

STRENGTHENING COMPETITION FOR
PRESCRIPTION DRUGS THROUGH PATENT
AND DRUG REGULATORY REFORM

A BLUEPRINT FOR REFORM

Over the last 30 years, drug prices in the U.S. have outpaced inflation by three-fold,¹ and thirty percent of Americans currently report not taking their medication as prescribed due to cost.² Retail spending on prescription drugs in the U.S. was \$335 billion in 2018, and by 2028, it is projected to reach \$560 billion.³ Policymakers on both sides of the aisle seek solutions to this critical issue.

Accelerating the entry of generic and biosimilar medicines is one policy objective often identified to decrease costs. Accomplishing this objective will require changes to U.S. laws and regulations, and more effective collaboration among different agencies. As the agency responsible for approving new drugs as well as generic and biosimilar products, the Food and Drug Administration (FDA) has a role to play.

But brand-name pharmaceutical companies also deploy many patent-related strategies⁴ that can make it difficult for would-be generic and biosimilar competitors to enter the marketplace and reduce costs. For example, some drugmakers obtain or apply for dozens - or in some cases hundreds - of patents⁵ to extend their monopolies in order to delay competition even though many of those patents cover trivial advances, which may subsequently be found invalid when challenged.

In light of the role patents play in the biopharmaceutical marketplace, the U.S. Patent and Trademark Office (PTO) also has a key function in addressing unjustified delays in the availability of lower-cost generic and biosimilar products. This will necessitate establishing coordination between the PTO and FDA, where currently little exists. Indeed, in response to an Executive Order by the Biden Administration,⁶ the FDA recently identified concerns over misuse and of the patent system and called for just this collaboration between PTO and FDA to support a competitive marketplace.⁷

This blueprint utilized I-MAK's Participatory Changemaking (PCM) model to synthesize information gathered through literature reviews, key informant interviews, and the convening of a diverse group of stakeholders. This process identified potential policy options to strengthen competition in the market. The recommendations were selected because they (i) have the potential to accelerate generic and biosimilar entry and (ii) are operationally feasible in the current system.

STRENGTHENING COMPETITION POLICY BLUEPRINT

LOWERING PRESCRIPTION DRUG COSTS THROUGH THE
U.S. PATENT AND TRADEMARK OFFICE AND U.S. FOOD
AND DRUG ADMINISTRATION



Strengthen the Process for Challenging Weak Patents at the PTO



1. **Create a single Patent Trial and Appeal Board (PTAB) challenge process** that allows all types of invalidity arguments to be raised.
2. **Reverse the policies** that allow the PTO to use “discretion” to deny challenges to possibly invalid patents on purely procedural grounds.
3. **Expedite post-grant patent review** for patents explicitly listed or related to approved products by the FDA (e.g., patents listed in the Orange Book or Purple Book).
4. **Improve the ability to search** PTAB decisions relating to Orange and Purple Book Patents.

Amend The Hatch-Waxman Act to Support Earlier Generic Entry



1. **Allow the FDA to recognize** PTAB decisions as legal authority to permit a generic drug to enter the market.
2. **Designate** certain new drug products for faster generic entry.
3. **Reform Orange Book listing practice** so that branded pharmaceutical companies only get one opportunity to list any and all patents that cover their product.

Expand Interagency Collaboration, Starting with Partnership Between PTO And FDA



1. **Require the FDA to share material** submitted as part of the drug approval process with the PTO.
2. **Allow the PTO to solicit and utilize FDA input** during examination and post grant review of Orange Book/Purple Book Patents.
3. **Require consultation** between the PTO and FDA on Patent Term Extension processes.



STRENGTHEN THE PROCESS FOR CHALLENGING WEAK PATENTS AT THE PTO

1. Create a single PTAB challenge process that allows all types of invalidity arguments to be raised

Problem: The Patent Trial and Appeal Board (PTAB) only considers certain patent disputes during two types of proceedings for challenging the validity of low-quality patents -- Post-Grant Review (PGR), which can be filed within the first nine months after a patent issues, and Inter Partes Review (IPR), which can only be filed after that window. Each procedure allows a third-party to petition the PTAB to take a second look at an issued patent, assess whether it was correctly granted, and cancel or amend any problematic claims. IPR provides a more limited review, with the PTAB assessing only whether the patent claims a truly new and non-obvious invention when compared to certain printed publications. PGR, on the other hand, considers all the key requirements for patentability, and a broader universe of evidence when evaluating whether the patent is valid. Consequently, nine months after issuance, a patent is immune from PGR review on important issues such as whether it fully describes the invention claimed or if it fits the kind of subject matter that is patentable.

Solution (Legislative): The America Invents Act statute (AIA) should be amended to create one harmonized PTAB process that allows challenges to be filed at any time after a patent is granted based on any of the key statutory requirements for patentability and based on broader types of prior art, as currently permitted for a PGR.

2. Reverse the policies that allow the PTO to use “discretion” to deny challenges to possibly invalid patents on procedural grounds

Problem: In recent years, the PTO has exercised discretion and adopted new policies that lead the PTAB to reject patent challenges filed under PGR and IPR for procedural reasons. This means the PTAB can deny an IPR or PGR challenge even if a case has legal merit and the PTAB may think that the patent is possibly invalid. These decisions, known as ‘discretionary denials’, cannot be appealed. Since 2017, discretionary denials have increased dramatically and negatively impacted the ability of manufacturers of generic and biosimilar drugs to use these proceedings to challenge weak patents that block competition.⁸

Solution (Administrative Action, Rulemaking, Legislative): A new PTO Director could reverse its position on discretionary denials by simply withdrawing the precedential decisions that created the policy, namely the *NHK Spring* and *Fintiv* decisions. However, more permanent changes are needed to preserve the positive impact of IPR and PGR. For example, the PTO should also engage in rulemaking to undo other recent policies that weaken IPR, and it should confirm that the preeminent factor in instituting an IPR petition is based on merit and the reasonable likelihood that at least one patent claim is invalid. Additionally, change is required to expand the range of prior art that could be considered in IPR, and to enable petitioners to appeal if they disagree with the PTAB’s decisions. Ultimately, legislation is the most clear and sustainable way to maximize IPR and PGR – and improve patent quality.

Case Study: Discretionary Denials

Invega Sustenna (paliperidone palmitate) is a monthly injectable schizophrenia drug marketed by Janssen and approved by the FDA in 2009. The patent listed in the Orange Book for the monthly dosing of the drug expires in 2031. In 2020 generic drugmaker Mylan challenged this patent at the PTAB. However, Mylan’s petition was dismissed by way of discretionary denial due to a parallel ongoing court proceeding on the same patent by another generic company. Had Mylan’s petition been accepted by the PTAB and Janssen’s patent found invalid, then generic entry could have occurred at least 7.5 to 10 years earlier if the FDA was allowed to recognize PTAB decisions (see page 5). The potential cost savings through these policy changes would be an estimated \$16.1 to \$19.6 billion dollars.⁹

3. Expedite post-grant patent review for patents explicitly listed or related to approved products by the FDA (E.g. patents listed in the Orange Book or Purple Book)

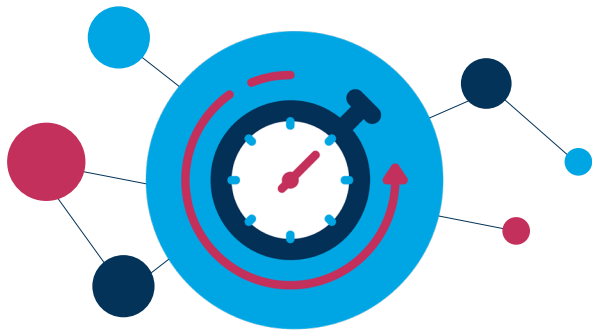
Problem: PTO review of IPRs and PGRs are completed within 18 months, but to achieve the critical public benefit of lower priced drug products expeditiously, this length of time is too long. When the Patent Office's decision--which typically triggers an appeal to the Federal Circuit that usually takes 12 months --that an Orange or Purple Book or related patent is invalid comes after a generic or biosimilar FDA approval, the public is harmed by delayed market entry and access to lower-cost products.

Solution (Administrative Action, Legislative): Given the importance of IPRs and PGRs to potentially bring generic and biosimilar drugs to market sooner, the PTO should expedite proceedings involving Orange Book and Purple Book patents to be completed in 12 months rather than the current standard of 18 months. To ensure this happens, Congress should designate a fast track to complete review of these critical patents more expeditiously.

4. Improve the ability to search PTAB Decisions Relating to Orange and Purple Book Patents

Problem: PTAB decisions are already made available publicly through the PTO website, but cannot be searched by drug product name.

Solution (Administrative Action): While the database can be searched by patent number or assignee, PTO could cross reference the Orange Book/Purple Book and also provide the drug products to which patents relate. This could be easily accomplished by the Patent Office on its own.



AMEND THE HATCH-WAXMAN ACT TO SUPPORT EARLIER GENERIC ENTRY

1. Allow the FDA to recognize PTAB decisions as legal authority to permit a generic drug to enter the market

Problem: The FDA can only allow a generic drug to enter the market if the relevant patents associated with the branded drug have expired or a district court has entered an order that they are invalid or not infringed. However, if the PTAB invalidates relevant patents related to a product, the FDA is not currently allowed to recognize that PTAB decision and allow a generic company to proceed towards market entry. In these scenarios, generic drug companies still have to take those PTAB decisions to the district court, seeking an order they can provide to the FDA. This adds another layer of delay, denying the FDA an opportunity to speed up generic competition that can lower drug prices.

Solution (Legislative): The Hatch-Waxman Act should be amended to harmonize current practices regarding the FDA's ability to recognize district court and PTAB decisions. This could also embolden generic companies to use the PTAB more often as a primary forum to invalidate patents, knowing they may be able to get immediate market entry from the FDA.

2. Designate certain new drug products for faster generic or biosimilar entry

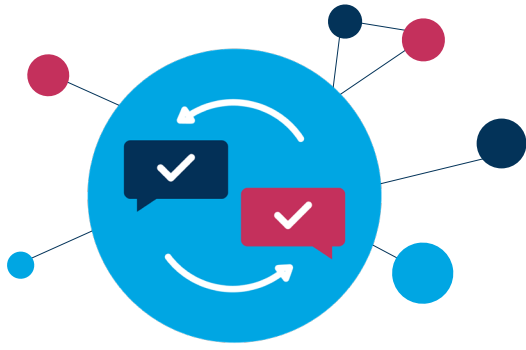
Problem: As a matter of public health, some therapies may need faster generic or biosimilar review by the FDA.

Solution (Administrative Action, Legislative): Some therapies should be designated by the FDA as justifying faster generic or biosimilar entry. For example, when a drug is not available and/or affordable, it would trigger such a designation. The Department of Health and Human Services (HHS), acting upon an Executive Order, should be directed to make such designations. Once designated, FDA could accelerate its review of a generic or biosimilar drug, similar to the emergency use authorization process. At the same time, the Hatch Waxman litigation or challenges at the PTAB could also be accelerated to resolve patent issues on a faster timetable parallel to approval. New statutory provisions would be required to ensure the judicial process keeps pace with the approval process.

3. Reform Orange Book listing practice so that branded pharmaceutical companies only get one opportunity to list any and all patents that cover their product

Problem: Branded pharmaceutical companies seeking to delay generic entry are able to time the issuance and listing of follow-on patents to delay the resolution of patent litigation. The Orange Book listing of follow-on and newly issued patents requires certification by generic applicants, which can trigger the branded companies to file new patent lawsuits. This can result in the delay of FDA approval and the market entry of generic versions.

Solution (Legislative): Orange Book listing practice should be reformed to prevent the serial listing of follow-on patents that create unexpected hurdles for generic entry. When filing a new drug application NDA holders should get one opportunity to list any and all patents that cover their product. Thereafter, no further Orange Book listing should be allowed. This practice would encourage the NDA holder to apply for and prosecute its patents quickly and efficiently, so that it is able to list its patents in the Orange Book in one comprehensive submission. Delay tactics arising from deferred patent prosecution would be discouraged. Changing the Orange Book listing practice would require Congressional intervention and likely an amendment of the Hatch-Waxman provisions.



EXPAND INTERAGENCY COLLABORATION, STARTING WITH PARTNERSHIP BETWEEN THE PTO AND THE FDA

1. Require the FDA to share material submitted as part of the drug approval process with the PTO

Problem: Patent applicants often have material relevant to their application that they submit to FDA but not the PTO because the disclosure obligations at PTO can be narrower than what is required by FDA. However, this information may be relevant to whether a patent should be granted for a claimed invention.

Solution (Administrative Action): The FDA recently published a letter¹⁰ to the PTO proposing a commitment to increased coordination between the two agencies relating to pharmaceutical patents. One recommendation is to mandate that material submitted to FDA in connection with product approval be disclosed to the PTO as well, so it can be considered during review of any relevant patent applications (e.g., those that may be listed in the Orange Book). This could assist a patent examiner in determining what knowledge the applicant already had in its possession and when it had such knowledge. For example, if the FDA requires routine experimentation to elucidate polymorphic forms of a drug substance during the product approval process, a patent examiner would likely find that information useful in evaluating the inventiveness of a subsequent patent application claiming various polymorphic forms¹¹ of the drug substance.¹² The sharing of information on drug products between FDA and PTO could be made through a memorandum of understanding between the two agencies that are kept confidential so as to avoid any issues relating to trade secrets.

Case Study: Sharing Approval Material

Sharing product approval material submitted to the FDA with the PTO could help evaluate whether associated patents meet the inventiveness standards. Revlimid (lenalidomide) is a cancer drug first approved by the FDA in 2005. The primary patent on the drug expired in October of 2019. Celgene also filed and was granted two additional patents covering polymorphic forms of the already patented compound lenalidomide. The two additional patents covering the polymorphic forms, expiring in 2024 and 2027, allowed Celgene to extend their patent protection on Revlimid. Had the FDA been able to share its materials on these polymorph patents with the PTO, specifically that polymorphic screening is part of the ordinary drug approval process and a result of routine experimentation, the PTO may have come to a different decision as to whether these additional patents should have been granted. In the event that the FDA material would have helped the PTO find the polymorph patents lacking inventiveness, then a generic version of Revlimid could have potentially entered the market six years earlier (2020 instead of 2026) and saved an estimated \$46 billion dollars.¹³

2. Allow the PTO to solicit and utilize FDA input during examination and post grant review of Orange Book/Purple Book Patents

Problem: Through its experience reviewing drug applications, the FDA may have an understanding of evidence that a claimed invention is already known or is common knowledge in a particular area of drug development that a patent examiner may not.

Solution (Administrative Action): FDA should be allowed to provide input during the examination of new patent applications and post grant review of patents in the Orange and Purple Book and related patent assets. FDA is in a unique position to understand what types of tests and data are required for an NDA submission, and would have knowledge of prior art and the level of skill in the art including whether claimed subject matter was derived from routine and even required routine experimentation done for regulatory reasons. Patent examiners and judges may lack this practical insight and this greater scrutiny during the patenting process and subsequent post grant review will cull out patents that contain subject matter borne out of routine regulatory experimentation.

This proposal could be implemented at both the examination level as well as the post grant review stage. The goal would be to reduce the number of obvious patents at the outset, and bolster the rigor of review in an IPR or PGR. An interagency working group could coordinate these efforts to ensure consistency with respect to review and standards, consistency over pharmaceutical art units at the PTO, and consistency between patent applicants' disclosures to the PTO and FDA. Implementing this change would require interagency coordination but may not require an act of Congress.

3. PTO should work with FDA on Patent Term Extension (PTE) Processes

Problem: The Hatch Waxman Act contemplates members of the public filing petitions with the HHS or FDA challenging the amount of time to which the patent is entitled to seek extension—this is a calculation that the statute leaves to HHS and the FDA, not to PTO. This is important because such extensions can delay generic entry if incorrectly granted. However, the public is hindered in filing petitions concerning patent term extensions because important information that is relevant for each patent is not readily available.

Solution¹⁴ (Administrative Action): PTO should coordinate with FDA to make it easy for the public to know when and how to file petitions with FDA to inform FDA of relevant facts that might affect the calculation of the appropriate length of PTE. To effectuate this, PTO should publicly list all of the PTE applications it receives, what drug(s) those applications pertain to, and the length of the extension requested. In addition, PTO should notify the public of any pertinent deadlines for public comment. The PTO has a webpage that lists all PTE applications granted (not received), and that list should be kept up to date.

ABOUT PARTICIPATORY CHANGEMAKING

This paper leveraged I-MAK's "Participatory Changemaking" (PCM) process, a multidimensional assessment of the patent system informed by real world insights and input from the public perspective. PCM brings together individuals from different geographic, political, personal, and professional backgrounds to generate new ideas of how to modernize the patent system. Interaction among stakeholder groups who hold different views about the role of patents in society is extremely limited, and a participatory process builds much needed connection and understanding between diverse participants. This multi-stakeholder approach delivers a policy blueprint that is implementable and inclusive of the public's interest, and that can create meaningful change.

This blueprint is a synthesis of literature review, interviews, and group dialogue with individuals and organizations representing stakeholders who hold or apply for patents, administer the system, and are affected:

- | | |
|------------------------------|----------------------|
| Patent lawyers | Consumers |
| Government agencies | Health system payers |
| Senior citizens | Affected communities |
| Patent judges | Academics |
| Healthcare advocates | Economists |
| Patent holders | Think tanks |
| Small and medium enterprises | Policymakers |
| Patients | Investors |
| Patent policy advocates | |

LEARN MORE ABOUT PCM AT

<https://www.i-mak.org/PCM>

ABOUT I-MAK

The Initiative for Medicines, Access, and Knowledge (I-MAK) is a 501(c)(3) organization with a mission to build a more just and equitable medicines system. Our framework integrates deep analytical research to influence policy, education to activate change, and partnerships to drive solutions. We bring decades of private-sector expertise and an evidence-based approach to this mission. Our work spans 50 countries and we collaborate with patients, drug manufacturers, patent offices, community leaders, public health professionals, policymakers, scientists, economists, and more across the globe. I-MAK's work on structural change in the patent system is featured regularly in the national and global press, as our data is cited in Congressional hearings and Committee reports. In early 2021, I-MAK proposed a 10 point plan¹⁵ to increase equity and competition through the patent system to help inform policy solutions going forward. I-MAK is committed to evidence-based research and education that will benefit American families and help lower drug prices, and therefore has never taken funding from the pharmaceutical industry.

LEARN MORE ABOUT I-MAK'S WORK AT

<https://www.i-mak.org/>



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ENDNOTES

¹ Drug Prices Outpaced Inflation Since the 1990's. USA Facts. 27 Jul 2021. <https://usafacts.org/articles/drug-prices-outpaced-inflation-since-the-1990s/>

² L Hamel, L Lopes, A Kirzinger, et al. Public Opinion on Prescription Drugs and Their Prices. Kaiser Family Foundation. 19 Oct 2021. <https://www.kff.org/health-costs/poll-finding/public-opinion-on-prescription-drugs-and-their-prices/>

³ SP Keehan, GA Cuckler, JA Poisal, et al. National health expenditure projections, 2019-28: Expected rebound in prices drives rising spending growth. Health Aff (Millwood). 2020;39(4):704-714. doi:10.1377/hlthaff.2020.00094

⁴ K Vokinger, A Kesselheim, J Avorn, et al. Strategies That Delay Market Entry of Generic Drugs. JAMA Intern Med. 2017;177(11):1665-1669. <https://doi.org/10.1001/jamainternmed.2017.4650>

⁵ House Oversight and Reform Committee. Drug Pricing Investigation. Majority Staff Report. December 2021. <https://oversight.house.gov/sites/democrats.oversight.house.gov/files/DRUG%20PRICING%20REPORT%20WITH%20APPENDIX%20v3.pdf>

⁶ The White House. Executive Order on Promoting Competition in the American Economy. 09 Jul 2021. <https://www.whitehouse.gov/briefing-room/presidential-actions/2021/07/09/executive-order-on-promoting-competition-in-the-american-economy/>

⁷ J Woodcock. U. S. Food & Drug Administration [Letter] 10 Sep 2021. <https://www.fda.gov/media/152086/download>

⁸ I-MAK. Lowering Prescription Drug Costs by Removing Barriers to Challenging Patents. Nov 2021. <https://www.i-mak.org/wp-content/uploads/2021/11/Removing-Barriers-to-Challenging-Patents-to-Help-Lower-Prescription-Drug-Costs-2021-11-30F.pdf>

⁹ Based on an I-MAK model of estimated revenue and spending for branded and generic Invega Sustenna from 2021–2031. The potential cost savings were calculated per year and summarized for the total period. The \$19bn estimate was based on the assumption of a generic product entering the market in 2021 following a successful PTAB challenge, while the \$16bn estimate assumed generic entry in mid-2023 following appeal by the patent holder. Broadly, the model is based on historical U.S. revenues of Invega products and incorporates projected annual growth rates of 5-9% during the ten-year period. A generic-eligible market was calculated and – consistent with historical examples of generic product pricing dynamics – prices for generic products reduced over time from 33% to 85% less than the branded product.

¹⁰ J Woodcock. U. S. Food & Drug Administration. [Letter] 10 Sep 2021. <https://www.fda.gov/media/152086/download>

¹¹ Many organic chemical compounds that form the active drug substance in a product inherently have different polymorphic forms. The different polymorphic forms of a compound can exhibit different properties that may affect physical properties, such as stability, of a product.

¹² Q6A Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances. <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/q6a-specifications-test-procedures-and-acceptance-criteria-new-drug-substances-and-new-drug-products>

¹³ Based on an I-MAK analysis of U.S. spending on Revlimid from 2020-2025. This six-year period reflects a hypothetical generic entry at the start of 2020 (given the primary '517 patent expiration in Q4 2019), to the start of 2026 when the actual settlement agreements with Celgene/BMS and various generic suppliers allow for unrestricted generic access. The potential cost savings were calculated as the difference between total spending on branded Revlimid versus generic equivalent each year. Key variables in the analysis period included, i) Revlimid revenues were projected based on actual figures through 2021 and modest projected annual growth rates of 5% were assumed for 2022-2025; ii) the share of U.S. revenue to total worldwide revenue was assumed to be 66%, based on available historical data; and iii) the discount of generic product to Revlimid was assumed to be 85%, consistent with recent small molecule generic pricing dynamics.

¹⁴ This solution was identified during our interview process by James Krellenstein and Christian Urrutia of PrEP4All and PrEP4All's counsel, Christopher Morten.

¹⁵ P Krishtel and T Amin. 10 Steps The Biden-Harris Administration Should Take To Bring Equity To Our Patent System. Medium. 17 Mar 2021. <https://medium.com/i-mak/10-steps-the-biden-harrisadministration-should-take-to-bring-equity-to-our-patentsystem-a50304bfe228>

Additional Resources

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