Your Generics & Biosimilars Industry

February 6, 2024

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

The Honorable Dr. Laurie E. Locascio
Under Secretary of Commerce for Standards and Technology
Director of the National Institute of Standards and Technology (NIST)
100 Bureau Drive
Gaithersburg, MD 20899

Re: Comments from the Association for Accessible Medicines Regarding Docket No. 230831-0207, "Request for Information Regarding the Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights"

Dear Director Locascio:

The Association for Accessible Medicines and its Biosimilars Council (collectively, "AAM") provides these comments in response to the National Institute of Standards and Technology's ("NIST") Request for Comments, titled "Request for Information Regarding the Draft Interagency Guidance Framework for Considering the Exercise of March-In Rights."[1]

AAM is the nation's leading trade association for manufacturers of FDA-approved generic and biosimilar prescription medicines. We aim to improve the lives of patients by advancing timely access to safe, effective, and affordable generic and biosimilar medicines.

Generic drugs and biosimilar medicines are vital to ensuring access to affordable healthcare. Generics represent more than 90% of all prescriptions dispensed in the United States, yet account for less than 18% of expenditures on prescription drugs.[2] Savings attributable to generics and biosimilars have kept nearly $2.9 trillion in the pockets of patients and taxpayers over the past ten years.[3] This increased affordability has also expanded access to critical medications that improve patient outcomes.

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[1] 88 Fed. Reg. 85593 (Dec. 8, 2023).

[2] Ass'n for Accessible Meds., *2023 The U.S. Generic & Biosimilar Medicines Savings Report* (Sept. 2023), https://accessiblemeds.org/sites/default/files/2023-09/AAM-2023-Generic-Biosimilar-Medicines-Savings-Report-web.pdf.

[3] *Id.*

AAM supports policies directed towards lowering prescription drug prices, increasing access to generic drugs, and harmonizing our patent system to ensure it encourages innovation but does not pose a barrier to Americans' timely access to live-saving generic and biosimilar medicines. While we appreciate the government's desire to achieve these same outcomes, we are concerned that NIST's proposal carries with it many "broad and unintended consequences" that, in AAM's view, risk doing more harm than good.[4]

Specifically, AAM is concerned that the proposal ignores and jeopardizes the vital role that generics and biosimilars play in ensuring the affordability and availability of medicine. Rather than making a handful of brand medicines more affordable, it is likely that NIST's proposal would in fact undermine pre-existing incentives, specifically under the Hatch-Waxman Act and the Biologics Price Competition and Innovation Act ("BPCIA"), for generic and biosimilar manufacturers.

II. MARCH-IN WOULD NOT BRING GENERICS OR BIOSIMILARS TO THE MARKET MORE QUICKLY

Competition from lower-priced generics and biosimilars is the single tested and proven solution to the challenge of brand drug prices. NIST's proposal will do nothing to further competition. And by leaving the door open to government-led manufacturing, march-in threatens to disincentivize the development of generic and biosimilar medicines that actually reduce costs for American consumers.

a. March-In Can Affect Only a Limited Subset of Patents

Practically speaking, constraints on the use of march-in make it a poor vehicle for bringing lower-cost generic and biosimilar medicines to market. In the U.S., brand-name pharmaceutical products are often protected by tens, and sometimes hundreds of patents. As an example, the top-ten best selling drugs in America today are protected by an average of 74 patents *each*.[5]

The government's march-in authority, on the other hand, applies to a very narrow class of patents—those "subject inventions" that were "conceived or first actually reduced to practice in the performance of work under a [government] funding agreement."[6] A 2019 study of the patents covering the 197 top-selling NDA drugs quantified that narrow class. It revealed that of the more than 1,110 patents listed in the Orange Book, less than 3% have the government-interest patent disclosure required for march-in.[7]

Even for the handful of drugs that *are* protected by at least one Bayh-Dole patent, a single march-in license will do nothing to address the other patents covering that drug. Indeed, after removing non-Bayh Dole patents from the equation, the same 2019 study found that march-in would cover

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[4] 88 Fed. Reg. at 85600.

[5] *Overpatented, Overpriced*, Initiative for Meds., Access, & Knowledge (Sept. 2022), https://www.i-mak.org/wp-content/uploads/2022/09/Overpatented-Overpriced-2022-FINAL.pdf.

[6] 35 U.S.C. §§ 201(e), 203(a).

[7] Genia Long, *Federal Government-Interest Patent Disclosures for Recent Top-Selling Drugs*, 22 J. Med. Econ. 1261, 1264 (2019).

the relevant patents for only two of the 197 drugs listed in the Orange Book.[8] And a recent study of the 361 new medicines approved by the FDA between 2011–2020 revealed that only five would have been statutorily eligible for march-in.[9]

NIST itself has recognized this roadblock, explaining: "if only one of several patents necessary to produce a product is subject to march-in, that likely weighs against march-in, since other licensees would need separate permission to use several other patents before they could make the product."[10]

Unfortunately, the growing number of patents covering a single invention narrows the number of drugs march-in could reach. That is why expanding the use of march-in would do very little, if anything, to make lower-cost generic and biosimilar medicines available to patients.

b. Generic and Biosimilars Can Achieve More for Patients Through Litigation Than March-In

Generics and biosimilar companies can achieve far more for patients in litigation—and far more quickly—than what the march-in proposal can achieve. If a set of patents becomes subject to march-in, it does not result in an invalidity finding of the relevant patents—only a license for a "responsible" licensee.[11] By contrast, invalidity findings rendered in district court litigation are typically preclusive across all future potential infringers.[12] Thus, if a single generic manufacturer is able to invalidate all of the patents covering a given drug, that manufacturer's success will open up the market for everyone. And once the number of generic drugs in the market increases, savings follow. For example, after generic challengers invalidated the key patents covering branded Tecfidera, the price per capsule fell from about $90 to less than $30 following generic approvals, resulting in annual savings of about $938 million.[13] And data show that when six or more generic competitors are present, "price reductions of more than 95%" will result.[14] That level of price reduction simply cannot be achieved by march-in.

These litigation victories will be reached much more quickly than march-in. The timing for Hatch-Waxman proceedings is well-established: there is a 30-month stay that coincides with district court proceedings.[15] In the BPCIA context, courts have acted decisively and quickly—as one

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[8] *Id.*

[9] *New study finds 92% of new FDA approved medicines have no federally funded intellectual property or patents*, VitalTransformation (Nov. 30, 2023), https://vitaltransformation.com/wp-content/uploads/2023/11/FINAL-march-in-press-release-30Nov2023-1.pdf.

[10] 88 Fed. Reg. at 85600.

[11] 35 U.S.C. § 203(a).

[12] *Blonder-Tongue Labs., Inc. v. Univ. of Ill. Found.*, 402 U.S. 313, 329 (1971).

[13] *Estimating Cost Savings from New Generic Drug Approvals in 2021*, FDA (Sept. 2023), https://www.fda.gov/media/172608/download?attachment.

[14] *Generic Competition and Drug Prices: New Evidence Linking Greater Generic Competition & Lower Generic Drug Prices*, FDA (Dec. 2019), https://www.fda.gov/media/133509/download.

[15] 21 U.S.C. §§ 355(c)(3)(C), (j)(5)(b)(iii).

example, Apotex received a final decision of noninfringement on its filgrastim product from the Federal Circuit approximately 25 months after being sued.[16] By contrast, march-in is extremely protracted. Indeed, once a march-in license is granted, any party "adversely affected" by an agency's march-in determination has the statutory right to *three separate levels of review*: agency review, an appeal to the U.S. Court of Federal Claims, and an appeal to the U.S. Court of Appeals for the Federal Circuit.[17] Each of these processes can take years, and the agency's march-in decision must be "held in abeyance" until the lengthy appellate process has been exhausted.[18] Thus, the generic and biosimilar processes work much more quickly than the protracted march-in processes, and will result in expedited patients access to lower-cost medicines.

III. MARCH-IN LICENSES WOULD INJECT UNCERTAINTY AND UNDERMINE GENERIC AND BIOSIMILAR DEVELOPMENT

March-in will also introduce substantial unpredictability into the development process for generics and biosimilars. For biosimilars, prospective manufacturers must invest as much as $300 million over 6–9 years just to develop the biosimilar[19]—which may fail clinical trials—and then must invest as much as "$10 million per suit" in patent litigation.[20] Similarly, in the Hatch-Waxman context, generics must decide—often years in advance—whether to file a paragraph IV certification to challenge brand-name patents listed in the Orange Book.[21] That decision is already fraught with uncertainty and unpredictability.[22]

March-in would only amplify this substantial uncertainty and would further undermine incentives for generic and biosimilar development, as detailed below. And this added uncertainty would have deleterious impacts for patients. In the Hatch-Waxman space alone, a single less paragraph IV challenge would result in approximately $1.7 billion in lost savings for patients.[23] Similarly, in the biosimilars context, biosimilars have already resulted in $24 billion in savings since 2015.[24]

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[16] *Amgen v. Apotex*, 712 F. App'x 985 (Fed. Cir. 2017) (affirming judgment of non-infringement).

[17] 35 U.S.C. § 203(b).

[18] *Id.*

[19] Miriam Fontanillo et al., *Three Imperatives for R&D in Biosimilars*, McKinsey & Co. (Aug. 19, 2022), https://www.mckinsey.com/industries/life-sciences/our-insights/three-imperatives-for-r-and-d-in-biosimilars.

[20] *FTC v. Actavis, Inc.*, 570 U.S. 136, 170 (2013) (Roberts, C.J., dissenting).

[21] 21 U.S.C. § 355(j)(2)(A)(iv).

[22] *The Hatch-Waxman 180-Day Exclusivity Incentive Accelerates Patient Access to First Generics*, Ass'n for Accessible Meds., https://accessiblemeds.org/sites/default/files/2022-06/AAM-Hatch-Waxman-180-Day-Exclusivity-Incentive-Accelerates-Patient-Access-First-Generics.pdf.

[23] William Schultz & Margaret Dotzel, *An Evidence Based Assessment of the BLOCKING Act* (May 2022), https://www.thefdalawblog.com/wp-content/uploads/2022/05/5-25-FINAL.pdf.

[24] *Generic & Biosimilar Savings Report*, *supra* note 2, at 3.

a. The Proposal Undermines Hatch-Waxman and BPCIA Incentives

(1) March-in undermines the sole incentive for challenging patents in Hatch-Waxman proceedings

March-in has the potential to cause the loss of the single most important incentive for generic developers to challenge brand-name patents—Hatch Waxman's 180-day exclusivity incentive. Since its introduction in 1984, Hatch-Waxman has ushered in countless lower-cost generic drugs and has achieved lasting benefits for taxpayers and patients alike. The Act enables generic manufacturers to develop products without incurring patent-infringement liability; to market products before relevant brand patents' expiration; and to efficiently challenge brand-companies' patents.[25]

Hatch-Waxman's 180-day exclusivity provision "is perhaps the most significant driver of competition—and lower prices—within the pharmaceutical industry."[26] Recognizing that challenging brand drugs is an expensive and risky endeavor, the Act grants 180 days of market exclusivity to the "first" generic applicant to file a paragraph IV certification. This exclusivity is the sole statutory incentive motivating generic manufacturers to challenge brand-name patents.

Incentivizing paragraph IV filings is of the utmost importance—challenges not only pave the way for approval of an initial generic drug, they open up the market to further generic competition, generating billions in potential savings. According to the FDA, first generics often reduce drug costs by 39%.[27] But once additional competitors follow suit, "price reductions often exceed 95%."[28]

It is easy to see how march-in could disrupt a generic manufacturer's expected 180-day exclusivity. For example, 180-day exclusivity could be effectively eliminated for other first filers if one of them receives a march-in license. Those first filers will have expended a substantial amount of time and effort challenging the subject patents, all to lose their exclusivity.

In these ways, march-in risks upsetting Hatch-Waxman's carefully crafted statutory regime. By weakening incentives for generic manufacturers, march-in could lead to fewer patent challenges, resulting in delayed access to lower-cost medicines.

(2) March-in undermines incentives in the BPCIA

March-in similarly undermines multiple incentives in the BPCIA. Under the BPCIA, the first approved interchangeable is eligible for up to 12 months of exclusivity.[29] To the extent that one first interchangeable receives a march-in license, interchangeable exclusivity could be severely

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[25] *The Hatch-Waxman Act: Over a Quarter Century Later*, Cong. Rsch. Serv. (Dec. 5, 2012), https://www.everycrsreport.com/files/20121205_R41114_03b8c7cd64a3a0e2558375b3bbc694613ee48546.pdf.

[26] *Hatch-Waxman 180-Day Exclusivity Incentive*, *supra* note 22, at 2.

[27] *Id.*

[28] *Id.*

[29] 42 U.S.C. § 262(k)(6).

undermined for another first interchangeable, as would be the investment in switching studies that FDA has called for in some circumstances.

Even more problematically, march-in severely disincentivizes the years-long, expensive development process for biosimilars. As noted above, prospective manufacturers must invest as much as $300 million over 6–9 years just to develop a biosimilar.[30] And those prospective manufacturers must generally engage in expensive phase III trials that could fail.[31] Knowing that march-in could be exercised at some point well-down this unpredictable, cost-intensive road would likely severely disincentivize these investments.

b. Alleged "Reasonable" Licenses That Exceed Generic and Biosimilar Profits Would Heavily Disincentivize Development

The massive unpredictability of what a "reasonable" license might be would also strongly disincentivize front-end investments and development work, particularly if that *license exceeds the entire profits of the generic or biosimilar*. Bayh-Dole contemplates requiring "the contractor, an assignee or exclusive licensee of a subject invention to grant a . . . license . . . upon *terms that are reasonable under the circumstances*, and if the contractor, assignee, or exclusive licensee refuses such request, *to grant such a license itself*[.]"[32]

In other words, the statute allows brand companies the freedom to propose terms for a "reasonable" license. But Bayh-Dole's failure to outline the factors that should be used to assess the reasonability of a march-in license risks contractors exploiting this freedom to request sky-high royalties.

Absent statutory guidance, brands or the government may turn to the *Georgia Pacific* factors, which are often cited when calculating a "reasonable" royalty. These factors consider pricing, profits, and value *at the brand rate*, including: "royalties received by the patentee for the licensing of the patent in suit"; the "existing value of the invention to the licensor as a generator of sales of his non-patented items; and the extent of such [] sales"; the "established profitability of the product made under the patent; its commercial success; and its current popularity"; and the "portion of the profit or of the selling price that may be customary in the particular business or in comparable businesses to allow for the use of the invention or analogous inventions."[33]

Historically, the calculation of a reasonable royalty in the pharmaceutical context has been subject to complex, time-consuming litigation that results in extremely high royalty demands from brand-name manufacturers. For example, in litigation concerning the drug Protonix®, the plaintiff sought

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[30] Fontanillo et al., *supra* note 19.

[31] Charlie Katebi, *Federal Barriers Make Biologic Drugs Unaffordable*, Am. First Pol'y Inst. (Nov. 29, 2023), https://americafirstpolicy.com/issues/federal-barriers-make-biologic-drugs-unaffordable.

[32] 35 U.S.C. § 203(a) (emphasis added).

[33] *Georgia-Pacific Corp. v. U.S. Plywood Corp.*, 318 F. Supp. 1116, 1120 (S.D.N.Y. 1970).

$2.7 billion in damages and ultimately settled with generic manufacturers for $2.1 billion.[34] The Federal Circuit has also affirmed "reasonable" royalty rates of 50% in the Hatch-Waxman context.[35] It has even stated that royalties can account for "the profits on sales [a brand] might lose as a result of granting a license,"[36] and that royalties can exceed the defendant's entire profit from the product.[37]

Licensing patents to generic manufacturers at a level that exceeds their profits, or at a level that effectively compensates brand companies for *their* lost profits, would injective massive unpredictability into decision making and severely disincentivize the development of lower-cost alternatives. And even though the statute contemplates the government's ability to step in and grant a license in the event a contractor's requests are unreasonable, the severe disincentives that march-in creates may have already stopped the generic or biosimilar at the starting block.

c. The Prospect of Government Manufacturing Will Further Disincentivize Development

Another risk tied to the expanded use of march-in is the accompanying uncertainty of government-led manufacturing efforts. Bayh-Dole gives the government the power to "grant [] a [march-in] license *itself*," as long as that license is granted to a "responsible applicant or applicants."[38] But nothing in the statute prevents the government from ultimately licensing the subject invention to itself, opening the door to government-led manufacturing.

Government manufacture will also severely disincentivize generic and biosimilar competitors from entering the marketplace and bringing lower cost medications to the American public. This could ultimately lead to drug shortages if, for example, the government cannot effectively supply the market with the licensed product. And this could not occur at a worse time—sustainability issues in the generic industry have reached perilous levels, with manufacturers "struggling to stay in business."[39] Moreover, biosimilar markets are not developing as predicted because of PBM practices and brand abuses.[40] Taking steps that could eliminate competitive opportunities for generics and biosimilars will certainly not help solve these problems.

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[34] *The Law on Damages In Generic Drug Launches Remains Vague*, Am. Conf. Inst. (Apr. 10, 2014), https://staging.americanconference.com/blog/the-law-on-damages-in-generic-drug-launches-remains-vague/.

[35] *AstraZeneca AB v. Apotex Corp.*, 782 F.3d 1324, 1333–37 (Fed. Cir. 2015).

[36] *Asetek Danmark A/S v. CMI USA Inc.*, 852 F.3d 1352, 1362 (Fed. Cir. 2017).

[37] *See Aqua Shield v. Inter Pool Cover Team*, 774 F.3d 766, 772 (Fed. Cir. 2014) (error to treat defendant's actual profits as royalty cap).

[38] 35 U.S.C. § 203(a) (emphasis added).

[39] Ike Swetlitz, *Teva Plans to Cut Back Generic Drug Production Even As Shortages Intensify*, Bloomberg (May 18, 2023), https://www.bloomberg.com/news/articles/2023-05-18/teva-plans-cuts-to-generic-drug-production-amid-shortages.

[40] Tristan Manalac, *AbbVie's Humira Maintains Market Dominance Amid Biosimilar Launches: Report*, BioSpace (Jan. 18, 2024), https://www.biospace.com/article/abbvie-s-humira-maintains-market-dominance-amid-biosimilar-launches-report/.

IV. CONCLUSION

AAM thanks NIST for the opportunity to comment on NIST's proposed, novel interpretation of the Bayh-Dole Act. Based on the ramifications we have outlined above, AAM opposes the suggested use of price as a reason to exercise march-in rights.