Novel AIA adversarial procedures for challenging validity of pharmaceutical patents

By Arlene Chow, Esq., and Ernest Yakob, Esq.
Hogan Lovells

Since September 2012, patent challengers have been able to take advantage of three new proceedings to attack patent validity at the U.S. Patent and Trademark Office under the America Invents Act: *inter partes* review, post grant review and a transitional program for covered business method patents. Each proceeding is conducted in an adversarial "trial" format before the Patent Trial and Appeal Board. These proceedings offer several advantages over traditional federal court litigation for those challenging patents — including pharmaceutical patents.

According to PTAB and DocketNavigator statistics, the absolute number of total and bio/pharma-related IPR petitions has doubled every nine months since October 2012. Because final outcomes thus far have strongly favored patent challengers, these numbers may continue to rise.

In the aftermath of the PTAB's initial decisions on pharmaceutical IPRs — with more sure to come in the near future — potential patent challengers will likely feel increasingly comfortable with the particularities of the

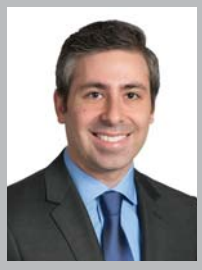
> Of the several advantages of AIA adversarial proceedings over conventional litigation, the lower invalidity standard is perhaps the most compelling.

AIA proceedings offer faster resolution (between 12 and 18 months), lower costs and technically trained judges. Perhaps most importantly, they also apply lower invalidity standard.

To date, *inter partes* review has been the focal point of post-AIA activity. According to PTAB statistics as of Jan. 1, nearly 90 percent of all AIA petitions have been IPR petitions. And of the 2,299 IPR petitions filed thus far, roughly 7 percent have involved biotechnology and pharmaceutical patents.

IPR process, which should produce more IPR filings.

Post-grant reviews, or PGRs, and transitional programs for covered business method patents, or CBMs, are additional attractive avenues for challenging pharmaceutical patents. These proceedings relate only to relatively recent patents for PGRs and only business method patents for CBMs, and data relating to their use in the pharmaceutical arena has yet to emerge. However, they offer the same advantages as IPRs. In addition, PGRs and CBMs allow for grounds of attack that are not available in IPRs, and they offer more immediate relief after the issuance of a new patent.



Arlene Chow (L) is a partner in the New York office of **Hogan Lovells**. She focuses her practice on patent litigation, post-grant proceedings and due diligence in the pharmaceutical, biotechnological and medical device industries. She can be reached at arlene.chow@hoganlovells.com. **Ernest Yakob, Ph.D.** (R), is an associate in the firm's New York office. His practice focuses on patent litigation, post-grant proceedings and due diligence in the pharmaceutical, biotechnological and medical device industries. He can be contacted at ernest.yakob@hoganlovells.com.

THE APPEAL OF AIA PROCEEDINGS

The bulk of current pharmaceutical patent litigation relates to abbreviated new drug application disputes involving generic-drug entry. It is anticipated that generic-drug manufacturers will take advantage of the novel AIA adversarial proceedings because of the benefits such proceedings provide

Of the several advantages offered by AIA adversarial proceedings compared with conventional litigation, the lower invalidity standard is perhaps the most compelling. Rather than "clear and convincing" evidence of invalidity, the standard of proof is merely "a preponderance of the evidence." In addition, claim terms are given their "broadest reasonable interpretation" in AIA proceedings, which can also ease the burden of proving invalidity over prior art.

In light of these standards, it is not surprising that IPR decisions have heavily favored patent challengers when compared with outcomes reached in federal district court cases. Based on statistics compiled with DocketNavigator as of Jan. 2, about 74 percent of nearly 200 IPR final decisions have canceled all challenged claims, while only 12 percent have upheld the validity of all challenged claims. The remaining 14 percent of IPR decisions have invalidated at least one challenged claim and maintained the validity of at least one challenged claim.

These numbers are slightly less dramatic with respect to bio/pharma matters, in which 61 percent of IPR decisions have canceled all challenged claims and 22 percent have upheld all claims. The sample size of about 18 decisions is too small to differentiate this subset from the statistics for all IPRs.

A comparison of IPR outcomes with those of U.S. district court cases filed over the same time period (from Sept. 16, 2012, to Jan. 2,

2015) demonstrates the PTAB's tendency to favor patent challengers in IPR proceedings. In particular, based on DocketNavigator statistics for 249 U.S. district court cases in which validity was decided, at least 60 percent of cases have *upheld* patent validity. For bio/pharma-related cases, patent holders are even more successful in U.S. district court. Although the number of those cases is relatively low at 44, at least 74 percent of them have upheld patent validity.

PTAB'S FIRST PHARMACEUTICAL-RELATED IPR DECISIONS

In June 2014 the PTAB issued four final IPR decisions (IPR2013-00116, IPR2013-00117, IPR2013-00118 and IPR2013-00119) on patents owned by South Alabama Medical Science Foundation and Merck & Cie, covering particular active metabolites of folate for use in treating folate deficiencies.

Although these IPRs did not involve traditional pharmaceutical patents, legal practitioners and commentators have heralded the decisions as the first pharmaceutical IPR decisions.

> The data thus far is clear that IPR proceedings will become a popular avenue for challenging the validity of patents, including pharmaceutical patents.

The PTAB held for the petitioner, Italian biotechnology company Gnosis SpA, finding that all the challenged claims were anticipated by, or obvious over, the prior art. In particular, the primary reference, Serfontein, taught most if not all of the claimed features but disclosed the use of "a suitable active metabolite of folate" without *explicitly* specifying the particular claimed active metabolites.

To the extent one of skill in the art would not have understood Serfontein to have taught the particular claimed active metabolites, the PTAB determined that a secondary reference, Marazza, did specifically disclose one of the claimed active metabolites for use in treating folate deficiency. Therefore, the claimed invention was at a minimum obvious over the combination of Serfontein and Marazza.

The PTAB rejected several counterarguments proposed by the patent owners, each to the effect that the state of the art at the time discouraged treatment of folate deficiency using the claimed active metabolites. Additionally, the PTAB determined that the evidence of record regarding objective indicia of non-obviousness was insufficient because there was no nexus between the evidence and the claimed subject matter. The evidence was either based on elements not reflected by the claims or tied to an element in the prior art.

The Gnosis IPR decisions demonstrate that, just as in other areas of technology, the PTAB is willing to invalidate all of the challenged claims of pharmaceutical-related patents and is willing to do so on both anticipation and obviousness grounds. These decisions also highlight the importance of a patent owner's own evidence in light of an IPR's "preponderance of the evidence" standard for invalidity.

In the Gnosis decisions, the PTAB readily accepted Gnosis' *prima facie* case and spent the bulk of its time rejecting the patent owners' arguments. Patent owners who anticipate AIA adversarial proceedings should therefore prepare their cases as early as possible, especially given the condensed timeline of these proceedings.

PTAB'S FIRST IPR DECISIONS ON PHARMACEUTICAL CLAIMS

Even though the PTAB is generating a record number of favorable outcomes for patent challengers in IPRs, it has also made it clear that a finding of invalidity is not merely a rebuttable presumption but must be supported by credible evidence. About six months after deciding the Gnosis petitions, the PTAB issued its first IPR decisions upholding the validity of a set of pharmaceutical patents in their entireties.

Amneal Pharmaceuticals LLC, a generic-drug manufacturer, filed three petitions for IPR (IPR2013-00368, IPR2013-00371 and IPR2013-00372) with respect to a set of patents owned by Supernus Pharmaceuticals Inc. relating to once-daily, sub-antimicrobial formulations of doxycycline. The claimed drug comprised specific amounts of immediate-release and delayed-release doxycycline. The primary reference cited by Amneal, Ashley '932, disclosed much of the claimed invention, but it did not teach the specific amounts of immediate-release and delayed-release doxycycline.

The main issue considered by the PTAB was whether a secondary reference, Sheth, suggested the claimed amounts of immediate- and delayed-release doxycycline. The PTAB found that Sheth did not teach or suggest the specific amounts of doxycycline claimed in the patents and the challenged claims were therefore all patentable.

> PGRs, which can only be filed in the first nine months after patent issuance or reissue, offer the most immediate avenue for challenging the validity of the patent.

The only claim term that required construction — and that was ultimately dispositive — was "delayed release." Interestingly, neither party offered a construction for this term in their principal briefs. Rather, the PTAB first raised the issue during oral argument. It ultimately found the broadest reasonable construction to be "release of a drug at a time other than immediately following oral administration."

In so finding, the PTAB rejected Supernus' argument that the term should also require that there be no substantial release in the stomach. Nevertheless, the PTAB still agreed with Supernus that Sheth did not teach a delayed-release drug and therefore could not have rendered obvious the claimed amount of delayed-release doxycycline. Weighing heavily into PTAB's reasoning was the testimony of Supernus' expert that Sheth only disclosed drug forms that provided *sustained* — but not *delayed* — release. Amneal did not offer any "credible evidence" to refute the testimony of Supernus' expert.

These decisions demonstrate the PTAB's willingness to reject obviousness arguments that stretch far beyond the actual teachings of the prior art. The Amneal IPRs also establish the importance of credible expert witness testimony that properly characterizes the asserted prior art. Despite the adversarial nature of IPRs, the PTAB's request that the parties offer further evidence regarding the meaning of the term "delayed release" demonstrates the relatively active role that the board is willing to assume in these proceedings.

PHARMACEUTICAL PGRS AND CBMS

Although nearly nine of 10 AIA petitions to date have been filed in IPR proceedings, PGRs and CBMs are also available to patent challengers, including drug companies. PGRs are similar to IPRs, but differ in some important respects. For example, an IPR petition can be filed with respect to any patent as long as no filing bar has been triggered. These filing bars apply if the petitioner has filed a previous declaratory judgment action for invalidity or served an infringement complaint on the petitioner more than a year before filing an IPR petition.

In contrast, PGRs are applicable only to patents with effective filing dates after March 16, 2013. For this reason, there have been few PGRs to date. As new pharmaceutical patents issue, they will be vulnerable to attack via PGR. Generic-drug manufacturer Accord Healthcare Inc. filed three of the PGR petitions filed to date (PGR2014-00010) against a patent on nausea drug Aloxi. Those petitions were terminated early due to settlement by the parties.

For relatively new patents, PGRs offer the most immediate avenue for challenging patent validity. While IPR proceedings are applicable to any patent eligible for PGR, an IPR petition for such a patent may only be filed nine months after issuance or reissue, or after the termination of a PGR of the patent. PGRs, in comparison, can only be filed during the first nine months after patent issuance or reissue.

In the context of pharmaceutical patents, PGRs therefore offer generic-drug manufacturers the ability to quickly resolve all potential validity issues with respect to new blocking patents. And unlike IPR proceedings, PGRs are not limited to prior art challenges. Because of the recent reinvigoration of Section 112- and Section 101-based validity challenges by the Federal Circuit and U.S. Supreme Court, the availability of such challenges makes PGRs particularly attractive. In fact, the lone pharmaceutical PGR petition to date was based entirely on Section 112 validity challenges.

Overall, the unique aspects of PGRs will likely make such proceedings popular among patent challengers.

> Comparing IPR outcomes with those of U.S. district court cases filed over the same time period underscores the tendency of the PTAB to favor patent challengers in IPR proceedings.

CBMs, which are restricted to business method patents, also have implications for the pharmaceutical realm. Like PGR proceedings, CBMs are not limited to prior art-based challenges. Unlike PGRs and some IPRs, however, CBMs can be filed at any time.

Generic-drug manufacturers Amneal, Par Pharmaceutical and Roxane Laboratories have already filed CBM petitions challenging Orange Book patents covering risk evaluation and mitigation strategies, or REMS, for the drug Xyrem.

The PTAB has yet to institute proceedings with respect to these petitions, and a threshold issue is whether REMS-based patents are covered business method patents. According to the petitioners, the challenged claims recite methods for centralized distribution of drugs through a central pharmacy, and the AIA's legislative history establishes that covered business methods should include "activities that are financial in nature, incidental to a financial activity or complementary to a financial activity." Until this issue is resolved, however, CBM challenges to REMS-related patents remain a possibility.

For prospective patent challengers, IPR, PGR and CBM proceedings offer advantages over district court patent litigation. Nonetheless, each AIA proceeding is distinct in terms of the patents that can be challenged, the timeframe during which a petition may be filed and the grounds upon which the challenge may be based. The data thus far is clear that IPR proceedings will become a popular avenue for challenging the validity of patents, including pharmaceutical patents.

Although there have only been a few PGR petitions filed to date, the unique aspects of PGR — especially the broad bases for attacking validity — will encourage patent challengers to consider this proceeding when applicable. PGRs may be an important tool for generic-drug manufacturers to quickly resolve validity issues of new blocking patents, and one PGR petition has already been filed for that purpose. Finally, CBM petitions have already been filed in the pharmaceutical area for challenging REMS-based patents, though the PTAB has yet to confirm the applicability of CBMs with respect to such patents.

Given these various alternatives available to pharmaceutical patent challengers — all of which are conducted in a condensed timetable — patent holders should anticipate these proceedings and do their best to prepare their cases as far in advance as possible. WJ