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BIOTECH: THE BATTLE OVER BIOSIMILARS

Sandoz may bring clarity to biosimilars rules

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The global biosimilars market accounted for approximately $1.3 billion in revenue last year. By 2020, revenue attributable to biosimilars is anticipated to increase to $35 billion as market share for biosimilar products grow in the North American, European and Asian markets. An important consideration driving the growth in the biosimilars market is the "patent cliff" facing several biologics. Ten biologics are projected to lose patent protection during the next four years (e.g., Humira, sales of which exceeded $10 billion in 2013, loses patent protection in 2016 and Johnson & Johnson's Remicade, which generated nearly $9 billion in sales in 2013, loses patent protection in Europe early next year, and in 2018 state-side). Revenue attributable to biologics coming off patent is estimated to be approximately $60 billion.

In addition to the ongoing patent cliff, biological innovators are faced with further market erosion from the imminent approval of biosimilars. Biosimilar products, as defined in the Biosimilars Price Competition and Innovation Act (BPCIA), are those that are either "highly similar" or have "no clinically meaningful differences" to an already licensed reference product.

The BPCIA mandates an exchange of patent information relevant to the reference product and the biosimilar (known colloquially as the "patent dance"). As the courts have begun interpreting the BPCIA, they have taken the position that that, in addition to the parties completing the patent dance, the biosimilars manufacturer must complete certain actions before it can successfully undertake a declaratory judgment action against a patent held by the manufacturer of the reference product. Key amongst these actions is the filing with FDA of an application for license to market a biosimilar product. Until very recently, the FDA had not even received an application for approval of a biosimilar. However, this has changed within the last month when Sandoz (Novartis' generic affiliate) and Celltrion Inc. announced submission of the first two biosimilars applications to the FDA.

In a recent case, the court confirmed the requirement that a biosimilar manufacturer and the innovator biologic company progress through and complete the complex "patent dance" to proceed. In November 2013, in *Sandoz Inc. v. Amgen Inc.*, the U.S. District Court for the Northern District of California granted Amgen Inc.'s and co-defendant Hoffmann-La Roche Inc.'s motion to dismiss a June 2013 complaint for declaratory judgment and patent invalidity and noninfringement concerning two patents covering Amgen's product Enbrel. The court interpreted the BPCIA to require a biosimilar manufacturer to at least submit an application for license to market before filing a declaratory judgment action. Because Sandoz had not filed an application with the FDA, the declaratory judgment action was premature.

Although Sandoz stated its intention to file an application to license its biosimilar product at some point in the future, the court found this intention was insufficient to create a "case or controversy," conferring jurisdiction on the court to decide the action. The U.S. Supreme Court's decision in *MedImmune Inc. v. Genentech Inc.*, 549 U.S. 118 (2007), clarified that the existence of a case or controversy is an essential element for determining Article III jurisdiction by the district court. The court dismissed the action.

Sandoz appealed the district court decision to the U.S. Court of Appeals for the Federal Circuit in March, arguing that the district court's decision "completely deprives federal courts of jurisdiction over any declaratory judgment action implicating a biosimilar product until after the FDA had already approved the product — a serious error that undermines the BPCIA's stated purpose of advancing competition for biologic drugs." Sandoz also argued that the court had jurisdiction even though Amgen did not threaten to sue Sandoz for patent infringement under the Supreme Court's holding in *MedImmune*.

Sandoz asserts that "the district court's contrary ruling defies both the plain text and very purpose of the BPCIA. The BPCIA contains no provision depriving courts of jurisdiction to resolve patent disputes where jurisdiction already existed, as here, before an FDA filing. While the BPCIA does contain certain limitations on declaratory judgment actions after a biosimilar application is submitted, those limitations do not apply to Sandoz's complaint, which was filed before any FDA application. The district court was not at liberty to impose a jurisdictional bar that does not exist in the statute's text, and its decision to create such a bar — without briefing on the issue, no less — was pure error."

Sandoz also asserts that the court misinterpreted the BPCIA's provisions by finding that a declaratory judgment action could not be initiated until the reference product and biosimilar manufacturers had completed the statutorily mandated exchanges of information. Sandoz argues an alternative interpretation in which the patent exchanges serve only as a prelude for an action for a patent owner's infringement lawsuit under Section 271(e)(2)(C), not a declaratory judgment: "The statute allows either party to file for declaratory judgment once a biosimilar applicant gives notice of its intention to market its product. Thus, even if the BPCIA applied, as the district court found, its provisions would expressly permit Sandoz's action here because Sandoz provided Amgen notice of its intention to commercially market its product before bringing this case."

In a second similar action this March, Celltrion Healthcare Co. filed suit in the U.S. District Court for the District of Massachusetts, seeking a declaratory judgment with respect to certain patents allegedly covering Janssen Biotech's biological product Remicade. Janssen countered with a motion to dismiss. The theories and arguments in both the complaint and motion closely track those in *Sandoz*. Thus, it is indeed likely that resolution of this lawsuit will, similar to *Sandoz*, require judicial interpretation of the complex patent resolution provisions added to the Public Health Service Act by the BPCIA, and of the effect of these provisions on a the Article III jurisdiction of the district court.

Ever since the BPCIA was enacted, attorneys have evaluated the patent litigation provisions of the act for guidance on which strategies to pursue. The Federal Circuit's interpretation of the act in *Sandoz* is likely to prove significant — particularly since it is the first. Manufacturers of reference products and biosimilars await further guidance from the Federal Circuit as to the metes and bounds of the new regime ushered in by the BPCIA.

Moreover, the FDA's decisions on the first biosimilar applications will be of importance for companies developing biosimilars and those defending their pioneer biologics. The FDA is under substantial pressure, including from Congress, to provide guidance on several remaining important issues regarding biosimilars, including whether there should be unique names for them, the scope of indications for which they can be approved, and standards for determining interchangeability, driven in large part by the intention of the Affordable Care Act to effect cost reductions through approval of biosimilars and the recent controversy over the pricing of new biologic products. Until uncertainty is resolved regarding the parameters of patent challenges under the BPCIA and the scope and type of data that will be required by FDA to support biosimilars applications, navigation of these processes will continue to be challenging for biosimilars manufacturers, leading to delay in the marketing of biosimilars notwithstanding the significant market demands for their introduction.

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