Manufacturers Face Potential Roadblock to Early Challenges to Biologic Drug Patents

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Biologic drugs have become increasingly popular in recent years, and now serve as standard treatment options for diseases such as diabetes, anemia, cancer, hepatitis, and multiple sclerosis.1 Biologics are a class of drugs or vaccines that are produced by manipulating a living tissue or microorganism.2 A “biosimilar” is a biologic drug product that is highly similar to a biologic drug previously approved by the U.S. Food and Drug Administration (“FDA”), with no clinically meaningful differences in safety, purity, or potency.3

The Patient Protection and Affordable Care Act, enacted on March 23, 2010, amended the federal Public Health Service Act (“PHSA”)4 to create an abbreviated pathway for FDA approval of biological drug products shown to be biosimilar or interchangeable5 with a previously approved reference (i.e., brand-name) biologic product.6 The new amended provisions of the PHSA are referred to as the “Biologics Price Competition and Innovation Act of 2009” (the “Biosimilars Act” or “BPCIA”).

The Biosimilars Act not only established new regulatory standards and procedures for approval of biosimilars, it also put in place a unique set of rules for identifying and resolving patent disputes involving proposed “follow-on” biologic (“FOB”) products. Until recently, however, no court had been called upon to interpret the BPCIA’s interweaving provisions.

A. The BPCIA “test case”

Amgen Inc. (“Amgen”) is a brand drug company that manufactures the biological drug etanercept, marketed under the brand name “Enbrel.” Enbrel is an injectable drug grouped within a class of medications called “biologic response modifiers” that work by suppressing

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1 See Kate S. Gaudry, Exclusivity Strategies and Opportunities in View of the Biologics Price Competition and Innovation Act, 66 FOOD & DRUG L.J. 587, 587 (2011). “Biologics can be composed of sugars, proteins, or nucleic acids or complex combinations of these substances, or may be living entities such as cells and tissues [and include] a wide range of products such as vaccines, blood and blood components, allergens, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins.” See What Are ‘Biologics’ Questions and Answers, http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CBER/ucm133077.htm.
2 See Gaudry, supra note 1, at 587.
3 See 42 U.S.C. § 262(i)(2).
5 See 42 U.S.C. § 262(i)(3) (defining “[t]he term ‘interchangeable’ or ‘interchangeability’ [to] mean[] that the biological product may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product”).
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the immune system to block proteins that contribute to the disease process. The FDA first approved Enbrel in 1998 for the treatment of moderate to severe rheumatoid arthritis.

On June 24, 2013, generic drug manufacturer Sandoz Inc. (“Sandoz”) filed a declaratory judgment action in the United States District Court for the Northern District of California seeking a declaration of patent noninfringement and invalidity against Amgen and Swiss drug maker Hoffman-La Roche Inc. (“Roche”), which owns two patents related to Enbrel that were exclusively licensed to Amgen. Sandoz sought a declaration that the biosimilar etanercept product it had been developing and taken steps to commercialize since 2004 would not infringe any valid claim of the two Roche patents covering Enbrel—all in anticipation of filing an application with the FDA for regulatory approval.

Amgen and Roche moved to dismiss the complaint on jurisdictional grounds. They argued first that the court lacked subject matter jurisdiction because “neither Roche nor Amgen have ever threatened Plaintiff or otherwise done anything to create a dispute of sufficient immediacy and reality to warrant a declaratory judgment action”; in particular, they argued against “declaratory judgment jurisdiction for a therapeutic where no FDA application had been filed and the requisite clinical trials had not yet been completed.” They asked that the court decline declaratory judgment jurisdiction because, practically speaking, “[a]djudication of the validity and infringement of the Roche patents would be unlikely to finally and conclusively resolve all underlying controversies that might be created by Sandoz’s importation, use, offer for sale or sale of an etanercept product upon FDA approval . ..”

Sandoz responded that “specific threats of infringement are not required” to confer jurisdiction but only a real and immediate conflict, which it claimed existed after “Amgen ha[d] trumpeted its ‘exclusivity’ under its new patents to the entire industry, time and again, and made clear its strategy for Enbrel depends on excluding all competition”—something Sandoz contended “leaves no doubt of [Amgen’s] intent to enforce the ’182 and ’522 patents against Sandoz.” Sandoz urged that “a declaratory judgment action [was] necessary to achieve patent certainty prior to Sandoz’s commercial marketing,” without which, Sandoz argued, “it will be required to shelve its product or risk the potential for significant liability by launching it.”

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7 See What is ENBREL?, http://www.enbrel.com/what-is-ENBREL.jspx.
10 See Complaint at ¶¶ 3, 72.
11 See Motion by Defendants, Amgen, Inc. and Hoffmann-La Roche, Inc. to Dismiss for Lack of Subject-Matter Jurisdiction or, Alternatively, to Decline to Exercise Declaratory Judgment Jurisdiction, Sandoz Inc. v. Amgen Inc. et al., 2013 WL 6000069 (N.D. Cal. Nov. 12, 2013) (No.: 3:13-cv-02904-NC).
12 See id. at 19, 21.
13 See id. at 22.
15 See id. at 1, 23. On the contrary, Sandoz asserted that “the BPCIA provides DJ actions can be filed by either party upon the biosimilar manufacturer’s notice of commercial marketing, which Sandoz has given here.” See id. at 24.
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On November 12, 2013, the California federal district court sided with Amgen and Roche and granted their motion to dismiss without prejudice, finding first that “Sandoz does not contend, and cannot contend, it has complied with its obligations under [the BPCIA] because . . . it has not, to date, filed an application with the FDA.”16 The BPCIA provides, in relevant part, that “[t]he subsection (k) applicant [i.e., the FOB maker] 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).”17 Then, “[i]f a subsection (k) applicant provides the application and information required under paragraph (2)(A), neither the reference product sponsor nor the subsection (k) applicant may, prior to the date notice is received . . . bring any action . . . for a declaration of infringement, validity, or enforceability of any patent . . . .”18 Here, the court reasoned, “Sandoz cannot, as a matter of law, have provided a notice of commercial marketing because . . . its etanercept product [was] not licensed under subsection (k).”19

The court further held that “Sandoz ha[d] not, at this time, established a real and immediate injury or threat of future injury that is caused by the defendants.”20 Specifically, it “submitted [no] evidence demonstrating defendants, by some means other than an express threat to sue, have subjected Sandoz to an ‘immediate’ threat of injury”; instead, the “public statements by Amgen that its patents cover etanercept, and that it defends the patents it owns . . . do not suffice to show an ‘imminent threat’ . . . .”21 Finally, and perhaps most importantly, the court ruled that “Sandoz’s allegation that it intends in the future to file an application with the FDA is insufficient to create a case or controversy” for purposes of establishing federal subject matter jurisdiction.22

B. What does it mean?

The November ruling, the first to interpret the litigation provisions of the Biosimilars Act, has no doubt created waves for manufacturers of biosimilars and may set a precedent with far-reaching implications. First among these is a requirement that a manufacturer of biosimilars must seek FDA approval for its version of a biologic drug before filing legal challenges to the patents on previously approved biologics. From a procedural standpoint, the court’s decision means (for the time being) that the “notice of commercial marketing” needed to trigger the right to file a declaratory action cannot attach to an unlicensed FOB, putting “patent certainty” further from reach.

The conclusions by the Northern District of California appear faithful to the provisions of the BPCIA but at the same time seem to be at odds with the law’s intended purpose of expediting approval of FOBs to foster increased competition among biologics manufacturers, with the ultimate goal being lower prices for these products. Whether other federal courts in California or elsewhere will similarly construe the BPCIA’s complex rules remains to be seen and is worth closely watching. Also interesting will be whether pushback against the law

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19 See Sandoz Inc., at *2 (internal quotations omitted).
20 See id. (internal quotations omitted).
21 See id.
22 See id. at *3.
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from health care industry participants of different stripes will prompt the FDA to issue clarifying regulations to simplify the BPCIA’s implementation.

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