COMMENTARY

Patent Claim Scope and Biosimilar Competition in the US and EU

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The US has found it hard to establish competition in the market for biologics, which are therapeutics derived from living cells. In the case of small-molecule drugs, the emergence of direct competition from generic drugs at the end of the exclusivity period has provided the impetus for price competition, leading to lower spending. In 2010, to spur competition in the biologics market, Congress created a simplified pathway for the US Food and Drug Administration (FDA) to approve comparable versions of biologic drugs called biosimilars. Biosimilar competition in the US has nonetheless remained weaker than in European peer countries. For example, as of August 2020, there were 52 biosimilars available in Germany, and only 15 in the US.[1] An important contributor to this "biosimilar gap" has been the fact that biosimilars to biologic blockbusters such as adalimumab (Humira) and etanercept (Enbrel) were only (or will only become) commercially available in the US several years after receiving FDA approval, while they were available in Europe years earlier.[2] Through the end of 2021, it took biosimilars a median of 301 days between receiving FDA approval and becoming available for use.[3] In one recent study, the median length of time between when a biologic drug was approved and when its first biosimilar was made available to US patients was 21.5 years.[4] This paucity of competition has contributed to high US spending on biologics. According to the Department of Health and Human Services, in 2022 41% of US drug expenditures was spent on biologics, which represented 16% of US prescriptions.[5]

Why has it taken so long for brand-name biologics such as Humira to face competition in the US, even after biosimilar rivals have been approved by the FDA? Why has it taken longer for biosimilars to enter the United States than Europe? The answer to both questions, at least in part, can be traced to the US patent system. Biologic manufacturers acquire dozens, in some cases hundreds, of US patents that cover every aspect of a medicine — the structure of its active ingredient, the composition of its formulation, its manufacturing process, its methods of use, and the devices for drug delivery. Armed with these so-called patent thickets, brand-name manufacturers assert approximately ten times as many patents in litigation against would-be biosimilar entrants in the US than in Canada or the United Kingdom (a hub for EU pharmaceutical patent litigation).[6] Similar differences are manifest among biologics in the US: biosimilars face longer delays coming to market in the US when more patents are asserted against them in litigation.[7]

Claim Breadth and Biosimilar Entry

There is thus good reason to think that the size of US biologic patent portfolios has slowed the pace of biosimilar entry. Bernard Chao's article in this issue complicates this finding by arguing that it is not simply the *number* of US patents, but their *breadth* that results in lengthy US-market delays.[8] Using Humira as a case

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study, Chao argues that the patent claims — the portions of the patent that define its power to exclude — are broader in Humira formulation patents issued by the US Patent and Trademark Office (PTO) than in otherwise highly similar patents issued by the European Patent Office (EPO). That, Chao contends, helps explain why US patents have provided a stronger shield against competition than European patents. In short, these patents are better for brand-name manufacturers because they allow their owners to exclude more products.

Chao's study takes advantage of the fact that pharmaceutical companies frequently file nearly identical patent applications (patent families) in both the US and Europe.[9] Different patent office processes and rules for patent evaluation sometimes lead the PTO and EPO to different results, both in terms of the number of patents issued and the nature of approved claims. Chao has uncovered striking differences between the claims of US Humira formulation patents and those in sibling European patents. For example, one of the broadest independent European patent claims for Humira's formulation specifies the stabilizer that must be deployed in a formulation to fall within the claim scope by dose range and type (10-14 mg/ml of mannitol). Corresponding independent US patent claims are much broader: they fail to specify a particular stabilizer (one claim requires only that the formulation include "a polyol," which is a broad category of organic compounds) or even fail to require a stabilizer at all (another independent claim covers a "stable liquid aqueous pharmaceutical formulation" meeting other criteria). The patents Chao analyzes follow this pattern more generally: the US patent claims are broader than European claims. This likely makes them more challenging to design around.

Though these results are novel and intriguing, it is hard to know how much claim scope explains US biosimilar entry patterns — or even the delayed entry of Humira biosimilars in the US as compared to Europe. Notably, patents covering drug formulations are only a part of a biologic drug's patent portfolio.[10] Are all Humira patents like this? Moreover, it will be difficult to pin slower US entry rates on any one factor. The US and EU biologic markets are different in many ways, adding many confounding variables. As Chao and Rachel Goode document elsewhere, brand-name biologic manufacturers assert many more patents in US litigation than they do in Europe.[11] Procedures for reviewing patents after issuance also differ between the jurisdictions.[12] The US has a novel (and much criticized) process designed to streamline biosimilar patent litigation.[13] And the US, which adopted legislation setting up a special regulatory process for biosimilar approvals several years after the EU, may just have needed time to catch up; indeed, differences between the US and EU in biosimilar availability appear to be narrowing, and biosimilar entry appears finally to be leading to meaningful declines in US spending.[14] Amid such differences, it is hard to know how much difference patent claim scope makes in explaining relatively slow entry by US biosimilars.

The PTO is perhaps best placed to take a leading role in answering these and other similar questions while pursuing policies that increase patent quality. The agency's leadership has started to show an appetite for policy research in recent years. In 2022, the PTO published the results of its first randomized control trial, which studied the effect of offering a sample of pro se applicants additional assistance. Similar work aimed at assessing measures to reduce issuance of low-quality patents — which might eventually be paired with an analysis of downstream effects on invention and competition — would be very valuable.

Directions for Future Research

Chao's study is a valuable contribution, one we expect to prompt interesting follow-on research into comparative claim scope. For example, are US pharmaceutical patent claims broader than EU patent claims in general? One approach to answering this question at scale would be to compare US and EU patent siblings using proxies for claim breadth, such as the length and number of independent claims.[15] Alternatively, researchers may be able to train large language mod-

The Journal of Law, Medicine & Ethics, 52 (2024): 439-442.

els (LLMs) to conduct replicable evaluations of patent claim breadth for thousands of patents.

Do patent examiner or patent office characteristics explain claim breadth? Michael Frakes and Melissa Wasserman have recently shown that when PTO examiners are pressed for time, they issue lower-quality patents.[16] It would be useful to know whether time pressure also leads examiners to issue claims with broader scope. Such research may also help disentangle whether claim breadth mostly reflects doctrinal differences between the US and the EU, as Chao suggests, or other institutional characteristics that lead to less exacting PTO reviews.

Finally, is broad claim scope associated with more robust patent protection for pharmaceuticals? Broad claim scope is favorable to patent owners in the sense that broad claims make it harder for rivals to design around a patent. But they can also be favorable to patent challengers, because such claims are easier to invalidate on obviousness grounds than narrow claims.[17] It is thus an open question whether broad claims are invariably helpful to patent owners, and if so to what degree.

Looking to the PTO

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Note

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2. V. L. Van de Wiele et al., "The Characteristics of Patents Impacting Availability of Biosimilars," *Nature Biotechnology* 1 (2022); "Etanercept Biosimilars Delayed until 2029 in US," *Generics and Biosimilars Initiative* (Jan. 14, 2022), *available at* <https://www.gabionline.net/biosimilars/news/etanercept-biosimilars-delayed-until-2029-in-us> (last visited June 20, 2024).
3. R. Williamson et al., "Are Manufacturing Patents to Blame for Biosimilar Market Launch Delays?" *Value Health* 27 (2024): at 289.
4. B. N. Rome et al, "Market Exclusivity Length for Drugs with New Generic or Biosimilar Competition, 2012–2018," *Clinical Pharmacology & Therapeutics* 109 (2021). Note that because biologics have only recently started facing competition, the sample size in the study was limited, considering four biologic molecules as compared with 264 small molecule therapies.
5. *See Competition In Prescription Drug Markets*, 2017-2022, U.S. Department of Health & Human Services 7 (2023), *available at* <https://aspe.hhs.gov/sites/default/files/documents/1aa9c46b849246ea53f2d69825a32ac8/competition-prescription-drug-markets.pdf> (last visited June 20, 2024) (calculation by authors from figures in Table 2). This disparity could be attributed in part to the fact that newer drugs are more likely to be biologics than small molecules, and hence protected from competition by both regulatory exclusivities and patents. In addition, biologics are more expensive to produce than most small molecule drugs, and so may in part for that reason remain more expensive after their exclusivity expires.
6. R. Goode and B. Chao, "Biological Patent Thickets and Delayed Access to Biosimilars, an American Problem," *Journal of Law & Biosciences* 9 (2022).
7. Williamson et al., *supra* note 3, at 291.
8. B. Chao, "USPTO's Lax Policy Leads to Humira Formulation Thicket," *Journal of Law, Medicine & Ethics* 52, no. 2 (2024). As Chao notes, whether current exclusivity periods are too long or too short depends in part on whether issued claims are justified (and on what effect patents have on innovation).
9. D. Bloomfield et al., "Improving the Quality of Drug Patents Through International Awareness," *BMJ* (2022), *available at* <https://www.bmj.com/sites/default/files/attachments/bmj-article/pre-pub-history/first_revised_article_1.1.22.pdf> (last visited June 20, 2024); M. D. Frakes and M. F. Wasserman, "Investing in Ex Ante Regulation: Evidence from Pharmaceutical Patent Examination," *American Economic Journal: Economic Policy* 15 (2023): 151.
10. See Van de Wiele et al., *supra* note 2.
11. Goode and Chao, *supra* note 6.
12. See generally "Special Theme — An Overview of Patent Litigation Systems Across Jurisdictions," *in World Intellectual Property Indicators* 2018, World Intellectual Property Org., *available at* <https://www.wipo.int/edocs/pubdocs/en/wipo_pub_941_2018-chapter1.pdf> (2018) (last visited June 20, 2024).
13. R. Feldman, "Dance of the Biologics," *Berkeley Technology Law Journal* (forthcoming 2024).
14. IQVIA estimates that annual real savings from biosimilars in the United States will increase from $13.2 billion in 2022 to $42.9 billion in 2027. See "Biosimilars in The United States 2023-2027: Competition, Savings, And Sustainability," *The IQVIA Institute for Human Data Science* 29 (2023). In May 2024, 51 biosimilars had received FDA approval, and 42 were available for use in the United States, according to Cardinal Health. "Biosimilars Landscape, Cardinal Health" (2024), *available at* <https://www.cardinalhealth.com/content/dam/corp/web/documents/Report/cardinal-health-biosimilar-launches.pdf> (last visited June 20, 2024). In November 2023, 79 biosimilars had received European Medicines Authority approval. Per Troein et al., "The Impact of Biosimilar Competition in Europe, *The IQVIA Institute for Human Data Science* 39-41 (2023).
15. A. C. Marco et al., "Patent Claims and Patent Scope," *Research Policy* 48 (2019): 1; J. M. Kuhn and N. C. Thompson, "How to Measure and Draw Casual Inferences with Patent Scope," *Journal of International Business Studies* 26 (2019): 5.

The Journal of Law, Medicine & Ethics, 52 (2024): 439-442.

16. See Frakes and Wasserman, *supra* note 9.
17. It is true that patents often contain dependent claims to narrow claim scope and avoid the danger of overly broad patent claims. But such dependent claims may not always narrow the claim sufficiently to avoid invalidation on obviousness grounds.
18. N. A. Pairolero et al., "Closing the Gender Gap in Patenting: Evidence from a Randomized Control Trial at the USPTO" (USPTO Econ. Working Paper, Paper No. 1, 2022), *available at* <https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4265093> (last visited June 20, 2024).
19. *See* Bloomfield et al., *supra* note 9; L. Larrimore Ouellette, "Patent Experimentalism," *Virginia Law Review* 101 (2015): 69. To be clear, we are not asserting that the Humira patents analyzed in Chao's study are low quality, or that broad claims are of lower quality as a rule.
20. *See* Terminal Disclaimer Practice to Obviate Nonstatutory Double Patenting, 89 Fed. Reg. 40,439 (May 10, 2024).

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