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***Inter partes* review in the life sciences industry**

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Inter partes review in the life sciences industry

By David I Berl, Michael Xun Liu and **Jingyuan Luo**, Williams & Connolly LLP

Inter partes review is a pathway established by the America Invents Act to permit challenges to patents before the United States Patent and Trademark Office's (USPTO) Patent Trial and Appeal Board (PTAB). As more than five years have passed since the PTAB issued the first final written decision in an *inter partes* review, an assessment of the role of *inter partes* reviews, their success rates and impact on pharmaceutical patent litigation is now feasible. Challenges to life sciences patents comprise only a small portion of all *inter partes* reviews, but they have transformed the landscape of every sector of pharmaceutical patent litigation, including Hatch-Waxman and biosimilar litigation. Although initially envisaged as a simplified alternative to complex and expensive litigation, in practice, *inter partes* reviews have often added a parallel dimension to life sciences patent litigation, albeit a dimension with a differing timeline, burden of persuasion, scope of discovery, evidentiary rules, and jurisdictional limits. This chapter examines the trends that can be adduced in life sciences *inter partes* reviews, analyses the interaction between *inter partes* review and Hatch-Waxman and biosimilar litigation, and concludes by addressing evolving legal issues that may change life sciences *inter partes* review practice in the coming years.

By the numbers: trends in life sciences *inter partes* review

At a high level, challenges to life sciences patents remain a small percentage of *inter partes* review petitions. The PTAB received 7,044 *inter partes* review petitions from 2014 to 2017. Of these, only 10.6% (745) involved life sciences patents. Moreover, *inter partes* reviews filed to challenge life sciences patents are generally perceived to be less likely to succeed. Analysis of *inter partes* review institution rates and success rates is confounded by the frequency and nature of settlement in *inter partes* review; settlement terms are generally not disclosed publicly and, although counted as *inter partes* reviews that did not result in invalidation (or, if settled earlier) institution, they may often reflect the achievement of the petitioner's competitive goals. Accordingly, statistics regarding the rates of institution and invalidation (an outcome that rendered at least one challenged claim unpatentable) must be considered with this significant proviso in mind.

Across all technology sectors, the PTAB instituted 55% of petitions and invalidated 24% of challenged patents. Although the institution rate for life sciences *inter partes* review petitions was only slightly below other fields at 50%, the invalidation rate was significantly lower at 14%. The invalidity rate is especially low for patents listed in the Food and Drug Administration's (FDA) Orange Book. Indeed, the USPTO's statistics indicate that 83% of all petitions challenging Orange Book patents resulted in the PTAB denying institution or finding the challenged claims patentable. In part, this lower invalidation rate may be ascribed to life sciences patents surviving serial challenges following an initial unsuccessful *inter partes* review, as well as the often fruitless efforts of non-competitors (including hedge funds) to challenge life sciences patents – phenomena less prominent in other technological sectors.

However, the low invalidation rate is also a consequence of results from the fact that approximately 57% of instituted life sciences *inter*

"Whereas the institution rate for all inter partes *review petitions has fallen steadily since 2014, the institution rate for life sciences petitions rose from 40% in 2014 to 51% in 2015"*

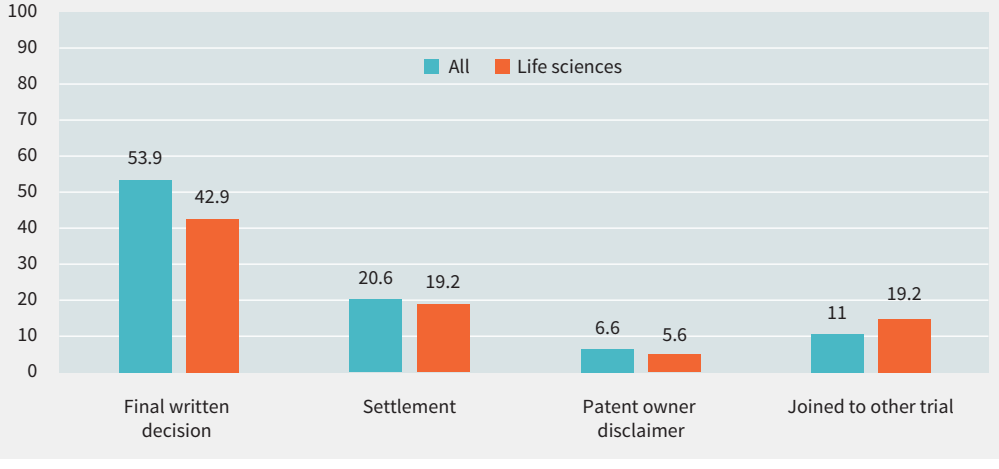
partes review petitions do not result in a final written decision of any kind. By comparison, across all technology sectors, approximately 46% of instituted petitions do not result in a final written decision. The primary reason for this difference is the higher rate of consolidation of multiple instituted *inter partes* review petitions challenging the same patent –19% of instituted petitions in the life sciences sector, compared to 11% for instituted petitions generally – due in large measure to *inter partes* review challenges to Orange Book patents (see Figure 1).

But the data also reflects the reality that the PTAB – initially criticised as a 'patent death squad' – has adjusted, both procedurally and substantively, to provide more opportunity for patent owners to advance their arguments and ultimately prevail. For example, adjustments of procedures to facilitate the submission of expert declarations in patent owner preliminary responses before institutions, and the relaxation of restrictions on sur-replies and claim amendments are explicitly directed to levelling the perceived playing field in a manner that is especially important in expert-driven life sciences proceedings.

Closer inspection of data reveals that the percentage of *inter partes* review petitions challenging life sciences patents has fluctuated over the years. From 2014 to 2018 the number of *inter partes* review petitions filed annually across all technologies consistently hovered between 1,600 and 1,800. By comparison, the percentage of life sciences *inter partes* reviews increased from 7.5% in 2014 to 10% in 2015 and 2016. Life sciences petitions peaked at 14% in 2017, at least partially as a result of a wave of initial petitions filed on patents covering biologic drugs. In 2018 this percentage dropped back to 8.4%.

A year-to-year review also confirms that life sciences patent claims are more likely to survive *inter partes* review. But invalidity rates for life sciences patents may be converging with the rates for other technology sectors. Whereas the institution rate for all *inter partes* review petitions has fallen steadily since 2014, the institution rate for life sciences petitions rose from 40% in 2014 to 51% in 2015. Since then, the institution rate for life sciences patents has remained steady and is now comparable with the institution rate for all *inter partes* reviews in 2016 and 2017. Although

FIGURE 1. Post-institution 2014-2018 (percentage of instituted *inter partes* review)



the invalidation rate for challenged life sciences patents remains low, the gap between life sciences patents and other patents will gradually close if the overall invalidation rate continues to decrease (see Figures 2 to 5).

Inter partes review and Hatch-Waxman litigation

Around half of all *inter partes* review petitions in the life sciences field are directed at patents covering FDA-approved drugs listed in the Orange Book. For generic pharmaceutical companies, *inter partes* reviews can help clear the path to market for their products. One recent study found generic drug companies filed more than 70% of *inter partes* reviews directed at Orange Book listed patents. The other petitions were filed by branded pharmaceutical companies, hedge funds and public interest groups.

As in other technology sectors, *inter partes* reviews are often used in conjunction with district court abbreviated new drug application (ANDA) litigation. More than 90% of *inter partes* reviews against Orange Book patents have co-pending district court litigation. For generic drug companies, there are advantages to challenging Orange Book patents through *inter partes* review. Substantively, the PTAB imposes a preponderance of the evidence standard for proving invalidity, whereas district courts require clear and convincing evidence. In theory, this distinction should make it easier for generic drug companies to prevail in the PTAB. In fact, generic drug companies have been more successful – even twice as successful, according to one study – in invalidating patents at the PTAB compared to the district courts.

Procedurally, *inter partes* review can affect Hatch-Waxman litigation in several important ways. After a branded pharmaceutical company sues an ANDA filer, the Hatch-Waxman Act requires the FDA to stay approval of the generic drug application for 30 months. This period allows a district court to resolve patent validity and infringement disputes before commercialisation

FIGURE 2. Institution rate (percentage of filed petitions)

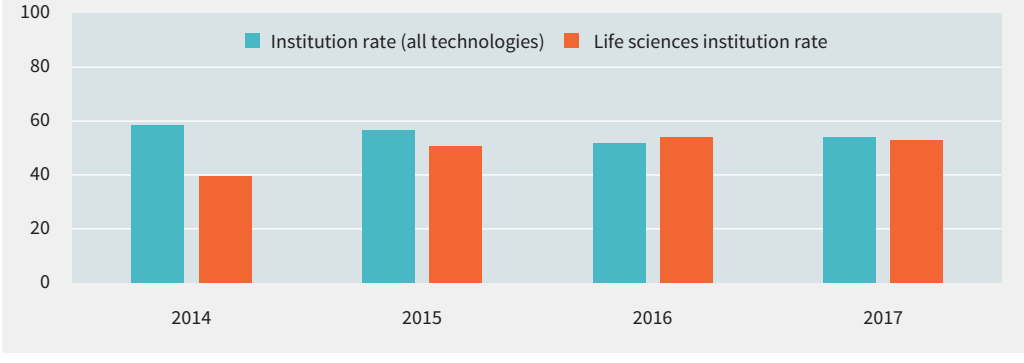
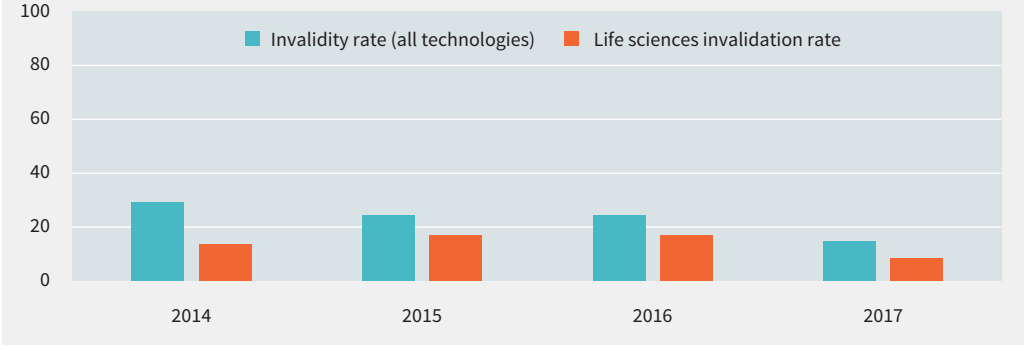


FIGURE 3. Invalidity rate (percentage of filed petitions)



"As in the Hatch-Waxman context, inter partes *review – with their lower burden of proof, no presumption of validity and no standing requirement – can be a valuable tool for challengers in biosimilar litigation under the Biologics Price Competition and Innovation Act"*

of the generic drug product. However, the district courts' practice of staying proceedings pending the PTAB's decision modifies this familiar timeline. In ANDA litigation, such a stay might prevent the district court from adjudicating validity within 30 months, as the *inter partes* review alone – from filing to final decision – takes approximately 18 months. Thus, by filing an *inter partes* review petition, ANDA filers can delay district court resolution of their case and create a risk of a pre-trial launch. Moreover, even where Hatch-Waxman litigation is not stayed by a parallel *inter partes* review proceeding, the parallel proceeding creates risks for branded manufacturers, which must balance and account for evidence in multiple proceedings with different scopes of discovery, evidentiary rules and burdens of persuasion. However, the risks run in both directions, as unsuccessful *inter partes* review challenges to patents in a procedurally more receptive forum renders successful prior art challenges in district court far less attainable, due to both formal estoppel pursuant to 35 USC Section 316(e) and the perception that patents that have survived *inter partes* review challenges are more likely to be valid. These risks may be mitigated, to some extent, by generic challengers pursuing prior art defences in *inter partes* review and non-prior art defences, if available, in litigation, thereby securing two opportunities to invalidate asserted claims.

Inter partes review and biosimilar litigation

As in the Hatch-Waxman context, *inter partes* review – with their lower burden of proof, no presumption of validity and no standing requirement – can be a valuable tool for challengers in biosimilar litigation under the Biologics Price Competition and Innovation Act. Unsurprisingly, as Biologics Price Competition and Innovation Act litigation has arrived, the number of *inter partes* review petitions filed against biologic drug patents has also increased, with a large number of challenges filed in 2017. The numerosity of patents often asserted in Biologics Price Competition and Innovation Act litigation, even in comparison to Hatch-Waxman litigation, presents challenges for district courts charged with adjudicating disputes; biosimilar applicants may attempt to elide these complexities, at least in part, by invalidating patents through *inter partes* review.

These biosimilar challenges are distinct from other *inter partes* reviews in two important

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respects. First, biologic drug patents often face multiple *inter partes* review challenges, while most patents outside the life sciences sector face only one or two challenges. Second, unlike other *inter partes* review challenges, particularly those in the Hatch-Waxman context, these challenges often pre-date district court litigation. Biosimilar manufacturers have found that *inter partes* review can be a useful tool for clearing the patent landscape and narrowing the scope of any potential district court Biologics Price Competition and Innovation Act litigation.

As in the Hatch-Waxman context, however, this strategy carries risk, as the failure to invalidate a claim in an *inter partes* review can severely compromise a biosimilar applicant's leverage before district court litigation even begins. In one prominent case, after failing to institute *inter partes* review petitions for two adalimumab (Humira) formulation patents in January 2016, Amgen entered into a settlement agreement with AbbVie in September 2017 not to commercialise its approved biosimilar product until 2023. While it is impossible to quantify the extent to which the failed *inter partes* review proceedings played a role in shaping the ultimate settlement, it undoubtedly weakened Amgen's litigation position and settlement posture.

Evolving legal issues

Broader changes to the PTAB and its procedures are also affecting how *inter partes* reviews are used in the life sciences industry. In *SAS Institute v Iancu*, the Supreme Court held that "when the Patent Office institutes an *inter partes* review, it must decide the patentability of all of the claims the petitioner has challenged". Before this decision, the PTAB's usual practice was to decide whether the petition raised a reasonable likelihood of unpatentability on a ground-by-ground, claim-by-claim basis. But after *SAS*, the PTAB must

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FIGURE 4. Institution and invalidation rates 2014-2018 (percentage of all petitions)

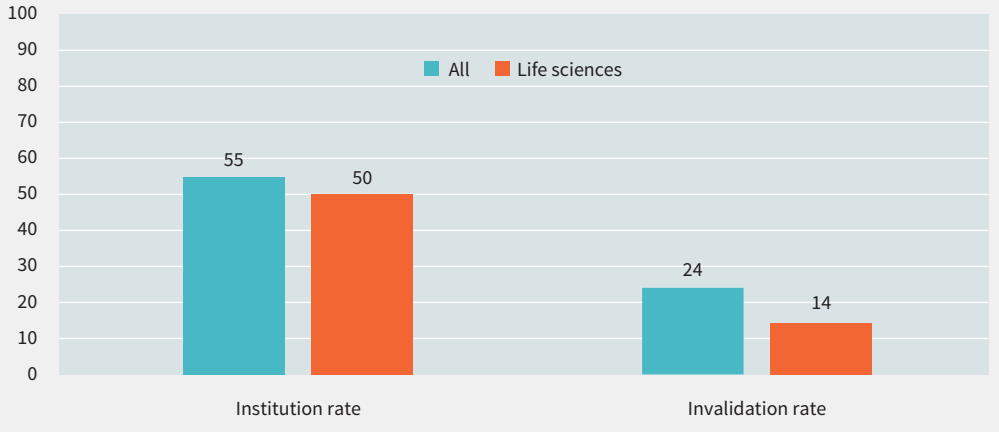
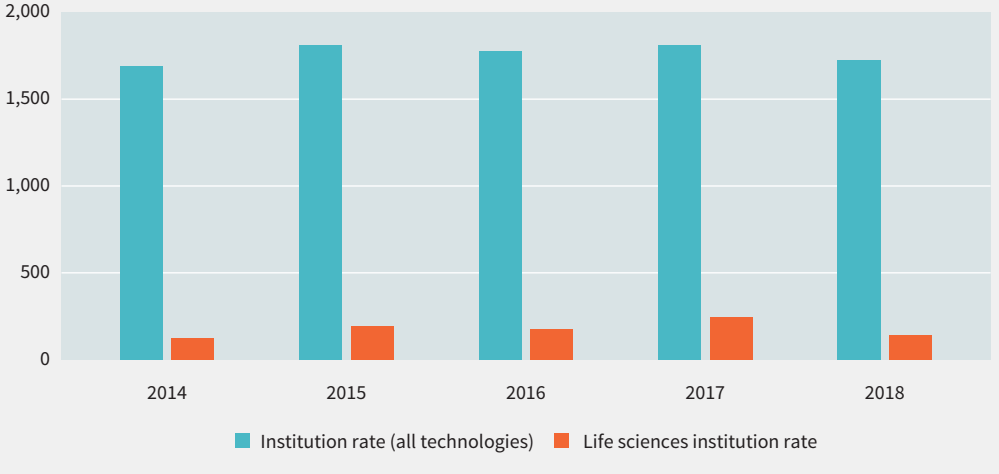


FIGURE 5. Annual *inter partes* rights petitions



decide whether to institute *inter partes* review on an all-or-nothing basis.

As a practical matter, *SAS* will likely expand the scope of estoppel based on *inter partes* review failure. Under 35 USC Section 315(e), the petitioner in an *inter partes* review "of a claim that results in a final written decision" is estopped from challenging that claim based on "any ground that the petitioner raised or reasonably could have raised". The Federal Circuit has held that estoppel under Section 315(e) only attaches to arguments addressed in a final written decision, as opposed to those on which the PTAB declined to institute. Prior to *SAS*, this rule permitted petitioners to avoid estoppel and thereby litigate in district court prior art invalidity challenges that were not instituted. However, after *SAS*, every challenged claim becomes part of the final written decision so long as the board institutes review. Therefore, with the consequences of failure even more pronounced, petitioners must carefully decide which claims to challenge and may opt for narrower *inter partes* review petitions.

Outside of the courts, the USPTO is also reforming the *inter partes* review process through administrative regulation. The USPTO recently promulgated rules to apply the *Phillips* standard for *inter partes* review claim construction in lieu of

the broadest reasonable interpretation. In theory, this rule change means that the PTAB should now interpret claims more narrowly. On a practical level, because the new rule makes the claim construction standard in the PTAB and district court identical, the PTAB is more likely to follow prior district court's claim constructions of the same claim term.

This rule change may also affect the relationship between ANDA litigation and *inter partes* review. The vast majority of *inter partes* reviews against Orange Book patents have co-pending district court litigations. When district courts and the PTAB applied different claim construction standards, the PTAB could reach an independent claim construction even if a district court had already construed the claim. But once the PTAB applies the *Phillips* standard for *inter partes* review, it will likely adopt any prior judicial claim constructions wholesale. To avoid this, petitioners may opt to file earlier *inter partes* review challenges, if they believe the PTAB is more likely to adopt a favourable claim construction.

Finally, although congressional action on *inter partes* review remains unlikely, there are pending legislative proposals that would have a dramatic impact on *inter partes* review in the life sciences realm. The Hatch-Waxman Integrity Act 2019, for example, would prohibit generic drug companies from petitioning for *inter partes* review or post-grant review of any Orange Book patent. Although unlikely to be enacted in its current form, this bill would remove *inter partes* review entirely from many important patents in the life sciences field. The bill also reflects the growing concern that, by providing an alternative and often parallel route to challenging Orange Book patents, *inter partes* review disrupts the balance between protecting innovation and promoting competition established by the Hatch-Waxman Act. *iam*

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