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Patents

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

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

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Part I of this two-part series noted that the Patent Trial and Appeal Board (PTAB) should not be considered a ''death squad'' for biotechnology and pharmaceutical patents in *inter partes* review (IPR) proceedings. Patent claims in biotech/pharma patents 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 decisions versus about 13 percent for all technologies.[1] Of 40 final PTAB written decisions after trial for biotech/pharma patents, no trial-instituted claims survived in 19.[2]

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[1] According to PTO statistics, as of 12/31/2015, 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); 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).

[2] For the period to 12/31/2015, biotech/pharma patentees had no trial-instituted claims survive final PTAB decisions in:

IPR2012-00006 – *Illumina, Inc. v. Trustees of Columbia University*

IPR2012-00007 – *Illumina, Inc. v. Trustees of Columbia University*

IPR2013-00011 –*Illumina, Inc. v. Trustees of Columbia University*

IPR2013-00102 – *Smith & Nephew v. Convactec Tech.*

IPR2013-00116 – *Gnosis v. S.Ala.Med.; note: S.Ala.Med. v. Gnosis, Appeal 14-1778 (Fed. Cir. 12/17/15) (obv. aff'd)*

IPR2013-00117 – *Gnosis v. Merck; note: Merck v. Gnosis, Appeal 14-1779 (Fed. Cir. 12/17/15)(obv. aff'd)*

IPR2013-00128 – *Intelligent Bio-Systems v. Illumina Cambridge*

IPR2013-00266 – *Intelligent Bio-Systems v. Illumina Cambridge*

IPR2013-00534 – *BioMarin v. Genzyme*

IPR2013-00537 – *BioMarin v. Genzyme*

IPR2013-00535 – *BioMarin v. Duke University*

IPR2013-00539 – *Butamax v. Gevo*

IPR2013-00590 – *Baxter Healthcare v. Millenium Biologix*

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Part I discussed particularly useful strategies for patent owners. Part II will discuss particularly useful strategies for petitioners.

Strategies for Petitioners

1. **Show the Primary Prior Art Document Favorably References a Secondary Prior Art Document That Discloses Claimed Feature(s) Not Found in the Primary Prior Art Document.**

In *Illumina v. Trustees of Columbia University* (IPR2012-00006), the challenged patent involved sequencing DNA by incorporating a base-labeled nucleotide analogue into a primer DNA strand, and then determining the identity of the incorporated analogue by detecting the label attached to the base of the nucleotide. The PTAB agreed with the petitioner that the primary prior art document's reference to a secondary prior art reference's fluorescent nucleotides would have provided a person of ordinary skill in the art (POSITA) with a reason to have used the labeling technique of the secondary prior art reference in the method of the primary prior art reference. The patent owner argued that the primary prior art document's base label nucleotide would not have been the ''starting point'' to make novel nucleotide analogues because of a preference for nucleotides with the label attached to the 3' –OH group. The PTAB did not find the patent owner's argument to be persuasive because there was an explicit description of base-labeled nucleotides in the primary prior art document, and no specific disclosure had been identified therein by the patent owner that disparaged these alternative nucleotide analogues, or which would have lead a POSITA to conclude that they were unsuitable for the ''sequencing DNA by synthesis'' purpose described by the primary prior art document.

2. **Argue Inherency.**

In *Ariosa v. Isis* (IPR2012-00022, IPR2013-00250 joined),[3] the challenged patent involved prenatal detection methods using noninvasive techniques by detecting foetal nucleic acids in serum or plasma from a maternal blood sample. The PTAB held that all that was required by the amplification step of claim 1 was a step of amplifying nucleic acid from a serum or plasma sample from a pregnant female, such as by polyermase chain reaction (PCR), as such amplified nucleic acid necessarily includes fetal nucleic acid, which necessarily includes paternally inherited nucleic acid. Further, the PTAB held that the detecting step did not require that the detected nucleic acid specifically be identified as being inherited from the father or even as being from the fetus, only that it be identified as containing some level of nucleic acid, which would include, necessarily, nucleic acid from the fetus that was inherited from the father. The PTAB held that one reference anticipated some claimed methods because it inherently detected paternally inherited nucleic acid of fetal origin. The PTAB held that the cases cited by the patent owner did not support its position that because experimental mistakes may have been made in the reference, the reference could not, under the law of inherency, anticipate the claimed methods.

3. **Demonstrate Motivation of POSITA to Pursue Development Despite Potential Hurdles.**

In *BioMarin v. Genzyme* (IPR2013-000534), the challenged patent involved treatment of Pompe disease using a claimed enzyme (GAA) biweekly. The record did not contain any evidence of human trials before the patent priority date. The PTAB found that a POSITA would have understood that to treat Pompe disease effectively using GAA, sufficient quantities of enzyme would have to reach the patient's muscle cells, which could potentially require high doses that could introduce safety and efficacy hurdles resolvable only with human clinical trials. Despite this recognized difficulty, however, the PTAB held that a POSITA would have been motivated to pursue the clinical development of the therapy disclosed in one reference, which disclosed all of the claim limitations except for a biweekly dosing schedule. The PTAB held that the evidence established that the selection of the dose and dosing schedule would have been a routine optimization of the therapy outlined in the primary reference.

4. **Demonstrate That the Primary Reference Serves as a Starting Point, and That a POSITA Striving to Develop a Stable Product Would Have a Reasonable Expectation of Success Based on the Solution Disclosed in a Secondary Reference.**

In *Noven Pharmaceuticals v. Novartis AG* (IPR2014-000549, IPR2014-00265 joined), the challenged patent was directed to a pharmaceutical composition (rivastigmine, an amine compound) in the form of a free base or acid addition salt, along with an antioxidant, and a diluent or carrier. At issue was whether a preponderance of the evidence established obviousness based on the teachings of a published U.K. patent application and a Japan Patent Office patent application. The petitioner

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IPR2014-00325 – *BioDelivery Sciences v. RB Pharmaceuticals*

IPR2014-00549 (IPR2015-00265 joined) – *Noven v. Novartis*

IPR2014-00550 (IPR2015-00268 joined) – *Noven v. Novartis*

IPR2014-00652 – *Endo v. Depomed*

IPR2014-00752 – *Eli Lilly v. Los Angeles Biomedical Research Institute*

IPR2014-00784 (IPR2015-00518 joined) – *Torrent v. Novartis AG*.

[3] Cited in Part I as a split decision with some but not all trial-instituted claims surviving.

asserted that the JPO application provided a POSITA a reasonable expectation that the rivastigmine transdermal patch formulation taught by the U.K. application would be unstable during long-term storage of two-to-three years. The petitioner asserted that the U.K. application served as a starting point for formulating a patch, and that a POSITA would have strived to develop stable pharmaceutical products with a commercially viable shelf life. In furtherance of that goal, according to the petitioner and its expert, one of the first steps a POSITA ''would have taken when formulating a drug product is to investigate the stability of the active component.'' The petitioner asserted that the POSITA would have been motivated to add an antioxidant, particularly tocopherol, as recited in claim 2 of the challenged patent, to the U.K. application's rivastigmine transdermal composition with a reasonable expectation of maintaining the stability of the patch during long-term storage, as this was the precise solution disclosed by the JPO application. The PTAB held that the petitioner had demonstrated that the challenged claims were unpatentable based on the combined teachings of U.K. application and the JPO application, or those teachings in combination with other prior art of record.[4]

5. **When an Obviousness Ground Is Based on a Single Reference, Also Include an Obviousness Ground Based on That Reference in View Of a Secondary Reference to Address the Weakest Obviousness Argument.**

In *Endo Pharmaceuticals v. Depomed* (IPR2014-000652), the patent described drugs formulated as unit oral dosage forms by incorporating them into polymeric matrices comprising a combination of poly(ethylene oxide) (PEO) and hydroxypropyl methylcellulose (HPMC). The patent disclosed that the matrices swell upon exposure to gastric fluid to a size large enough to promote retention and release the drugs into the upper gastrointestinal (GI) tract, rather than the lower portions of the GI tract. The petitioner alleged that the trial-instituted claims (claims 1, 3-5, and 10-13) were obvious in view of a primary reference, Ground 1, and were also obvious in view of that reference in view of a secondary reference, Ground 2. The PTAB held that the petitioner had shown that all of the trial-instituted claims were obvious in view of the primary reference, with the exception of claim 10, which claimed a specific PEO:HPMC weight ratio. Although the primary reference did not disclose a polymeric matrix made from a combination of PEO and HPMC, it did disclose a short list of polymers to be used individually in producing a solid matrix for controlled drug release, of which HPMC and PEO were particularly preferred polymers. The primary reference also taught that polymers could be combined to form a polymatrix, and did not limit which polymers could be combined or suggest that certain polymers would not function properly in a combination matrix. The PTAB agreed with the petitioner that the petitioner had shown that all trial-instituted claims, including claim 10, were obvious in view of the primary and secondary references. The secondary reference disclosed combinations of PEO and HPMC within the ratio set forth in claim 10. The PTAB found that the references were directed to similar issues and disclosed PEO and HPMC as swellable hydrophilic polymers, and that a POSITA would have considered the collective teachings of the secondary reference compatible with the teachings of the primary reference and would apply the disclosures in combination. But for Ground 2, claim 10 would have survived the IPR.[5]

6. **Show That the Patent Owner's Own Declarant Wrote a Paper That Contradicts That Declarant's Testimony in the IPR.**

In *Torrent Pharmaceuticals v. Novartis AG* (IPR2014-000784, IPR2015-00518 joined), the patent described a solid pharmaceutical composition suitable for oral administration, wherein the composition comprises sphingosine-1 phosphate (SIP) receptor agonist and a sugar alcohol, wherein the sugar alcohol may suitably be mannitol. The PTAB stated that the fact that the inventors may have discovered a new advantage of a combination of prior-art ingredients is not sufficient to render the claims patentable, as long as there was some reason to combine the prior-art teachings that those ingredients should be used. The patent owner argued that the petitioner failed to prove a reason to combine the two cited references. The PTAB found that the combination of teachings strongly suggested that mannitol disclosed in one cited reference likely would have been a target of investigation to a POSITA interested in finding an expedient compatible with the SIP receptor (fingolimod) disclosed in the other cited reference. The PTAB also found that a third prior art reference directly instructed that the two ingredients should be combined. The patent owner argued that the third prior art reference's teaching of the combination was irrelevant because the third prior art reference was limited to liquid-phase pharmaceutical compositions, as opposed to the claimed sold oral dosage forms. The PTAB found that an article written by the patent owner's own declarant (which the petitioner submitted into evidence) stated otherwise: ''Most, but not all, drug degradations in the solid state take place via chemical mechanisms that are identical to those that occur in solution. Hence, a mechanistic understanding gained from solution studies can be very helpful.'' The PTAB cited this article by the patent owner's own declarant in support of its holding that the petitioner had shown a reason to combine the teachings of the cited references.

Conclusion

While it is typically more difficult to use IPR proceedings to knock out claims of biotech/pharma patents versus claims of other technologies, the above exemplary IPRs demonstrate that there are successful strategies for petitioners. Since petitioners must carry the burden of proof on invalidity, they would be well-served to consider whether these exemplary strategies apply to the

[4] The petitioner presented similar evidence in IPR2014-00550 (IPR2014-00268 joined) in connection with another patent, and the PTAB also found that the petitioner had demonstrated unpatentability of the challenged claims of this other patent.

[5] The PTAB held that the petitioner failed to demonstrate that the trial-instituted claims were unpatentable for obviousness over a third reference in view of the secondary reference.

facts at issue in their matters, and if so, prepare their IPR papers accordingly.

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