



Addressing Patent Thickets To Improve Competition and Lower Prescription Drug Prices

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 \$378 billion in 2021 (\$1,147 per person), and by 2031 it is projected to reach \$592 billion.³

The issue of patent thickets and its impact on drug prices is particularly relevant to discussions of equity in medicines and healthcare policy. Patent thickets refer to the practice of amassing numerous patents around a single product or technology, creating a barrier to market entry for potential competitors.

Research from I-MAK and academics has highlighted how brand-name companies often file multiple patents for the same drug to extend their market exclusivity. One type of patenting activity that happens in a thicket is when drugmakers apply for, and get, numerous patents after the Food and Drug Administration (FDA) approves a product. For example, I-MAK found that on average, 66% of patent applications on the top ten selling drugs in 2021 were filed after the FDA approval for a drug.⁴ Drugmakers have a strong incentive to protect the revenue stream by any means permitted under current patent law, and the drug's outsized importance to the company's bottom line leads to aggressive patenting activity. As a result, new drugs, generic and biosimilar medicines, and other health technologies face significant barriers to entry, which can keep prices high and limit access for patients.

To address these structural inequities and barriers, there needs to be a rethinking of the current standards for how pharmaceutical patents, in particular secondary patents on approved products, are granted by the U.S. Patent and Trademark Office (PTO). This is necessary for accelerating the entry of generic and biosimilar medicines. Equally, it is also important for changing the current incentives of the patent system and to encourage companies to invest in genuinely new inventions and medicines as opposed to focusing on preserving the life cycle of existing products. Policymakers on both sides of the aisle seek solutions to these critical issues, which affect the affordability and accessibility of medicines for patients, healthcare providers, and both public and private payers.

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 to reduce drug prices, and (ii) address patent thickets and improve patent quality.

Addressing Patent Thickets

POLICY BLUEPRINT

Four approaches and six solutions identified for lowering drug costs through patent reform



Strengthen Transparency, Public Participation, and Evidence-Based Policy

Create a mandatory requirement for drugmakers to provide the PTO and FDA with all patents and patent applications they own or license relating to a product, and make that information available to the public.



Strengthen the Obviousness Standard for Secondary Patents

1. Methods of use for indications disclosed or claimed in the primary patent for a product should make subsequent claims in secondary patents obvious.
2. Polymorph/crystalline patents should be considered obvious and unpatentable.
3. Create an independent panel of experts and patients at the PTO to assist in the examination of secondary patent applications related to approved products.



Secondary Pharmaceutical Patents Should Not Qualify for Presumption of Validity

Remove the presumption of validity for secondary pharmaceutical patents to shift the burden of proof, deter brand name manufacturers from asserting a thicket of weak patents, reduce the cost and time of litigation, and speed up generic and biosimilar entry.



'Use it or Lose it': Reducing Manufacturing Process Patent Thickets for Biologics

Given the twelve years of FDA exclusivity brand name biologic manufacturers have to change or modify their manufacturing process, biosimilar manufacturers should be allowed to request cancellation of any process patents that are not being used in relation to the product towards the end of this period.



STRENGTHEN TRANSPARENCY, PUBLIC PARTICIPATION, AND EVIDENCE-BASED POLICY

Create a mandatory requirement for drugmakers to provide the PTO and FDA with all patents and patent applications they own or license relating to a product, and make that information available to the public in a user-friendly format.

PROBLEM

Despite the growing body of evidence and public concern that brand-name drugmakers build patent thickets in order to delay competition and extend their market monopoly to maintain high drug prices,⁵ there remains strong opposition and denial of these findings from policymakers, academics, and the pharmaceutical industry.⁶

More transparency and access to patent data on pharmaceutical products is essential. Currently there are two public sources for patent information relating to branded products: the FDA Orange Book⁷ and the Purple Book⁸. However, it is well accepted that these public sources should not be solely relied upon to identify the complete range of patent claims that may be asserted or used by a brand name drug company to delay or block generic and biosimilar competition. For example, the FDA Orange Book does not require drug companies to submit all of its patents that cover or relate to a product. Nor does it require the listing of patent applications.⁹ Similarly, although the recent Purple Book Continuity Act of 2020 now requires the listing of patents for branded biologic products, the information is only limited to granted patents that are enforced as part of the patent litigation process against a particular biosimilar entrant. This excludes patent applications and other granted patents that a company may have in its patent thicket that it may assert against a different biosimilar entrant.¹⁰ As a result, large numbers of patents and patent applications

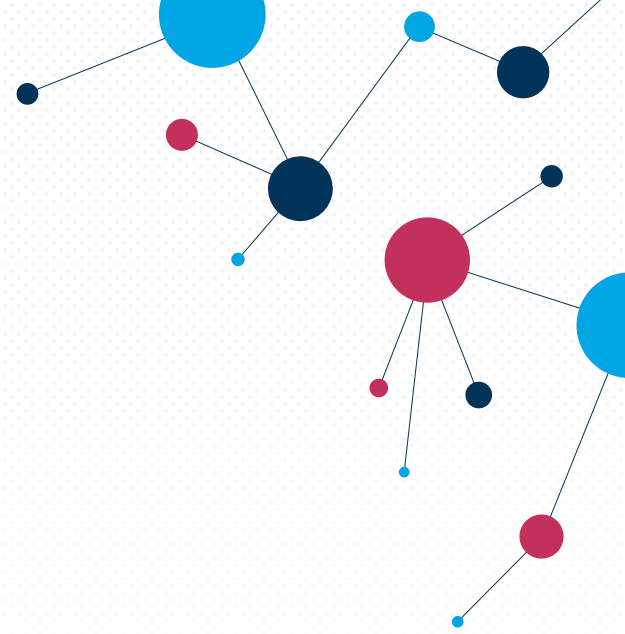
claiming or related to branded products are not publicly identified with those products.

Although the PTO provides a public database to search patents, it is only useful for those who have the resources and expertise to analyze the technical information provided in a patent document and its claims.¹¹ Searching for a patent by the active ingredient, brand name, or other search terms, can return dozens, hundreds, and thousands of patents in the results that are not associated with or cover that product, its manufacture, or its use. Simply publishing all patents and offering a database for searching does not actively promote transparency and greater participation by the public, policymakers, and those that may be affected by companies' patenting practices. Moreover, without the complete patent information that companies hold on brand-name drugs, policy cannot be evidence-based given this information asymmetry, which is one of the reasons why I-MAK created the Drug Patent Book.¹²

SOLUTION

(ADMINISTRATIVE ACTION, RULEMAKING, LEGISLATIVE)

The PTO, working with the FDA, should require that brand name drugmakers provide details of patent applications and granted patents covering or which could be asserted in relation to a product once it has been approved by the FDA. This information should also include patent applications and granted patents relating to a product that competitors may be able to work around to avoid infringement, as well as acquired and licensed patents. Companies should be required to provide this information within 30 days of a drug being approved. Details of all subsequent patent applications filed after FDA approval that relate to a product should be provided to the PTO within 30 days on an ongoing basis. The PTO should then tag such patent applications and granted patents with the drug's branded and generic names in its searchable database, in a user-friendly format. Making this information more transparent will not only help examiners identify related patents to a product and their novelty and obviousness assessments, it also brings greater public access, participation, and clarity to the policy-making process. Failure to provide this information within the required time period should mean such patents are not enforceable in litigation. ♦





STRENGTHEN THE OBVIOUSNESS STANDARD

Improve the obviousness standard in relation to the examination of secondary patents, such as methods of use, polymorphs, salt forms, and formulation patents.

- 1** | METHODS OF USE FOR INDICATIONS DISCLOSED OR CLAIMED IN THE PRIMARY PATENT FOR A PRODUCT SHOULD MAKE SUBSEQUENT CLAIMS IN SECONDARY PATENTS OBVIOUS.

PROBLEM

Pharmaceutical products are often approved to treat more than one condition (indication). In order to block competitors from researching or developing competing products using the same or related compounds or antibodies, the primary patents filed by companies are often very broad. Given that a company will have already established the mechanism of action of a compound or antibody before filing the primary patents, these primary patents will often disclose all the various indications that can potentially be treated by a compound or antibody, while also specifically claiming some of them. Companies will then file separate and subsequent patent applications covering aspects that the original description disclosed or claimed in the primary patents. Very often these secondary patent applications will separately claim the already disclosed indications from the primary patents as new inventions by specifying a dosage amount (e.g., once-daily dosing) or other marginally refined features in order to avoid the patent application being rejected on the grounds of obviousness.¹³ Under current law, these secondary patent applications covering methods of use for different indications disclosed or claimed in an existing patent are usually considered non-obvious. These types of secondary patents not only

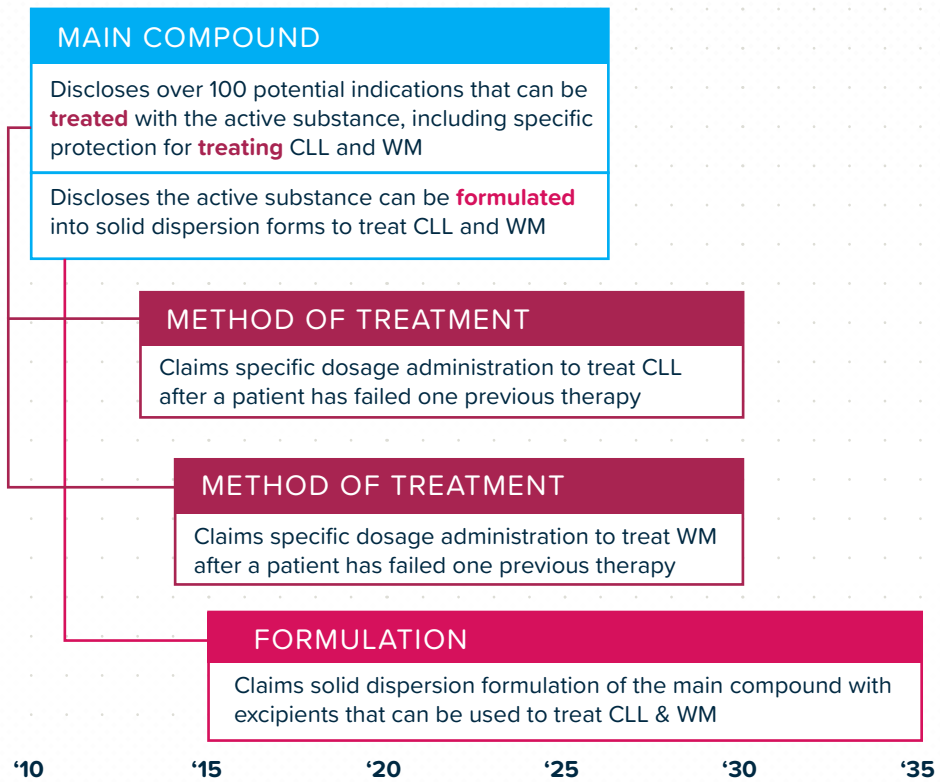
allow drugmakers to build out their patent thicket, they also help extend the period of protection resulting in the delay of generic and biosimilar competition.¹⁴

SOLUTION

(ADMINISTRATIVE ACTION, RULEMAKING, LEGISLATIVE)

Congress should pass legislation whereby a secondary patent claiming a method of use for an indication which has already been disclosed and/or claimed in a primary patent relating to a product is obvious and, therefore, unpatentable. The PTO should change its examination guidelines and practice in accordance with such legislation. ♦

AbbVie's drug Imbruvica (ibrutinib) is a small molecule drug approved to treat a variety of B cell cancers, including leukemia and lymphoma. In one of its primary patents (U.S. Patent 7,514,444 expiring December 28, 2026), AbbVie disclosed over 100 potential indications that ibrutinib and related compounds may treat, as well as claiming specific protection for a method of treating chronic lymphocytic leukemia and Waldenstrom's macroglobulinemia. Subsequently, AbbVie filed and was granted separate patents for a method treating Waldenstrom's macroglobulinemia and chronic lymphocytic leukemia with a specific dosage (U.S. Patent No. 9125889 expiring July 31, 2031 and U.S. Patent No. 9801881 expiring June 3, 2031). These patents add five years of extra patent protection beyond the primary patent 7,514,444. Notably, because of these and other later expiring patents, generic companies have settled with AbbVie and will only now enter the market in 2032 as opposed to in 2027 after the primary patent expires. The five years of additional patent protection is expected to help AbbVie secure over \$7 billion in U.S. revenue.¹⁵



WM = WALDENSTROM'S MACROGLOBULINEMIA

CLL = CHRONIC LYMPHOCYTIC LEUKEMIA

PROBLEM

In 2000, the FDA published guidance setting out how polymorph/crystalline forms of small molecule compounds should be monitored and controlled by companies for new drug substances and products.¹⁶ The guideline states:

“Some new drug substances exist in different crystalline forms that differ in their physical properties. In cases where differences exist that have been shown to affect drug product performance, bioavailability, or stability, then the appropriate polymorph should be specified.”

The guidance explains how physicochemical measurements and techniques are commonly used to determine whether multiple forms exist, and when and how polymorph/crystalline forms should be monitored and controlled. As polymorph/crystalline forms are inherent in the original compound and are found through screening, they are inevitably lacking in novelty and are obvious. Despite the FDA guidance on the routine testing and experimentation for polymorph/crystalline forms in order to achieve marketing approval, the PTO and courts have consistently determined these forms to be inventive and patentable on the grounds

that they are ‘unpredictable.’¹⁷ This practice of patenting polymorph/crystalline forms allows drugmakers to prolong their patent protection on a product beyond the primary patents and block potential alternative routes generic competitors might take. The patenting of polymorph/crystalline forms not only delays competition and allows drug prices to be kept high, it also adds to the patent thickets companies seek to create.

SOLUTION

(ADMINISTRATIVE ACTION, RULEMAKING, LEGISLATIVE)

Congress should pass legislation making polymorph/crystalline patents obvious and, therefore, unpatentable. The PTO should change its examination guidelines and practice in accordance with such legislation. ♦

CASE STUDY: POLYMORPH PATENTS FOR REVLIMID

Celgene’s Revlimid (lenalidomide) is a cancer drug first approved by the FDA in 2005. The primary patent U.S. Patent No. 5,635,517 expired in October 2019. Celgene also filed and was granted several additional patents covering polymorph/crystalline forms of the already patented compound lenalidomide.¹⁸ During litigation, Celgene entered into settlements with generic companies, which allow for limited generic volume launch until January 2026. Only after January 2026 will the generic companies that settled be able to enter the market with unlimited volumes that will help further drive prices down. A key patent that resulted in generic companies settling to delay competition was U.S. Patent No. 7,465,800 covering a polymorph of the compound lenalidomide. This patent is set to expire on April 27, 2027, adding nearly seven additional years of high prices through patent protection beyond the primary patent. Had generic versions entered the market in 2020 when the primary patent expired, it could have potentially saved payers an estimated \$46 billion dollars.¹⁹ Notably the corresponding patent in Europe, EP 1667682, was invalidated in 2021 allowing for earlier generic entry there.²⁰

3 | CREATE AN INDEPENDENT PANEL OF EXPERTS AND PATIENTS AT THE PTO TO ASSIST IN THE EXAMINATION OF SECONDARY PATENT APPLICATIONS RELATED TO APPROVED PRODUCTS

PROBLEM

Research shows that, on average, an examiner at the PTO spends 19 hours reviewing a patent application, which can run from a handful of pages to several hundred.²¹ This short time frame includes an examiner needing to learn the technology behind the claimed invention, as well as searching for and reviewing the relevant evidence (prior art) to assess whether the application meets all the requirements of patentability. In contrast, an attorney drafting an application or defending against infringement charges will spend considerably more time than this, even orders of magnitude more. The PTO acknowledges that there has not been a comprehensive reevaluation of examination time management practices since the current examination time expectancies were established in the 1970s.²² This is despite the significant increase in patent applications filed since the 1970s and the more than doubling of the number of pharmaceutical patents being granted between 2005 and 2015.²³

The problem is further compounded when it concerns the examination of secondary patents on pharmaceutical products. In addition to having limited time to carry out the examination, examiners typically lack the experience of working in the pharmaceutical industry and drug development, including knowledge of the commonly practiced techniques that are obvious to the field.

Common examples of this could include how a salt form is selected for a small molecule compound, various routine formulation techniques, or manufacturing processes that are standard practice but are often allowed to be patented.²⁴ Simply relying on prior published patents and non-patent literature as prior art during examination does not always capture what is known and commonly practiced in the field. Such techniques may not be published or specifically cover the particular claimed invention in question, but would nevertheless be relevant to an obviousness assessment for one skilled in the relevant field. Also, patent

applicants regularly assert they have ‘unexpected’ or ‘surprising’ results and advantages by providing data (e.g., bioavailability or stability data) in order to overcome examiner objections. However, scrutiny of this data would benefit from a review by independent experts who have previously practiced in the pharmaceutical industry, comparing clinical trial and efficacy data and public interest lawyers familiar with pharmaceutical patent prosecution and validity standards.

SOLUTION

(ADMINISTRATIVE ACTION, RULEMAKING)

The PTO should set up an independent panel who are vetted to exclude those with ties to the brand name or generic/biosimilar industry, comprising of pharmaceutical scientists, clinical trial and efficacy data experts, physicians, public interest patent and intellectual property attorneys, academics, and patients affected by the drug in question to assist examiners in the examination of secondary patent applications covering or related to approved products. The panel should be a permanent fixture that has a rotating set of experts. This solution would be complemented by increased transparency of patent applications covering or related to approved products as described above on page 4 in order to ensure the panel only reviews applications related to marketed products. ♦



SECONDARY PHARMACEUTICAL PATENTS SHOULD NOT QUALIFY FOR PRESUMPTION OF VALIDITY

PROBLEM

Under the legal doctrine known as the presumption of validity, courts are obligated to defer to the PTO's initial determination that a claim made in a patent qualifies for protection unless the defendant can show by "clear and convincing" evidence that the PTO made an error granting the patent.²⁵ Given the limited time that patent examiners have to examine patent applications, and the fact that secondary pharmaceutical patents are often invalidated when there is no settlement, this burden of proof unfairly favors brand name pharmaceutical companies defending their patents. As a result of the presumption, brand manufacturers are likely to assert weaker secondary patents and create a thicket of patents that are too costly for generic and biosimilar companies to litigate. This strategy often results in settlements that delay competition and even reward brand name manufacturers with royalty payments.²⁶

SOLUTION

(LEGISLATIVE)

Congress should pass legislation that the presumption of validity does not apply to secondary pharmaceutical patents on an approved product. Changing the presumption of validity for secondary pharmaceutical patents would shift the burden of proof, help deter brand name manufacturers from asserting a thicket of weak patents, reduce the cost and time of litigation, and speed up generic and biosimilar entry. ♦



‘USE IT OR LOSE IT’: REDUCING MANUFACTURING PROCESS PATENT THICKETS FOR BIOLOGICS

PROBLEM

A growing body of research has shown that patent thickets play a key role in delaying competition and access to biosimilars in the U.S.²⁷ One study shows that on average nine times more patents are asserted against biosimilars in the U.S. than in Canada, and twelve times more patents are asserted when compared to the U.K. At the same time, biosimilars are entering the UK, Europe and Canadian markets more quickly than they do in the U.S.²⁸ Data from biosimilar litigation shows that the manufacturing process patents are the patent type most asserted by a substantial margin.²⁹ For example, I-MAK’s research on the drug Keytruda found that manufacturing process patents accounted for 40% of all patents identified in relation to the product.³⁰ A number of these patents are broad in nature and may cover the reference product manufacturing process as approved by the FDA. However, it is also the case that many of these manufacturing process patents were never intended to be used in relation to the product. They are entirely for defensive purposes to block alternative routes of manufacture that a biosimilar competitor may seek to adopt.

SOLUTION

(ADMINISTRATIVE ACTION, RULEMAKING, LEGISLATIVE)

A “use it or lose it” system should be created for biologic manufacturing process patents. Brand-name biologics receive 12 years of marketing exclusivity from the FDA when a product is approved. Any changes in the manufacturing process must be reported to the FDA according to whether the modification is substantial, moderate, or minimal.³¹ Given the 12 years of exclusivity brand name biologic manufacturers are given to change or modify their manufacturing process, biosimilar manufacturers should be allowed to request cancellation of any patents that are not being used in relation to the product towards the end of this period. The cancellation request for non-use would be akin to what exists under the Lanham Act for trademarks.³² The patent holder would then carry the burden to prove to the PTO and FDA whether a process claimed in a patent is being used in relation to the brand name product in question. In the event that the patent holder is unable to show how the manufacturing process claimed in a patent is being used for the product in question, the patent will be canceled and be unenforceable in litigation. This solution would help to prevent companies squatting on knowledge they have no intention of using other than to block competition, extract settlements, and royalties. ♦

About Participatory Chngemaking

This blueprint leveraged I-MAK’s “Participatory Chngemaking” (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
- Government agencies
- Senior citizens
- Patent judges
- Healthcare advocates
- Patent holders
- Small and medium enterprises
- Patients
- Patent policy advocates
- Consumers
- Health system payers
- Affected communities
- Academics
- Economists
- Think tanks
- Policymakers
- Investors

LEARN MORE ABOUT PCM AT [I-MAK.ORG/PCM](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. I-MAK is committed to evidence-based research and education that will benefit American families and help lower drug prices, and therefore have never taken funding from the pharmaceutical industry, including generic and biosimilar companies.

LEARN MORE ABOUT I-MAK’S WORK AT [WWW.I-MAK.ORG](https://www.i-mak.org)

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Endnotes

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¹⁷ Routine testing and information relating to polymorph/crystalline forms are provided by the drugmaker to the FDA during the Investigational Drug Application phase, but is not made public. The FDA maintains this information as a trade secret, often for several years, before a drugmaker will file patent applications covering the various polymorph/crystalline forms that have been tested.

¹⁸ *Supra*, 12

¹⁹ I-MAK, Strengthening Competition for Prescription Drugs Through Patent and Drug Regulatory Reform. February 28, 2022. Accessed Oct. 30, 2023. <https://www.i-mak.org/strengthening-competition-blueprint/>

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