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Comments of the Pharmaceutical Research and Manufacturers of America in Response to the USPTO's Notice on *Joint USPTO–FDA Collaboration Initiatives; Notice of Public Listening Session and Request for Comments* (Docket No. PTO-P-2022-0037)

February 6, 2023

The Pharmaceutical Research and Manufacturers of America (PhRMA) is pleased to submit these comments in response to the United States Patent and Trademark Office's (USPTO's) and the U.S. Food and Drug Administration's (FDA's) Notice of Public Listening Session and Request for Comments regarding *Joint USPTO-FDA Collaboration Initiatives*.[1] PhRMA appreciated the agencies holding the Public Listening Session. PhRMA participated in the Public Listening Session and is submitting these comments to address additional topics.

PhRMA represents the country's leading innovative biopharmaceutical research companies, which are devoted to discovering and developing medicines that enable patients to live longer, healthier, and more productive lives. Since 2000, PhRMA's member companies have invested more than $1.1 trillion in the search for new treatments and cures, including an estimated $102.3 billion in 2021 alone.

PhRMA thanks the agencies for holding a public listening session and for requesting stakeholder comments on USPTO-FDA collaboration and engagement. PhRMA appreciates that the agencies are seeking public participation on important innovation policy issues; a transparent policymaking process is beneficial for all stakeholders. Further, we applaud the agencies' stated "commitment to ensuring our innovation system strikes the appropriate balance—encouraging meaningful innovation in drug development while supporting a competitive marketplace that can promote greater access to medicines for American families."[2] The President's Executive Order on Promoting Competition in the American Economy similarly recognizes the importance of preserving this balance,[3] which is critical not only to promoting biopharmaceutical innovation and access but also to ensuring that the United States continues to serve as a leader in biopharmaceutical innovation. Any new policies emerging from the agencies' collaborations should be tailored to preserve this balance.

In brief, PhRMA comments as follows:

- PhRMA has not seen reliable evidence of systemic issues within the U.S. patent system or the FDA drug approval process that would warrant substantial changes in intellectual

[1] 87 Fed. Reg. 67,019-67,022 (Nov. 7, 2022).

[2] *Id.* at 67,020.

[3] *See* Exec. Order. No. 14,036, § 5(p)(vi) (July 9, 2021) (directing FDA to write a letter to the USPTO "to help ensure that the patent system, while incentivizing innovation, does not also unjustifiably delay generic drug and biosimilar competition beyond that reasonably contemplated by applicable law").

property (IP) laws. Any changes to IP laws or policies should be based on sound evidence, not false narratives, flawed data, or unsupported assertions.

- PhRMA supports training USPTO examiners on relevant and publicly available FDA resources if helpful to examiners.

- Assertions that practitioners and drug sponsors are making inconsistent statements to FDA and USPTO lack sound evidentiary support. Critics focus on a single biopharmaceutical case, which does not indicate a widespread problem warranting creation of a broad, resource-intensive information sharing infrastructure between the agencies. To the extent that any such statements occur, they are rare and are already discouraged by the severe penalty for inequitable conduct. Although we view increased information sharing between the agencies as unwarranted, any such sharing initiatives must comply with existing laws protecting proprietary information and should be designed to avoid chilling investment in innovative biopharmaceuticals.

- FDA does not play a role in proceedings under the Leahy-Smith America Invents Act (AIA) more generally, so collaboration between the agencies as to AIA proceedings is not warranted. PhRMA supports changes to FDA's regulation on the amendment and withdrawal of patent information in the Orange Book upon a final decision from a court or the Patent Trial and Appeal Board (PTAB) to align with the Orange Book Transparency Act (OBTA).

- The agencies' existing processes to share information on patent term extension (PTE) applications work well, and no changes are needed.

- We support the agencies' continued publication of important information about PTE applications and FDA reviews of drug and biologic applications, consistent with the law, and recommend keeping this information up to date.

- We believe changes to IP laws and policies on use codes, method-of-use patents, and "skinny labeling" are unjustified.

    - Generic and biosimilar applicants already enjoy significant discretion to pursue labeling carve-outs that can undermine IP protections. No changes are warranted based on the *GSK v. Teva* case, which is consistent with precedent that generic drug manufacturers are responsible for ensuring that their labeling and other statements do not induce infringement of an innovator's method-of-use patents. Any attempt to respond to *GSK v. Teva* by adopting an even more permissive approach to skinny labeling would undercut incentives to study new uses of approved drugs and is especially unwarranted while the Supreme Court considers whether to take the case.

    - FDA's role in patent listing should remain ministerial. The agency lacks the expertise, resources, and statutory authority to review generic labeling to ensure it avoids patent infringement, e.g., by construing patent claims. USPTO should remain uninvolved in patent listing. It does not have jurisdiction with respect to patent

enforcement or claim construction, nor does it have expertise in the safety and effectiveness issues presented by generic labeling.

- Congress has provided a mechanism for applicants submitting abbreviated applications to advance delisting allegations: the statutory counterclaim in court. A recent case shows claim construction by a federal court can be necessary to resolve these counterclaims, underscoring the appropriateness of the courts as a forum for delisting disputes.

- Changes to Orange Book listing practice also would be premature in light of the recent enactment of the OBTA, the Government Accountability Office's (GAO) forthcoming report on the Orange Book, and FDA's ongoing consideration of public comments on this topic.

- PhRMA believes that patents that relate to a risk evaluation and mitigation strategy (REMS) should (indeed, must) be listed whenever they meet the statutory listing criteria. Requiring FDA to identify "REMS patents" would raise concerns given FDA's ministerial role in patent listing.

- We disagree that patents are being "misuse[d]" to "improperly delay competition." As explained more fully below, stakeholders advancing these "concerns" rely on flawed data, false narratives, and unsubstantiated hypotheses.

- In response to the Request for Comment's request for input on additional topics, we believe that (1) FDA should publish prompt reference product exclusivity decisions at the time of biologic approval; (2) that patient groups and other stakeholders interested in participating in the patent prosecution process can use existing mechanisms to submit printed publications that are relevant to examination; and (3) that there is no statutory requirement for a claimed biopharmaceutical invention to show medical benefit or any other value-based characteristic to result in a patent, and such a requirement would not only depart from the statute but raise technology neutrality concerns.

I. Introduction

IP protections are essential to ensure that American patients continue to have access to an array of medicines, including novel medicines that serve unmet medical needs, and to promote a robust and successful American economy. The United States is an innovation leader, including in biopharmaceutical research and development (R&D), and the U.S. patent system is a major driver of this innovation. Patents incentivize R&D by both large and small entities in the biopharmaceutical industry and help provide the opportunity to recoup investment costs if a patented invention (or a combination of inventions) ultimately leads to a commercial product. They are also critically important for incentivizing post-approval R&D that can result in reduced side effects, efficacy in a different patient population or disease, or new dosage forms or forms of administration that can improve patient adherence or convenience, leading to better patient outcomes. Particularly in the biopharmaceutical space, without properly calibrated patent protection, the financial and time costs and risks necessary to develop groundbreaking new

medicines and post-approval innovations could be prohibitive. Indeed, without the protections afforded by the U.S. patent system, many lifesaving and life changing medicines and medical breakthroughs would not have been realized. Both the USPTO and FDA have key roles to play in ensuring that the innovation system both promotes development of novel medicines and uses and advances competition, and any interagency collaboration should ensure this balance is maintained.

We support the agencies' request that commenters "submit research and data" to support their comments.[4] We view this step as essential particularly when a commenter is advocating for a change to existing law or policy. PhRMA believes that current IP laws and policies are functioning as intended and that any changes to IP laws and policies should be based on sound evidence, not unsubstantiated allegations or flawed research. As described more fully in these comments, we believe that many proponents of change are advancing misleading narratives that are not grounded in accurate data. In the absence of evidence-based rationales for changes to the law or agency policy, the agencies should continue their work carrying out the relevant statutory directives that continue to make the U.S. a leader in biopharmaceutical innovation.

A. A Change to Current IP Law or Policies Is Not Warranted.

Developing a drug—starting from synthesizing a molecule in a laboratory and onward to conducting clinical trials, obtaining FDA approval, and then bringing a drug to market—is a long and increasingly expensive process. The time required to develop a drug and bring it to market averages 10 to 15 years.[5] Protocols for clinical trials have become significantly more complex in recent years; for example, Phase II and III protocols generally involve 263 procedures per patient, supporting approximately 20 endpoints, and the number of procedures per patient has increased 44% since 2009.[6] Phase III clinical trials generate an average of 3.6 million data points, which is three times the amount collected 10 years ago.[7] All of these increased complexities contribute to the increasing cost of biopharmaceutical R&D.[8] Indeed, R&D costs have increased by approximately 8.5% per year over the past decade.[9] The average R&D cost per new drug is $2.6 billion, which includes the cost of laboratory research, clinical trials, and expenditures for drugs that do not reach the market.[10]

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[4] 87 Fed. Reg. at 67,021.

[5] *See* PhRMA, *The Dynamic U.S. Research and Development Ecosystem*, at 1 (2021) [hereinafter Dynamic R&D].

[6] *See Rising Protocol Design Complexity Is Driving Rapid Growth in Clinical Trial Data Volume, According to Tufts Center for the Study of Drug Development*, GLOBENEWSWIRE (Jan. 12, 2021).

[7] *See id.*

[8] *See Dynamic R&D*, *supra* note 5.

[9] Research and Development in the Pharmaceutical Industry, Congressional Budget Office, at 16 (Apr. 2021).

[10] *See* Joseph A. DiMasi, Henry G. Grabowski, & Ronald W. Hansen, *Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs*, 47 J. HEALTH ECON. 20-33, at Abstract (2016) (in 2013 dollars).

On top of increasing costs, the risks of biopharmaceutical R&D are significant: most drugs fail to obtain FDA approval.[11] The odds of success are also getting slimmer. More than 20% of drugs developed in the 1980's and 1990's reached the market, but now fewer than 12% of drugs that enter Phase I clinical trials are approved by FDA and marketed.[12] For example, an analysis of investigational drugs developed for nine different cancers between 1998 and 2020 revealed that 1,315 investigational drugs were unsuccessful, and only 111 gained FDA approval.[13] These statistics reflect a uniquely complex and treacherous R&D pathway for biopharmaceuticals compared to innovative products in other fields of technology.

After a drug product is approved, biopharmaceutical sponsors often continue to invest in R&D to explore additional potential benefits for patients. In some cases, additional research determines that a medicine can also be used to treat different states of the same disease, such as earlier stages of cancer. Additional research may also demonstrate the medicine can be used to treat completely different conditions including different forms of cancer, or different diseases altogether. In other cases, additional research may lead to increased safety or effectiveness, new dosage forms, or new forms of administration of a medicine that can improve patient adherence or convenience, leading to better patient outcomes. For instance, orally disintegrating tablets enable treatment of patients with difficulty swallowing, and new products combining previously approved active ingredients can lead to treatments that are more effective, reduce risks of developing resistance and other adverse events, and reduce pill burden.[14]

An FDA report on new drug therapy approvals in 2022 highlights a wide range of new uses and new dosage forms of approved medicines as critical treatment advances, particularly for cancer patients, children, and those impacted by rare diseases.[15] In fact, many of these post-approval research advances brought first-time treatments for patients. For example:

- A new treatment for "HER2-low" breast cancer, which historically has had limited treatment options.

- A first-time treatment for chronic weight management in patients six years and older with obesity due to a rare genetic disorder known as Bardet-Biedl syndrome.

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[11] *See Dynamic R&D*, *supra* note 5, at 2.

[12] *See* Research and Development in the Pharmaceutical Industry, *supra* note 9, at 16-17.

[13] *See* PhRMA, *Researching Cancer Medicines: Setbacks and Stepping Stones*, at 3 (2020). For example, setbacks in Alzheimer's disease medicine development highlight the complexity of Alzheimer's research—there is just a 2% success rate in treatments. Between 1998 and 2021, there were 198 unsuccessful investigational drugs for Alzheimer's disease. *See* PhRMA, *Researching Alzheimer's Medicines: Setbacks and Stepping Stones*, at 1 (2021). And between 1998 and 2017, 146 investigational medicines that were in clinical development to treat and potentially prevent Alzheimer's were halted while only four new medicines were approved to treat symptoms of the disease. *See* PhRMA, *Researching Alzheimer's Medicines: Setbacks and Stepping Stones*, at 3 (2018).

[14] *See* FDA, Guidance for Industry, New Chemical Entity Exclusivity Determinations for Certain Fixed-Combination Drug Products, at 2, 7 (Oct. 2014) (discussing the benefits of combination therapies).

[15] FDA, New Drug Therapy Approvals 2022 (Jan. 10, 2023).

- A first-time treatment for pediatric patients with juvenile myelomonocytic leukemia, a rare blood cancer primarily impacting young children.

- Two treatments approved for use in combination to treat pediatric patients whose tumors express a BRAF mutation.

Innovations that can improve patient care and the patient experience should continue to be incentivized. Indeed, post-approval research is a significant investment. Without patents to safeguard the investment made to develop new uses, which may require a significant investment and take three to twelve years to develop,[16] there would be little incentive to continue R&D on a drug product after it has been approved. Indeed, IP protection for post-approval innovation should be strengthened, not weakened. FDA already generally permits follow-on (i.e., generic and biosimilar) applicants to omit patent-protected indications from their labeling while obtaining approval for other indications.[17] However, their products nevertheless may be used for the protected indication, including through automatic substitution of generics for listed drugs.[18] Any new policies should avoid further undermining the incentives for development of new uses of approved drugs.

As previously noted, the biopharmaceutical industry is committed to working every day to discover and develop new treatments and cures for patients battling serious and life-threatening diseases such as cancer, Alzheimer's, heart disease, and, most recently, COVID-19. These new treatments and cures are made possible by the American system of IP protections. Given the increasing cost of bringing a biopharmaceutical product to market and the increasing percentage of drugs that fail to reach the market, IP protections are more important than ever to protect investment in biopharmaceutical R&D.

The substantial investments related to biopharmaceutical R&D also fuel the U.S. economy. IP-intensive manufacturing industries drive economic progress and collectively support 57.6 million American jobs,[19] including more than 4.4 million jobs supported by the biopharmaceutical industry and contribute approximately $1.4 trillion in economic output when direct and indirect effects are considered.[20] Strong and predictable IP protections in the United

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[16] *See* Erika Lietzan, *Paper Promises For Drug Innovation*, 26 GEO. MASON L. REV. 168, 177-78 (2018); Benjamin N. Roin, *Solving the Problem of New Uses*, at 5 (Draft Oct. 14, 2016).

[17] *See* FDCA § 505(j)(2)(A)(viii); 21 C.F.R. § 314.127(a)(7); Public Health Service Act § 351(k)(2)(A)(i)(III); FDA, Draft Guidance for Industry, Biosimilars and Interchangeable Biosimilars: Licensure for Fewer Than All Conditions of Use for Which the Reference Product Has Been Licensed, at 3-4, 8 (Feb. 2020) [hereinafter Biosimilars and Interchangeable Biosimilars Guidance] ("an applicant may choose to seek licensure of a proposed biosimilar or interchangeable biosimilar for fewer than all of the reference product's licensed conditions of use based on an assessment by the applicant that one or more of the reference product's licensed conditions of use is protected by patent").

[18] *See* Jesse C. Vivian, *Generic Substitution Laws*, U.S. PHARMACIST (June 19, 2008) (describing automatic substitution for generic drugs).

[19] *See* PhRMA, IP in the Economy (last visited Feb. 1, 2023).

[20] *See* TEConomy Partners, LLC, *The Economic Impact of the U.S. Biopharmaceutical Industry: 2020 National and State Estimates*, at 1, 14-15 (Mar. 2022).

States also signal to other jurisdictions the critically important economic benefits of IP. But most importantly, they enable investment in medical innovations that give patients hope for new and better treatments.

The accomplishments of the United States in promoting development of both innovative and follow-on biopharmaceuticals are due in no small part to the balance Congress struck in both the Hatch-Waxman Amendments and the Biologics Price Competition and Innovation Act (BPCIA).[21] Both Acts were intended to promote competition by establishing a pathway for abbreviated applications while preserving incentives for innovation. Before the enactment of Hatch-Waxman, generic drugs were only about 19% of all dispensed prescriptions,[22] but Hatch-Waxman has been an overwhelming success in enabling generic access. Indeed, generics currently comprise up to 92% of all drug prescriptions dispensed, up from 75% in 2009.[23] Biosimilar products also are providing patients with additional choices. Interchangeable biosimilar products have recently been approved, and the biosimilar market has expanded rapidly in recent years. Growth in the biologics and biosimilar market is projected to continue, suggesting that the carefully balanced incentives of the BPCIA are working as intended.[24] Accordingly, both laws have robustly facilitated competition from follow-on products in the U.S. marketplace.

Indeed, it is incentives for innovation that should be strengthened, particularly for novel drugs and innovative uses of existing drugs. Although some commentators have alleged that generic products are unnecessarily delayed from market entry, data do not support this allegation. For example, innovator drugs in a 1995-2019 cohort have been found to have an average market exclusivity period from market launch of the innovator drug to the launch of the first generic of between 12.2 and 14.6 years.[25] In addition, since enactment of Hatch-Waxman in 1984, patent challenges from generic companies (in the form of paragraph IV certifications and subsequent Hatch-Waxman lawsuits) have been filed more frequently and earlier in the lifecycle of innovator drugs. Generic companies often file such challenges as soon as possible under the law—in the case of a new chemical entity, as early as four years after approval—and recent data show a trend towards more new molecules experiencing paragraph IV filings while also having

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[21] *See* Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585; Biologics Price Competition and Innovation Act of 2009, Pub. L. No. 111-148, §§ 7001-7003, 124 Stat. 804.

[22] *See* PhRMA, What is Hatch-Waxman? (June 2018).

[23] *See* IQVIA Institute for Human Data Science, *The Use of Medicines in the U.S. 2022: Usage and Spending Trends and Outlook to 2026*, at 39 (Apr. 2022); IQVIA Institute for Human Data Science, *Medicines Use and Spending in the U.S. A Review of 2018 and Outlook to 2023*, at 5 (May 2019).

[24] *See Global Biosimilars Market Growing to Exhibit a Noteworthy CAGR of 22.9% by 2033, Key Drivers, Growth and Opportunity Analysis - Research Nester*, GLOBENEWSWIRE (Oct. 12, 2022); *The Global Biologics Market Is Projected to Grow at a CAGR of 8.82% By 2032: Visiongain Reports Ltd*, GLOBENEWSWIRE (Oct. 12, 2022).

[25] *See* Henry Grabowski et al., *Continuing trends in U.S. brand-name and generic drug competition*, 24 J. MED. ECON. 908, 911 (2021); *see also* Erika Lietzan & Kristina Acri née Lybecker, *Solutions Still Searching for a Problem: A Call for Relevant Data to Support "Evergreening" Allegations*, 33 FORDHAM INTELL. PROP., MEDIA & ENT. L.J., at 41 (2022) (forthcoming) (finding that 224 new drug applications averaged 11.3 years of market exclusivity and new chemical entities averaged 13.34 years).

fewer years from brand launch to the first paragraph IV filing.[26] Given that a patent term generally is 20 years from filing, these data show that the patent system has not been unjustifiably delaying generic drug "beyond that reasonably contemplated by applicable law."

To maintain a thriving market for both innovator and follow-on drug products, innovator companies must continue to have incentives to make the risky, substantial investment in the R&D necessary to bring new drugs to market and to keep innovating after a medicine is first approved and used by patients. In the absence of such incentives, fewer new treatments would make it to FDA approval and to patients, which would upset the balance intended by Hatch-Waxman and the BPCIA. The U.S. is a global leader in biopharmaceutical R&D and, as a result, patients in the U.S. generally enjoy the fastest and broadest access to innovative medicines in the world.[27] This access to biopharmaceutical products has the ability to offset other, much more significant and long-term costs related to adverse health outcomes. Without robust R&D, fewer medicines would be available, which could lead to worse health outcomes and, ultimately, more expensive medical care.

B. Any Changes to the IP System Should be Based on Evidence.

Given the need for strong and reliable incentives for development of new and improved medicines, any changes to IP laws or policy should be made on the basis of sound evidence, not flawed data or unsupported assertions. PhRMA has not seen reliable evidence of systemic issues within the U.S. patent system or the FDA drug approval process that would warrant substantial changes in IP laws. Instead, false narratives regarding biopharmaceutical patents have pervaded. Senator Tillis, Ranking Member of the Senate Judiciary Committee Subcommittee on Intellectual Property, recently noted this problem in letters to FDA and the USPTO, which identified concerns with the accuracy and transparency of research from the I-MAK on the role of patents in drug pricing and the "Evergreen Drug Patent Search" database from the U.C. Hastings College of the Law. The letters noted that "several of the main sources driving the narrative that patents are to blame for high drug prices do not appear to meet [the] fundamental criteria" of being "based on accurate facts and data from reliable, unbiased sources."[28] With respect to I-MAK in particular, commentators have noted that I-MAK may have counted the patents protecting a sponsor's drug to include abandoned patent applications, patents held by third parties, patents that expired after actual generic launches, and patents that do not cover the approved product or the approved method of using it,[29] leading to artificially inflated numbers

[26] *See* Grabowski, *supra* note 25, at 914.

[27] *See* Kevin Haninger, *New analysis shows that more medicines worldwide are available to U.S. patients*, PHRMA (June 5, 2018).

[28] Letter from Sen. Thom Tillis to Dr. Janet Woodcock and Mr. Drew Hirshfeld, at 1 (Jan. 31, 2022); *see also* Letter from Sen. Thom Tillis to Dr. Robert Califf and Mr. Drew Hirshfeld, at 1 (Apr. 1, 2022) ("[S]ources are based on opaque methodologies, and appear to contain inaccurate or incomplete information that may be misleading policymakers"); Eileen McDermott, *Mossoff Policy Memo for Hudson Institute Calls for Transparency from I-MAK on Data Used in Drug Pricing Debate*, IPWATCHDOG (Jan. 21, 2022).

[29] *See* Statement of Corey Salsberg, Vice President and Global Head Intellectual Property Affairs for Novartis, Listening Session, at 6 (Jan. 19, 2022); Adam Mossoff, *Unreliable Data Have Infected the Policy Debates Over Drug Patents*, HUDSON INST. (Jan. 2022).

and significant discrepancies with actual generic launch dates. We agree that agencies and lawmakers should be "armed with all the key facts and data needed to make sound public policy decisions regarding drug pricing."[30] We urge FDA and the USPTO to ensure that any policy changes implemented as part of their partnership are based on reliable evidence.

Evidence-based policy making should not place undue emphasis on speculation or outlier cases. For example, an academic article by Arti K. Rai & W. Nicholson Price II alleges that patent applicants may be making inappropriate conflicting statements in submissions to the USPTO and FDA in order to circumvent the on-sale bar to patentability under 35 U.S.C. § 102(a)(1).[31] The authors cite no evidence that such conflicting statements are a problem necessitating policy reform. Instead, they emphasize statistics regarding litigation over manufacturing process patents and provide no proof that any of the implicated patents were procured based on inconsistent statements to the agencies. Also, seeking to create the perception of a problem of inconsistent statements in the biopharmaceutical space where there is none, other proponents of this theory cite *Belcher v. Hospira*.[32] This case does not indicate a widespread problem. In fact, the court imposed a severe penalty, deeming the patent unenforceable and awarding attorney fees under 35 U.S.C. § 285. Other safeguards already exist, including the duty of disclosure to USPTO[33] and the strong incentives for submitters of abbreviated applications to identify and raise issues related to inconsistent statements in litigation challenging patents. Existing law thus is sufficient to prevent such fraudulent activity from occurring.

Similarly, we have not seen evidence to justify any further changes to patent listing practice for small molecules. Congress recently amended the law in the OBTA and has mandated additional steps to gather evidence on listing issues, including a GAO Report due this year. FDA also has received comments on Orange Book listing issues and "is continuing to evaluate these issues."[34] The agency has noted that there are a "diversity of viewpoints," and "there is not a consensus view around specific proposed changes" to be made to the Orange Book listing process.[35] We believe that any changes to patent listing practice should be made based on sound evidence and further believe that any such changes remain premature while the congressionally mandated steps to gather evidence remain incomplete.

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[30] Letter from Sen. Thom Tillis to Dr. Robert Califf and Mr. Drew Hirshfeld, *supra* note 28, at 3.

[31] *See* Arti K. Rai & W. Nicholson Price II, *An administrative fix for manufacturing process patent thickets*, 39 NATURE BIOTECH. 20 (2021).

[32] *Belcher Pharms., LLC v. Hospira, Inc.*, 11 F.4th 1345 (Fed. Cir. 2021).

[33] *See* 87 Fed. Reg. 45,764 (July 29, 2022) (Federal Register Notice describing and clarifying the duty of disclosure owed to the USPTO and the public), which is discussed in relation to Question 2 below.

[34] Docket No. FDA-2020-N-1127. After reopening the docket in response to the Orange Book Transparency Act, the comment period was extended to April 15, 2021. *See* Docket No. FDA-2020-N-1127-0024; FDA Letter to Avadel CNS Pharms. LLC (July 21, 2022), *Avadel CNS Pharms., LLC v. Becerra*, Case No. 22-02159 (D.D.C.), Exh. 15, at 9-10, n.34.

[35] FDA, The Listing of Patent Information in the Orange Book, Report to Congress, at 24.

Overall, PhRMA agrees with the Patent Public Advisory Committee that "policymakers should not focus myopically on so called 'low quality' patents or 'gaming' of the system."[36] Instead, as the Committee notes, "[t]he proper focus, as the USPTO recognizes, is more broadly cast – any change in law, policy, or procedure should be focused on supporting innovation for economic growth and the betterment of society," which is the "True North" of the U.S. patent system.[37] In view of this background, PhRMA presents the following comments in response to the Request for Comments.

II. PhRMA's Responses to the Request for Comment's Questions

Question 1: What publicly available FDA resources should be included when training USPTO patent examiners on tools they can use to assess the patentability of claimed inventions?

To the extent that these resources are not already included resources in USPTO trainings, FDA's Drugs@FDA database, the Orange Book, and the Purple Book could be included. Ensuring that these FDA resources are routinely updated would be helpful to the USPTO and stakeholders more generally, as discussed below. PhRMA recognizes that the USPTO has already taken steps to provide additional training to examiners and to expand the resources to which examiners have access.

Question 2: What mechanisms could assist patent examiners in determining whether patent applicants or patent owners have submitted inconsistent statements to the USPTO and the FDA? Please explain whether such mechanisms present confidentiality concerns and, if so, how those concerns could be addressed.

Allegations that practitioners and drug sponsors are making inconsistent statements to FDA lack sound evidentiary support. To the extent that such statements occur, they are rare and are already harshly penalized. Moreover, if any new information-sharing arrangements between FDA and the USPTO are established, these arrangements must comply with existing law.

A. The Submission of Inconsistent Statements to the USPTO and to FDA Is Not a Widespread Problem.

Assertions that practitioners and drug sponsors are making inconsistent statements to FDA and USPTO lack sound evidentiary support. In particular, the Rai and Price article does not establish that a widespread problem exists. Although there have been over 5,000 Hatch-Waxman cases since 2000,[38] we have identified no case in which the current framework did not function as intended—i.e., the small number of cases involving inconsistent statements to FDA and the USPTO concerning a biopharmaceutical have resulted in a finding that the patent is

[36] Letter to the President of the United States, Patent Public Advisory Committee, 2022 Annual Report (Nov. 1, 2022).

[37] *Id.*

[38] *See* Docket Navigator Database (last visited Feb. 3, 2023) (identifying 5,321 ANDA cases filed in district court from 2000 to date).

unenforceable. Thus, to the extent that any such statements occur, they are rare and are already discouraged.

Rai and Price suggest that practitioners and sponsors may be making inconsistent statements to the USPTO and FDA, which allows manufacturing patents to issue, and that these manufacturing patents are "improperly chill[ing] competition."[39] Rai and Price suggest that the claims in post-approval manufacturing patents necessarily lack novelty or non-obviousness because the drug or biologic is known or because they necessarily claim known or obvious extensions of existing processes.

Rai and Price misunderstand the complexity and iterative nature of biologic manufacturing. As other commentators have noted, the greater number of patents associated with biologics is commensurate with "the complexity of the innovation that biologic drugs (as well as gene therapies and other recent pharmaceutical marvels) encompass."[40] There also is nothing problematic or nefarious about continuous improvement in manufacturing process throughout a biological product's marketing history; instead, such improvements benefit patients. For example, improvements can be made in scale up of manufacturing processes or in response to the sustained need to manufacture safe and effective doses of the biologic. These manufacturing improvements can lead to better products or production and can be patentable. Such patenting may occur after FDA approval for a marketed product. Thus, the authors' focus on whether the process patent was filed more than a year after FDA approval is fundamentally flawed because these manufacturing improvements may and do occur *after* the biologic's initial approval. Furthermore, biosimilar developers can and do design around manufacturing patents, and such patents are not necessarily prohibitive to biosimilar market entry.[41] Although not the focus of the Rai and Price article, generic manufacturers also can and do design around manufacturing patents.

Rai and Price also emphasize statistics regarding litigation over manufacturing process patents and provide no proof that any of the implicated patents were procured based on inconsistent statements to the agencies. Instead, they allege that "it is possible" that certain asserted manufacturing patents were improperly granted. Such speculation should not form the basis for novel policies. The article's conclusion and any policy changes stemming from it are thus unsupported. The article demonstrates only that these authors have an unproven theory.

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[39] Rai & Price, *supra* note 31, at 21.

[40] Laura Karas, *Pharmaceutical Patents on Manufacturing Methods: Groundless or Well-Supported?*, BILL OF HEALTH (Feb. 16, 2021).

[41] *See, e.g.*, *Amgen Inc. v. Sandoz Inc.*, 923 F.3d 1023 (Fed. Cir. 2019) (summary judgment of noninfringement of patent directed to protein purification process); *Amgen Inc. v. Apotex Inc.*, 712 F. App'x 985 (Fed. Cir. 2017) (finding noninfringement of patent directed to methods of refolding recombinant proteins); *Amgen Inc. v. Mylan Inc.*, No. 17-cv-01235-MRH (W.D. Penn. Sept. 16, 2019) (stipulating to noninfringement of patent directed to a purification process).

Other stakeholders alleging a widespread problem of inconsistent statements regarding biopharmaceuticals cite *Belcher v. Hospira*[42], but they do not cite any examples where the law did not work. This outlier case does not indicate a problem, particularly given the more than 5,000 Hatch-Waxman cases that were filed in U.S. district courts.[43] Instead, *Belcher* underscores the harsh penalties for inconsistent statements. As in *Belcher*, withholding information known to be material to patentability can result in a finding of inequitable conduct. "[T]he remedy for inequitable conduct is the 'atomic bomb' of patent law"[44] because the entire patent is held unenforceable and it can also render related patents and applications unenforceable, jeopardizing a significant portion of a company's patent portfolio for a technology. *Belcher* thus demonstrates that existing law already imposes severe penalties for fraudulent activity that are an effective deterrent for inconsistent statements. Rai and Price acknowledge this point but claim there is a "relatively remote threat of a subsequent court finding of inequitable conduct."[45] The authors also lament that "defendants alleging inequitable conduct must show strong evidence of specific intent to mislead the USPTO."[46] Other commentators have similarly expressed concern that intent must be proven while also asserting that biopharmaceutical companies intentionally make contradictory statements to USPTO and FDA.[47] Far from being a drawback, the intent requirement ensures that allegations of misrepresentations are based on facts instead of speculation. Moreover, their concern appears overstated: the *Belcher* court found the requisite level of evidence "although there was no direct evidence of deceptive intent."[48]

Citations to other cases fare no better. One stakeholder cites a 1989 case, *Merck v. Danbury,* in which the patent was held unenforceable.[49] This nearly 34-year-old case is the only other biopharmaceutical case we have seen cited beyond *Belcher*, and, as in *Belcher*, the system worked: the patent was held unenforceable. In this regard, the case served as a deterrent to inconsistent statements by highlighting the sharp penalties for them. Other cited cases, including the *Bruno* and *Baxter* cases, are not biopharmaceutical cases at all.[50] Instead, they are medical device cases. These are therefore irrelevant to a docket focused on ensuring that "our patent system properly and adequately protects innovation while not unnecessarily delaying getting generic, biosimilar, and more affordable versions of pharmaceuticals into the hands of

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[42] *Belcher Pharms., LLC v. Hospira, Inc.*, 11 F.4th 1345 (Fed. Cir. 2021).

[43] *See supra* note 38.

[44] *Therasense, Inc. v. Becton, Dickinson & Co.*, 649 F.3d 1276, 1288 (Fed. Cir. 2011) (internal quotations and citation omitted).

[45] Rai & Price, *supra* note 31, at 20-21.

[46] *Id.* at 22.

[47] *See* S. Sean Tu, *FDA Reexamination: Increased Communication Between the FDA and USPTO to Improve Patent Quality*, 60 HOUS. L. REV. 403, 428-29 (2022).

[48] *Belcher Pharms., LLC v. Hospira, Inc.*, 11 F.4th 1353 (Fed. Cir. 2021).

[49] *Merck & Co., Inc. v. Danbury Pharmacal, Inc.*, 873 F.2d 1418 (Fed. Cir. 1989); *see* Tu, *supra* note 47, at 407 n.8.

[50] *Bruno Indep. Living Aids, Inc., v. Acorn Mobility Servs., Ltd.*, 277 F. Supp. 2d 965 (W.D. Wisc. 2003), *aff'd*, 394 F.3d 1348 (Fed. Cir. 2005); *Baxter Int'l, Inc. v. CareFusion Corp.*, No. 15-cv-9986, 2017 WL 1049840 (N.D. Ill. Mar. 20, 2017).

Americans who need them."[51] Indeed, their citation by authors concerned about drug patent issues[52] underscores the scarcity of reported cases involving biopharmaceuticals.

In addition to the threat of patent unenforceability, other existing mechanisms also guard against inconsistent statements. The existing duty of candor and disclosure to the USPTO in the context of patent prosecution described in 37 C.F.R. § 1.56 has worked well and discourages practitioners from withholding from the USPTO information material to patentability.[53] Given guidance from the courts, including in *Therasense v. Becton, Dickinson and Co.*, 649 F.3d 1276 (Fed. Cir. 2011), and *Helsinn Healthcare S.A. v. Teva Pharmaceuticals USA, Inc.*, 139 S. Ct. 628 (2019), any reasonable practitioner would understand their duty to disclose to USPTO information that they are aware of that is related to prior commercial uses of a claimed manufacturing process if that information is material to patentability.[54] In addition, litigants challenging the validity of one or more patents have significant incentives to identify (and the ability to access) prior art that is material to patentability and that can serve to invalidate patents. Contrary to the claims of another commentator, litigants are able to do so even though they must plead inequitable conduct with particularity.[55] Innovators routinely produce their marketing applications and FDA correspondence during infringement litigation, and generic and biosimilar sponsors can already scrutinize these documents for inconsistent statements. They can amend their Answer to add inequitable conduct allegations should they see any evidence of inconsistent statements. The lack of more reported cases of inequitable conduct stemming from inconsistent statements—commentors cite only a single biopharmaceutical case from the last nearly 34 years—suggests that inconsistent statements are not a substantial issue.

Given that the contours of the duty of disclosure and inequitable conduct are well understood, there is confusion surrounding the USPTO's issuance of its Federal Register Notice regarding the Duties of Disclosure and Reasonable Inquiry During Examination, Reexamination, and Reissue, and for Proceedings Before the Patent Trial and Appeal Board (Duty Notice).[56] The disclosure obligation is tied to what is material to the claimed invention. It does not extend beyond the scope of the claimed invention. Moreover, the Federal Circuit recognizes a very limited duty to reasonably inquire about material information related to patentability, but only where "the surrounding factual circumstances would cause a reasonable attorney to understand

[51] 87 Fed. Reg. at 67,020.

[52] *See* Tu, *supra* note 47, at 407 n.8.

[53] *See also* Manual of Patent Examining Procedure § 2001 (Duty of Disclosure, Candor, and Good Faith).

[54] *See, e.g.*, *GS Cleantech Corp. v. Adkins Energy LLC*, 951 F.3d 1310 (Fed. Cir. 2020) (affirming finding of inequitable conduct based on failure to disclose pre-critical date sales).

[55] *See* Tu, *supra* note 47, at 409-11. Dr. Tu's article states that "[t]he Federal Circuit invalidated patents in thirty-one cases from 2005-2018[,] [h]owever eighteen of those thirty-two (sic) cases dealt with FDA drug and device regulated products." *Id.* at 408 n.10. Although he states that these cases involved inequitable conduct, the article does not demonstrate that these cases involved inconsistent statements.

[56] 87 Fed. Reg. 45,764 (July 29, 2022).

that relevant and questionable material information should be assessed."[57] Given the questions that have been raised regarding the Notice, PhRMA appreciates the USPTO's decision to organize a panel discussion regarding the duty of disclosure and duty of reasonable inquiry on February 23, 2023,[58] and looks forward to USPTO providing greater clarity to stakeholders during that discussion on the scope of these duties and on the meaning of the Duty Notice. PhRMA requests that USPTO provide an opportunity to comment following the panel discussion.

Suggestions that FDA-USPTO information sharing will help USPTO assess the "on sale" bar are also misguided. These issues are highly fact-intensive and, in many respects, most appropriately assessed by Article III courts. For example, assessment of the "on sale" bar requires interpretation of non-patent legal issues such as whether there has been an "offer for sale" under the Uniform Commercial Code as well as extensive factual analysis and discovery. These activities are outside examiner expertise and would drain agency resources.

Ultimately, Rai and Price and other commentators do not provide sound evidence of inconsistent statements to FDA and the USPTO warranting policy changes—and certainly not the creation of a novel infrastructure for FDA-USPTO information sharing that could overburden both agencies, distract from fulfillment of their missions, and raise confidentiality concerns, as discussed in the next section.

B. Any Mechanisms Adopted by USPTO to Further Reduce the Risk of Inconsistent Statements Must Align with Protections for Confidential Information.

PhRMA believes that creation of a new information sharing infrastructure between USPTO, and FDA is unwarranted given the lack of evidence concerning inconsistent statements and the significant agency burdens associated with implementing such an infrastructure. If FDA and the USPTO nevertheless do adopt new information-sharing arrangements, these arrangements must comply with existing law, including protections on trade secret and confidential commercial information.

The fact that the agencies have very different confidentiality practices will pose a challenge to new information sharing mechanisms. USPTO's general position is that information material to patentability must be disclosed to the public. Although a petition to expunge may request that USPTO maintain secrecy of confidential information, USPTO takes the position that it nevertheless will publicly disclose any information that is material to

[57] *Brasseler, U.S.A. I, L.P. v. Stryker Sales Corp.*, 267 F.3d 1370, 1385 (Fed. Cir. 2001). As noted in *Brasseler*: "There is no need for an attorney to pursue a fishing expedition to obtain information." *Id.* at 1382. The Duty Notice does not discuss this case. Instead, the Duty Notice indicates that the Examiner may compel disclosure of information that is not material to the claimed invention. Such compelled disclosure raises significant confidentiality concerns, as discussed later.

[58] *See* https://www.uspto.gov/about-us/events/uspto-host-virtual-panel-discussion-duty-disclosure-and-duty-reasonable-inquiry, last visited Feb. 5, 2023.

patentability upon patent issuance.[59] In contrast, to implement Exemption 4 of the Freedom of Information Act, the Federal Trade Secrets Act, and section 301(j) of the Federal Food, Drug, and Cosmetic Act (FDCA), FDA has long had in place regulations that protect the confidentiality of proprietary information submitted to the agency.[60] Although Rai and Price suggest that the agencies should share manufacturing process information, FDA has long recognized that this highly sensitive information is trade secret information subject to legal restrictions on sharing.

Section 301(j) of the FDCA prohibits the "revealing, other than to the Secretary or officers or employees of the Department" of Health and Human Services, "any information acquired under authority of section [505, among others] concerning any method or process which as a trade secret is entitled to protection."[61] New drug applications are submitted under section 505, as are the investigational new drug applications pursuant to which biologics are developed. Further, section 351(j) of the PHSA, provides that the FDCA, which includes section 301(j), applies to biologics.[62] Section 702(d) of the FDCA authorizes FDA to share "full and complete information with respect to such questions relating to drugs as the [USPTO] may submit concerning any patent application" but does not qualify or limit the more specific provisions of section 301(j).[63]

FDA's regulation at 21 C.F.R. § 20.85 implements the above provisions. It provides that "[a]ny [FDA] record otherwise exempt from public disclosure may be disclosed to other Federal Government departments and agencies," except that special rules apply for trade secret and confidential commercial information, which can be released only as specified by the relevant statutory provisions, including section 301(j).[64] Thus, the regulation recognizes that trade secret information protected by section 301(j) of the FDCA cannot be shared beyond the Department of Health and Human Services and requires that any information sharing must be subject to a written agreement prohibiting further disclosure without FDA's permission. FDA's regulations more broadly recognize that trade secret (including manufacturing process information) and confidential commercial information in FDA files are protected from disclosure.[65] FDA's NDA

[59] *See* 37 C.F.R. § 1.59 (describing scope and process for expungement); Manual of Patent Examining Procedure (MPEP) § 724.02 (a petition to expunge will be denied if materials are found to be material to patentability).

[60] *See* 21 C.F.R. Part 20; FDCA § 301(j); 18 U.S.C. § 1905; 5 U.S.C. § 552; *see generally* 39 Fed. Reg. 44,602 (Dec. 24, 1974).

[61] FDCA § 301(j).

[62] *See* PHSA § 351(j).

[63] *Cf. Genus Med. Techs. LLC v. FDA*, 994 F.3d 631, 638 (D.C. Cir. 2021) (referencing the "old and familiar rule" of statutory construction that "the specific governs the general" (internal quotations and citation omitted)).

[64] 21 C.F.R. § 20.85 ("Any disclosure under this section shall be pursuant to a written agreement that the record shall not be further disclosed by the [receiving] department or agency except with the written permission of the Food and Drug Administration.").

[65] *See* 21 C.F.R. § 20.61(c).

and BLA regulations also expressly prohibit the disclosure of manufacturing methods or processes.[66]

Any information sharing mechanism must respect these existing legal protections provided by statute and regulation. To the extent FDA can share relevant information with the USPTO consistent with these requirements, the agencies should ensure that legally protected information is not inadvertently or deliberately disclosed by USPTO. USPTO, therefore, is likely to need new procedures that ensure appropriate segregation of materials received from FDA and fulfillment of the contractual conditions required by 21 C.F.R. § 20.85, including by providing equivalent protections to shared information as FDA would provide. The agencies also should ensure that they provide appropriate notice and an opportunity to object to proposed disclosures, consistent with their regulations,[67] and that they have appropriate processes for identifying information that may be confidential. Contrary to suggestions made at the listening session, it would be insufficient to simply delay the disclosure of manufacturing process information in FDA's hands until after FDA approval. FDA's regulations recognize that this information remains protected even after a medicine's approval.[68] Manufacturing process information continues to have significant commercial value after approval, including because platform technology may be used across new and approved products.

Similar protections should apply to any information submitted directly to USPTO that is not material to the claimed invention. Manufacturing information is protected not only by the above federal laws but also by state trade secret law.[69] Requiring its submission even when not material to patentability and then publicly disclosing the information would destroy the value of these trade secrets and compromise incentives for developing this information. Significantly, disclosure of trade secret information—particularly paradigmatic trade secret information on manufacturing processes—could be considered a taking under the Takings Clause of the Fifth Amendment to the U.S. Constitution.[70] The USPTO must therefore be mindful of these confidentiality issues, particularly in light of the Duty Notice, since its currently established procedures are inadequate to address stakeholders' legitimate concerns regarding these issues.

[66] *See id.* §§ 314.430(g)(1), 601.51(f)(1).

[67] *See id.* § 21.61(e) (describing procedures for objecting to disclosure of documents held by FDA).

[68] *Id.* §§ 314.430(g), 601.51(f).

[69] *See, e.g.*, Virginia Uniform Trade Secrets Act, Va. Code Ann. § 59.1-336 *et seq.*

[70] *See Ruckelshaus v. Monsanto Co.*, 467 U.S. 986 (1984).

Question 3: What are the opportunities and challenges related to the use of AIA proceedings to address the patentability of claims in pharmaceutical and biotechnological patents, including with respect to how such proceedings may intersect with Hatch-Waxman paragraph IV disputes and the Biologics Price Competition and Innovation Act "patent dance" framework that biosimilar applicants and reference product sponsors use to address any patent infringement concerns?

PhRMA acknowledges that AIA proceedings fall within the jurisdiction and expertise of the USPTO. In contrast, FDA has neither the mandate nor the expertise to address issues pertaining to such proceedings. Accordingly, this question is not an appropriate topic for FDA-USPTO collaboration.

PhRMA does, however, recommend that FDA align its regulation on the amendment and withdrawal of patent information in the Orange Book upon a final decision from a court or the Patent Trial and Appeal Board (PTAB) to align with the requirements in the OBTA.[71] The OBTA amended section 505(j)(7) of the FDCA to require that an NDA holder notify FDA when "any claim of the [Orange Book listed] patent has been cancelled or invalidated pursuant to a final decision issued by the [PTAB] or by a court, from which no appeal has been, or can be taken" and if "a patent[,] . . . or any patent information for such drug" does not meet Orange Book listing requirements.[72] A written notification must be submitted within 14 days of the cancellation or invalidation decision, and the notification must also request that the patent or patent information be amended or withdrawn consistent with the decision by the court or the PTAB.[73] Upon receipt of the notification and a copy of the decision, FDA must amend or remove the patent or patent information as requested and in accordance with the decision, unless there is an existing 180-day exclusivity period that relies on a certification to the listed patent.[74]

FDA should amend its regulations to align with the OBTA and should expressly note that the relevant PTAB decision or the court decision must be a final decision from which no appeal has been or can be taken. For PTAB decisions, this conclusion flows from the use of the terms "final" and "cancellation" in amended section 505(j)(7). Under the Patent Act, USPTO "shall issue and publish a certificate canceling any claim of the patent finally determined to be unpatentable, confirming any claim of the patent determined to be patentable, and incorporating in the patent by operation of the certificate any new or amended claim determined to be patentable" if the PTAB issues a final written decision "and the time for appeal has expired or any appeal has terminated."[75] This proposal best harmonizes section 505(j)(7) with the procedural requirements under the Patent Act and will avoid waste of administrative resources from needing to revisit prior amendments to the Orange Book based on appeals. We support

[71] Orange Book Transparency Act of 2020, Pub. L. No. 116-290, 134 Stat. 4889; *see* Comment by PhRMA, Docket No. FDA-2020-N-1127, at 2-3 (Apr. 15, 2021).

[72] FDCA § 505(j)(7)(D).

[73] *See* FDCA § 505(j)(7)(D)(i)-(ii).

[74] *See id.* § 505(j)(7)(D)(iii).

[75] 35 U.S.C. § 328(b).

FDA's implementation of the OBTA as described. We also believe further changes to FDA's limited ministerial role in AIA issues are unwarranted given that Congress recently addressed AIA issues and their relationship to Orange Book listing in the OBTA and decided that only small adjustments are needed.

More generally, we disagree that there are "opportunities and challenges" relating to AIA proceedings and their intersection with Hatch-Waxman and BPCIA disputes. PhRMA does not believe there should be a special role for AIA proceedings in only the biopharmaceutical context. AIA proceedings, for example, *inter partes* review (IPR), were designed as an alternative to litigation and were not designed to operate in concert with or in the context of Hatch-Waxman or the BPCIA.[76]

PhRMA also disagrees with the characterization that there have been "so few filings of AIA proceedings" on biopharmaceutical patents.[77] The PTAB Orange Book patent/biologic patent study cited in the Request for Comments states that 4% of all AIA petitions challenge Orange Book patents and 2% of all AIA petitions challenge biologic patents.[78] The number of AIA proceedings generally tracks the number of Hatch-Waxman and BPCIA cases involving invalidity disputes.[79] In particular, for biologics, there was an increase in AIA proceedings between 2015 and 2017,[80] potentially due to the recent enactment of BPCIA and the bolus of applications prepared and filed during that time for biosimilars. In the last few years, the number of AIA proceedings for patents covering biologics has generally decreased to a steady level. This trend is consistent with the number of approved biosimilar applications over time, as shown below.

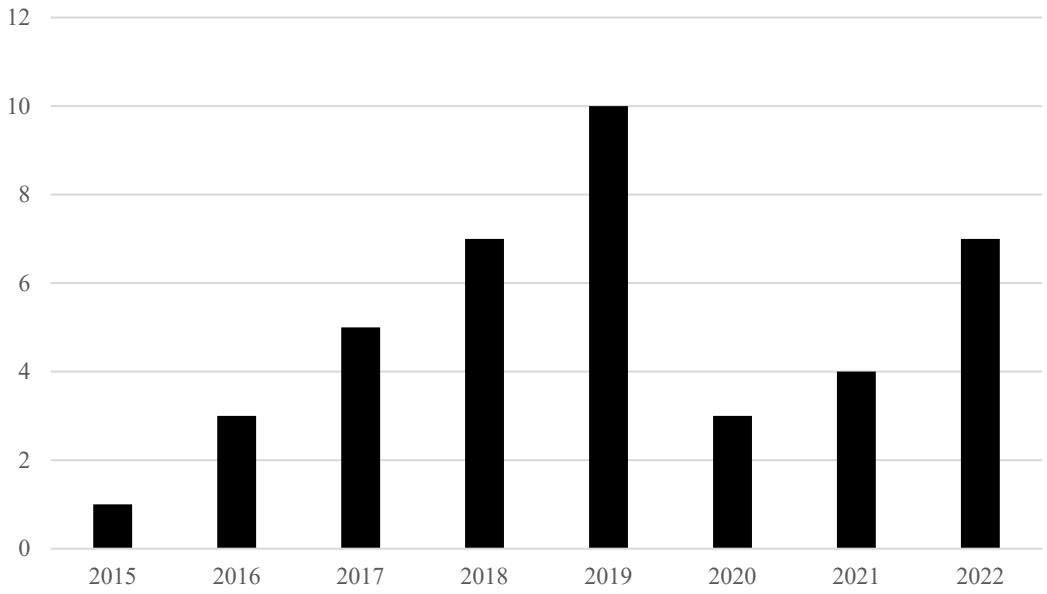
[76] *See* Patent Public Advisory Committee, 2022 Annual Report, at 1 (Nov. 1, 2022) ("[T]he majority of IPR proceedings have parallel proceedings in district court – increasing rather than decreasing costs for patent holders.").

[77] 87 Fed. Reg. at 67,021 ("[T]he USPTO will also work with the FDA to assess why there have been so few filings of AIA proceedings on Orange Book-listed patents and biologic patents and why the number of AIA filings for pharmaceutical patents has generally declined.").

[78] *See* PTAB Orange Book patent/biologic patent study (FY21 Q3, June 2021).

[79] *See* Amy C. Madl & Jill K. MacAlpine, *Patent Trial and Appeal Board Releases Updated Orange Book/Biologic Patent Study*, OUTSOURCED PHARMA (Oct. 20, 2021) (describing a decrease in IPR petitions from FY15 to FY21 for Orange Book-listed patents and a "small but volatile" number of IPR petitions challenging IPR petitions over the same period, which "tracks the decline in [ANDA] case filings").

[80] *See* PTAB Orange Book patent/biologic patent study (FY21 Q3, June 2021).



Number of Approved Biosimilars in the U.S. Per Year[81]

In any case, available evidence also may reflect short-term trends and does not warrant policy changes. In particular, the number of AIA proceedings and associated biosimilar applications might be cyclical and not due to any defect or deficiencies in the statutory or policy framework.[82]

Other factors also may affect the number of IPRs concerning biopharmaceutical patents. There are established procedures to litigate biopharmaceutical patents under Hatch-Waxman and the BPCIA, which may be more appealing to patent challengers than pursuing IPR proceedings. For example, 180-day exclusivity encourages generic applicants to be the first applicant to challenge Orange Book-listed patents via a paragraph IV certification. There is no comparable incentive to challenge such patents via AIA proceedings. Further, a generic sponsor often cannot opt out of Hatch-Waxman proceedings, so a generic sponsor may see no need to engage in duplicative AIA challenges.

Further, challengers are unlikely to find the so-called "smoking gun" prior art that would serve as a basis for a successful IPR challenge in the biopharmaceutical space. IPRs are principally based on prior art, and biopharmaceutical patents go through rigorous examination processes, often in more than one country. Multiple prior art searches are conducted, and examination reports collect all relevant prior art. Indeed, examiners at the USPTO have access

[81] FDA, Biosimilar Product Information (last visited Feb. 1, 2023).

[82] The data show that the number of AIA petitions challenging biological patents also varies and may be cyclical. For FY2013, there were 4 petitions, followed by 4 in FY2014, 14 in FY2015, 42 in FY2016, 75 in FY2017, 32 in FY2018, 27 in FY2019, 8 in FY2020, and 23 through the third quarter of FY2021. *See* PTAB Orange Book patent/biologic patent study (FY21 Q3, June 2021). In addition, there were 8 pending biosimilar applications in FY2021. *See* FDA-TRACK: BsUFA Historical Performance - Biosimilar Applications and Supplements (Sept. 30, 2022).

to state-of-the-art databases to assist with prior art searches. Therefore, AIA proceedings may not be as beneficial for patents directed to biopharmaceuticals as they might be as to patents directed to other technologies.

Finally, PhRMA believes that any initiatives directed solely at biopharmaceutical patents are not permissible. Technology-specific initiatives or rules directed at only one industry would conflict with the legislative intent of Congress in establishing AIA proceedings and could be contrary to U.S. obligations under the World Trade Organization (WTO) Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS).[83]

Question 4: How can the USPTO and the FDA reinforce their collaboration and information exchange in relation to determining whether a patent qualifies for a patent term extension (PTE) and the length of any extension under 35 U.S.C. 156, as described in the Manual of Patent Examining Procedure § 2756? Identify any specific areas for improvement in the effectiveness of the current USPTO–FDA process for adjudicating applications for PTE and in the opportunity for public comment on such applications.

PhRMA appreciates the work that USPTO and FDA do to collaborate and share information in determining whether a patent qualifies for a PTE and the length of any such extension. PhRMA believes that the current collaboration and information exchange between USPTO and FDA for assessing PTE eligibility provides an example of a developed system that works well.

Regulations regarding PTE exist for functions undertaken by USPTO and FDA.[84] The USPTO's Manual of Patent Examining Procedure describes the Director's responsibilities with respect to eligibility, and the current system allows both the USPTO and FDA "to process applications efficiently and to conserve resources."[85] The existing memorandum of understanding between the agencies "establishes procedures for exchanging information between FDA and [USPTO] regarding regulatory review period determinations, due diligence petitions and informal FDA hearings under the law."[86]

Upon receipt of a written request from the USPTO, FDA will provide information regarding eligibility for patent term extension: "(1) whether a product has undergone a regulatory review period within the meaning of 35 U.S.C. 156(g) prior to commercialization, (2) whether the marketing permission was for the first permitted commercial marketing or use of that product, or, in the case of recombinant DNA technology, whether such commercial marketing or use was the first permitted under the process claimed in the patent, and (3) whether the patent term extension application was submitted within 60 days after the product was

[83] *See* TRIPS Agreement, art. 27.1.

[84] *See* 37 C.F.R. Subpart F; 21 C.F.R. Part 60.

[85] MPEP § 2756.

[86] Memorandum of Understanding Between The Patent and Trademark Office and The Food and Drug Administration, MOU 225-86-8251 (1986).

approved, as well as any other relevant information."[87] Confidential documents and information are not exchanged during this process, and so the memorandum does not address confidentiality. Instead, FDA verifies certain statutory requirements and conveys to the USPTO whether they have been fulfilled. In addition, the current system protects confidential matter. For example, if information is confidential and has been given to FDA, that information stays with FDA, reducing the risk that confidential information is inadvertently disclosed while ensuring that the USPTO has FDA-verified information.

With respect to the opportunity for public comment, PhRMA notes that there is already a process for public comment during review of a PTE application, and it has been well developed in the regulations.[88] Upon determination of the regulatory review period, "any person" can request reconsideration of the calculated regulatory review period or may challenge a sponsor's diligence within 180 days of publication of the regulatory review period.[89]

We disagree with calls to abolish PTE for certain types of patents, e.g., patents covering biological products, made in connection with the listening session. One commentator claimed that "patent term extensions appeared to extend biologic drug market exclusivities beyond the standard regulatory exclusivity for biologics" and suggested rethinking whether biologics should receive PTE.[90] PTE is intended to restore some of the patent term that is lost due to the time a marketing application is under review by FDA and by statute, is equally available for drugs and biologics.[91] The rationale for PTE is equally applicable to drugs and biologics, both of which undergo regulatory review periods leading to lost effective patent life. At bottom, the commentator appears to ask the agencies to depart from the PTE statute and to take issue with the length of PTE; he suggests substitution of a different maximum number of years of patent life with PTE (12 years) plucked from a different statute with different purposes (i.e., the reference product exclusivity statute). But Congress already considered the appropriate length of time for a product's effective patent term from the extended patent when it established a 14-year period, which is measured from the time of FDA approval up to patent expiration and includes any term added due to PTE.[92] In addition, the commentator considers the extended patent's impact on biosimilar entry only, but PTE may have commercial value for other types of competition. Eliminating PTE for patents covering biological products also would be discriminatory and could disincentivize development of biological products. We disagree that the agencies can or should change PTE for biologics.

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[87] *Id*.

[88] *See, e.g.*, 21 C.F.R. §§ 60.30-60.36.

[89] 21 C.F.R. § 60.30(a).

[90] *See* Statement of Victor Van de Wiele, Listening Session, at 3-4 (Jan. 19, 2022).

[91] *See* 35 U.S.C. § 156.

[92] 35 U.S.C. § 156(c)(3); *see* 130 Cong. Rec. 23,060 (Representative Kastenmeier referring to the 14-year period as the "heart of the compromise"); 130 Cong. Rec. 23,057 (Representative Waxman noting that "[this] bill represents a compromise among divergent and sharply differing interests").

Overall, the PTE process has been found to work well, and PhRMA opposes any changes to the current PTE system.

Question 5: The FDA already publishes PTE applications on www.regulations.gov, and the USPTO publishes PTE applications on its Patent Center portal (https://patentcenter.uspto.gov/), which replaced the Public Patent Application Information Retrieval (PAIR) system. The USPTO also recently provided centralized access to a listing of PTE applications filed during the last five years at www.uspto.gov/patents/laws/patent-term-extension/patent-terms-extended-under-35-usc-156. This list includes the patent application number, patent number, link to the electronic file wrapper in Patent Center, PTE application filing date, and trade name identified in the PTE application. The status of each PTE application, including disposition, may be determined by reviewing the electronic file wrapper in Patent Center. What additional information would be useful to include on this web page?

PhRMA appreciates the work that both the USPTO and FDA do to ensure publication of information that is important to the industry and to the public, consistent with the law. The USPTO currently provides the public with information regarding PTE applications and other pertinent information. In addition, FDA also provides the public with information regarding labeling, summary reviews forming the bases for drug approval, and the like. PhRMA emphasizes that keeping this information up to date is important to ensure that all parties—whether government agencies, private companies, or the general public—have access to accurate and current information.

Question 6: What policy considerations or concerns should the USPTO and the FDA explore as they relate to method of use patents and, as applicable, associated FDA use codes, including with respect to generic drug, 505(b)(2), and biosimilar applicants who do not seek approval for (i.e., who seek to carve out from their labeling) information related to a patent-protected method of use (sometimes described as "skinny labeling")?

PhRMA does not believe that changes to law or agency policy are necessary regarding method-of-use patents, use codes, and labeling carve-outs. The current practices and policies concerning skinny labeling weigh in favor of generic sponsors, which disincentivizes R&D on already approved drugs. If any changes are made, however, PhRMA urges the agencies to ensure that incentives for innovation in the study of new uses are not compromised.

A. Generic and Biosimilar Applicants Enjoy Significant Discretion to Pursue Labeling Carve-Outs—Even Where They Can Undermine IP Law and Policies—and the Agencies Should Avoid Further Undercutting Incentives for Studying New Uses.

FDA often permits both ANDA applicants and biosimilar applicants to omit patent- and exclusivity-protected uses from their labeling.[93] Moreover, generic drugs routinely are

[93] *See, e.g.*, 21 C.F.R. § 314.94(a)(8)(iv); Biosimilars and Interchangeable Biosimilars Guidance, *supra* note 17, at 3-4.

substituted for the prescribed listed drug even in a protected indication,[94] and products approved in abbreviated applications may be prescribed for an exclusivity-protected use despite the IP. These realities already substantially undermine incentives for further study of approved drugs.[95] FDA and the USPTO therefore should carefully weigh any changes regarding skinny labeling and ensure that any changes do not further degrade incentives for innovation. In particular, no changes are warranted based on *GlaxoSmithKline LLC v. Teva Pharmaceuticals USA, Inc.*[96] In addition to being unwarranted as described below, any changes based on the case also would be premature given that the Supreme Court is considering a petition to a writ of certiorari and has requested the Solicitor General's views on the petition.[97]

Contrary to various claims made by some generic companies,[98] the Federal Circuit's *GSK v. Teva* opinion did not reshape the induced infringement landscape for skinny-labeled generic drugs. Rather, the Federal Circuit applied the unremarkable principle that generic drug manufacturers are responsible for ensuring that their labeling and other statements do not induce infringement of an innovator's method-of-use patents. As background, to obtain approval with skinny labeling, the generic applicant files a "section viii statement" indicating that the patent "does not claim a use for which the applicant is seeking approval."[99] Crucially, making this statement comes with a responsibility: the applicant must delete from its labeling all mentions of the patented uses.[100] If a generic applicant's labeling ineffectively carves out the patented use, or if the applicant discusses the patented use in its promotional materials, it may be held liable for induced infringement.[101] In *GSK v. Teva*, the Federal Circuit found that substantial evidence supported a jury verdict that Teva's labeling and marketing materials for its generic carvedilol product induced infringement of GSK's patent claiming a method of using carvedilol to decrease mortality caused by congestive heart failure.[102] The jury heard evidence regarding Teva's marketing efforts, catalogs, press releases, and testimony from Teva's own witnesses, showing that Teva encouraged carvedilol sales for the patented use.[103] Indeed, claims that the case

[94] *See Bristol-Myers Squibb Co. v. Shalala*, 892 F. Supp. 295, 296 (D.D.C. 1995) (stating that a therapeutic equivalence rating "allows pharmacists to substitute the generic version of [a product] for the original product.").

[95] *See* Lietzan, *supra* note 16, at 183-91.

[96] *GlaxoSmithKline LLC v. Teva Pharms. USA, Inc.*, 7 F.4th 1320 (Fed. Cir. 2021).

[97] *See Teva Pharms. USA, Inc. v. GlaxoSmithKline LLC*, No. 22-37, 143 S. Ct. 80 (Mem.) (Oct. 3, 2022) (inviting the Solicitor General to file a brief).

[98] *See, e.g.*, Br. of Amicus Curiae Alvotech in Support of Pet'r, *Teva Pharms. USA, Inc. v. GlaxoSmithKline LLC*, No. 22-37, 2022 WL 3448299 (Aug. 12, 2022); Br. for Mylan Pharms. Inc. as Amicus Curiae In Supp. of Pet'r, *Teva Pharms. USA, Inc. v. GlaxoSmithKline LLC*, No. 22-37, 2022 WL 3448297 (Aug. 12, 2022).

[99] FDCA § 505(j)(2)(A)(viii).

[100] *See* 21 C.F.R. § 314.94(a)(12)(iii)(A); FDA, Letter to Dexmedetomidine Hydrochloride Injection NDA Holder/ANDA Applicant, Docket No. FDA-2014-N-0087, at 6 (Aug. 18, 2014) (citing 21 CFR 314.92(a)(1) and 314.94(a)(12)(iii)).

[101] *See* 35 U.S.C. § 271(b).

[102] *See GlaxoSmithKline LLC*, 7 F.4th at 1330.

[103] *See id.* at 1335.

fundamentally rewrote induced infringement law are belied by subsequent case law.[104] *GSK v. Teva* is not the first Federal Circuit case to find inducement when the generic claimed it used skinny labeling,[105] and it fully aligns with how inducement analysis has always worked: claims are assessed on a fact-specific basis based on the generic applicant's labeling and other statements. The case confirms that generic companies may obtain approval of their drugs for *off-patent* uses, if they refrain from discussing *patented uses* in their labeling and promotional activities. Indeed, the skinny-labeling provisions of Hatch-Waxman were never intended to provide generic companies *carte blanche* to encourage their drugs' use for patented indications without facing liability for induced infringement.[106] Instead, they were meant to balance the two goals of encouraging development of new uses for approved drugs and enabling generic entry for off-patent uses. Patents provide much-needed incentives to study approved products for new uses, and the current skinny labeling framework, coupled with pharmacy substitution, already provides a windfall to generic sponsors (due to automatic substitution) and undermines incentives to invest in new-use research. Tipping the balance further toward benefitting generics through changes to skinny labeling practice would upend the Hatch-Waxman balance and ultimately come at the cost of new treatments for patients.

There is also no need to change the labeling carve-out practice for biologics. The prevalence of biosimilars with skinny labels suggests that biosimilar companies are motivated to bring biosimilars to market and are able to do so despite the existence of patents or exclusivity covering the innovator biologic. Per one publication, out of 33 approved biosimilars, 22 (66.7%) had a skinny label for which carved-out information was protected by patents or regulatory exclusivities.[107] There is therefore no evidence of any concerns with biosimilar applicants' ability to carve-out protected information, and FDA is not precluded from approving a biosimilar based on its labeling containing patented information.

B. The USPTO Should Not Be Involved in the Patent Listing Process, and FDA's Role Should Remain Ministerial.

No policy changes are warranted to FDA's review of skinny labeling or related issues concerning method-of-use patents and use codes. The current approach aligns with the agencies' statutory authority and expertise, and Congress has recently spoken to these issues. FDA has stated that "a fundamental assumption of the Hatch-Waxman Amendments is that the courts are the appropriate mechanism for the resolution of disputes about the scope and validity of patents."[108] We agree. Whether labeling submitted by a generic drug, section 505(b)(2), or

[104] *See Amarin Pharma, Inc. v. Hikma Pharms. USA Inc.*, 578 F. Supp. 3d 642 (D. Del. 2022).

[105] *See, e.g.*, *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1060 (Fed. Cir. 2010).

[106] *See Abbreviated New Drug Applications and 505(b)(2) Applications*, 81 Fed. Reg. 69,580, 69,598 (Oct. 6, 2016) (FDA has "agree[d] that the use code is not intended to substitute for the . . . ANDA applicant's review of the patent and the approved labeling.").

[107] Alexander C. Egilman et al., *Frequency of Approval and Marketing of Biosimilars With a Skinny Label and Associated Medicare Savings*, Research Letter, JAMA INTERNAL MED., at E2 (Nov. 28, 2022).

[108] 68 Fed. Reg. 36,676, 36,683 (June 18, 2003).

biosimilar applicant reads on a patent-protected method-of-use is a matter of patent enforcement and is firmly within the purview of the courts.

With respect to use codes, FDA's role is and should remain ministerial. The agency properly reviews generic drug labeling to confirm that omissions of exclusivity-protected information "do not render the proposed drug product less safe or effective than the [RLD]" for the labeled uses,[109] in line with the agency's public health mission. The agency lacks the expertise, resources, and statutory authority to review generic labeling to ensure it avoids patent infringement, e.g., by construing patent claims. For these reasons, we disagree with a commentator from the listening session who argued FDA should abolish use codes and construe patent claims.[110] The responsibility to omit a patented use from generic labeling has always fallen upon the generic applicant. Use codes are limited in their number of characters and only provide an abbreviated summary of the scope of the patent claims. FDA has "agree[d] that the use code is not intended to substitute for the . . . ANDA applicant's review of the patent and the approved labeling."[111] FDA has managed the mechanics of listing of use codes, and FDA's ministerial role should not be disturbed.

The same commentator—Professor John R. Thomas—also called for USPTO to become involved in construing patent claims in lieu of use code practice.[112] Regarding the suggestion that the USPTO become substantively involved with use codes, the USPTO does not have jurisdiction with respect to claim construction in the patent enforcement context. These tasks are squarely within the province of an Article III court. Moreover, USPTO may not have access to the materials from the NDA that could be needed to assess whether a patent is to be listed in the Orange Book and granting USPTO access could implicate confidentiality concerns. The agency also lacks expertise in the safety and effectiveness issues that FDA considers in reviewing generic labeling. For these reasons, we disagree with Professor Thomas's suggestion.

Neither FDA nor the USPTO should become involved with challenges to use codes beyond what is already permitted by law. Congress has already provided a mechanism for applicants submitting abbreviated applications to advance delisting allegations: the statutory counterclaim in court.[113] As evidenced by *Jazz Pharmaceuticals, Inc. v. Avadel CNS Pharmaceuticals, LLC*, claim construction is often necessary to determine whether a patent is properly listed in the Orange Book.[114] Determining listability also may entail review of sensitive business information and other confidential material that the USPTO is not well-equipped to protect, as discussed above. Similarly, FDA does not have the resources or expertise to conduct

[109] 21 C.F.R. § 314.127(a)(7).

[110] *See* Comment from John R. Thomas, Docket No. PTO-P-2022-0037-0010, at 2-3.

[111] 81 Fed. Reg. 69,580, 69,598 (Oct. 6, 2016).

[112] *See* Comment from John R. Thomas, *supra* note 110, at 3.

[113] *See* FDCA § 505(c)(3)(D)(ii)(I).

[114] *See Jazz Pharm., Inc. v. Avadel CNS Pharms., LLC*, No. 21-691-GBW, 2022 WL 17084371, at *1 (D. Del. Nov. 18, 2022) (denying Avadel's first motion for judgment on the pleadings regarding the delisting counterclaim because the delisting arguments "depend in no small part on claim construction").

claim construction, given the need for extensive fact development and expert testimony to inform claim construction. These matters are appropriately handled by federal courts. Any agency processes to pre-vet these issues would conflict with the role of the courts and raise due process questions about whether the agencies properly considered all evidence relevant to the scope of the claims.

Other proposals are also inconsistent with the agencies' statutory roles. For example, in a 2015 proposed rule, FDA proposed to defer to the section 505(b)(2) or ANDA applicant's interpretation of the scope of the listed patent in the event of a use code dispute. Specifically, under the proposed rule, if a follow-on applicant commenced a use code challenge, FDA proposed that it would "review the proposed labeling for the 505(b)(2) application or ANDA with deference to the 505(b)(2) or ANDA applicant's interpretation of the scope of the patent."[115] This proposal is inconsistent with FDA's ministerial role in patent listing issues. Such deference also would invite gamesmanship and frivolous challenges, in which the follow-on applicant files a use code challenge specifically to secure automatic deference to the section 505(b)(2) or ANDA applicant rather than submit to an evaluation of the listing on the merits. Overall, PhRMA believes that FDA's role in the patent listing process should remain ministerial, and USPTO should remain uninvolved in this process, consistent with the agencies' statutory authorities and longstanding practices.

C. Congress Recently Clarified the Orange Book Listing Criteria for Patents, and Further Changes Are Unwarranted.

If the agencies intend to limit the scope of patents listed in the Orange Book, for example, method-of-use or "REMS patents," it is premature for agencies to revisit these issues (1) so soon after Congress has addressed patent listing in the OBTA, (2) while GAO's report on the Orange Book is under preparation, and (3) while FDA continues to review its docket on listing issues.[116] In addition, limiting the scope of patents that may be listed in the Orange Book would also undermine the Hatch-Waxman compromise.

The public listing of patents in the Orange Book furthers Congress's intent for Hatch-Waxman to strike a balance between competing interests. Namely, patent listing provides (1) transparency as to the existence of relevant drug and method-of-use patents; (2) an opportunity for patent litigation subject to a 30-month stay of approval of a generic application,[117] which allows for the early, efficient, and orderly resolution of patent issues before the marketing of the proposed generic product and the potential for damages; and (3) the potential for 180-day exclusivity for generic first applicants,[118] which provides a key incentive to challenge listed patents. Listing patents in the Orange Book, along with their associated use codes, helps generic companies identify patents that could affect the market entry of a proposed generic drug under Hatch-Waxman and promotes the early and streamlined analysis of patent

[115] 80 Fed. Reg. 6801, 6826 (Feb. 6, 2015) (proposed rule); *see also* Docket No. FDA-2011-N-0830.

[116] *See* Docket No. FDA-2020-N-1127.

[117] *See* FDCA §§ 505(c)(3)(C), 505(j)(5)(B)(iii).

[118] *See id.* § 505(j)(5)(B)(iv).

issues. In contrast, limiting patents that could be listed in the Orange Book would impede these objectives. If new limitations on the scope of patents listed were introduced, the Orange Book would not serve its notice function because only some of the relevant patents would be included. Yet, a generic company would still need to identify other such patents, increasing the burden on generic companies.

Adding new limitations on patent listing also would disrupt the orderly patent resolution process that exists under Hatch-Waxman. Such disruption comes with no promise of faster or increased generic market entry. Without patent listing and a 30-month stay, generic applicants might fail to identify a relevant patent before bringing a generic drug to market and risk liability for damages or become subject to injunctive relief. An alternative patent enforcement process at the time of generic launch also would involve costly, time-pressured actions for preliminary injunctions that would deprive innovators of the opportunity to enforce or defend their patents prior to generic launch, a benefit that Hatch-Waxman was meant to provide. Further, an at-risk launch would require the parties to litigate damages-related issues, which would increase the cost, time, and complexity of patent litigation and potentially subject generic applicants to significant damages. Restricting the number of listed patents also would limit opportunities for 180-day exclusivity. Indeed, without the opportunity for 180-day exclusivity, generic applicants might not invest in developing a product at all.

Overall, PhRMA believes that the current Orange Book listing requirements are working as intended and should not be changed.

Question 7: What policy considerations or concerns should the USPTO and the FDA explore in relation to the patenting of risk evaluation and mitigation strategies associated with certain FDA-approved products? What other types of patent claims associated with FDA-regulated products raise policy considerations or concerns for the USPTO and the FDA to evaluate?

PhRMA believes that patents are not, and should not be, excluded from eligibility for listing in the Orange Book solely on the ground that they relate to a REMS. The statute does not exclude from listing patents otherwise meeting the listing criteria based on the subject matter to which they relate. A "REMS patent" must be listed if it meets these criteria set forth in the statute[119] and in 21 C.F.R. § 314.53—i.e., if it claims an approved method-of-use of a drug as described by the approved labeling. Indeed, given FDA's ministerial role in patent listing, it would be difficult for the agency to administer an alternative framework in which "REMS patents," however ill-defined, were excluded from listing. The agency would need to identify such patents, which would entail interpretation of patent claims. FDA lacks the expertise, statutory authority, and resources to perform this task.

PhRMA reiterates that "REMS patents" as a category are listable in the Orange Book if they meet the listing requirements and should remain listable. In particular, for method-of-use patents, pursuant to 21 C.F.R.§ 314.53, a patent must be listed if it "claim[s] indications *or other*

[119] *See* FDCA § 505(b)(1).

conditions of use for which approval is sought or has been granted in the NDA."[120] In the absence of a REMS, certain drug products may not be approved by FDA, and REMS is thus an "other condition of use."[121] Accordingly, there is a basis for listing "REMS patents" in the Orange Book.

Further, it is not clear that changing the listing requirements for "REMS patents" or precluding their listing entirely would lead to more or faster market entry for generic drug products, as described previously.[122] For example, "REMS patents" covering drug products could be asserted in litigation after launch of the generic product, which could result in an injunction against the generic sponsor and monetary damages. These are the very outcomes that Hatch-Waxman's premarket litigation framework was intended to avoid.

Finally, questioning the listing of "REMS patents" is also unwarranted in light of Congress' recent enactment of the OBTA and the open processes at both the GAO and FDA to consider Orange Book listing issues.

Question 8: Apart from, or in conjunction with, the initiatives set forth in the USPTO Letter, what other steps could the USPTO and the FDA take collaboratively to address concerns about the potential misuse of patents to improperly delay competition or to promote greater availability of generic versions of scarce drugs that are no longer covered by patents?

PhRMA does not agree that concerns about "the potential misuse of patents to improperly delay competition" are well-founded. Patents have a long and important history in U.S. innovation, and the mere existence of a patent or patents covering an innovative biopharmaceutical product does not mean that patents are "improperly delaying competition."

As noted in the introduction, data from I-MAK and the U.C. Hastings Evergreen Drug Patent Search Database have fueled false narratives about excessive patenting, but these data and inferences from them have been called into serious question.[123] Given the findings of Professors Mossoff, Lietzan, and Acri, the timing of generic and biosimilar market entry strongly suggests that inferences and conclusions of I-MAK and based on the U.C. Hastings Evergreen Drug

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[120] 21 C.F.R. § 314.53(b) (emphasis added).

[121] FDCA § 505-1(a)(1).

[122] *See supra* Question 6.

[123] *See, e.g.*, Letter from Sen. Thom Tillis to Dr. Janet Woodcock and Mr. Drew Hirshfeld, *supra* note 28, at 2 ("I-MAK appears to be a primary source of data regarding the role of patents in drug pricing . . . [but] the organization does not transparently disclose or explain its underlying data, and the data differs by orders of magnitude from public sources like the US Orange Book and court filings."); *see also* Letter from Sen. Thom Tillis to Dr. Robert Califf and Mr. Drew Hirshfeld, *supra* note 28, at 1 (I-MAK's claims that drugs "are often protected by dozens or hundreds of patents each, with an alleged effect of blocking generic competition for 30 to 50 years longer per drug" have "serious flaws, inaccuracies, and biases in the methods and calculations."); Adam Mossoff, *supra* note 29, at 2-3 ("I-MAK claims to be the authoritative source on the number of patents covering drugs and drug treatments," but there are serious discrepancies, for example, claiming that Lyrica is covered by 68 patents but failing to explain why the Orange Book lists only 3 patents.).

Patent Search Database about the timing of follow-on entry are false.[124] The patent system is not being exploited and is working as intended.

With respect to the agencies' concern about the "availability of generic versions of scarce drugs that are no longer covered by patents," PhRMA notes that, if there are no patents covering drugs or scarce drugs, generic sponsors are free to launch generic versions of those drugs. In particular, Congress has established incentives to promote the development of certain generic drug products. For example, the FDA Reauthorization Act of 2017 created a pathway for the designation of a drug with "inadequate generic competition" as a competitive generic therapy (CGT).[125] Such a designation comes with incentives such as expedited development and review of an ANDA for a CGT and 180-day exclusivity for certain first approved applicants for CGTs.[126] Accordingly, Congress has already provided a policy response to this concern. To the extent that there is any "potential misuse of patents to improperly delay competition," such alleged patent misuse is an antitrust issue within the authority of the Federal Trade Commission or the U.S. Department of Justice.

Question 9: What additional input on any of the initiatives listed in the USPTO Letter (1(a)–1(h)), or any other related suggestions for USPTO–FDA collaboration, should the agencies consider?

To increase transparency about IP issues, we urge FDA to publish prompt reference product exclusivity decisions at the time of biologic approval. The Purple Book FAQ says that "FDA has not made a determination of first licensure for each 351(a) biological product included in the Purple Book. The absence of a date of first licensure in the Purple Book does not mean that a biological product on the list is not, or was not, eligible for" reference product exclusivity.[127] FDA's current approach has led to widespread confusion about the availability of reference product exclusivity. This uncertainty sows doubt and discourages investment in both reference products and biosimilars. In addition, we also urge FDA to publish prompt exclusivity decisions for small molecule drugs. Prompt publication of these exclusivity decisions would provide much-needed clarity and transparency.

PhRMA also acknowledges that the agencies are seeking comments regarding procedures for collecting broader stakeholder input. We agree that stakeholder input is important to fully understand issues in the industry and that stakeholders should have the opportunity to engage with the agencies, comment on open dockets, and participate in public listening sessions. PhRMA does not agree, however, that stakeholders should be involved in the confidential aspects of patent prosecution. As noted by USPTO personnel at the public listening session, there is an existing mechanism under 35 U.S.C. § 122(e) for third parties to submit patents, published patent applications, and other printed publications that are relevant to the examination

[124] *See* Lietzan & Acri, *supra* note 25, at 46.

[125] FDA Reauthorization Act of 2017, Pub. L. No. 115-52, 131 Stat. 1070.

[126] *See* FDCA § 506H.

[127] FDA, Purple Book Database of Licensed Biological Products, FAQs (last visited Feb. 1, 2023).

of a patent application. Stakeholders seeking to engage with the patent prosecution process should file such third-party pre-issuance submissions.

PhRMA has long supported patient-focused drug development (PFDD)[128] and FDA's efforts to incorporate the patient voice into its regulatory decision-making. The patient voice is critical to understanding how patients (and their caregivers) view a disease or condition, and these perspectives can help inform evaluation of a medicine's benefits and risks and provide the context for FDA's regulatory decision-making. We have strongly supported efforts to further enhance PFDD and FDA's ongoing activities in this space,[129] including the PFDD-related commitments described in the Prescription Drug User Fee Act (PDUFA) commitment letter.[130]

While PhRMA supports and acknowledges the appropriateness of incorporating the patient voice in FDA's understanding of risks and benefits to support FDA's regulatory decision-making, it is not an appropriate metric for USPTO's decision-making as suggested by certain speakers at the public meeting. Indeed, there is no statutory requirement for the claimed invention to show medical benefit or any other value-based characteristic. Patent examiners have the important role of analyzing patent applications for compliance with statutory requirements. Our current patent system entitles a person to a patent unless certain exclusionary conditions exist; the subject of a patent must be novel, non-obvious, and must also meet written description and enablement requirements.[131] Although a "new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent,"[132] utility has been broadly interpreted. No specific medical benefit or value-based characteristic is required. Any such proposals to evaluate patent applications go against the long-standing and successful patent system that has made the U.S. a leader in innovation, and to the extent the proposals apply only to biopharmaceutical inventions, they would raise issues as to their technology neutrality.

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[128] FDA defines PFDD to mean a "systematic approach to help ensure that patients' experiences, perspectives, needs, and priorities are captured and meaningfully incorporated into drug development and evaluation." FDA, CDER Patient-Focused Drug Development (July 27, 2022).

[129] In 2022 alone, FDA published a number of guidance documents relating to PFDD. *See, e.g.*, FDA, Draft Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders, Patient-Focused Drug Development: Selecting, Developing, or Modifying Fit-for-Purpose Clinical Outcome Assessments (June 2022); FDA, Guidance for Industry, Food and Drug Administration Staff, and Other Stakeholders, Patient-Focused Drug Development: Methods to Identify What is Important to Patients (Feb. 2022).

[130] The commitments industry negotiated in the PDUFA Commitment letter include: (1) expanding FDA staff training and external outreach to sponsors and other involved stakeholders with emphasis on PFDD methods and tools-related guidance; (2) FDA engagement with external experts to support the review of patient experience data; (3) issuing a request for information and holding multiple public workshops on PFDD-related methodological issues, including the submission and evaluation of patient experience data in the context of benefit-risk assessment and product labeling; and (4) publishing draft guidance on use and submission of patient preference information to support regulatory decision-making. *See* FDA, PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2023 Through 2027.

[131] *See* 35 U.S.C. §§ 102, 103, 112.

[132] *Id*. § 101.

III. Conclusion

PhRMA thanks the USPTO and FDA for reaching out to stakeholders regarding various aspects of the agencies' collaboration initiatives. PhRMA welcomes further dialogue with the agencies regarding the various matters addressed in these comments.

Respectfully submitted,

/s/	/s/
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