Bloomberg BNA

BNA's Patent, Trademark & Copyright Journal®

VOL. 91, NO. 2256 APRIL 8, 2016

Patents

In Part I of a two-part article, the author provides useful strategies for patent owners in inter partes review proceedings in biotechnology and pharmaceutical patents.

A Patent Owner's Guide to Handling IPRs in the Higher-Survival Patent Arena of Biotech and Pharmaceuticals

BY ROBERT H. RESIS

In October 2013, about one year after *inter partes review* (IPR) proceedings became available, the chief judge of the Federal Circuit called the Patent Trial and Appeal Board (PTAB) a ''death squad.''[1] Certainly, a high percentage of early IPR petitioners succeeded in getting the PTAB to hold patent claims invalid, and the number of IPRs filed has steadily climbed.[2] Patent claims in biotechnology and pharmaceutical patents, however, have much higher IPR survival rates than claims in patents for all technologies. When an IPR is instituted and a trial completed, biotech/pharma patents have all trial-instituted claims survive about 43 percent on final PTAB written decision versus about 13 percent for all technologies.[3]

Of 40 final PTAB written decisions after trial for biotech/pharma patents, the patentee had all trial-instituted claims survive in 17,[4] and no trial-instituted claims survive in 19, and some, but not all trial-

[1] At the annual meeting of the American Intellectual Property Law Association on Oct. 25, 2013, during a question-and-answer session, then Judge Randall Rader stated that PTAB was ''acting as death squads, kind of killing property rights.'' Rader Regrets *CLS Bank* Impasse, Comments on Latest Patent Reform Bill, Bloomberg BNA's Patent, Trademark and Copyright Journal (87 PTCJ 14, 11/1/13).

[2] According to PTO statistics, the number of IPR petitions filed by fiscal year was 514 (FY 2013), 1,310 (FY 2014), and 1,737 (FY 2015).

[3] According to PTO statistics, as of Dec. 31, 2015, 732 IPR trials reached final written decision, with the following results: all trial-instituted claims survived in 96 trials (13 percent of final written decisions), and no trial-instituted claims survive in 529 trials (72 percent of final written decisions), and some, but not all trial-instituted claims, survive in 107 trials (15 percent of final written decisions).

[4] For the period to Dec. 31, 2015, biotech/pharma patentees had all trial-instituted claims survive final PTAB decision in:
IPR2013-00276 – *Ariosa v. Verinata*; note: Appeal 15-1215 (Fed. Cir. 11/16/15) (vacated & remanded)
IPR2013-00277 – *Ariosa v. Verinata*; note: Appeal 15-1226 (Fed. Cir. 11/16/15) (vacated & remanded)
IPR2013-00368 – *Amneal v. Supernus*
IPR2013-00371 – *Amneal v. Supernus*
IPR2013-00372 – *Amneal v. Supernus*
IPR2013-00390 – *Sequenom v. Stanford*

Robert H. Resis, a principal shareholder with Banner & Witcoff Ltd., Chicago. Resis was part of Amgen's successful trial team in Amgen Inc. vs. Chugai Pharmaceuticals, et al., a leading biotechnology patent case. He has successfully prosecuted patents in a variety of arts, including chemical, medical device and pharmaceutical, and has implemented U.S. Patent and Trademark Office post-grant review procedures.

 ISSN 0148-7965

instituted claims, survive in four.[5] Particularly useful strategies for patent owners are discussed below.

Strategies for Patent Owners

1. **Point to Prior Art Incompatibility.**

In *Ariosa v. Verinata* (IPR2013-00276, -00277), the patent claimed methods of noninvasive prenatal testing for the presence of fetal chromosomal abnormalities. The patent owner's expert testified why the ''tags'' of one reference could not be incorporated into methods described in another reference due to incompatibility. The PTAB found that although the petition and accompanying declarations pointed to disparate elements in the three references, and attempted to map them to elements of the challenged claims, virtually no effort was made to explain how or where the references differed from the challenged claims, how a person of ordinary skill in the art (POSITA) would go about combining their disparate elements, or what modifications a POSITA would necessarily have made in order to combine the disparate elements. The PTAB held that the petitioner did not provide an ''articulated reason[] with some rationale underpinning to support the legal conclusion of obviousness.''[6]

2. **Show Construed Claim Term Not Disclosed in Prior Art.**

In *Amneal v. Supernus* (IPR2013-00368), the claimed formulations could be used to inhibit activity of collagen destruction enzymes associated with human diseases, such as rosacea, without provoking undesired side effects attendant to an antibacterial dose. The PTAB held that a secondary reference did not disclose a ''delayed release'' portion as claimed. The PTAB credited the declaration testimony of the patent owner's expert that inclusion of a water-soluble polymer coating of the secondary reference results in release of the drug promptly after administration, and that the petitioner did not cite credible evidence to refute that testimony. The PTAB noted that although the patent owner's expert conceded that there must be some lag while the polymer hydrates, it further credited his testimony that this lag, essentially the time required to wet the material, would not be considered a ''delay'' in connection with the construed claim term. Thus, the PTAB held that the challenged claims were not shown to be unpatentable.

3. **Provide Sufficient Evidence to Corroborate Actual Reduction to Practice Before the Filing Date of § 102(e) Art Cited by the Petitioner.**

In *Sequenom v. Stanford* (IPR2013-00390), the patent described prenatal diagnosis methods that allow detection of chromosomal aberrations without the use of invasive techniques, such as amniocentesis, which pose potentially significant risks to both fetus and mother. The PTAB agreed with the patent owner that a reference relied upon in every instituted ground of unpatentability did not qualify as prior art under § 102(e) because the invention recited in the patent claims was reduced to practice before the non-provisional filing date of the reference. The petitioner did not contend that the relied upon disclosures of the reference were entitled to the benefit of an earlier provisional application. Instead, the petitioner argued that the patent owner failed to advance evidence, independent of the inventor's testimony, which sufficiently corroborated the asserted reduction to practice before the reference's nonprovisional filing date. The PTAB concluded that the patent owner established an actual reduction to practice before the relevant date through a draft of an article that one of the inventors sent to a non-inventor but coauthor of the article. The PTAB found that the testimony of the non-inventor/coauthor corroborated that the draft was in fact a copy of the document that he received from the inventor before the reference's nonprovisional filing date.[7]

IPR2013-00517 – *Intelligent Bio-Systems v. Illumina Cambridge*
IPR2014-00115 – *Apotex v. Wyeth*
IPR2014-00360 (IPR2014-01365 joined) – *Amneal v. Endo*
IPR2014-00376 – *Monosol v. Arius*
IPR2014-00377 – *Purdue Pharma v. Depomed*
IPR2014-00378 – *Purdue Pharma v. Depomed*
IPR2014-00379 – *Purdue Pharma v. Depomed*
IPR2014-00654 – *Endo v. Depomed*
IPR2014-00656 – *Endo v. Depomed*
IPR2014-00676 – *Phigenix v. Immunogen*
IPR2014-00693 – *Eli Lilly v. Los Angeles Biomedical Research Institute*

[5] For the period to Dec. 31, 2015, biotech/pharma patentees had some trial-instituted claims survive final PTAB decision in:
IPR2012-00022 (IPR2013-00250 joined) – *Ariosa v. Isis* (split)
IPR2013-00124 – *Int'l Flavors v. USA* (substitute claims 27-44 patentable, substitute claim 45 not patentable)
IPR2013-00401 (consolidated with IPR2013-00404) – *Cyanotech v. Univ. of Illinois* (split)
IPR2014-00003 (IPR2014-00556 joined) – *Aker v. Neptune* (split)

[6] On appeal, the Federal Circuit vacated the finding of nonobviousness, and remanded the IPRs due to the PTAB's language in the final written decisions that left open the distinct possibility that the PTAB incorrectly limited its consideration of an exhibit, which Ariosa alleged showed the background knowledge that a POSITA would have possessed at the relevant time. *Ariosa v. Verinata Health Inc.*, Appeal Nos. 2015-1215, and -1226 (Fed. Cir. Nov. 16, 2015).

[7] In *Sequenom v. Stanford* (IPR2014-00337), the PTAB denied the petitioner's second IPR Petition against the claims of the patent, holding that the provisional application of the reference was neither a patent nor an application for patent published under 35 U.S.C. § 122(b), and therefore, was not one of

4. **Provide Evidence of Years of Research and Testing to Manipulate Different Variables to Come Up With the Claimed Inventions.**

In *Purdue Pharma v. Depomed* (IPR2014-00377), the patent described drugs formulated as unit oral dosage forms by incorporating them into polymeric matrices comprised of hydrophilic polymers that swell upon imbibition of water to a size large enough to promote gastric retention of the drug during the fed mode. The PTAB found that each limitation of claim 1 was known in the prior art, as demonstrated by the teachings of a published article and a patent. The patent owner argued that the petitioner failed to demonstrate a motivation to combine the cited references with a reasonable expectation of success. The PTAB noted that in contrast to the testimony of the petitioner's expert that it would take him ''a week'' to come up with the claimed invention, the patent owner pointed to one inventor's testimony that it took ''years of research and testing in the laboratory to manipulate different variables . . . to come up with the claimed inventions.'' The PTAB also noted that another inventor testified that a POSITA would not have reasonably expected to successfully achieve the claimed invention given that a ''vast array of structural considerations affect polymer and matrix properties.'' The PTAB held that although the references may have interrelated teachings, the petitioner failed to explain persuasively *how* or *why* a POSITA would have combined the ''swelling'' and ''substantially intact'' features of the prior art patent formulation with the formulation disclosed in the article.[8]

5. **Demonstrate Why a POSITA Would Not Modify the Primary Reference According to a Secondary Reference.**

In *Endo Pharmaceuticals v. Depomed* (IPR2014-00656), the patent was the same at issue in IPR2014-00377, *supra*. The PTAB found that each limitation of claim 1 was separately disclosed by at least one cited reference. Similar to the prior IPR, the PTAB found that although the references may have interrelated teachings, and were intended to solve the same problem of controlled drug release, the petitioner failed to explain persuasively *how* or *why* a POSITA would have combined the various features of the cited references in the manner recited in the claims. The PTAB noted that the petitioner's declarant testified about several formulation considerations that impact drug release, including polymer ratio, type of polymer used, and particle size, and that formulating a reliable gastric retentive controlled release dosage form is ''very difficult.'' Given that testimony, the PTAB credited the testimony of the patent owner's declarant that ''[m]atrices formulated with a given polymer in a dosage form can result in different release controlling mechanisms, depending on the details of the matrix formulation and drug solubility characteristics.'' The PTAB stated that the petitioner failed to identify any combinations of the cited references that would be most promising to try. In contrast, the patent owner's declarant credibly explained why a POSITA would not have a reasonable expectation of success in combining the references. For example, the patent owner's declarant testified that a POSITA would expect the drug release characteristics of a secondary reference to change if the disclosed dosage forms were reformulated to remain substantially intact. The patent owner's declarant also explained that a POSITA reading the primary reference would not modify that dosage form according to another secondary reference, since the primary reference was an ''improvement'' of the formulation of the secondary reference in that the polymers described in the primary reference were not cross-linked and ''inherently safer.''[9]

6. **Provide a Prior Art Publication, Closer to Time of Invention Than the Petitioner's Primary Reference, That Counters the Petitioner's Arguments Relied Upon by the PTAB to Institute.**

In *Phigenix v. Immunogen* (IPR2014-00676), the patent was directed to immunoconjugates comprising a humanized anti-body known as huMAb4D5-8 (sold as HERCEPTIN®) linked to a maytansinoid toxin, for treating tumors in humans. In deciding to institute the IPR, the PTAB found that the petitioner made a sufficient showing that an ordinary artisan would have had reason to substitute the mouse antibody in the immunoconjugate of the primary reference, published in 1992, with the humanized antibody disclosed in the prior art HERCEPTIN® Label. After institution, the patent owner submitted a 1999 prior art publication that described a Phase I clinical study of human patients receiving an immunoconjugate (erb-38) fused to a toxin wherein the patients experienced ''hepatic injury'' (liver toxicity). The 1999 prior art submitted by the patent owner concluded that ''targeting of tumors with antibodies to erbB2 that are armed with . . . toxic agents may result in unexpected organ toxicities due to erbB2 expression on normal tissues.'' The PTAB held that the petitioner had not established by a preponderance of the evidence that the general statements in the 1992 primary reference, in view of teachings years later in the HERCEPTIN® Label, the 1999 prior art submitted by the patent owner, and other evidence regarding liver toxicities, would have motivated an ordinary artisan to substitute the mouse antibody of the 1992 primary reference with HERCEPTIN® on the basis that one would have expected the modified immunoconjugate to work to treat human tumors.[10]

Conclusion

As shown above, the PTAB should not be considered a ''death squad'' for biotech/pharma patents. The exemplary biotech/pharma IPRs above demonstrate that there are successful strategies for patent owners. Patent

two types of documents that may be relied upon under 35 U.S.C. § 102(e) to show that claims are unpatentable.

[8] The patent owner presented similar evidence in IPR2014-00378 and -00379 in connection with other patents, and the PTAB also found that the petitioner failed to demonstrate unpatentability.

[9] The patent owner presented the similar evidence in IPR2014-00654, involving another patent, and the PTAB also found that the petitioner failed to demonstrate unpatentability of the claims of that patent. In IPR2014-00654, the patent in was the same patent at issue in IPR2014-00378, *supra*.

[10] The petitioner's appeal to the Federal Circuit (Appeal No. 16-1544) was docketed on February 2, 2016.

owners would be well-served to consider whether these exemplary strategies apply to the facts at issue in their matters and, if so, prepare their IPR papers accordingly.

  PTCJ ISSN 0148-7965