Your Generics & Biosimilars Industry

July 9, 2024

Via Federal eRulemaking Portal (https://www.regulations.gov)

The Honorable Katherine K. Vidal
Under Secretary of Commerce for Intellectual Property
Director of the United States Patent and Trademark Office
Madison Building
600 Dulany Street
Alexandria, VA 22313-1450

Re: Comments from the Association for Accessible Medicines Regarding Docket No. PTO-P-2024-0003 "Terminal Disclaimer Practice to Obviate Nonstatutory Double Patenting"

Dear Director Vidal,

The Association for Accessible Medicines and its Biosimilars Council (collectively, "AAM") is pleased to provide these comments in response to the U.S. Patent and Trademark Office's ("Office") Notice of Proposed Rulemaking, titled "Terminal Disclaimer Practice to Obviate Nonstatutory Double Patenting." Specifically, these comments respond to the Office's notice proposing a rule in which "the USPTO will not issue a patent to a common owner or inventor with a claim that conflicts with a claim of a second patent unless the terminal disclaimer includes an additional agreement that the patent with the terminal disclaimer will not be enforced if any claim of the second patent is invalidated by the prior art."[1]

AAM is the nation's leading trade association for manufacturers and distributors of FDA-approved generic and biosimilar prescription medicines. AAM's core mission is to improve the lives of patients by advancing timely access to safe, effective, and affordable generic and biosimilar medicines. Generics represent greater than 90% of all prescriptions dispensed in the United States, but account for only 18.2% of expenditures on prescription drugs, saving patients and payers more than $2.9 trillion over the past ten years.[2] Our members' products are used in billions of prescriptions every year.

AAM supports the Office's proposed rule. AAM supports a strong and robust patent system to encourage and enable innovation, and thanks the Office for its work in examining and issuing high-quality patents. AAM's member companies frequently obtain and assert patents themselves. Unfortunately, low-quality patents sometimes issue, in part due to the Office's current policies and procedures relating to terminal disclaimers to obviate obviousness-type double patenting. Such policies and procedures have enabled brand-name pharmaceutical companies to amass low-quality patents that pose significant barriers to patients' timely access to life-saving generic and biosimilar medicines. These patents accordingly discourage and disable innovation, while also leading directly to higher health-care costs by closing off market alternatives and foreclosing the savings that generic competition can bring.

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[1] 89 Fed. Reg. at 40439-40 (May 10, 2024).

[2] AAM, The U.S. Generic & Biosimilar Medicines Saving Report, Sept. 2023, at 7-8, https://accessiblemeds.org/sites/default/files/2023-09/AAM-2023-Generic-Biosimilar-Medicines-Savings-Report-web.pdf.

AAM previously submitted comments in response to the Office's October 4, 2022 request for comments regarding the Office's terminal disclaimer practices.[3] As AAM explained, large patent estates harm patients and the healthcare system, and make it impossible for generic and biosimilar companies to economically challenge such patents. AAM recommended that to address this issue, the Office should treat the filing of terminal disclaimers as strong evidence of obviousness.

AAM applauds the Office's recent efforts to "reduce barriers to market entry and lower costs for consumers."[4] As the Office aptly recognizes, "multiple patents tied by terminal disclaimers that are directed to obvious variants of an invention could deter competition due to the prohibitive cost of challenging each patent separately in litigation or administrative proceedings."[5] Particularly in the pharmaceutical industry, abusive overpatenting practices by brand-name pharmaceutical companies are a significant issue, leading to costly litigation and delayed patient access to lower-cost alternatives. AAM accordingly supports the Office's efforts to address this problem and restore necessary balance to the patent system.

I. AAM and Its Members Have A Strong Interest Against Abusive Overpatenting Practices

Generic and biosimilar pharmaceutical companies are uniquely affected by abusive overpatenting practices, in large part due to the Hatch-Waxman Act and the Biologics Price Competition and Innovation Act ("BPCIA"). These statutory schemes were designed to create a robust generic and biosimilar drug marketplace, and, as a whole, have been successful in balancing the need for innovative drug therapies while enabling generic and biosimilar pharmaceutical companies to offer patients affordable medicines. However, some brand-name pharmaceutical companies have found ways to slow the availability of affordable generic and biosimilar medicines by abusing the patent system and extending patent-supported monopolies for years. Such abusive patenting practices are particularly problematic in the pharmaceutical industry because—as summarized below—the Hatch-Waxman Act and BPCIA often make it necessary for generic and biosimilar companies to "clear the decks" and challenge a significant number of patents before entering the market.

Under the Hatch-Waxman Act, generic pharmaceutical companies must address any and all patents identified by brand-name pharmaceutical companies before entering the market. The statute sets forth a framework that requires brand-name pharmaceutical companies to identify all patents that allegedly claim the "drug" or any "method of using [the] drug" for which a claim of patent infringement could reasonably be asserted against an unauthorized user.[6] These patents are subsequently published in "Approved Drug Products with Therapeutic Equivalence Evaluations," commonly known as the "Orange Book."[7] Before obtaining FDA approval of an Abbreviated New Drug Application ("ANDA"), generic pharmaceutical companies must submit a "certification" to each patent listed in the Orange Book in connection with the brand-name drug.[8] A "Paragraph IV" certification asserts that the listed patent is invalid, unenforceable, and/or will not be infringed and, on that basis, the applicant seeks FDA approval of the generic product prior to patent expiration.[9] Upon submitting an application containing a Paragraph IV certification, the statute requires the generic pharmaceutical company to notify both the patent holder and brand-name pharmaceutical company.[10] If the patent holder or brand-name pharmaceutical company file

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[3] *See* 87 Fed. Reg. at 60130 (Oct. 4, 2022); *see also* AAM Comments, Docket No. PTO–P–2022–0025.

[4] 89 Fed. Reg. at 40440 (May 10, 2024).

[5] *Id.* at 40439.

[6] *See* 21 U.S.C. §§ 355(b)(1), (c)(2); 21 C.F.R. §§ 314.53(b)(1), (c)(2).

[7] 21 C.F.R. § 314.53(e).

[8] 21 U.S.C. § 355(j)(2)(A)(vii); 21 C.F.R. § 314.94(a)(12).

[9] 21 U.S.C. § 355(j)(2)(A)(vii)(IV); *see also* 21 C.F.R. § 314.94(a)(12)(i)(A)(4).

[10] 21 U.S.C. § 355(j)(2)(B).

an infringement suit within 45 days, FDA will automatically stay the approval of the ANDA for a period of 30-months.[11] Congress intended that these 30 months would give the parties sufficient time to resolve their patent dispute before the ANDA applicant introduced its generic product to the market.[12]

The BPCIA, too, presents unique procedural issues that often require biosimilar companies to address many patents pre-launch. Under the BPCIA, biosimilar pharmaceutical companies may notify the reference biologic product sponsor that it filed an Abbreviated Biologics License Application ("aBLA") within 20 days of the FDA's acceptance of the aBLA.[13] Within 60 days of receiving such notice, the biologic product sponsor identifies a list of unexpired patents for which a claim of infringement could reasonably be made.[14] The biosimilar applicant then has 60 days to provide detailed invalidity, unenforceability, and/or non-infringement contentions for each of the identified patents.[15] In response, the biologic product sponsor provides the factual and legal basis for its opinion that such patent will be infringed by the biosimilar applicant.[16] Over many months, the parties engage in negotiations concerning which patents could properly be subject to a patent infringement suit, which culminates with the reference product sponsor filing a complaint for patent infringement in district court.[17] The BPCIA framework can result in the assertion of a substantial number of patents.[18]

II. The Proliferation of Large Patent Estates Covering Obvious Variants Of the Same Invention Impedes Competition and Harms Patients

The cost of prescription drugs remains high, in part due to patent holders improperly extending their patent rights over single inventions. For decades, brand-name drug manufacturers have engaged in a variety of patenting practices devised to obtain numerous overlapping patents. These practices can be used as an end run around the basic principle that "although the terms of the claims may differ," "no patent can issue for an invention actually covered by a former patent, especially to the same patentee."[19]

Patent thickets are becoming increasingly prevalent, particularly in the context of biologics. A frequently cited example is Humira®, a biologic indicated for rheumatoid arthritis that resulted in 132 issued patents, almost twice as many patent applications, and a litigation with 74 asserted patents.[20] It has been estimated that between 2015-2019 alone, "delayed entry of biosimilars due to patenting has cost the U.S. health care system an astounding $7.6 billion in lost savings."[21] This is unsurprising, as it has been estimated that biosimilar medicines reduce prescription prices by 20-60%.[22] Often, the later-filed patents claim small, incremental changes that do not represent genuine innovation or benefit patients. Worse, brand-name pharmaceutical companies often use later-filed patents to obtain claims with a broader scope

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[11] 21 U.S.C. § 355(j)(5)(B)(iii); 35 U.S.C. 271(e)(2)(A).

[12] *Ben Venue Labs., Inc. v. Novartis Pharm. Corp.*, 146 F. Supp. 2d 572, 579 (D.N.J. 2001).

[13] 42 U.S.C. § 262(l)(2).

[14] *See* 42 U.S.C. § 262(l)(3)(A).

[15] 42 U.S.C. § 262(l)(3)(B).

[16] 42 U.S.C. § 262(l)(3)(C).

[17] 42 U.S.C. § 262(l)(4)-(5).

[18] *See, e.g.*, Complaint at ¶ 1, *AbbVie v. Boehringer Ingelheim Int'l GMBH*, No. 1:17-cv-01065-MSG-RL (D. Del. Aug. 2, 2017) (asserting 74 patents).

[19] *Miller v. Eagle Mfg. Co.,* 151 U.S. 186, 198 (1894).

[20] Complaint at ¶ 1, *AbbVie*, No. 1:17-cv-01065-MSG-RL (D. Del. Aug. 2, 2017).

[21] Biosimilar Council, *Failure to Launch: Patent Abuse Blocks Access to Biosimilars for America's Patients: Part I* (June 2019), *available at* https://biosimilarscouncil.org/wp-content/uploads/2019/10/Failure-to-Launch-Part-1.pdf.

[22] *See, e.g.*, Barclays Bank PLC, Biosimilars Monthly: Mar 2020 Edition at 11 (Mar. 21, 2020).

than the parent patent. Yet these low-quality—and often non-innovative—patents effectively delay generic and biosimilar competition and can force generic and biosimilar pharmaceutical companies into years of slow-moving and costly litigation.

In fact, from the time the key patent on Humira® was set to expire in 2016, AbbVie raised the list price by 60%, generating an additional $114 billion in revenue for the company.[23] AbbVie's clear intent was to accumulate patents because they increase costs and constitute barriers for potential biosimilar competitors. Indeed, external, peer-reviewed research has found that the Humira® patent estate is comprised of 80% duplicative patents.[24] This practice is entirely allowed by PTO rules.

Nor is this merely a Humira® problem: numerous other large brand-name pharmaceutical companies have purportedly followed this exact same strategy.[25] One example is Vascepa®, a drug containing a form of purified fish oil that is covered by roughly 70 patents in the Orange Book—many of which issued with terminal disclaimers.[26] As another example, a brand-name pharmaceutical company recently filed two complaints asserting a total of 31 patents against a single ANDA filer for a generic version of the drug Galafold®.[27] The brand-name pharmaceutical company has continued to prosecute additional patents, with nearly 60 patents currently listed in the Orange Book in connection with Galafold®, all stemming from a handful of patent families.[28] Peer-reviewed data shows that, of all the patents litigated against biosimilars between 2010 and 2023, 48% of them contained terminal disclaimers.[29]

These masses of duplicative patents create a numbers game for generic and biosimilar companies that ultimately harms patients. Challenging a large patent estate requires generic and biosimilar manufacturers to engage in years of costly litigation, yet the process of obtaining additional patents is comparatively quite simple. For example, although a "duplicative patent[] may cost as little as $25,000 to obtain," challengers will pay, on average, "$774,000 to challenge that patent" in administrative proceedings and "even more" to bring a similar challenge in district court.[30] Given these mounting costs, uncertainties, and long litigation timelines, the sheer number of "patents directed to obvious variants of an invention" often make even the easiest of legal challenges "prohibitively expensive."[31] The incentive to bring these cases is further reduced by the fact that, even after a successful challenge to "one or [] several of these patents,"

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[23] Rebecca Robbins, *How a Drug Company Made $114 Billion by Gaming the U.S. Patent System*, N.Y. Times (Jan. 28, 2023), https://www.nytimes.com/2023/01/28/business/humira-abbvie-monopoly.html.

[24] Rachel Goode & Bernard Chao, *Biological Patent Thickets and Delayed Access to Biosimilars, an American Problem*, 9 J.L. & Biosciences, 19 (Sept. 2022).

[25] Robbins, *supra* note 23; *see also* Dulan Lokuwithana, *Merck Leans on New Keytruda Formulation to Avoid Patent Cliff*, Seeking Alpha (Dec. 2, 2022), *available at* https://seekingalpha.com/news/3913649-merck-leans-on-new-keytruda-formulation-to-avoid-patent-cliff.

[26] *See* Orange Book, Vascepa®, *available at* https://www.accessdata.fda.gov/scripts/cder/ob/patent_info.cfm?Product_No=001&Appl_No=202057&Appl_type=N (accessed on June 24, 2024).

[27] Complaint at ¶ 1, *Amicus Therapeutics v. Teva Pharm. USA, Inc.*, Nos. 1-22-cv-01462, 1-22-cv-01462 (D. Del. Nov. 7, 2022).

[28] *See* Orange Book, Galafold®, *available at* https://www.accessdata.fda.gov/scripts/cder/ob/patent_info.cfm?Product_No=001&Appl_No=208623&Appl_type=N (accessed on June 24, 2024).

[29] Sean Tu, Rachel Goode, & William B. Feldman, *Biological Patent Thickets and Terminal Disclaimers*, JAMA Vol. 331(4), 335-337 (2023).

[30] Goode & Chao, *supra* note 24, at 19.

[31] 87 Fed. Reg. at 60131 (Oct. 4, 2022).

a generic manufacturer "do[es] not necessarily enter the market . . . [and] may simply face more patent roadblocks."[32]

These duplicative patents also create a timing game for generic companies that ultimately harms patients. Brand-drug manufacturers are increasingly filing multiple, serial litigations against generic companies based on later-issued, secondary patents, many of which are terminally disclaimed to earlier adjudicated patents.[33] This emerging phenomenon provides brand-drug manufacturers multiple bites at the apple to obtain an injunction or monetary damages, increases costs for generics, and extends the risk and uncertainty for generics—all of which could not only delay entry of lower-cost generics but also divert resources away from the launch of other generic products. This practice subverts the intent of Hatch-Waxman to lower the burdens and speed up the market entry of generics. To the contrary, serial litigation enables brand-drug manufacturers to indefinitely extend the dispute resolution process far beyond the 30-month stay.

The net result is delayed patient access to lower-cost generics and biosimilar medicines. As shown in the chart below, time to market entry—and thus the time to lower-cost alternatives—is adversely tied to the number of asserted patents:[34]

Results – Large patent thickets correlate with delayed biosimilar market entry in the US

- A comparison of the mean # patents asserted against biosimilars vs mean # months delay to launch (time lapse between regulatory approval and launch of a each biosimilar).
- On average, **7x more patents** are asserted against biosimilars in the US compared to Canada and the UK.
- On average, there is **4x longer delayed launch** of biosimilars in the US compared to Canada and the UK.

United States		Canada		United Kingdom	
Mean # of patents	Mean # months delay launch	Mean # of patents	Mean # months delay launch	Mean # of patents	Mean # months delay launch
17.1	**30.3**	**2.5**	**7.7**	**2.4**	**7.6**

Because the table includes averages (mean values), only those biosimilars that faced litigation are included into the calculation. The 30 biosimilars within this study are copies of 9 branded biological drugs. For example, there are 5 biosimilars of Humira within the 30 biosimilars under study. Two of those Humira biosimilars were sued under 62 and 10 patents respectively whereas 3 of those Humira biosimilars entered into pre-litigation patent settlements. Therefore, the average number of patents litigated against a Humira biosimilar in the US is (62+10)/2 = 36. The same method of calculation was used across all biosimilars.

As shown above, the time to entry in the United States for biosimilars is nearly four times that of Canada and the United Kingdom, and the number of patents asserted in the United States is nearly eight times the number in those countries.[35] The United States plainly lags behind other countries in timely providing

[32] Goode & Chao, *supra* note 24, at 3.

[33] *See, e.g., Vanda Pharms. Inc. v. Teva Pharms. USA, Inc.*, No. 22-7528 (D.N.J. Feb. 10, 2023) (granting defendants' motion to transfer a subsequent litigation to the original litigation's venue and describing how Vanda filed serial litigations against Teva and Apotex).

[34] Goode & Chao, *supra* note 24, at 3.

[35] *Id.*

patients with lower-cost medicines, and it does so in large part due to the number of patents asserted against generic and biosimilar companies pre-launch.[36]

III. AAM Supports the Office's Efforts to Combat Abusive Overpatenting

There is no more fundamental rule of patent law than that an inventor is entitled to only a single patent for an invention. That is because a single patent "endow[s] [its] holders with superpowers, but only for a limited time."[37] A central corollary to that rule is that a patentholder cannot obtain a patent claim on an obvious variant of an existing claim. The obviousness type double-patenting ("ODP") doctrine ensures that a patentee receives one period of exclusivity for an invention—a period that cannot be extended through subsequent claims covering obvious variations of the invention. The limits imposed by the ODP doctrine are important not only to the general health of the patent system, but they are critical as applied to drug patents.

While the ODP doctrine critically limits the patent term for obvious variants of the same invention, the Office's current practices fail to protect competitors from large patent estates rooted in ODP. Under the Office's current practices, "claims in patents tied by a terminal disclaimer filed under 37 CFR 1.321(c) or (d) to obviate nonstatutory double patenting must be separately challenged on validity grounds."[38] Terminal disclaimers have accordingly permitted industry patentholders to engage in gamesmanship that has kept low-cost generics and biosimilars out of the market. Brand-name pharmaceutical companies have abused the system to obtain later patents that claim small, incremental changes that are neither genuinely innovative nor beneficial to patients. Yet these non-innovative and oftentimes duplicative patents are effective at their primary goal: delaying generic competition through protracted patent litigation (and sometimes through multiple, serial patent litigation) and extending patent-supported monopolies on brand-name drugs beyond the maximum statutory limits.

The Humira® patent estate discussed above illustrates how the Office's current practices enable brand-name pharmaceutical companies to engage in abusive overpatenting. As shown in the table below, the Humira® patent estate is dominated by duplicative patent families, with two separate patent families in the Humira® patent estate comprising 36 separate patents linked by terminal disclaimers:[39]

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[36] *Id.*

[37] *Kimble v. Marvel Ent., LLC.*, 576 U.S. 446, 451 (2015).

[38] 89 Fed. Reg. at 40441 (May 10, 2024).

[39] Goode & Chao, *supra* note 24, at 4, 10–11.

Case study: the Humira patent thicket (USA)

- The Humira patent thicket contains 73 granted US patents that are directed to the product, formulation or method of treatments (the core thicket).
- The 73 US patents (core Humira thicket) are derived from only 8 patent families. Within each patent family, many patents are linked by terminal disclaimers and so are not patentably distinct.
- 59 of the Humira patents are non-patentably distinct from other members. **80% of the US Humira patents are not directed to non-obvious inventions.**

Core Humira Patent Thicket (USA)

	Patented subject matter and earliest granted family member	Number of granted US patents within each family	Number of granted US linked by terminal disclaimers within each family (non-patentably distinct)	% of Humira patents within each family that are non-patentably distinct
Humira patent family 1	Basic product patent US6090382	10	10	100%
Humira patent family 2	Primary indications US8889135	7	4	57%
Humira patent family 3	Formulation (single concentration) US8216583	21	21	100%
Humira patent family 4	Secondary indications US8889136	18	15	83%
Humira patent family 5	Purity level US8916153	8	8	100%
Humira patent family 6	Treatment of hidradenitis suppurativa US8747854	2	2	100%
Humira patent family 7	Treatment of juvenile diseases US8999337	3	3	100%
Humira patent family 8	Formulation (double concentration) US8420081	4	4	100%

The originator of Humira, Abbvie, also owns 70 platform (drug agnostic) manufacturing patents, not shown above

Despite the significant overlapping subject matter in the Humira patent estate, as the Office acknowledges, "competitors attempting to enter the market . . may have to defend against patents to obvious variants of a single invention despite the presence of terminal disclaimers," exposing such competitors to unnecessary high litigation costs.[40] This holds true here. Biosimilar pharmaceutical companies must go 36-for-36 in challenging these patents despite their overlapping nature. Yet AbbVie needs to prove infringement of only a single claim in a single one of those patents to delay the biosimilar manufacturer's market entry until patent expiration. The system has fallen out of balance, and the phenomenon of multiple patenting is largely to blame.

AAM supports the Office's efforts to combat overpatenting through the filing of obvious variants of the same invention.[41] AAM believes that such efforts will only promote—and not hurt—competition. Brand-name pharmaceutical companies have options when faced with an ODP rejection during prosecution—they can choose to fight the rejection on the merits if they believe that the rejected claims are patentably distinct, or they can avoid that dispute and file a terminal disclaimer. Indeed, the Office recognizes that such options exist, noting that "[t]o the extent an applicant believes claims are patentably distinct, they may either challenge the rejection or move those claims to an application in which a terminal disclaimer has not been,

[40] 89 Fed. Reg. at 40441 (May 10, 2024).

[41] AAM notes that while the Office's proposal would significantly restore balance to the patent system, it does not fully address all overpatenting practices involving terminal disclaimers. As noted above, brand-name pharmaceutical companies often file terminal disclaimers in connection with later-filed patents claiming obvious—yet broader—variants of claims recited by earlier-filed patents. The broader claims recited by the later-filed patent may be more susceptible to an invalidity challenge, yet the Office's proposed rule attaches consequences only if a claim of the narrower, earlier-filed patent is finally held unpatentable or invalid. *See id.* at 40440 (explaining that "a terminal disclaimer under the proposed rule would be unidirectional, encumbering only the patent with the terminal disclaimer and not the conflicting patent"). To address this issue, AAM recommends that the Office require disclaimants to agree that the prosecution history of patents tied by terminal disclaimers will become part of the prosecution record. Such a rule would enable litigants to assert, when appropriate, the doctrines of prosecution history estoppel and prosecution history disclaimer based on prosecution arguments concerning any patents tied by terminal disclaimers.

and will not be, filed."[42] The Office's proposal merely attaches consequences to an applicant's voluntary decision to choose the latter option—consequences that could greatly promote competition and provide patients with earlier access to lower-cost medicines.

IV. Conclusion

AAM thanks the Office for its tireless efforts in ensuring the high quality of the United States patent system. The suggestions outlined above represent meaningful steps that the Office should take to improve the quality of future patents and to combat existing, low-quality patents that burden patients' timely access to life-saving generic and biosimilar medicines.

Sincerely,

/s/

Association for Accessible Medicines

[42] 89 Fed. Reg. at 40441 (May 10, 2024).