d at 1357–60.

Our conclusion is consistent with our cases under the Hatch-Waxman Act. As noted above, we have found no justiciability where a declaratory-judgment plaintiff had not filed an application for the FDA approval required to engage in the arguably infringing activity. On the other hand, where we have found a case or controversy in the Hatch-Waxman setting, we have focused on the presence of an application for the required FDA approval. *See*, *e.g.*, *Caraco*, 527 F.3d at 1295 ("Caraco has a complete generic drug product that has been submitted to the FDA for approval, and no additional facts are required to determine whether this drug product infringes the claims of Forest's '941 patent."); *Glaxo, Inc. v. Novopharm, Ltd.*, 110 F.3d 1562, 1571 (Fed. Cir. 1997) ("Novopharm also indicated that it had submitted an ANDA accompanied by data sufficient to make FDA approval imminent. Thus, unlike *Telectronics* . . . the threat of Novopharm entering the U.S. market was not years away . . . .") (internal quotation marks omitted).

The Supreme Court and this court have indicated that Congress may act to "articulate chains of causation that will give rise to a case or controversy where none existed before"—thus, in some circumstances, effectively creating justiciability that attenuation concerns would otherwise preclude. *Massachusetts v. EPA*, 549 U.S. 497, 516–18 (2007); *see Consumer Watchdog v. Wis. Alumni Research Found.*, 753 F.3d 1258, 1261 (Fed. Cir. 2014). But Sandoz, in its current posture, cannot invoke any statutory relaxation of otherwise-applicable immediacy and reality requirements. Congress has not specifically provided for suits where the potential infringer has not filed an FDA application for the approval required before it can undertake the activity that might expose it to liability.

In the Hatch-Waxman Act, Congress did provide for certain early adjudications of patent issues that would be presented by future market-entry activity in the FDA setting. It created an "artificial" act of infringement to allow suit by a patent holder, 35 U.S.C. § 271(e)(2)(A); *Bayer Schering Pharma AG v. Lupin, Ltd.*, 676 F.3d 1316, 1318 (Fed. Cir. 2012); and in the BPCIA, Congress extended the provision to biological products, 35 U.S.C. § 271(e)(2)(C). The essential requirement for such actions, however, is the defendant's filing of the FDA application needed for market entry—an application that defines what the applicant would be permitted to do (upon approval) and thus circumscribes and dominates the assessment of potential infringement. *See Ferring B.V. v. Watson Labs., Inc.-Fla.*, 764 F.3d 1401, 1408–09 (Fed. Cir. 2014) (discussing earlier cases). Sandoz has not filed such an application. Accordingly, no congressional judgment aids Sandoz in diminishing the significance of the present uncertainties about whether and when an adjudication will be needed and what issues it will involve if it occurs.

At the same time, Sandoz has not shown that it will suffer an immediate and substantial adverse impact from not being able to seek or secure a patent adjudication before filing an application for FDA approval. Sandoz cannot lawfully enter the market now anyway, wholly apart from the '182 and '522 patents, so there is no question of its taking immediate action that risks building up infringement liability. And while Sandoz has alleged that it has begun investing in expansion of a production facility in Europe, and that the potential American market influenced the expansion decision, it has not argued to us that it is suspending or even delaying this investment until a patent adjudication occurs or that it would do so upon receiving an adverse patent judgment. *See* J.A. 2009, 2055–56, 4047–51; Sandoz Opening Br. at 17, 53–54; Sandoz Reply Br. at 25. To the extent that particular hardships can affect the overall evaluation, we see none

in the circumstances of this case that override the contingency problems that lead us to conclude that Sandoz does not meet the Article III requirements of immediacy and reality.

Our resolution of this case makes it unnecessary for us to address the district court's BPCIA rationale. We also do not decide whether, once an application is filed under the BPCIA, that statute forecloses a declaratory-judgment action concerning whether the ultimate marketing of the application-defined product would infringe under 35 U.S.C. § 271(a).

CONCLUSION

For the foregoing reasons, we affirm the judgment of the district court.

AFFIRMED