Unpacking The Latest Trends In Biologics-Related IPRs

By **Justin Rosinski, Michael Green, Richard Praseuth and John Josef Molenda** (June 4, 2021)

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In a previous Law360 guest article,[1] we analyzed statistical trends in the 98 biologics-related inter partes review petitions filed in the first four and a half years of the IPR procedure, namely Sept. 16, 2012, to April 12, 2017. As part of that analysis, we explored the underlying bases for those trends and how they related to concurrent developments in the biologics and biosimilars industry.

We also focused on the types of patents challenged and the success rates of those challenges, including institution rates and ultimate outcomes following trial before the Patent Trial and Appeal Board.

From this preliminary data we concluded that IPRs are a potent weapon for challenging biologics-related patents, both on the part of innovators seeking to launch new biologics and biosimilars applicants seeking to launch biosimilar versions of existing biologics.[2]

Over the last four years, namely April 13, 2017, through May 13, 2021, 120 new biologics-related IPR petitions and nine post-grant review petitions have been filed.[3] At the same time, many challenges, both old and new, have achieved resolution, thereby providing deeper insight into outcomes before both the PTAB and the U.S. Court of Appeals for the Federal Circuit.

We examine the new data below to provide a more comprehensive picture of the statistical trends in biologics-related IPRs and PGRs and endeavor to explain the reasons underlying those trends.

Overall Timing and Volume of Biologics-Related IPR Petitions, Including Types of Patents Challenged

Timing and Volume of Filings

With an eight-and-a-half-year time frame to draw from, we have acquired a robust data set of 218 biologics-related IPR petitions to analyze. The timing of those petitions is summarized below in Figure 1:

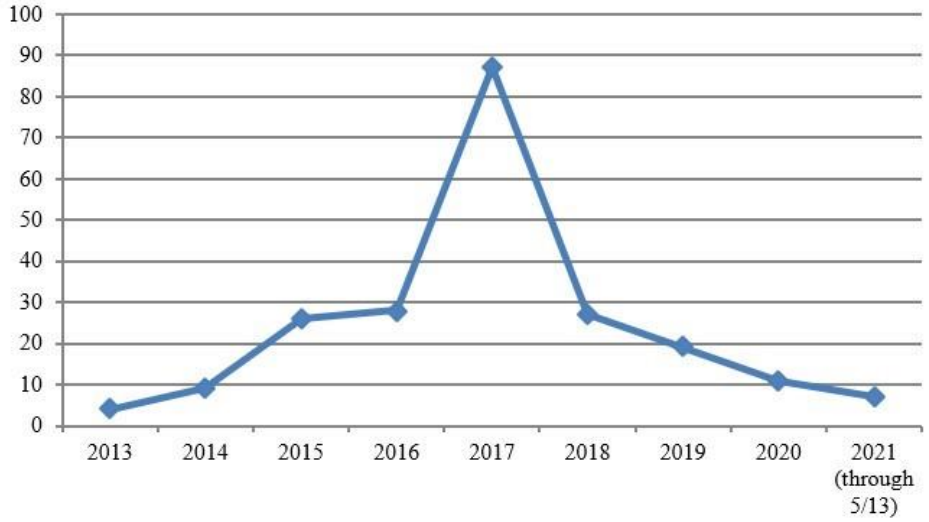

Figure 1 Number of biologics-related petitions filed between September 16, 2012 and May 13, 2021.[4]

After a slow start in 2013 and 2014 with a mere 13 petitions combined,[5] those numbers rose to about 25 per year in 2015 and 2016, a trend likely explained by various companies having advanced their biosimilar programs to the point where IPR-based challenges would play a key role in bringing their products to market.[6]

This trend accelerated greatly in 2017, which turned out to be the high-water mark for biologics-related IPR petitions, with a total of 87 petitions being filed that year and accounting for almost 40% of the 218 biologics-related IPR petitions filed since the inception of the IPR procedure.

As in 2015 and 2016, this spike in petitions in 2017 appears to be correlated with the advancement of biosimilar development programs relating to aging biologics such as AbbVie Inc.'s Humira and Genentech Inc./F. Hoffmann-La Roche Ltd.'s Rituxan, Herceptin and Avastin products. Indeed, biosimilar developers Coherus Biosciences and Sandoz International GmbH filed 13 IPR petitions against Humira-related patents in 2017.[7]

Also in that year, petitioners including Celltrion/Teva Pharmaceuticals Ltd. Inc., and Pfizer Inc. filed 21 IPR petitions against Rituxan-related patents; petitioners including Celltrion/Teva, Boehringer Ingelheim, Pfizer/Hospira Inc. and Samsung Bioepis Co. Ltd. filed 30 IPR petitions against Herceptin-related patents; and Boehringer Ingelheim filed one petition against a protein purification patent relating to Avastin, Rituxan and Herceptin.[8]

Overall, such IPR-based challenges to patents relating to aging biologics ultimately proved to be an effective way to clear the patent landscape[9] and facilitate settlement.[10]

Moreover, in 2017 several innovators similarly availed themselves of the IPR procedure to clear a path for their products. For example, vaccine manufacturers Merck Sharp & Dohme Corp., Sanofi SA and SK Biosciences together filed 10 IPR petitions challenging several patents in Pfizer's Prevnar estate.[11]

Likewise, Sanofi Genzyme and Regeneron Pharmaceuticals Inc, which together developed

Dupixent for the treatment of, inter alia, asthma and atopic dermatitis, filed three IPR petitions challenging claims of Amgen Inc./Immunex's U.S. Patent No. 8,679,487 to anti-IL-4 receptor antibodies.[12]

Following 2017, the number of biologics-related IPR petitions precipitously declined: The three-year period from 2018 to 2020 had an average of only 19 biologics-related petitions filed per year, less than the average of 21 that were filed in the three-year period from 2014 to 2016. This drop-off can be at least partially explained by the fact that only three challenges were brought against patents relating to Humira, Rituxan, Herceptin and Avastin during that time frame, as opposed to 65 in 2017 alone.

Since 2017, petitioners have focused on patent estates relating to a variety of other products including GlaxoSmithKline PLC's Synflorix,[13] Teva's Ajovy,[14] Alexion Pharmaceuticals Inc.'s Soliris,[15] and uniQure NV's Factor IX experimental gene therapy product.[16] Likewise, petitioners have focused on a variety of research tool patents, including Regeneron's challenges to patents relating to Kymab's transgenic mice.[17]

Types of Patents Challenged

In our prior analysis of the first four and a half years of the IPR procedure, we determined that of the 98 petitions analyzed, over half involved challenges to method-of-treatment patents (50), while composition-of-matter patents (18), formulation patents (16) and method-of-manufacturing patents (14) each represented approximately 16% of challenges.[18]

Of the 120 petitions filed in the subsequent four years, the majority again involved challenges to method-of-treatment patents (48).

Challenges to composition-of-matter patents (36) doubled relative to the previous period, and method-of-manufacturing patent challenges (27) likewise considerably increased. Formulation patents, however, were infrequently challenged, with only nine new petitions being filed since our last report. This data is depicted below in Figure 2:

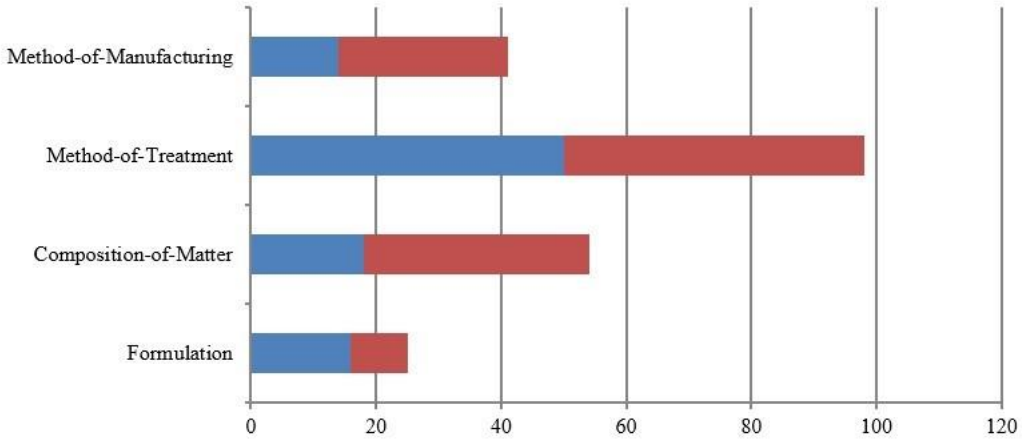

Figure 2 Types of patents challenged in biologics-related IPR petitions between September 16, 2012 and April 12, 2017 (blue bars) and from April 13, 2017 to May 13, 2021 (red bars).

Figure 2 reveals that across the entire eight-and-a-half-year time frame, the most challenged patents have been method-of-treatment patents (98/218 petitions). As noted in

our earlier article, this may be due to their perceived vulnerability to obviousness attacks and to their ability to serve as key patents blocking biosimilar entry since they are often directed to indications and dosage regimens set forth in the reference product's label.[19]

Interestingly, the second-most challenged patents were composition-of-matter patents (54/218 petitions). While this patent type likewise plays a central role in blocking market entry, the volume of challenges for this patent type is somewhat counterintuitive given that it is often difficult to locate invalidating prior art for biologics-related patents and that they are more commonly challenged for lack of written description[20] and/or lack of enablement,[21] grounds that may not be raised in an IPR proceeding.[22]

Nonetheless, many of these petitions challenged patents relating to blockbuster drugs, so these challenges were likely essential to enable petitioners to market their respective biosimilar products.

Method-of-manufacturing patents (41/218 petitions), on the other hand, were challenged at a somewhat lower rate than composition-of-matter patents, which again may be attributable to difficulties in locating invalidating prior art.[23]

In any event, since our last article, examples of specialized processes recently challenged include conjugation of bacterial saccharides in the production of vaccines,[24] methods for refolding proteins,[25] transgenic mouse platforms for the production of chimeric human-nonhuman antibodies,[26] and diphtheria toxin expression systems.[27]

The least-challenged patents were formulation patents (25/218 petitions). Only nine new petitions were filed between April 13, 2017, and May 13, 2021. The relatively small number of total challenges is surprising given that formulation patents, like method-of-treatment patents, are commonly viewed as particularly vulnerable to obviousness attacks.

The need to clear a path through these types of patents, however, may not be immediate or necessary given that companies' product formulations may differ from the claimed formulations, making noninfringement arguments more effective. In any event, of the new petitions filed challenging formulation patents, nearly half of those petitions were directed to injectable formulations containing vascular endothelial growth factor antagonists.[28]

Institution and Final Written Decisions of Biologics-Related IPRs

We next explore how the PTAB has approached instituting biologics-related IPRs and ultimately rendering final written decisions on the IPRs that it institutes. Turning first to institution,[29] the data reveals that institution rates tend to favor challengers, with the PTAB instituting 58% of petitions (105/180) and denying 42% of petitions (75/180), as may be seen in Figure 3 below:

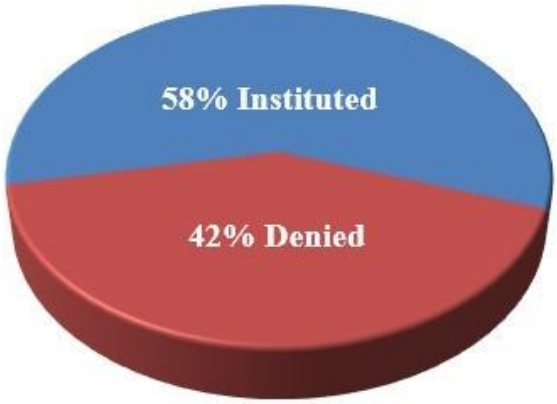

Figure 3 Disposition of petitions at the institution phase from September 16, 2012 to May 13, 2021.

Turning next to institution rates by patent type, Figure 4 reveals that the PTAB instituted a surprising 70% of IPRs involving composition-of-matter patents (33/47), showing that petitioners were in fact able to locate strong biologics-related prior art in a number of challenges.

Figure 4 further reveals that the PTAB instituted over 50% of IPRs challenging method-of-treatment patents (46/79), a figure consistent with the perceived vulnerability of such patents and instituted about the same percentage of method-of-manufacturing patents (18/34), again despite potential concerns over locating sufficiently strong prior art.

Interestingly, the data showed that challenges to formulation patents were instituted at a rate of 40% (8/20), despite formulation patents being viewed as particularly vulnerable to obviousness attacks. This data underscores the importance of formulation patents in the lifecycle management of biologics-related products.

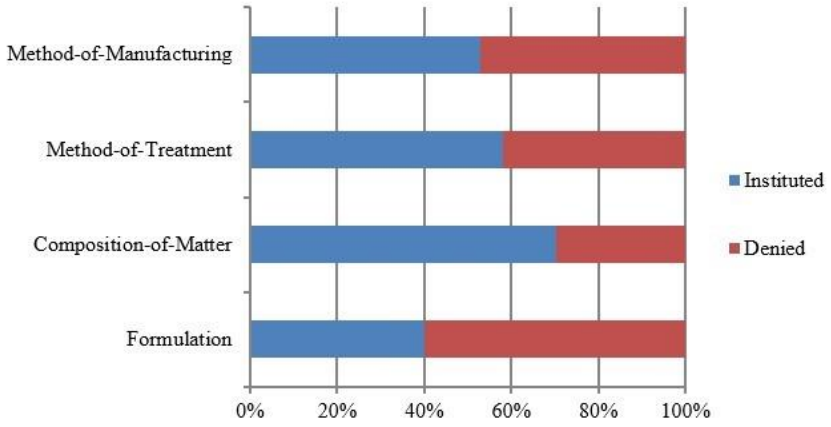

Figure 4 Types of patents challenged and percent disposition at the institution stage from September 16, 2012 to May 13, 2021.

As of May 13, 105 biologics-related IPRs had progressed passed the institution stage, with 71 resolved by a final written decision on the merits, 32 resolved by settlement/termination, and two not yet resolved by the PTAB.

Focusing on the 71 petitions resolved on the merits, we find that petitioners in the biologics space have seen considerable success. As depicted in Figure 5 below, nearly 75% of cases were resolved in favor of the challenger (53/71), and roughly 25% were resolved in favor of the patentee (18/71):

Figure 5 Disposition of cases post-institution from September 16, 2012 to May 13, 2021.

As for ultimate disposition per patent type, the data shows that petitioners succeeded in proving at least one claim unpatentable in a remarkable 91% of IPRs involving composition-of-matter patents (20/22), as well as 68% of IPRs involving method-of-treatment patents (26/38).

Petitioners challenging formulation patents achieved success in about 83% of IPRs (5/6) and 40% of IPRs (2/5) involving method-of-manufacturing patents, but this data should be viewed with caution given the limited number of final written decisions on the merits. This patent-specific data is summarized below in Figure 6:

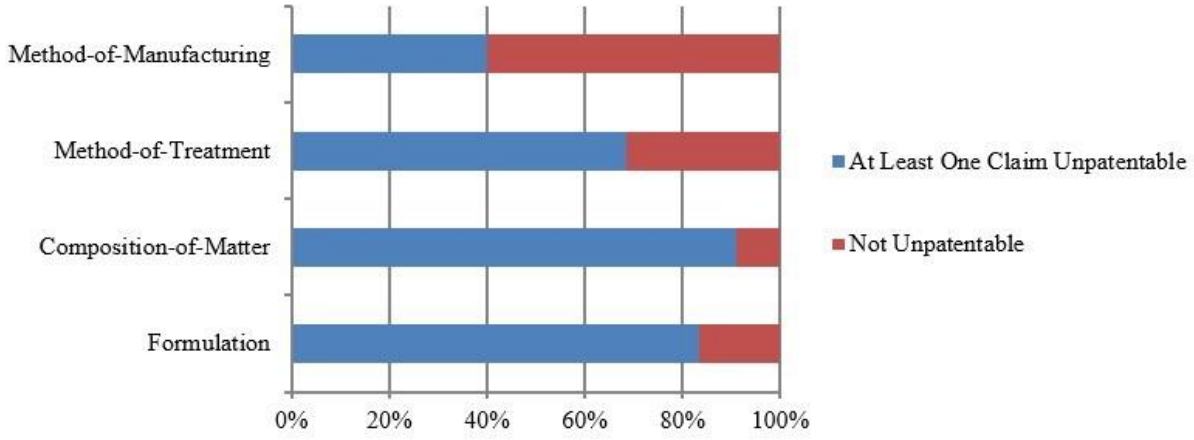

Figure 6 Percent disposition after institution stage per patent type from September 16, 2012 to May 13, 2021.

Appellate Dispositions of Biologics-Related IPRs

Turning next to biologics-related IPR appeals, 61 final written decisions, two institution stage decisions and two preinstitution stage decisions have been appealed from the PTAB to the Federal Circuit, representing nearly 30% of all biologics-related IPR petitions filed since the inception of the IPR procedure.[30]

Excluding the 25 appeals that were either settled or pending at the time of this article and focusing on the remaining 40 appeals, as shown in Figure 7 below, the Federal Circuit affirmed 29 decisions on every issue (73%), vacated/remanded six (15%), and dismissed the remaining five (12%):[31]

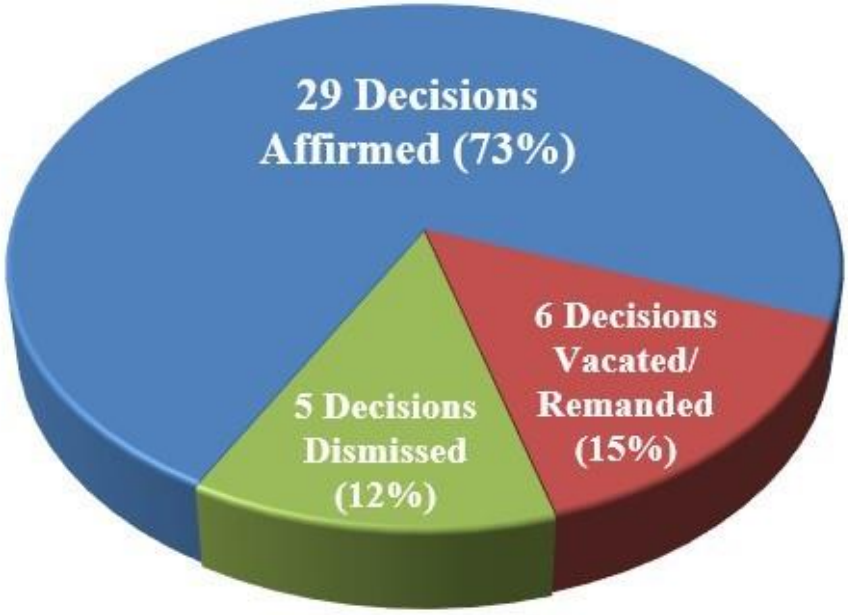

Figure 7 Appellate dispositions of 40 cases from September 16, 2012 to May 13, 2021.

This high affirmance rate may largely be attributed to the high degree of deference the Federal Circuit gives the PTAB's factual findings underlying its patentability determinations.[32]

Focusing on the 29 affirmances, the lion's share involved patents relating to Herceptin (seven), Copaxone (six), Humira (five) and Lumizyme (three), while the six vacated and remanded cases all pertained to one Prevnar-related patent and one protein folding patent that Amgen had asserted against Neulasta and Neupogen biosimilars in co-pending litigation.

And perhaps not surprisingly given the high value of the products involved, just over 85% (61/71) of IPR final written decisions pertaining to biologics-related patent challenges were appealed to the Federal Circuit, though as noted above, the vast majority were affirmed.

Biologics-Related Post-Grant Review

IPRs are by far the post-grant procedure of choice for challenging biologics-related patents relative to PGRs.[33] Indeed, not a single biologics-related PGR petition was filed from the inception of the procedure on Sept. 16, 2012, through 2017, with only a single PGR petition being filed in 2018 and only two being filed each year in 2019 and 2020.

The biopharma industry's disinterest in filing PGR petitions is largely attributable to the potentially Draconian estoppel impact arising from PGR proceedings on district court litigations involving the same challenged patent, an impact that is potentially far greater than with IPRs.[34] But in 2021, we have witnessed an interesting uptick in PGR challenges to biologics-related patents, with four such challenges having been filed in the first five months of this year.

Looking at the nine PGR petitions by patent type, six petitions challenged composition-of-matter patents (67%), two petitions challenged method-of-treatment patents (22%), and one petition challenged a method-of-manufacturing patent (11%), with no petitions challenging formulation patents (0%). There was some degree of overlap in specific products being targeted, with the nine PGR petitions covering six different biologics products.

Given that written description and enablement are among the most effective arguments employed to challenge biologics-related patents, particularly composition-of-matter patents, it follows that all nine PGR petitions involved a written description challenge and seven of those PGR petitions additionally included enablement challenges. The frequency of statutory grounds alleged in the nine PGR petitions is presented below in Figure 8:

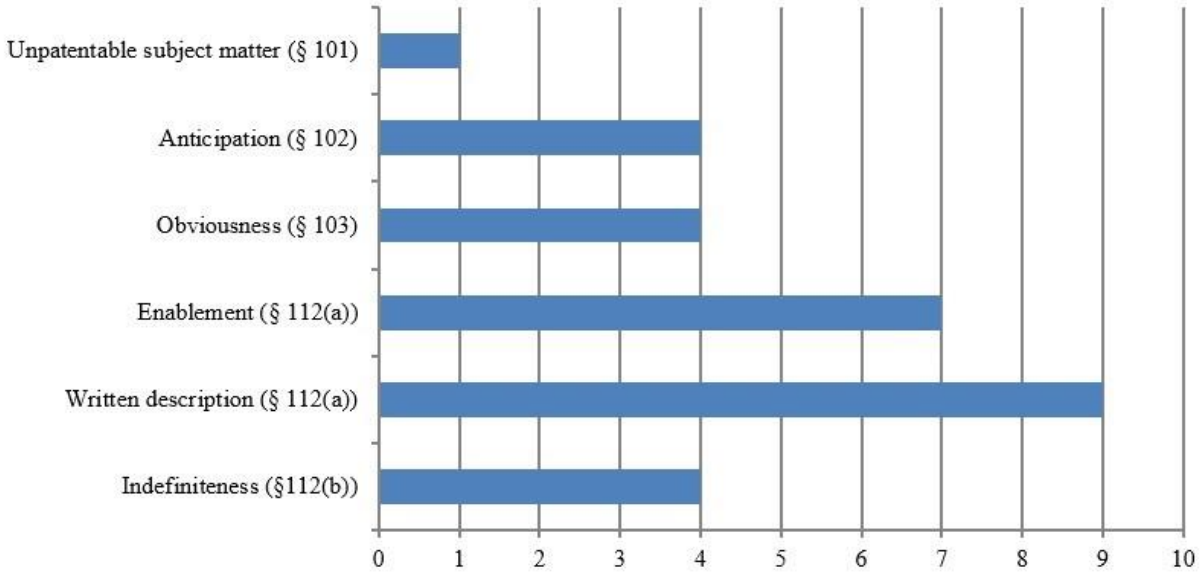

Figure 8 Frequency of statutory grounds alleged in PGRs filed through May 13, 2021.

With respect to the resolution of these nine PGRs, four have reached the institution stage (each being instituted), with two progressing to find at least one claim unpatentable, one settling, and one post-institution PGR still pending. The remaining five PGRs are all still pending an institution decision.

While any conclusions that may be drawn from the existing PGR data must be viewed with caution because of the limited number of PGR petitions filed to date, it is fair to say that there appears to be an increased willingness to challenge biologics-related patents via PGR despite the potential estoppel effects that may later apply in litigation.

Conclusion

With over eight and a half years of data to analyze, including an additional four years of data since our last Law360 guest article, we have been able to provide a more comprehensive picture of the statistical trends in biologics-related IPRs.

Of the 218 IPR petitions filed during this period, the lion's share continues to be challenges to method-of-treatment patents (45%), with many fewer challenges to composition-of-matter patents (25%), method-of-manufacturing patents (19%) and formulation patents (11%).

We found that the overall institution rate for biologics-related IPR petitions tends to favor challengers, with the PTAB granting 58% of petitions and denying 42% of petitions. As for specific patent type, institution rates were over 70% for composition-of-matter patents, about 55% for method-of-treatment and method-of-manufacturing patents, and 40% for formulation patents.

For the 71 instituted IPRs that reached a final written decision, we observed that petitioners achieved considerable success, with roughly 75% of the decisions holding at least one reviewed claim unpatentable. With respect to patent type, petitioners achieved particular success in IPRs involving composition-of-matter patents (91%), formulation patents (83%) and method-of-treatment patents (68%), with method-of-manufacturing patents (40%) trailing behind.

As for biologics-related IPR appeals, 85% of final written decisions from biologics-related IPRs were appealed to the Federal Circuit. While this rate of appeal is appreciable, over 73% of those decisions were nonetheless affirmed on every issue, a statistic that mirrors the overall affirmance rate of appeals of IPR decisions from the PTAB.

Moreover, the last four years have witnessed the biopharma industry starting to take advantage of the PGR procedure, with a total of nine biologics-related PGR petitions filed since 2018. While this limited data must be viewed with caution in view of the small number of PGR petitions filed to date, there does appear to be an increased willingness to challenging biologics-related patents despite the potential estoppel effects.

In sum, the data suggests that IPRs and PGRs will continue to be an attractive and effective weapon for biopharmaceutical companies to challenge biologics-related patents, both from the standpoint of innovators and biosimilar applicants. We expect the biopharmaceutical industry to continue availing itself of both procedures as market conditions and product launches warrant, and we look forward to continuing to analyze future statistical trends and the reasons underlying them.

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Disclosure: Steptoe & Johnson represents Sanofi and affiliated entities, Regeneron, Sandoz, Alexion, AbbVie and Amgen, but not in the matters discussed in this article.

[1] J. Molenda & R. Praseuth, Current Trends in Biologics-Related Inter Partes Reviews, Law360 (July 20, 2017) available at https://www.law360.com/articles/942459/current-trends-in-biologics-related-inter-partes-reviews (last visited May 24, 2021).

[2] Id.

[3] For purposes of this article, a biologics-related IPR or PGR is a proceeding involving a patent directed to protein or nucleic acid compositions or formulations thereof, methods of manufacturing those compositions and formulations, or methods of treating a disease with such compositions and formulations. An IPR or PGR involving a diagnostic patent is excluded from this definition.

[4] In our prior article we reported 27 biologics-related IPRs being filed in each of 2015 and 2016, whereas here, we report 26 and 28 petitions, respectively, being filed in those years. That is because we revaluated our categorization of two of those petitions as biologics IPRs, concluding that one of the 2015 petitions was improperly included in our analysis, while one of the 2016 petitions was improperly excluded from our analysis.

[5] As discussed previously, likely reasons for the biopharma industry's initial slow embrace of the IPR procedure included an historical reluctance by the pharmaceutical industry to employ post-grant procedures, a general unfamiliarity with the new IPR procedure, and an insufficient development of biosimilar programs, such that the need to clear a path for a product was not yet sufficiently immediate. See Molenda & Praseuth, supra note 1, at 2.

[6] Id.

[7] These petitions followed eight IPR petitions filed against Humira®-related patents by petitioners including Amgen, Coherus, and Boehringer Ingelheim in the 2015-2016 time frame.

[8] These petitions followed seven IPR petitions filed against Rituxan®-related patents by petitioners including Boehringer Ingelheim, Celltrion/Teva and two IPR petitions filed against Herceptin®-related patents by petitioners including Mylan and Pfizer/Hospira, in the 2014 to

2016 time frame. Additionally in 2016, the licensing company bioeq IP AG filed a petition against one patent directed to both Rituxan® and Herceptin®, and Pfizer/Hospira filed a petition against a protein purification patent relating to Rituxan®, Herceptin®, and Avastin®.

[9] For example, Pfizer successfully challenged a Rituxan®-related method-of-treatment patent, Pfizer Inc. v. Biogen, Inc., IPR2017-01168 (filed Apr. 28, 2017, challenging claims of U.S. Patent No. 8,821,873), while Samsung Bioepis successfully challenged a Herceptin®-related composition-of-matter patent, Samsung Bioepis Co. v. Genentech, Inc., IPR2017-02139 (filed Sept. 29, 2017, challenging claims of U.S. Patent No. 6,407,213).

[10] Amgen, which is developing a biosimilar of Alexion's Soliris® product, initiated IPR challenges to three of Alexion's Soliris®-related patents, inducing an early-entry settlement that avoided costly litigation under the Biologics Act. See C. Wilgoos, Biosimilar Maker Leverages IPR to Avoid Patent Dance and Obtain Early Market Entry, Kramer Levin Bio Law Blog at 2 (June 22, 2020), available at https://www.kramerlevin.com/en/perspectives-search/biosimilar-maker-leverages-ipr-to-avoid-patent-dance-and-obtain-early-market-entry.html (last visited May 21, 2021); see infra note 15 (itemizing Soliris®-related IPRs and associated patents). And as early as 2016, Mylan employed an IPR strategy to challenge certain Herceptin®-related patents, Mylan Pharm. Inc. v. Genentech, Inc., IPR2016-01693 & IPR2016-01694 (both filed Aug. 30, 2016, challenging claims of U.S. Patent No. 6,407,213), ultimately reaching a global settlement with Genentech/Roche that resulted in the termination of those IPR challenges. See, e.g., Press Release, Mylan N.V., Mylan Announces Global Settlement and License Agreements with Genentech and Roche on Herceptin®, PRNewswire (Mar. 13, 2017), available at https://www.prnewswire.com/news-releases/mylan-announces-global-settlement-and-license-agreements-with-genentech-and-roche-on-herceptin-300422255.html (last visited May 16, 2021). In 2017, Sandoz likewise employed an IPR strategy to challenge certain Humira®-related patents and also reached a global settlement terminating those challenges. Sandoz Inc. v. AbbVie Biotech. Ltd., IPR2017-02105 (filed Sept. 14, 2017, challenging claims of U.S. Patent No. 9,090,689) & IPR2017-02106 (filed Sept. 14, 2017, challenging claims of U.S. Patent No. 9,067,992). See, e.g., Press Release, Sandoz, Sandoz announces global resolution of biosimilar adalimumab patent disputes, securing patient access (Oct. 11, 2018), available at https://www.sandoz.com/news/media-releases/sandoz-announces-global-resolution-biosimilar-adalimumab-patent-disputes (last visited May 23, 2021).

[11] See Merck Sharp & Dohme Corp. v. Wyeth LLC, IPR2017-01194 (filed Mar. 29, 2017, challenging claims of U.S. Patent 8,895,024); IPR2017-01211 & IPR2017-01215 (both filed Mar. 30, 2017, challenging claims of U.S. Patent No. 9,399,060); IPR2017-01223 (filed Mar. 31, 2017, challenging claims of U.S. Patent No. 9,399,060). Merck Sharp & Dohme Corp. v. Pfizer, Inc., IPR2017-02131 & IPR2017-02132 (both filed Sept. 19, 2017, challenging claims of U.S. Patent No. 9,492,559); IPR2017-02136 & IPR2017-02138 (both filed Sept. 20, 2017, challenging claims of U.S. Patent No. 9,492,559). Sanofi Pasteur Inc. v. Pfizer, Inc., IPR2018-00187 & IPR2018-00188 (both filed Nov. 20, 2017, challenging claims of U.S. Patent No. 9,492,559). These petitions were on top of three IPR petitions that Merck Sharp & Dohme filed in 2016. See Merck Sharp & Dohme Corp. v. Wyeth LLC, IPR2017-00378 & IPR2017-00380 (both filed Dec. 1, 2016, challenging claims of U.S. Patent No. 8,562,999); IPR2017-00390 (filed Dec. 2, 2016, challenging claims of U.S. Patent No. 8,562,999).

[12] See Sanofi-Aventis U.S. LLC v. Immunex Corp., IPR2017-01129 (filed Mar. 23, 2017); IPR2017-01879 (filed July 28, 2017); IPR2017-01884 (filed July 31, 2017).

[13] See Merck Sharp & Dohme Corp. v. GlaxoSmithKline Biologicals SA, IPR2018-01229 &

IPR2018-01236 (both filed June 11, 2018, challenging claims of U.S. Patent No. 8,753,645); IPR2018-01234 & IPR2018-01237 (both filed June 11, 2018, challenging claims of U.S. Patent No. 9,265,839); IPR2019-00230 & IPR2019-00241 (both filed Nov. 7, 2018, challenging claims of U.S. Patent No. 9,422,345). Pfenex also filed three IPR petitions all challenging claims of the '345 patent. Pfenex Inc. v. GlaxoSmithKline Biologicals SA, IPR2019-01027 & IPR2019-01028 (both filed May 6, 2019); IPR2019-01478 (filed Aug. 9, 2019).

[14] See Eli Lilly and Co. v. Teva Pharm. Int'l GmbH, IPR2018-01422 (filed Aug. 8, 2018, challenging claims of U.S. Patent No. 9,340,614); IPR2018-01427 (filed Aug. 8, 2018, challenging claims of U.S. Patent No. 8,597,649); IPR2018-01423 (filed Aug. 8, 2018, challenging claims of U.S. Patent No. 9,266,951); IPR2018-01424 (filed Aug. 8, 2018, challenging claims of U.S. Patent No. 9,346,881); IPR2018-01425 (filed Aug. 8, 2018, challenging claims of U.S. Patent No. 9,890,210); IPR2018-01426 (filed Aug. 8, 2018, challenging claims of U.S. Patent No. 9,890,211); IPR2018-01710 (filed Sept. 28, 2018, challenging claims of U.S. Patent No. 8,586,045); IPR2018-01711 (filed Oct. 1, 2018, challenging claims of U.S. Patent No. 9,884,907); IPR2018-01712 (filed Oct. 1, 2018, challenging claims of U.S. Patent No. 9,884,908).

[15] See Amgen Inc. v. Alexion Pharm., Inc., IPR2019-00739 (filed Feb. 28, 2019, challenging claims of U.S. Patent No. 9,725,504); IPR2019-00740 (filed Feb. 28, 2019, challenging claims of U.S. Patent No. 9,718,880); IPR2019-00741 (filed Feb. 28, 2019, challenging claims of U.S. Patent No. 9,732,149).

[16] See Pfizer Inc. v. uniQure BioPharma BV, IPR2020-00388 (filed Jan. 4, 2020, challenging claims of U.S. Patent No. 9,249,405); IPR2021-00925 & IPR2021-00926 (both filed May 11, 2021, challenging claims of U.S. Patent No. 9,982,248); IPR2021-00928 (filed May 11, 2021, challenging claims of U.S. Patent No. 10,465,180).

[17] See Regeneron Pharm., Inc. v. Kymab Ltd., IPR2019-01577 (filed Sept. 20, 2019, challenging claims of U.S. Patent No. 9,505,827); IPR2019-01578 (filed Sept. 20, 2019, challenging claims of U.S. Patent No. 9,434,782); IPR2019-01579 (filed Sept. 20, 2019, challenging claims of U.S. Patent No. 9,447,177); IPR2019-01580 (filed Sept. 20, 2019, challenging claims of U.S. Patent No. 10,064,398); IPR2020-00389 (filed Jan. 3, 2020, challenging claims of U.S. Patent No. 10,165,763).

[18] See Molenda & Praseuth, supra note 1, at 2. For simplicity, we characterized the patents based on the predominant claim type (composition-of-matter, formulation, method-of-manufacturing, or method-of-treatment), although some of the challenged patents contain more than one claim type. We have followed that approach here, as well.

[19] See id.

[20] See, e.g., Amgen Inc. v. Sanofi, 872 F.3d 1367 (Fed. Cir. 2017); AbbVie Deutschland GmbH & Co. v. Janssen Biotech, Inc., 759 F.3d 1285 (Fed. Cir. 2014).

[21] See, e.g., Amgen Inc. v. Sanofi, 987 F.3d 1080 (Fed. Cir. 2021).

[22] See Molenda & Praseuth, supra note 1, at 2.

[23] Id.

[24] See supra, note 13.

[25] See Kashiv BioSciences, LLC v. Amgen Inc., IPR2019-00791 (filed Mar. 7, 2019, challenging claims of U.S. Patent No. 8,940,878); IPR2019-00797 (filed Mar. 7, 2019, challenging claims of U.S. Patent No. 9,643,997). Fresenius Kabi USA, LLC v. Amgen Inc., IPR2019-00971 (filed Apr. 14, 2019, challenging claims of U.S. Patent No. 9,856,287); IPR2020-00314 (filed Dec. 20, 2019, challenging claims of U.S. Patent No. 9,856,287). Lupin Ltd. v. Amgen Inc., IPR2021-00326 (filed Dec. 15, 2020, challenging claims of U.S. Patent No. 9,856,287).

[26] See supra, note 17.

[27] See Merck Sharpe & Dohme Corp. v. GlaxoSmithKline Biologicals SA, IPR2019-00230 & IPR2019-00241 (both filed Nov. 7, 2018, challenging claims of U.S. Patent No. 9,422,345). Pfenex also filed three IPR petitions challenging claims of the '345 patent. Pfenex Inc. v. GlaxoSmithKline Biologicals SA, IPR2019-01027 & IPR2019-01028 (both filed May 6, 2019); IPR2019-01478 (filed Aug. 9, 2019). Seemingly in response, GSK petitioned to challenge claims to a Pfenex patent to a similar expression platform. GlaxoSmithKline Biologicals SA v. Pfenex Inc., IPR2020-00890 (filed May 7, 2020, challenging claims of U.S. Patent No. 8,530,171); IPR2020-00962 (filed May 27, 2020, challenging claims of U.S. Patent No. 8,530,171). It is worth noting that these diphtheria toxin expression systems are integral to the preparation of pneumococcal vaccines. See supra, note 11.

[28] See Regeneron Pharm., Inc. v. Novartis Pharma AG, IPR2020-01317, IPR2020-01318, IPR2020-01320 (all filed July 16, 2020, challenging claims of U.S. Patent No. 9,220,631); IPR2021-00816 (filed Apr. 16, 2021, challenging claims of U.S. Patent No. 9,220,631).

[29] Our analysis of overall institution rates and institution rates for specific patent types does not include the 12 of 218 petitions that were pending as of May 13, 2021, as well as the 26 of 218 petitions that had settled, leaving 180.

[30] Of those 65 appeals, 44 appeals (68%) were from final written decisions in which at least one claim was held unpatentable, 17 appeals (26%) were from final written decisions in which no claims were held unpatentable, 2 appeals (3%) were from denials of institution, and 2 appeals (3%) were from petition dismissals on sovereign immunity grounds. By patent type, 40 appeals (61%) involved method-of-treatment patents, 15 appeals (23%) involved composition-of-matter of patents, 5 appeals (8%) involved method-of-manufacturing patents, and 5 appeals (8%) involved formulation patents.

[31] This affirmance rate is remarkably consistent with other reported affirmance rates of IPR decisions across all technologies. See, e.g., Daniel F. Klodowski et al., Federal Circuit PTAB Appeal Statistics Through April 30, 2021, Finnegan At The PTAB Blog (May 20, 2021), available at https://www.finnegan.com/en/insights/blogs/at-the-ptab-blog/federal-circuit-ptab-appeal-statistics-through-april-30-2021.html (reporting that IPR decisions were affirmed on every issue at a rate of 74%). Moreover, each of the six appeals that the Federal Circuit vacated and remanded was in light of Arthrex Inc. v. Smith & Nephew, Inc., 941 F.3d 1320 (Fed. Cir. 2019), which held that the Secretary of Commerce's appointment of the Administrative Patent Judges who decide IPRs violated the Appointments Clause of the U.S. Constitution. The Supreme Court has granted certiorari. Smith & Nephew, Inc. v. Arthrex, Inc., 141 S. Ct. 551 (Oct. 13, 2020) (No. 19-1452) (argued Mar. 1, 2021). The Federal Circuit dismissed four of the appeals on standing and/or mootness grounds and one appeal because it had been consolidated with another appeal regarding the same patent in which all claims were held unpatentable.

[32] See In re Gartside, 203 F.3d 1305, 1315 (Fed. Cir. 2000) (establishing substantial evidence standard as the standard of review for Patent Appeal Board fact finding).

[33] As distinguished from IPR petitions, which can only be filed no earlier than nine months after a patent issues, PGR petitions must be filed within the first nine months of patent issuance. Compare 35 U.S.C. § 311(c) (IPR) with 35 U.S.C. § 321(c) (PGR). And while IPRs allow for the assertion of only anticipation (§ 102) and obviousness (§103) as grounds for unpatentability, PGRs allow for the assertion of any ground of unpatentability, most notably written description (§ 112(a)), enablement (§ 112(b)), and indefiniteness (§ 112(b)). Compare 35 U.S.C. § 311(b) (IPR) with 35 U.S.C. § 321(b) (PGR).

[34] As is the case with IPR estoppel, PGR estoppel applies to "any ground that the petitioner raised or reasonably could have raised during that [review proceeding]." Compare 35 U.S.C. § 315(e)(2) (IPR) with U.S.C. § 325(e)(2) (PGR). While both estoppel provisions extend to preclude the introduction of prior art that "reasonably could have [been] raised" but which was not raised in the review proceeding, the reach of PGR estoppel is inherently far greater, given that it extends to all statutory grounds available to assert for invalidity. Compare Barbara Clarke McCurdy et al., Where Are We Now? Are You Estopped or Not?, Finnegan at the PTAB Blog (Feb. 19, 2020), available at https://www.finnegan.com/en/insights/blogs/at-the-ptab-blog/where-are-we-now-are-you-estopped-or-not.html (IPR estoppel) (last visited May 23, 2021) with David Maiorana, PGR Estoppel Applies to Unasserted Art, Jones Day PTAB Litigation Blog (Sept. 3, 2020), available at https://www.ptablitigationblog.com/pgr-estoppel-applies-to-unasserted-art/ (PGR estoppel) (last visited May 23, 2021).