Biotechnology Innovation Organization
1201 New York Ave., NW
Suite 1300
Washington, DC, 20005
202-962-9200

COMMENTS OF THE BIOTECHNOLOGY INNOVATION ORGANIZATION (BIO) TO THE USPTO NOVEMBER 7, 2022 REQUEST FOR COMMENTS OF USPTO-FDA COLLABORATION, 87 FR 67019

I. INTRODUCTION

On behalf of its member organizations, Biotechnology Innovation Organization ("BIO") respectfully submits this Comment in response to the United States Patent and Trademark Office's (the "Patent Office" or "PTO") November 7, 2022 Request for Comments. *See* 87 FR 67019 (the "RFC").[1]

BIO is the world's largest trade association representing biotechnology companies, academic institutions, state biotechnology centers, and related organizations across the United States and in more than 30 other nations. BIO members include virtually every major pharmaceutical developer in the United States including, by way of illustrative example, every developer of an FDA-approved COVID-19 vaccine in the United States (*i.e.*, Pfizer, Johnson & Johnson, Moderna, and Novavax). BIO members include startup companies developing their first commercial products to multi-national Fortune 500 pharmaceutical corporations. Importantly, BIO's innovators include stakeholders at every phase of the patenting process, including members who engage in patent prosecution, patent licensing, and patent assertion and challenges in civil litigation and before the Patent Office.

Before turning to the questions presented in the RFC, BIO wishes to clarify some of the misconceptions and unwarranted concerns that were raised at the January 19, 2023 Listening Session. Specifically, BIO seeks to address some of the false and misleading narratives and improper criticisms of the patents procured by drug and biopharmaceutical innovators. As set forth in BIO's response to RFC-1, the empirical data does not support the allegations of "evergreening," "patent thickets," and "product hopping." On the contrary, the data suggests that the current set of compromises that Congress reached in enacting the Drug Price Competition and Patent Term Restoration Act ("Hatch-Waxman") and Biologics Price Competition and Innovation Act ("BPCIA") (as amended) are working efficiently and effectively to promote continued innovation in the drug and biopharmaceutical industry while at the same time providing generic and biosimilar manufacturers incentives and mechanisms to enter the marketplace and provide competitively priced drugs.

[1] On February 1, 2023, BIO submitted a response to the PTO's October 4, 2022 Request for Comments (87 FR 60130) ("RFC-1"), which raises concerns and issues similar to those presented in this RFC. Accordingly, BIO incorporates by reference its submission in response to RFC-1. A copy of which is filed herewith as an exhibit.

II. PRELIMINARY STATEMENT

In many instances, collaboration between government agencies can operate efficiently to achieve common goals as is the case with the FDA and PTO in analyzing and granting Patent Term Extensions ("PTE"). However, the stated purpose of this RFC and the proposed collaboration, "[t]o advance President Biden's Executive Order on 'Promoting Competition in the American Economy' and to promote greater access to medicines for American families," lacks focus and seems misdirected given the separate and distinct missions and roles of the PTO and FDA. Neither agency is tasked with the responsibility or authority for setting drug pricing, reimbursement, insurance coverage or the like. Yet, the Executive Order seems to suggest that if the two agencies worked more closely together, drug pricing would decrease and competition would increase.

Moreover, the factual predicate underlying the Executive Order and the perceived need for the two agencies to find additional areas of collaboration appears to be inaccurate and misleading. There is no evidence that the drug and biopharmaceutical industries are obtaining patents that are different in scope, quality, duration, or number compared to any other industry. Empirical evidence shows that drugs and biologics developed by biopharmaceutical innovators are not covered by a disproportionate number of patents and they are not being used to extend patent terms. As set forth in BIO's response to RFC-1, the average number of patents listed in the Orange Book for each new molecular entity (NME) is between **3 – 5 patents**, and the average number of patents that are the subject of BPCIA litigation is **7 patents** – far from the "hundreds" of patents or "patent thickets" that are alleged to overwhelm putative competitors with avalanches of litigation. The average effective market life of a drug covered by patents from FDA approval to generic entry has been stable at **12.5-13.5 years**, which is far less than 20-year statutory patent term and the "decades" of "evergreening" that are also alleged to exist.[2]

Misleading Narrative About Patents as a "Numbers Game" – Given large numbers of related, overlapping, and "weak" biopharmaceutical patents, the costs of challenging them in IPR or district court litigation is cost-prohibitive and functions as a deterrent to biosimilar applicants (*i.e.*, if it costs $1M to challenge one of these patents, challenging a dozen or more costs more than $12M)
False: In practice, the cost to challenge multiple patents – especially those that are related or claim priority to the same family member – is not significantly greater than the cost to challenge one patent. Typically, the challenges overlap with respect to cost drivers: the same experts are used with each patent; the art used to challenge validity is typically the same or similar; overlapping IPR proceedings can be consolidated; counsel is the same and the underlying litigation is also the same. The notion that the sheer number of patents acts as a cost barrier to biosimilar development and/or challenges by biosimilar applicants is not borne out in practice.

[2] Additional data can be found in Appendix A, which BIO compiled in responding to the PTO's October 4, 2022 Request for Comments. See 87 FR 60130, available at: https://www.regulations.gov/comment/PTO-P-2022-0025-0111

Another false narrative that continues to be repeated is that the delay in biosimilar approval is due to the excessive number of patents that are granted to U.S. Biopharmaceutical companies. *See, e.g., Goode and Chao*, "*Biological patent thickets and delayed access to biosimilars, an American problem*," Journal of Law and the Biosciences, 1–24 (2022).[3] But when biosimilar approval-to-launch intervals are compared to the actual number of patents asserted against them in BPCIA litigation, it is clear that there is no such correlation as is evident from the table and chart below.[4]

Litigation	Accused Biosimilar	Reference Product	Number of Patents Litigated[5]	Time from Approval to Launch (months)
Amgen v. Coherus, No. 17-546 (D. Del.)	UDENYCA (pegfilgrastim-cbqv)	NEULASTA	1	2.1 months
Amgen v. Hospira, Nos. 18-1064, 20-561 (D. Del.)	NIVESTYM (filgrastim-aafi)	NEUPOGEN	1	2.5 months
Amgen v. Hospira, No. 20-201 (D. Del.)	NYVEPRIA (pegfilgrastim-apgf)	NEULASTA	1	6.8 months
Janssen v. Celltrion, No. 17-11008 (D. Mass.)	INFLECTRA (infliximab-dyyb)	REMICADE	2	7.5 months
Amgen v. Hospira, No. 15-839 (D. Del.)	RETACRIT (epoetin alfa-epbx)	EPOGEN/ PROCRIT	2	5.9 months
Amgen v. Sandoz, No. 16-2581 (N.D. Cal.)	ZIEXTENZO (pegfilgrastim-bmez)	NEULASTA	2	0.3 months

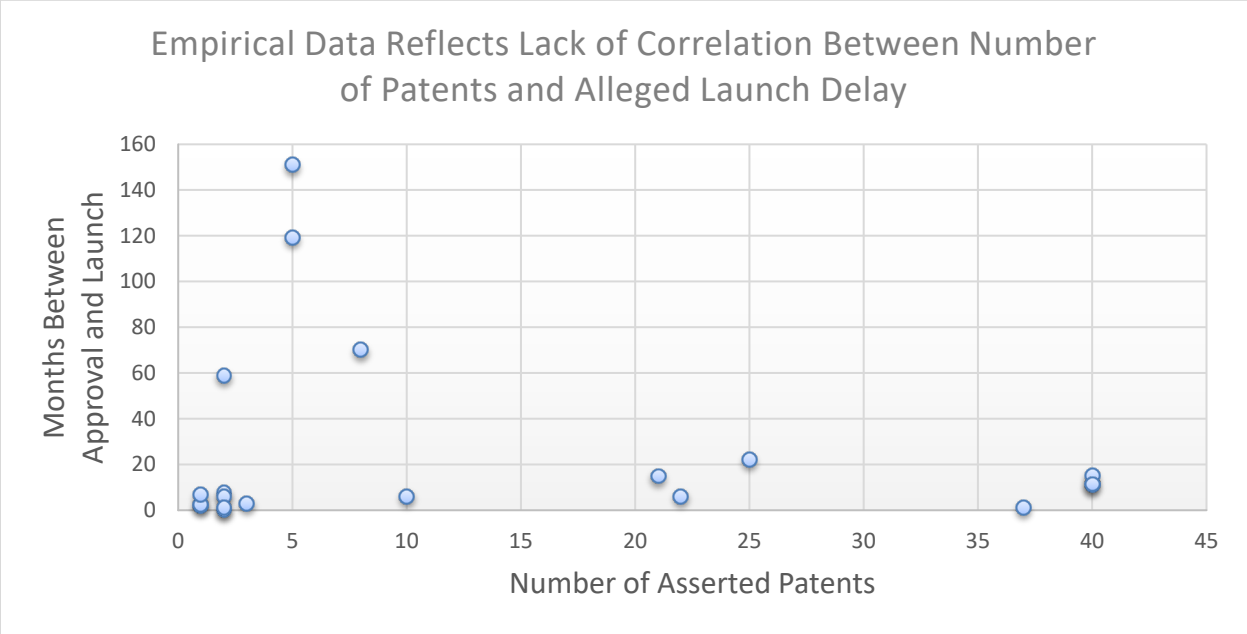
[3] The authors themselves recognized that within their data there was a single outlier (Enbrel: etanercept) responsible for skewing the data set owing to the fact that two patents at issue were pre-GATT with a patent term of 17 years from the date of grant (effectively 34 years).

[4] Data table includes all U.S. biosimilar products that have been subject to district court litigation, have received FDA approval, and for which a launch date is known. Biosimilars that do not meet these criteria cannot be included because it is not possible to establish a period of "launch delay" for a product that has not yet received FDA approval (i.e. that could not be launched anyway). For example, Goode and Chao, at n.3 above, make repeated reference to Alvotech's adalimumab biosimilar which has been accused of infringing over 60 patents as an example of purported patent over-enforcement leading to delayed market access. Their paper did not mention that the biosimilar in question does not have FDA approval. See *FDA holds back Alvotech's Humira biosimilar over manufacturing issues*, available at: https://www.biopharmadive.com/news/alvotech-humira-biosimilar-fda-reject-crl-manufacturing/631213/

[5] Largest Number of Patents Asserted in Complaint or Amended Complaint; the number of patents actually asserted at trial is equal to or less than the number cited herein.

Litigation	Accused Biosimilar	Reference Product	Number of Patents Litigated[5]	Time from Approval to Launch (months)
Amgen v. Mylan, No. 17-1235 (W.D. Pa.)	FULPHILA (pegfilgrastim-jmdb)	NEULASTA	2	1.1 months
AbbVie v. Sandoz, No. 18-12668 (D.N.J.)	HYRIMOZ (adalimumab-adaz)	HUMIRA	2	59 months
Janssen v. Samsung Bioepis, No. 17-3524 (D.N.J.)	RENFLEXIS (infliximab-abda)	REMICADE	3	3.1 months
Immunex v. Sandoz, No. 2:16-01118 (D.N.J.)	ERELZI (etanercept-szzs)	ENBREL	5	151.1 months
Immunex v. Samsung Bioepis, No. 19-11755 (D.N.J.)	ETICOVO (etanercept-ykro)	ENBREL	5	119.3 months
AbbVie v. Boehringer Ingelheim, No. 17-1065 (D. Del.)	CYLTEZO (adalimumab-adbm)	HUMIRA	8	70.2 months
AbbVie v. Amgen, No. 16-666 (D. Del.)	AMJEVITA (adalimumab-atto)	HUMIRA	10	6.1 months
Genentech v. Samsung Bioepis, No. 18-1363 (D. Del.)	ONTRUZANT (trastuzumab-dttb)	HERCEPTIN	21	15 months
Genentech v. Pfizer, No. 19-638 (D. Del.)	ZIRABEV (bevacizumab-bvzr)	AVASTIN	22	6.1 months
Genentech v. Amgen, Nos. 17-1407 LEAD, -1471, 19-602 (D. Del.)	MVASI (bevacizumab-awwb)	AVASTIN	25	22.2 months
Genentech v. Amgen, No. 18-924 (D. Del.)	KANJINTI (trastuzumab-anns)	HERCEPTIN	37	1.2 months
Genentech v. Pfizer, No. 17-1672 (D. Del.)	TRAZIMERA (trastuzumab-qyyp)	HERCEPTIN	40	11.2 months
Genentech v. Celltrion, Nos. 18-095, -1025 (D. Del.)	HERZUMA (trastuzumab-pkrb)	HERCEPTIN	40	15.1 months
Genentech v. Celltrion, Nos. 18-574, -11553 (D.N.J.)	TRUXIMA (rituximab-abbs)	RITUXAN	40	11.5 months

Moreover, the data plotted below dispels yet another common misconception; namely, that there are impenetrable delays to the launch of Biosimilars. On the contrary, based on the 38 approved biosimilars, the median time for launch following approval of the biosimilar is 7.5 months.

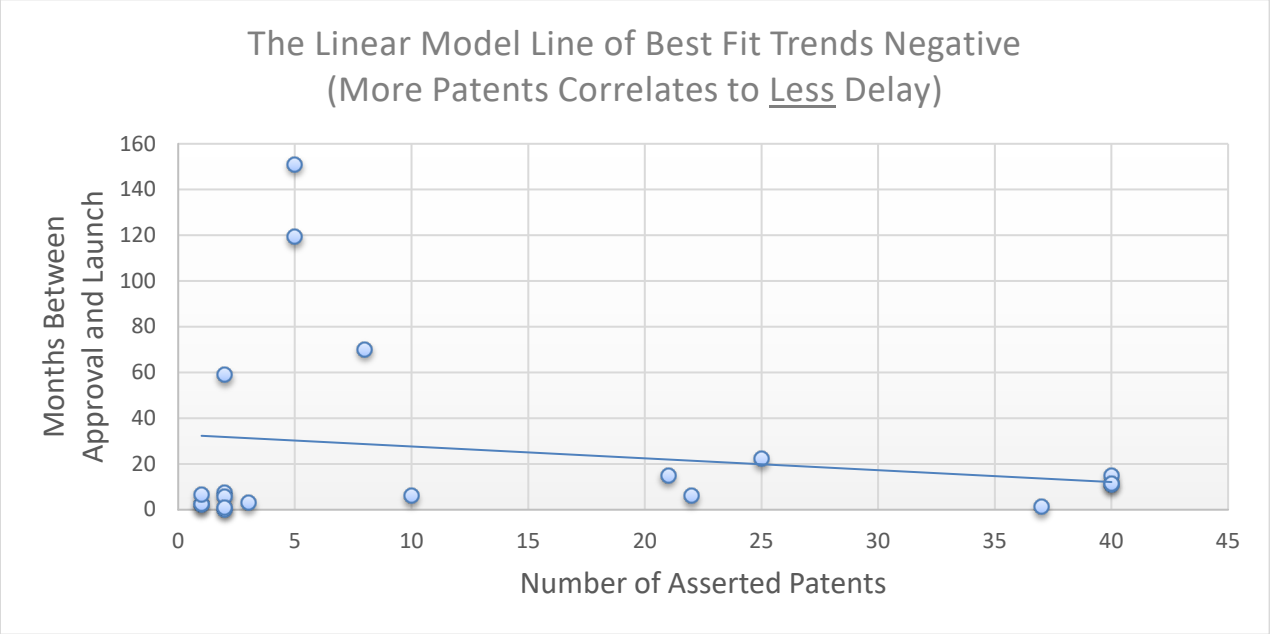


The "thicket" hypothesis claims that greater numbers of patents contribute to greater delays in biosimilar launches. ("[A] trend emerges: as the mean number of patents increases in the USA, so does the duration of the delayed biosimilar launch." Goode and Chao at 16). But the available data on biosimilars litigation simply do not support that notion. As the number of litigated patents increases, the amount of alleged delay does not. For example, one BPCIA litigation involving 37 patents resulted in a biosimilar launch "delay" of 1.2 months, while another BPCIA litigation involving 5 patents led to 151.1 month launch differential period.

Put simply, variation in the number of asserted patents cannot explain variation in the interval between biosimilar approval and launch. Unsurprisingly, a linear regression of this data has virtually no statistical explanatory value (r^2 = .0286)—that is, the number of patents does not explain 97.14% of the variation in the amount of time it takes to launch an approved biosimilar. Instead, the difference in time from approval to launch appears to be driven by matters wholly unrelated to number of asserted patents.

If anything, the linear line of best fit (below) suggests a weak <u>negative</u> relationship between number of asserted patents and alleged delay (i.e., *greater* numbers of asserted patents are associated with *less* delay). But another way to interpret the data is that there simply is no relationship (linear or otherwise) between the number of patents and the amount of alleged delay; patents do not increase or decrease time-to-launch for biosimilars. Indeed, the data suggests that

the number of patents is wholly uncorrelated to the amount of time it takes to launch a biosimilar. Thus, policymakers interested in speeding up the time to launch should look elsewhere than patent counting exercises, and reforms at the USPTO are unlikely to favorably impact that policymaking goal.[6]



The initiatives suggested by the RFC questions are not likely to foster "generic drug and biosimilar competition." Exec Order, Section 5(p)(vi). Biotechnology and pharmaceutical patents are of paramount importance to drug development given the staggeringly high costs of research, development and drug approval, all in light of the high degree of appropriability once a drug is approved, if such drug is approved at all. Biotechnology and pharmaceutical patents are needed to spur innovation and promote the progress of life sciences. Moreover, patent protection on subsequent improvements incentivizes further innovation that results in significant improvements for patient and therapeutic outcomes. As stated succinctly by the Pharmaceutical Research and Manufacturers of America: "Innovation shouldn't stop once a new drug becomes available to patients. Additional patent protections only cover enhancements to a product and allow

[6] *Goode & Chao* discuss only 8 of the 20 biosimilar launches discussed herein, but even their narrow subset reaches the same result—a scattering of data points without a correlation between number of asserted patents and months between biosimilar approval and launch. And, as detailed above, analysis of the full data set shows a lack of any correlation.

companies to continue working to improve medicines, making them more effective for patients – whether reducing side effects or finding a new disease a medicine can treat."[7]

Misleading Narrative About "Secret" Manufacturing Patents– In the face of competition, biopharmaceutical companies surprise challengers with patents claiming manufacturing processes that were filed years after the underlying biologic was approved and launched. These patents block market entry and must be invalid.[8]
False: There are multiple reasons why valid patents covering manufacturing processes are filed and obtained years after the original launch and none of those reasons are improper. The simplest explanation is that claimed manufacturing improvements were invented *after* the reference biologic was approved. It is common for biological originators to optimize manufacturing processes so that existing drugs can be made more efficiently, economically, or with greater purity. Improved or alternative processes for manufacturing the same biologic may be first developed for commercial use only years after approval, and putative biosimilar competitors are not required to copy those process improvements. Put simply, there is nothing "illogical" about such patents, nor do they "block" biosimilars. The suggestion that later-patented manufacturing processes were secretly being practiced by biopharmaceutical originators is pure conjecture, and BIO is aware of no instance where this supposed practice has been documented. One common misconception regarding the duration of patent protection for a given drug is that innovators game the system to obtain periods of patent protection that extend beyond the 20-year period. This is simply false. After-invented improvements, such as new methods of manufacture or new resins for protein purification that did not exist at the time of the original drug patent are distinct inventions independently qualified to receive patent protection. If the patent covering the drug itself is expired, generic or biosimilar manufacturers are free to produce and sell the drug using other methods of manufacture that existed at the time of the original drug patent. That the new, after-invented method of manufacture is protected for a period beyond the duration of the original drug patent does not mean that the original drug patent is somehow extended, or that the original drug itself enjoys a period of patent protection extending beyond the 20-year period.

III. RESPONSE TO QUESTIONS IN THE RFC

Q1. What publicly available FDA resources should be included when training PTO patent examiners on tools they can use to assess the patentability of claimed inventions?

As a preliminary matter, the PTO needs to remain industry-agnostic when it comes to promulgating rules and regulations governing the issuance of patents. This question, however, appears to be targeted only at the biotechnology and pharmaceutical industry. If FDA resources were to be included when training PTO patent examiners, then all examiners or examiners within other art units must also be trained by other agencies such as the FAA, EPA, SEC, NRC, USDA, or DOT. Singling out those examiners in the biotechnology and pharmaceutical art units to receive

[7] https://phrma.org/policy-issues/Intellectual-Property

[8] *See, e.g., W. Nicholson Price II & Arti K. Rai*. "How logically impossible patents block biosimilars." Nature Biotechnology 37: 862–863.

specialized training from FDA ignores the examiners' qualifications and/or the hiring process, and places undue emphasis on subject matter that is unrelated to patent eligibility or patentability. .

It is BIO's understanding that FDA already has authority to inspect PTO records for purposes of enforcing the FDCA, and the USPTO in turn has the ability to request full and complete information from the FDA relating to questions raised by any drug patent application, and to have FDA conduct additional research into such questions. (21 USC 372(c) and (d)). Patent examiners are also able to require information directly from applicants if they deem that information reasonably necessary to the examination of an application. And applicants are under a duty to disclose material information under Rule 56. Given these tools which are already available to the two agencies, it would be helpful to better understand what it is in the FDA record that the PTO would expect to find. In BIO's members' experience, FDA regulatory dossiers are not very efficient or fruitful sources of prior art that cannot be accessed from other sources. Well-heeled and sophisticated litigants in patent infringement litigation have reviewed their adversaries' regulatory filings for decades with very few instances of finding "killer" prior art. It appears that FDA records have been of primary interest not as a source of prior art, but in order to find out what the patentee knew, or has been saying, *about* that prior art.

Proponents seeking to prevent the issuance of patents seem to believe that greater FDA involvement is likely to expose potentially patentability-destroying events (such as prior secret commercial use of later-patented manufacturing processes), or that it could lead to the discovery of so-called inconsistent statements. But as discussed above, the existence of secret prior commercial uses is pure conjecture. And an arguably inconsistent statement, made non-publicly to the FDA, is not prior art.

FDA training materials could be useful only to the extent they highlight the existence, location, and search methods for **publicly available** FDA resources. Only those resources that are publicly available are pertinent in examining a patent application; confidential discussions and submissions made by drug applicants have no relevance, weight or bearing on the subject matter of patentability. At the same time, the FDA requires clear, candid, and confidential discussions and disclosures from drug applicants without the fear of retribution from the PTO using such information to preclude legitimate patents from being granted. The public record before the FDA is available to the public and litigants in Hatch-Waxman and BPCIA litigation have made use of such records for many years. Thus, questions about inconsistent positions taken in publicly available records is already accessible and in use by those persons and entities who are motivated to challenge the patentability of any patent. Additionally, PTO examiners already have available some of the best and most powerful online databases and search engines available. If, however, FDA can assist examiners in how to use those tools and identify other means to access **publicly available** information during the patenting process, the BIO members believe that such training could be useful.

It is important to keep in mind that patent applicants are subject to a robust duty to disclose all information known to that individual to be material to patentability. *See* 37 CFR §1.56 ("Each individual associated with the filing and prosecution of a patent application has a duty of candor and good faith in dealing with the Office, which includes a duty to disclose to the Office all information known to that individual to be material to patentability as defined in this section."). This

includes a duty to disclose publicly available FDA resources and publicly available information submitted to the FDA which is known to the applicant and that bears on the issue of patentability. The penalty for failing to comply with this requirement for even just one claim in a patent is severe -- it can render unenforceable the entire patent issued from the application in question, and it may also result in unenforceability of other patents in the family as well; a result that has been called the "atomic bomb" of patent law. *Therasense, Inc. v. Becton, Dickinson and Co.,* 649 F.3d 1276, 1288-89 (Fed. Cir. 2011) (*en banc*) ("[T]he remedy for inequitable conduct is the 'atomic bomb' of patent law. Unlike validity defenses, which are claim specific, inequitable conduct regarding any single claim renders the entire patent unenforceable. Unlike other deficiencies, inequitable conduct cannot be cured by reissue or reexamination. Moreover, the taint of a finding of inequitable conduct can spread from a single patent to render unenforceable other related patents and applications in the same technology family. Thus, a finding of inequitable conduct may endanger a substantial portion of a company's patent portfolio.").

Finally, results from other jurisdictions suggest that a more expansive collaboration would not likely enhance the patent prosecution process. Brazil, for example, experimented with a similar approach with ANVISA—the Brazilian FDA—playing a role in the patent prosecution process, until that role was revoked in August 2021. ANVISA was then excised from the patent process because its involvement was deemed wasteful, inefficient, duplicative, and caused delays. The Office of the United States Trade Representative hailed this development as a "positive step" in light of concerns about lengthy "pendency of patent applications and the impact on the effective patent term."[9]

Q2. What mechanisms could assist patent examiners in determining whether patent applicants or patent owners have submitted inconsistent statements to the PTO and the FDA? Please explain whether such mechanisms present confidentiality concerns and, if so, how those concerns could be addressed.

This question appears to assume that patent owners are submitting inconsistent statements to the PTO and FDA that bear on the issue of patentability, and that this suspected conduct may be sufficiently common to warrant procedural changes in patent examination. BIO members do not believe that such an assumption is well-founded, as that there is basically no evidence of such practices. With respect to inconsistent statements the PTO only points to two cases: a 30 year-old case of a 510(k) medical device applicant and a more recent case of a 505(b)(2) new drug applicant. In each instance, the applicant *relied* for FDA approval on publicly known prior art predicate devices or reference drugs that were neither found by the PTO nor brought to the PTO's attention by the applicant during patent examination. These are hardly typical scenarios in the innovator biopharmaceutical industry, and a thin reed for instituting systemic policy change. And, as noted above, if the information is publicly available, patent examiners already have access to such information when considering issues of patentability. Suggesting that the PTO exert significant effort to access regulatory information beyond that

[9] https://ustr.gov/sites/default/files/IssueAreas/IP/2022%20Special%20301%20Report.pdf.

which is publicly available is neither relevant to the issues or patentability nor practical in any manner for several reasons.

First, given the varied standards that exist among the agencies, consistency and conversely inconsistency are nearly impossible to assess—the issues before the PTO and FDA are apples-to-oranges. For example, an invention may be non-obvious under the PTO's standards for patentability but may nevertheless provide a predictable and reliable safe and efficacious outcome in support of a new drug application. Or an existing drug manufactured via a new process may retain its FDA approval while the new method of manufacture may be patentable. Statements that are clear and reasonable in one context to one agency, may take on a different meaning when excised and imported into another.

Second, sorting through all of the FDA submitted materials (rather than what is already publicly available) would put an enormous burden on PTO examiners and may not provide any new or additional information relevant to patentability. Drug patent applications would be inevitably delayed by requiring review of voluminous FDA-submitted materials.

Third, the public relies on published patent prosecution histories which would pose confidentiality issues if confidential FDA materials were considered by the examiners and made part of the record.

Fourth, to the extent that this proposed initiative means that patent owner "statements" made to FDA will now be used to deny patentability at the PTO, this would create new legal grounds of unpatentability under Sections 102 and 103 for non-published statements. A non-public statement, even an arguably inconsistent one, is not prior art. Neither the PTO nor FDA has the power to create new substantive law, and Congress has not seen fit to amend the Patent Act to include such non-public "statements" as either grounds for invalidity or as a condition of patentability.

As previously noted, there are already mechanisms in place that are used successfully in litigation whereby a patent challenger may obtain FDA submitted materials in litigation under the protections of a confidentiality order that may be then used in that litigation to analyze whether so-called inconsistent statements were made that should have an impact on patentability. And although those mechanisms exist, they have only been useful in a small handful of cases in the last 40 years; the most recent was in the case of *Belcher Pharmaceuticals, LLC v. Hospira, Inc.*, 11 F.4th 1345 (Fed Cir. 2020). And the mechanism employed in that case worked—there was a finding of inequitable conduct on the part of the patentee (who was also the principal involved in preparing and participating in the NDA process) that resulted in the court holding that the patent was unenforceable. The existing mechanisms work; the fact that this circumstance does not arise frequently does not suggest that the PTO and FDA should create some new form of inter-agency information sharing. There is no data to support that the PTO is being deprived relevant information.

Nevertheless, the USPTO recently expressed its views regarding the disclosure obligations underlying its concerns about a party's submission of inconsistent statements to

USPTO and FDA.[10] However, as presented in the July Notice, USPTO's description of the duty of reasonable inquiry appears to be broader than the courts and USPTO previously have recognized.

The Federal Circuit recognizes a "duty of reasonable inquiry," in the context of the doctrine of inequitable conduct, that is triggered when the factual circumstances "would cause a reasonable attorney to understand that relevant and questionable material information should be assessed."[11] This duty is limited in scope and the Federal Circuit "has repeatedly reaffirmed the proposition that '[a]s a general rule, there is no duty to conduct a prior art search, and thus there is no duty to disclose art of which an applicant could have been aware.'"[12] Instead, the duty recognized by the Federal Circuit arises *only* when an attorney is "on notice of certain factual issues which may have been material to the prosecution of the patent application."[13] Thus, "a duty to investigate does not arise where there is no notice of the existence of material information" and "[t]he mere possibility that material information may exist will not suffice to give rise to a duty to inquire; sufficient information must be presented to the attorney to suggest the existence of specific information the materiality of which may be ascertained with reasonable inquiry."[14]

This duty of reasonable inquiry is also limited to individuals who are substantively involved with an application's preparation or prosecution and have actual, subjective knowledge of facts warranting further investigation.[15] Importantly, the duty to disclose "applies only to individuals, not to organizations."[16] Thus, absent *actual* knowledge of facts material to patentability or facts and circumstances warranting further investigation, individuals with a duty to disclose are not under an obligation to further investigate, nor are they charged with the knowledge of facts known by others in an organization that could be material to patentability.[17]

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[10] *See*, 87 Fed. Reg. 45,764, July 29, 20221 (the "July Notice").

[11] *Brasseler, U.S.A. I, L.P. v. Stryker Sales Corp.*, 267 F.3d 1370, 1385 (Fed. Cir. 2001).

[12] *Frazier v. Roessel Cine Photo Tech, Inc.*, 417 F.3d 1230, 1238 (Fed. Cir. 2005) (quoting *FMC Corp. v. Hennessy Indus., Inc.*, 836 F.2d 521, 526 n.6 (Fed. Cir. 1987) and collecting cases).

[13] *Brasseler*, 267 F.3d at 1385; *id.* at 1382 ("There is no need for an attorney to pursue a fishing expedition to obtain information.").

[14] *Id.* at 1382.

[15] *Id*. at 1383 ("Once *an attorney, or an applicant, has notice* that information exists that appears material and questionable, *that person* cannot ignore that notice in an effort to avoid *his or her* duty to disclose.") (emphasis added); 37 C.F.R. § 1.56(c).

[16] USPTO, Manual of Patent Examining Procedure (MPEP) § 2001.01.

[17] *See, e.g.*, *Inline Packaging, LLC v. Graphic Packaging Int'l, LLC*, 351 F. Supp. 3d 1187, 1205 (D. Minn. 2018).

The July Notice, however, suggests a duty of reasonable inquiry that would go beyond what the Federal Circuit has recognized.[18] By suggesting that the duty of reasonable inquiry may require a review of submissions to FDA where there is no notice of the existence of material information and based solely on the mere possibility that material information may exist, this statement could suggest a duty of disclosure that would be contrary to Federal Circuit law. As the Federal Circuit has explained, "[t]here is no need for an attorney to pursue a fishing expedition to obtain information."[19]

Further, the July Notice states that "[d]eliberate schemes or established practices" to shield practitioners "from obtaining knowledge of material information" violates the duty of candor and good faith under 37 C.F.R. § 1.56(a).[20] But, "walling off the patent prosecution practitioners from the attorneys seeking FDA approval" may be necessary for legitimate reasons. For example, it might be necessary to erect such a screen to comply with protective orders, patent prosecution bars or ethical considerations. An organizational structure that separates patent and regulatory lawyers also might be an appropriate business practice that reflects the different job functions and skills of each group. Moreover, the patent owner and marketing applicant might be two different entities that have an arm's length relationship.

In each of these ways, the July Notice describes a duty of reasonable inquiry that would be broader in scope than the Federal Circuit and the USPTO previously have recognized. If this is the case, BIO asks that USPTO clarify its description of the duty of reasonable inquiry to more precisely conform to existing law. Such clarification will enable stakeholders to more accurately assess the confidentiality implications that would result from any disclosure to the USPTO of trade secrets or confidential commercial information that may be required by the duty of reasonable inquiry.

Q3. 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?

Hatch-Waxman Act and BPCIA litigation typically proceed on a statutory and/or procedural timeline created by Congress and implemented by the Courts. By enacting the Hatch-Waxman

[18] 87 Fed. Reg. at 45,766 ("[t]his reasonable inquiry may comprise reviewing documents that are submitted to or received from other Government agencies, including the FDA. If any reviewed document is material to the patentability of a pending matter before the [USPTO], such as a patent application (including a reissue application), a reexamination proceeding, or an issue pending before the PTAB, the party has a duty to submit the information to the USPTO.").

[19] *Brasseler*, 267 F.3d at 1382.

[20] 87 Fed. Reg. at 45,767.

Act and the BPCIA, Congress created a streamlined, efficient approach to litigating drug patents for generics and biosimilars. Congress worked to strike a delicate balance between patent holders and challengers. Compromises to exclusivity and drug patent challenges were reached after much analysis and debate from consumers and industry experts, and those compromises are reflected in the rules and regulations governing Hatch-Waxman Act and BPCIA litigation.

Notwithstanding the operation of the two statutory schemes, generic and biosimilar applicants have made good use of the AIA's post-grant review process to challenge various drug patents. *See, e.g.*, https://www.bigmoleculewatch.com/bpcia-patent-litigations/. With an institution rate of 77%, petitioners for *inter partes* review of biotechnology and pharmaceutical patents have achieved successes no better or worse than in other technologies.[21] Thus, there is no need to create any exceptions or changes to the rules governing the AIA's post-grant review process given the procedures Congress created in the relevant acts and the existing rules governing AIA practice. Moreover, any discourse surrounding the allegedly high costs of challenging multiple patents in post-grant review proceedings or at the District Court level is refuted by the benefit challengers see from economies of scale, especially when the patents are in the same family (discussed above). With the same experts and overlapping prior art references, there is a negligible difference between the cost of challenging one patent and challenging multiple patents in the same family.

Q4. How can the PTO 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 PTO-FDA process for adjudicating applications for PTE and in the opportunity for public comment on such applications.

Under current practice, the PTO determines the period of PTE that is granted, if any. The "FDA's primary responsibility is to [determine] a product's eligibility for patent term restoration and to provide information to PTO regarding a product's regulatory review period." Additionally, "FDA also has the responsibility for due diligence petitions and due diligence hearings." [22]

While current practice seems to work well, the determination of PTE eligibility and the duration of PTE is ripe for a true joint effort between the two agencies, especially given that the PTO currently makes the determination based on events that occurred under FDA supervision. The current process for assessing PTE eligibility and the duration is a clear, well-established six-step procedure that delineates the roles and responsibilities of each agency[23]:

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[21] https://www.uspto.gov/sites/default/files/documents/ptab__aia_fy2022_roundup.pdf

[22] https://www.fda.gov/drugs/cder-small-business-industry-assistance-sbia/small-business-assistance-frequently-asked-questions-patent-term-restoration-program

[23] *Id.*

1. The applicant must show that the patent has not expired.

2. The applicant must establish that the patent has not previously been extended.

3. The patent owner or its agent must submit an application for patent term restoration that includes details about the patent and the activities undertaken to secure FDA approval.

4. The applicant must establish the product was subject to a regulatory review period before its commercial marketing or use.

5. The applicant must show that the product either represents the first permitted commercial marketing or use of the product after such regulatory review period or, in the case of a product manufactured under a process patent that primarily uses recombinant deoxribonucleic acid (DNA) technology, represents the first permitted commercial marketing or use of a product manufactured under the process claimed in the patent.

6. The applicant must submit the application for patent term restoration to PTO within 60 days of FDA approval of the commercial marketing application.

The agencies, however, could collaborate to make the determination of PTE eligibility and the duration by a joint decision by both agencies. This could make the process easier and more streamlined, and makes good sense given that PTE necessitates an assessment by both agencies. The ultimate authority for granting the PTE petition should remain, however, with PTO given that the end result may be the extension of a patent term.

Q5. The FDA already publishes PTE applications on www.regulations.gov, and the PTO publishes PTE applications on its Patent Center portal (https://patentcenter.PTO.gov/), which replaced the Public Patent Application Information Retrieval (PAIR) system. The PTO also recently provided centralized access to a listing of PTE applications filed during the last five years at www.PTO.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?

In addition to what is already being published, information that explains why the patent is eligible for PTE would be useful to the public and industry. Such information would be helpful in gauging the likelihood of obtaining PTE and the length of PTE. For example, details about the overall FDA approval process that took place, including the overall timeline, the number of meetings and committees involved and the amount of PTE sought, would be helpful data points so that the public and biopharmaceutical industry can have a better understanding of the circumstances for which PTE has been and will be granted, while at the same time provide some level of expectation regarding the extension period.

Q6. What policy considerations or concerns should the PTO 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")?

While these considerations and concerns are important to both innovators and generics and biosimilar applicants, they are unrelated to issues of patentability. The question of whether a novel method of use can be patented or whether such patent is valid is wholly separate from whether FDA can approve a 505(b)(2) application or an ANDA that contains a label with less than all approved indications. As such, there appears to be no legitimate role for PTO to play in this regard. In addition, 505(b)(2) applications are more commonly used by generic manufacturers, not innovators.

Notwithstanding, the FDA's use of, and reliance on, use codes is ripe for further discussion. Use codes serve little purpose in the patent context, given that a generic challenger is perfectly capable of reading and interpreting patent claims just like anyone else, and is obligated to review and consider the claims of the method of use patent, regardless of what the use code says. BIO members have expressed diverse views about the value of use codes, and many believe that FDA's use of codes has created problems and confusion within the biopharmaceutical industry and the public. To the extent that the FDA requires assistance in making a determination as to whether a patent claims an approved method of use, the FDA can – and should – consult with the patent owner. The patent owner is in the best position to understand the full scope and reach of its patent. The use of use codes (restricted to 250 characters) as a surrogate for the full scope of a patent and all of its claims is not appropriate or warranted.

Whether a generic drug manufacturer correctly carves out information related to a patent-protected method of use is ultimately a question of infringement, left in the first instance for the patent owner to assess, for the defendant to dispute, and ultimately for the courts to adjudicate. Neither the FDA nor the PTO should abridge those rights and responsibilities through the use code mechanism.

Q7. What policy considerations or concerns should the PTO 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 PTO and the FDA to evaluate?

A Risk Evaluation and Mitigation Strategy (REMS) is a drug safety program that the FDA may require for certain medications with serious safety concerns. REMS programs help ensure that the benefits of the medication outweigh its risks. By way of example provided by the FDA, Lilly's Zyprexa Relprevv, a long-acting injectable anti-psychotic medication used to treat schizophrenia in adults, can cause post-injection delirium sedation syndrome, symptoms of which include sedation, coma, and delirium which occurred in clinical studies within 3 hours of

treatment.[24] The risk is small (less than 1 percent), but the FDA required Zyprexa Relprevv's manufacturer to develop a REMS program to ensure that the drug is administered only in certified health care facilities that can observe patients for at least three hours and provide the medical care necessary in case of an adverse event.[25] While the FDA evaluates the need for a REMS program based on the safety, efficacy and adverse effects of a drug, patents covering a specific REMS program that presents a novel and nonobvious method for assessing drug safety must be evaluated by the PTO on its own merits. In short, a specific REMS program is assessed, evaluated and analyzed differently by FDA and PTO (when it appears in a patent application). An assessment by one agency has nothing to do with the other. If the conditions for patentability are met, patents covering a REMS program should be granted regardless of whether, when or how the REMS program came about or was implemented.

The question whether a so-called REMS patent should be listed in the Orange Book is separate from the PTO's determination of patentability. FDA is aware of long-standing uncertainty in this regard, but has yet to issue definitive guidance.

Q8. Apart from, or in conjunction with, the initiatives set forth in the PTO Letter, what other steps could the PTO 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?

BIO incorporates by reference its response to the PTO's October 4, 2022 Request for Comments, see 87 FR 60130 (available at: https://www.regulations.gov/comment/PTO-P-2022-0025-0111) and the data included therein, which appears in Appendix A hereto.

In short, a significant body of publicly-available data belie the assertion that "generics are taking longer to reach the market and prices continue to rise." Generics today are reaching the market no sooner or later than they did 30 years ago, but are acquiring more market share at a faster rate than ever before. Generic manufacturers challenge patents more often, earlier, and acquire market share faster. When innovators have developed improved or next-generation products, generic manufacturers have routinely entered the market with generic versions of both the original product and the improved formulation. In 50% of the cases, generic entry for the original and new formulations occurred around the same time. In the other half of the cases, generic versions of original products compete against branded second-generation products while patients and prescribers are free to choose between such product alternatives. Accordingly, there is no grounds or data to support the notion that generic drug manufacturers are being improperly delayed or lack the incentive to create generic versions of certain drugs. On the contrary, nearly 90% of all prescriptions filed in the US are filed with generic versions of an innovator drug.

[24] https://www.fda.gov/drugs/drug-safety-and-availability/risk-evaluation-and-mitigation-strategies-rems
[25] *Id.*

Q9. What additional input on any of the initiatives listed in the PTO Letter (1(a)-1(h)), or any other related suggestions for PTO-FDA collaboration, should the agencies consider?

The Patent Act, as amended in the Leahy–Smith America Invents Act and implemented, already provides the means for obtaining "robust and reliable patents [] needed to incentivize and protect the immense research and development investment essential to bringing such products to market and to spur the collaboration necessary for quick and speedy drug and biologic development."

One key goal of the Executive Order is to use robust and reliable patents "to incentivize and protect the immense research and development investment essential to bringing such products to market and to spur the collaboration necessary for quick and speedy drug and biologic development." It is the pharmaceutical innovators and patent-holders who invest heavily in research and development to quickly bring new drugs to the market. Studies estimate that it costs, on average, $2.8 billion to bring a new drug to market. Wouters OJ, McKee M, Luyten J (March 2020). "Estimated Research and Development Investment Needed to Bring a New Medicine to Market, 2009-2018". JAMA. 323 (9): 844–853. In exchange for their disclosure of these drugs and associated innovations to the public, pharmaceutical innovators are granted patents. Generic manufacturers are able to capitalize on not only the public disclosures made by pharmaceutical innovators, but the clinical data they provide to the FDA as well. Use of this information enables generic manufacturers to offer drugs at a low cost. Without the information and investment provided by pharmaceutical innovators, generic manufacturers would need to incur the costs of both research and development and clinical trials, which would result in higher drug prices.

In addition, the patent examination process as it currently exists works to weed out obvious variations and prevent the issuance of patents that are not patentably distinct. Thus, any fears of "evergreening" or "patent thickets" are unwarranted. The patent law is clear that one invention yields one patent. As an additional check, post-grant proceedings such as *inter partes* review and post-grant review provide effective, low-cost means for reviewing biotech and pharmaceutical patents. *Inter partes* review and post-grant review frequently narrow the scope of claims, either via amendment, disclaimer, or developments in the prosecution history. *Aylus Networks, Inc. v. Apple Inc.*, 856 F.3d 1353 (Fed. Cir. 2017). If a patentee succeeds in avoiding an invalidation based on prior art by showing that its invention is narrowly targeted to a new improvement, its statements to the PTO are binding, especially statements made in an *inter partes* review proceeding. Finally, the narrative that the PTO is somehow issuing poor quality biotechnology and pharmaceutical patents implies that the PTO is failing to properly examine patent applications, which is simply untrue.

IV. CONCLUSION

Biotechnology and pharmaceutical companies are critically important in both their promotion of innovation and the resulting positive social returns generated by their innovation. The concerns stated in President Biden's Executive Order surrounding the industry's perceived patent practices are unfounded and inconsistent with empirical evidence. The data indicate that a discrete number of patents are associated with biotechnology and pharmaceutical innovations similar to other industries.

Our patent system in its current form includes robust checks at each level of the prosecution system and post-grant review. At the prosecution level, rigorous examining procedures prevent the issuance of patents that would be obvious or lack novelty. At the post-grant level, administrative proceedings including *Inter Partes* Review and Post Grant Review allow third parties an opportunity to challenge the validity of a patent. Finally, judicially crafted doctrines, such as obviousness type double patenting and unenforceability due to unclean hands operate as an additional level of checks on issued patents.

There is no tenable basis for the FDA to take on a role in the issuance of patents, nor is there a tenable basis for the PTO to take on a role in the approval of drugs. Each agency has its own discrete function and expertise. Save for the limited areas identified in this Comment where collaboration may be appropriate, there is no apparent need to impose any new or any additional restrictions on either agency. Any new initiative that would require the two agencies to work together in carrying out their respective functions would not "promote greater access to medicines for American families."

Respectfully Submitted,

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By: /s/ *Michael Sitzman*
Michael Sitzman
Hon. Jim Greenwood
Christian F. Chessman
Monica De Lazzari
DLA Piper LLP (US)
500 Eighth Street, NW
Washington, DC 20004

Counsel for BIO

By: /s/ *Hans Sauer*
Hans Sauer
Vice President, Intellectual Property
Biotechnology Innovation Organization (BIO)
1201 New York Ave NW Ste. 1300,
Washington, DC 20005

Appendix A

Statistical Category	Empirical Data	Source
Patent Quantity Data		
Average ranking of drug and biopharmaceutical companies among the top 300 patent holders	198th Constitute 2.6% of the top 300 patent holders	https://ipo.org/wp-content/uploads/2022/01/2021-Patent-300%C2%AE-IPO-Top-Patent-Owners-List-FINAL.pdf
Average number of patents listed in the Orange Book per drug – New Molecular Entities (NMEs)	3 - 5 patents	*Kapczynski et al. PLOS Online 2012* *Grabowksi et al. J. Health Econ. 3 (2017) 33-59* *Hemphill and Sampat, J. Health Econ. 31 (2012) 327-339* *Oulette, Mich. Telecom. Tech. L.R. 17 (1) (2010)* *Van de Wiele et al., Health Affairs 41(8) (2022) 1117-24* *Lietzan and Acri*, 2022 available at: https://papers.ssrn.com/sol3/papers.cfm?abstract_id=4230310 https://www.patentdocs.org/2019/01/guest-post-the-final-score-2018-drug-biologic-patent-approvals.html https://onpointanalytics.com/pharma/patent-proliferation/
Average number of non-active ingredient (AI) patents listed for each NME in the Orange Book	2 patents	*Kapczynski et al*. PLOS Online 2012 *Grabowski et al*. J. Health Econ. 3 (2017) 33-59 *Walsh et al.*, JAMA Int'l Medicine 181, (2021) 995
Percentage of patents added to the Orange Book with priority dates coming ***after*** FDA approval of the NME	6%	BIO Study of 138 NMEs between 2004-2019.

Statistical Category	Empirical Data	Source
Average number of biologic patents involved in BPCIA litigation	7 patents	https://www.bigmoleculewatch.com/bpcia-patent-litigations/ https://purplebooksearch.fda.gov/
Average number of patents obtained per $10M spent on R&D	5.5 for the top 20 patentees 0.5 for drug and biopharmaceutical companies (92% lower)	https://ipo.org/wp-content/uploads/2022/01/2021-Patent-300%C2%AE-IPO-Top-Patent-Owners-List-FINAL.pdf *Shackelford, B.* (2013, February) One in Five U.S. Businesses with R&D Applied for a U.S. Patent in 2008. Retrieved from https://www.nsf.gov/statistics/infbrief/nsf13307/. *Wolfe, R.* (2019, May 13) Business Research and Development and Innovation: 2016. Retrieved from https://ncses.nsf.gov/pubs/nsf19318/.
Patent Term Data		
Average time to generic entry	13.3 years.	*Lietzan* and *Acri* report an average time to generic entry of 13.3 years. *Beall et al.* (2019) reported average time to generic market entry as 13.75 years for eighty-three top-selling drugs. *Gupta* (2020) reports an average time to generic entry of 13.3 years for a set of 370 drugs. *See* https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3748158
Average effective market life from FDA approval to generic entry	12.5 years	Data from *Wang et al.,* JAMA Internal Med 175 (2015) 635
Average market exclusivity period for drugs with sales greater than $250 million in the year prior to generic entry	12.5 years	*Grabowski H, Long G, Mortimer R, Boyo A.* Updated trends in US brand-name and generic drug competition. J Med Econ. 2016 Sep;19(9):836-44. doi: 10.1080/13696998.2016.1176578. Epub 2016 Apr 20. PMID: 27064194.

Statistical Category	Empirical Data	Source
Overall average market exclusivity period for drugs experiencing initial generic entry in 2013-2014	13.6 years	*Grabowski H, Long G, Mortimer R, Boyo A.* Updated trends in US brand-name and generic drug competition. J Med Econ. 2016 Sep;19(9):836-44.
Median time from FDA approval to patent expiration	10.4 years	*Kapczynski et al.* PLOS Online 2012 *Grabowksi et al.* J. Health Econ. 3 (2017) 33-59 *Hemphill and Sampat,* J. Health Econ. 31 (2012) 327-339 *Oulette,* Mich. Telecom. Tech. L.R. 17 (1) (2010) *Van de Wiele et al.,* Health Affairs 41(8) (2022) 1117-24
Litigation and Other Data		
Average Time from Brand launch to first Paragraph IV Notice challenging listed patents	6.3 years (down from 18.7 years in 1995)	*Grabowski et al.* J. Med. Econ. 24 (2021) 908-917
Percentage of NMEs experiencing Paragraph IV challenges to listed patents	81% (up from 9% in 1995)	*Grabowski et al.* J. Med. Econ. 24 (2021) 908-917
Number of BPCIA cases since inception of the Act	30 resolved; 4 pending	https://www.fda.gov/drugs/biosimilars/biosimilar-product-information
Reference biologics for which biosimilars are approved and launched	10	*Biehn & Nell*, AmerisourceBergen, U.S. Biosimilar Report (Dec. 2022)
Reference biologics for which biosimilars are approved but not yet launched	1	*Biehn & Nell*, AmerisourceBergen, U.S. Biosimilar Report (Dec. 2022)