STRATEGIES IN *INTER PARTES* REVIEW PROCEEDINGS FOR BIOTECH/PHARMA PATENTS

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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 enjoyed success getting the PTAB to hold patent claims invalid, and the number of IPRs filed has steadily climbed.[2] Biotech/pharma patents, however, have a greater success rate in surviving an IPR than patents in other technologies. First, almost 40 percent of IPR petitions have been denied for patents in Tech Center 1600 (Biotechnology and Organic),[3] whereas about 21 percent of IPR petitions for all technologies have been denied.[4] Second, even when an IPR is instituted, biotech/pharma patents have all challenged claims survive about 33 percent on final PTAB decision versus about 23 percent for all technologies.

Of 18 final PTAB decisions for biotech/pharma patents, the patentee had all challenged claims survive in six,[5] and no challenged claims survive in 10,[6] and some, but not all challenged claims, survive in two.[7] Particularly useful strategies for petitioners and patent owners are discussed below.

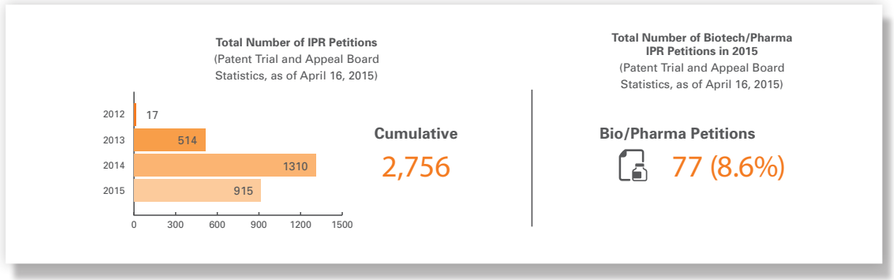
STRATEGIES FOR PETITIONERS

1. **Argue 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. Illumina argued that claims were obvious in view of Tsien and Prober I. Specifically, Illumina contended that Tsien's reference to Prober I's fluorescent nucleotides would have provided a person of ordinary skill in the art (POSITA) with a reason to have used Prober I's labeling technique in Tsien's method. Columbia argued that Tsien'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 Columbia's argument to be persuasive because there was an explicit description of base-labeled nucleotides in Tsien, and no specific disclosure had been identified in Tsien by Columbia 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 Tsien.

2. **Argue Inherency.**

In *Ariosa v. Isis* (IPR2013-00022, IPR2012-00250 joined), the challenged patent involved prenatal detection methods using non-invasive techniques by detecting foetal nucleic acids in serum or plasma from a maternal blood sample. The patent taught that the claimed methods may be used to screen for Down's syndrome and other chromosomal aneuploidies, to detect other conditions. The PTAB held that the same claim construction from its institution decision applied, i.e., 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 PCR, as such amplified nucleic acid 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 the Kazakov reference anticipated the claimed methods because it inherently detected paternally inherited nucleic acid of fetal origin. The PTAB held that the cases cited by Isis did not support its position that because experimental mistakes may have been made in Kazakov, Kazakov 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. BioMarin demonstrated 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.

STRATEGIES FOR PATENT OWNERS

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

In *Ariosa v. Verinata* (IPR2013-00276, -00277), the challenged patent involved a method for determining the presence or absence of fetal aneuploidy – a condition in which a fetus carries an abnormal number of chromosomes – by determining the relative amounts of non-random polynucleotide sequences from a chromosome suspected of being aneuploidy, and from a reference chromosome or a chromosome region, in a cell-free sample from a pregnant woman. Verinata argued that a "tagging" method of one reference would not have been combinable with another reference's use of restriction digestible primers. The PTAB found that although the petition and accompanying declarations point to disparate elements in the three references, and attempt

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[**IPR**, FROM PAGE 7]

to map them to elements of the challenged claims, virtually no effort was made to explain how or where the references differ from the challenged claims, how one of ordinary skill in the art 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 Ariosa did not provide an "articulated reason[] with some rationale underpinning to support the legal conclusion of obviousness."

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2. Submit Evidence of Patentability.

In *Int'l Flavors v. USA* (IPR2013-00124), the patent involved a method for repelling arthropods, which are known to transmit diseases and pose a serious threat to public health worldwide. The patent claimed methods of treating an object or area with an arthropod repelling effective amount of at least one isolongifolenone analog having a particular formula. The USA provided several publications, as well as an expert declaration, to demonstrate the level of ordinary skill in the art, as well as the non-obviousness of features to demonstrate patentability of proposed, substitute claims. The PTAB found that the evidence cited by the USA demonstrated that even small changes in structure can change the biological activity of an insect repellant. The PTAB also found that the prior art did not provide a reason to modify, and did not provide a reasonable expectation that such modifications would result in a compound with desired insect repellant activity.

3. Show Construed Claim Term Not Disclosed in Prior Art.

In *Amneal v. Supernus* (IPR2013-00368), the patent involved sub-antimicrobial formulations of doxycycline. 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 credited the declaration testimony of Supernus' expert that inclusion of a water-soluble polymer coating of the secondary reference's secondary loading portion results in release of the drug promptly after administration, and that Amneal did not cite credible evidence to refute that testimony. The PTAB noted that although Supernus' 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. The PTAB agreed with Supernus that the secondary reference did not disclose a "delayed release" portion. Thus, the PTAB held that the challenged claims were not unpatentable.

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 both petitioners and patent owners. ■

1. At the annual meeting of the American Intellectual Property Law Association on October 25, 2013, during a question-and-answer session, then Chief Federal Circuit Judge Randall Rader stated that PTAB was "acting as death squads, kind of killing property rights." http://www.law360.com/articles/482264.
2. According to PTO statistics, the number of IPR petitions was 514 (FY 2013), 1,310 (FY 2014), and 915 (FY 2015). As of April 16, 2015, that correlates to a pace of about 3,150 for FY2015.
3. For Tech Center 1600, Biotechnology and Organic, of 109 IPR petition institutions decided, 39 percent (43) were denied, 15 (14 percent) were granted, and 47 percent (51) were granted and denied (for period of 2/1/2013 to 4/10/2015).
4. For all technologies, of 1,765 of all IPR petitions institutions decided, 21 percent (366) were denied, 18 percent (320) were granted, and 61 percent (1079) were granted and denied (for period of 2/1/2013 to 4/10/2015).
5. For the period to 4/10/2015, biotech/pharma patent had all challenged claims survive final PTAB decision in:
IPR2013-00276 and IPR2013-00277 – *Ariosa v. Verinata*
IPR2013-00368, -00371, and -00372 – *Amneal v. Supernus*
IPR2013-00517 – *Intelligent Bio-Systems v. Illumina Cambridge*
6. For the period to 4/10/2015, patent owners had no challenged claims survive final PTAB decision in:
IPR2012-00006, -00007, -00011 – *Illumina, Inc. v. Trustees of Columbia University*
IPR2013-00117 – *Gnosis v. Merck*
IPR2013-00128, -00266 – *Intelligent Bio-Systems v. Illumina Cambridge*
IPR2013-00534, -00537 – *BioMarin v. Genzyme*
IPR2013-00535 – *BioMarin v. Duke University*
IPR2013-00590 – *Baxter Healthcare v. Millenium Biologix*
7. For the period to 4/10/2015, patent owners had some claims survive final PTAB decision in:
IPR2013-00124 – *Int'l Flavors v. USA* (substitute claims 27-44 patentable, substitute claim 45 not patentable)
IPR2013-00022 (IPR2012-00250 joined) – *Ariosa v. Isis* (split)