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Post-Grant Proceedings Are Important For Biosimilars

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Patent certainty is a major goal of generic drug manufacturers — whether small molecule or biologic. However, compared to their small molecule brethren, biosimilar developers potentially face a much more complicated patent thicket because of the complexity of producing a biologic drug. The Biologics Price Competition and Innovation Act introduced one mechanism by which patent certainty may be obtained prior to market approval. But in recent litigations, biosimilar applicants who have sought to circumvent the BPCIA have been unsuccessful in their efforts to obtain early resolution of their patent disputes in district court. Thus, biosimilar applicants will increasingly look to post-grant patent challenges at the U.S. Patent and Trademark Office as a mechanism for obtaining early and fast patent certainty.

The BPCIA and Recent Legal Challenges

Though the BPCIA established a mechanism to resolve patent disputes that relate to a new biosimilar drug, biosimilar applicants have attempted to circumvent the BPCIA's process and obtain early patent-dispute resolution in district court. Section 351(l) sets forth a detailed patent-exchange procedure, commonly referred to as the "patent dance," by which the reference product sponsor and the biosimilar applicant determine which patents will be the subject of a first wave of litigation. The triggering event for the patent dance is U.S. Food and Drug Administration acceptance of the biosimilar application for review. Twenty days after acceptance, the biosimilar applicant must provide the reference product sponsor a copy of its application along with information that describes the processes used to manufacture the biosimilar product.

Sandoz v. Amgen[1] was the first instance in which the Federal Circuit had the opportunity to address the scope of the BPCIA. At issue in Sandoz was a declaratory judgment action Sandoz Inc. filed against Amgen Inc. and Hoffman-La Roche Inc. on June 24, 2013, in U.S. District Court for the Northern District of California. Sandoz's complaint sought a declaratory judgment that two patents owned by Roche, and exclusively licensed to Amgen, were invalid, unenforceable, and would not be infringed by the commercial marketing of Sandoz's biosimilar version of Enbrel (etanercept), which is Amgen's blockbuster biologic for treating rheumatoid arthritis. However, when Sandoz filed its complaint, it had not yet filed a biosimilar application with the FDA, nor had it even finished clinical trials.

Amgen moved to dismiss Sandoz's complaint, asserting that the district court lacked jurisdiction to hear the case because an immediate and real controversy between the parties did not exist. The court granted Amgen's motion, noting that the BPCIA "sets specific limitations on the timing of any litigation arising from the filing of an application" for approval to market a biosimilar and that neither party engaged in a series of statutorily mandated exchanges of information related to patents in dispute. In this case, Sandoz had not even started the patent-exchange process by filing its application for approval. On appeal, Sandoz argued that the patent litigation provisions of the BPCIA only govern the statutory patent infringement litigation authorized by the BPCIA after the actual filing of a biosimilar application, and do not apply to declaratory judgment actions in general.

The Federal Circuit affirmed the district court's dismissal of Sandoz's complaint, concluding that Sandoz had not alleged an injury of sufficient immediacy and reality to create subject matter jurisdiction. The court, however, specifically declined to address the district court's interpretation of the BPCIA as barring a lawsuit by either party until the parties have engaged in the statutorily-mandated patent dance. The Federal Circuit stated that its decision was limited to the particular facts before it, and did not address the issue of whether the BPCIA forecloses declaratory judgment actions outside of the patent dance.

The latest salvo between Sandoz and Amgen came on Oct. 24, 2014, when Amgen sued Sandoz for not disclosing the process by which Sandoz's biosimilar filgrastim product, EP2006, is produced.[2] At issue in Amgen is the BPCIA provision that specifies that a biosimilar maker "shall provide" a copy of its application to the reference product sponsor within 20 days of the application's acceptance by the FDA. Amgen argues that Sandoz violated the BPCIA by refusing to provide its application, but Sandoz notes that the BPCIA authorizes legal action when biosimilars developers choose not to comply. Specifically, Sandoz argues:

There will be circumstances where the Applicant will want to provide the Sponsor a copy of the Application within twenty days of acceptance by FDA, and then engage in other Section (l) provisions by which the parties try to resolve patent disputes. 42 U.S.C. § 262(l)(2)-(4). There will be other circumstances, however, where it makes little sense for the Applicant to provide its Application within that time period. That decision triggers specified consequences—notably including allowing the Sponsor to sue immediately to enforce patents claiming the biological product, or a use thereof. 42 U.S.C. § 262(l)(9)(C). Sandoz made such a choice here, the consequence of which is that Amgen had the right to bring a patent infringement action immediately—which it did.[3]

With FDA approval now granted on March 6, 2015, Amgen has urged a California court to block the biosimilar launch. A decision on the preliminary injunction is expected very soon.

In a recent decision, the U.S. District Court for the Southern District of New York refused to allow a biosimilar applicant to use the declaratory judgment process to avoid complying with the patent-exchange provisions of the BPCIA. See Celltrion Healthcare Co. Ltd. et al. v. Kennedy Trust for Rheumatology Research.[4] There, Celltrion filed a 351(k) application for FDA approval of Remsima, a Remicade biosimilar, and it filed a declaratory judgment action rather than invoke the patent-exchange provisions of the BPCIA. In response, the Kennedy Institute filed a motion to dismiss Celltrion's complaint for failure to state a claim, and the district court granted the motion.

In dismissing the case, Judge Paul Crotty explained that "The BPCIA purposefully keys its dispute resolution procedures to the occurrence of certain events on the path to FDA approval. Celltrion has failed to show why this carefully crafted and well-timed procedure should be avoided here."[5]

Increased Importance of Post-Grant Proceedings for Biosimilar Developers

The above-described cases cast doubt on the ability of a biosimilar developer to bring an action that is outside the patent dance prescribed by the BPCIA, be it prior to filing a biosimilar application (Sandoz) or after (Celltrion). These cases thus highlight the utility of post-grant challenges before the USPTO as a tool for obtaining early patent certainty. With over 2,500 inter partes reviews having been filed since Sept. 16, 2012, IPRs have proven to be an attractive option for adjudicating patentability in view of prior art patents and printed publications. And as more patents become eligible for post-grant review, PGR will be used increasingly — particularly given the ability to challenge patents on any statutory ground in a PGR proceeding. Notably, an IPR or PGR petitioner does not need declaratory judgment jurisdiction to file a petition to challenge a patent.

Although not used as often in the biotech/pharma sector,[6] IPR has proven to be a potent weapon to induce settlement for generic drug manufacturers in abbreviated new drug application litigations. Instituting trial in about 77 percent of all cases petitioned, the Patent Trial and Appeal Board has canceled approximately 80 percent of all claims for which trial was instituted, and canceled 74 percent of all claims that were initially challenged by the petitioner.[7] If one considers the lower standard of proof required to nullify patent claims, the speed of trial, the diminished costs compared to district court litigation, and the high patent claim "kill" rate, it is easy to see that IPRs can provide tremendous leverage to biosimilar developers.

Pharma sector IPRs have recently been in the media spotlight because of the filings by Kyle Bass, the founder of hedge fund Hayman Capital Management, on behalf of the Coalition for Affordable Drugs. These first IPRs have challenged patents owned by Acorda Therapeutics, which develops drugs that primarily target neurological functions in people with multiple sclerosis. However, Acorda is likely not going to be alone in their fight with Bass. In a recent speech in Oslo, Norway, Bass stated that he plans to challenge the patents of 15 pharmaceutical companies by IPR, and "we are not going to settle."[8]

There are limited statistics available for patent challenges for pharmaceuticals in general. However, the PTAB recently issued what is believed to be the first final written decision in a biopharmaceutical case. In IPR2013-00537, BioMarin Pharmaceutical Inc. challenged the patentability of two patents owned by Genzyme that cover its drug Myozyme (alglucosidase alfa). Myozyme is a lysosomal glycogen-specific enzyme indicated for use in patients with Pompe disease (GAA deficiency). In its decision, the PTAB found that all claims of both challenged patents were obvious in view of the prior art.[9]

Initially, potential petitioners were hesitant to file IPRs because of the possibility the patent owner could amend claims, and because of the statute's estoppel provisions. But these concerns arguably are illusory. In the nearly 2.5 years since IPRs were introduced, only two motions to amend claims have been granted — and one of them was unopposed.[10] This incredibly low success rate owes itself to the fact that the PTAB has strictly interpreted the rules governing claim amendments and has placed a heavy burden on the patent owner to demonstrate patentability of any new or amended claims.[11]

And history has shown that this is a very difficult burden to bear. With respect to the estoppel provisions, it is important to note that estoppels do not attach until the PTAB issues a final written decision, and the estoppel is limited to grounds that one raised or reasonably could have raised in the post-grant proceeding. Many patent challengers believe they stand a better chance of showing unpatentability over the prior art at the PTAB than in district court, thus minimizing concerns regarding estoppels. Also, the effect of estoppels can be mitigated by strategically timing the filing of IPR petitions

relative to the timing of any potential litigation.

The threat of IPR is surely not lost on reference product sponsors, and they undoubtedly seek to mitigate the risks of IPR with each portfolio that covers their biologic. Because IPR proceedings can create an uphill battle for patent owners, reference product sponsors must bear in mind the possibility of IPRs when prosecuting patent applications. A proactive approach can help prepare for, or mitigate against, IPR attacks.

Such a proactive approach can include one or more of the following strategies: (1) for important applications, filing several applications under expedited examination to obtain quick allowance of pending claims, thereby limiting any potential impact of patent owner's estoppel arising from a post-grant proceeding; (2) filing patents with robust claim sets that include claims of varying scope to decrease the likelihood that a motion to amend claims will be necessary for claims to survive a post-grant proceeding; (3) introducing claims narrowly tailored to important embodiments; (4) including a glossary of claim terms in a specification to avoid application of an unreasonably broad claim interpretation; and (5) if available, submitting objective evidence of non-obviousness, supported by expert declarations, to have a well-developed prosecution record that can ward off an IPR or be relied upon in the early stages of the IPR.

Biosimilar applicants that are reluctant to participate in the BPCIA's patent-exchange process will increasingly use post-grant challenges at the USPTO to obtain patent certainty, particularly in light of recent decisions dismissing such early disputes from district court.

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[1] Sandoz Inc. v. Amgen Inc., 2014-1693 (Fed. Cir. Dec. 5, 2014).

[2] U.S. District Court for the Northern District of California, Case #: 3:14-cv-04741-RS

[3] Id. Dkt. 45, p. 3 (Jan. 23, 2015).

[4] Case No. 14 Civ. 2256 (PAC)(Dec. 1, 2014).

[5] Id. Dkt. 32, p. 10 (Dec. 1, 2014).

[6] For fiscal year 2015, approximately 7 percent of IPRs have been filed in Bio/Pharma (Art Unit 1600), compared to 66 percent in the Electrical/Computer arts - http://www.uspto.gov/ip/boards/bpai/stats/aia_statistics_120414.pdf

[7] For all USPTO Art Units.

[8] http://www.reuters.com/article/2015/01/07/pharmaceuticals-haymancapital-idUSL3N0UM42O20150107

[9] IPR2013-00537, Paper No. 79 (Feb. 23, 2015).

[10] International Flavors & Fragrances Inc. v. U.S. Department of Agriculture, IPR2013-00124 (May 20, 2014) (Paper 12) was unopposed; Riverbed Technology, Inc. v. Silver Peak Systems, Inc., IPR2013-00402 (Dec. 30, 2014) (Paper 35); IPR2013-00403 (Dec. 30, 2014) (Paper 33).

[11] Idle Free v. Begstrom, IPR2012-00027.
