IP PROTECTIONS FOR MEDICINES

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Intellectual property protections for medicines encourage investment in the time consuming, uncertain and expensive process of developing drugs that can improve and extend life. In addition, the U.S. intellectual property framework allows for the streamlined entry of generic and biosimilar medicines, which are a key contributor to reducing healthcare cost. This has created an environment where the U.S. is typically the first country to receive an approved medicine and where more than 90% of all prescriptions filled at the pharmacy are low-cost generics. [1,2,3]

While patent protections and regulatory exclusivity are in effect the patent holder has rights to enforce the patents and exclusively market a medicine. When the protections expire other companies can develop copies of the medicine, typically at a lower price. This has motivated interest in reducing exclusive rights to drug developers. The counter position is that without intellectual property protection there will not be the same degree of investment in research and development, including expensive and often unsuccessful clinical trials.

This whitepaper is a simple explanation of the system of intellectual property protection for medicines in the U.S., including the special protections offered for certain types of clinical data development. It also addresses misconceptions about biopharmaceutical intellectual property in the U.S.

INTELLECTUAL PROPERTY FOR MEDICINES:
Patent Protections and Regulatory Exclusivities

Intellectual property protection grants the patent owner the right to exclude others from making, selling, using or importing their invention. A patent in the U.S. has a basic term of no more than 20 years for all patented inventions including those incorporated within medicines.[4] Then, with the limited exception of patent term extensions (PTE), the patent expires, and the invention can be copied and marketed by others. PTE may be applied to offset delays from obtaining FDA approval.[5] However, these extensions cannot extend the patent beyond 14 years from FDA approval.

For most medicines, the manufacturing of the chemical or biologic agent is neither the highest value nor the costliest part of developing the invention. After identifying the potential medicine in drug discovery phases, there is a high cost of developing a medicine or vaccine that the clinical data demonstrates is safe and effective to be used

1 For simplicity “medicines” refers to medicines and vaccines throughout .

2 FDA Office of Generic Drugs Office of Generic Drugs 2021 Annual Report

3 Mulcahy, Andrew W., Comparing New Prescription Drug Availability and Launch Timing in the United States and Other OECD Countries. Santa Monica, CA: RAND Corporation, 2024.

4 20 years from the earliest priority date

5 A patent term may be extended up to five years for the first approval of a new active ingredient.

in humans. This takes roughly 10-15 years with an estimated cost of $1bilion to more than $2 billion, when including the cost of capital, failed attempts and costing hundreds of millions of dollars in outlays for a successful drug.[6,7] Furthermore, while a patent has a 20 year term, small molecules have historically experienced generic entry after 13 to 14 years. Medicines with larger revenues experience face more patent challenges and earlier generic entry.[8]

Because developing the clinical data that demonstrates the safety and efficacy of a medicine is both high cost and carries sizeable risk of lost capital, Congress recognized the need to create additional incentives to support the investment in certain types of medicines. As a result, a number of regulatory exclusivities may be granted by the FDA. Regulatory exclusivity allows the exclusive rights to market the medicine or to use the information collected in clinical trials. It is granted by the FDA at the time of drug approval and runs concurrent with the patent term. No application may be submitted during the 5-year exclusivity period. This is typically five years for most small molecule medicines. For large molecule medicines the FDA cannot approve a biosimilar application for 12 years.[9] For small molecules, an FDA applicant can file for additional indications and receive additional three years of regulatory data exclusivity for those developments if a new clinical study was required. While regulatory exclusivity is in effect, another company cannot, except within very limited circumstances, receive FDA approval to market the originator medicine as a generic or biosimilar alternative.[10]

The FDA grants certain medicines additional regulatory exclusivities to encourage investment in clinical development in therapeutics that have a higher development cost or a lower expectation of profitability. This includes:

- Additional six months for studies in pediatric populations, added to the existing market, data or orphan exclusivity
- Seven years of exclusivity granted to drugs for “orphan” diseases that affect fewer than 200,000 people in the U.S.
- Five years added for certain type of infectious disease medicines

When a generic small molecule is approved, the generic is nearly always automatically substituted for a branded drug, except in limited circumstances.[11] So, unlike other inventions, a branded drug is largely moved out of use by government regulation. The first generic to a branded drug approved by the FDA is given 180 day exclusive

6 Congressional Budget Office, Research and Development in the Pharmaceutical Industry, April 2021

7 JA DiMasi , Grabowski, RW Hansen. Innovation in the pharmaceutical industry: New estimates of R&D costs. J Health Econ. 2016;47:20-33

8 Grabowski HG, Long G, Mortimer R, Bilginsoy M. Continuing trends in U.S. brand-name and generic drug competition. J Med. Econ. 2021; 24:1, 908–91

9 The regulatory data protection for biologics was established in the Affordable Care Act, policymakers established a longer period of protection relative to small molecules likely because of the higher cost of clinical development for biologic agents.

10 Another company can submit an application for FDA review while the originator drug still has active data exclusivity. FDA will not accept a generic application while the originator drug has an active regulatory exclusivity, but FDA would accept another application from a different company for the same active ingredient if supported by a new applicants own data. Regulatory exclusivity can be shorted from five to four years with a particular type of challenge to a patent (paragraph IV). The details of that process are more extensive than will be included in this whitepaper.

11 For example a physician indicates “dispense as written” on the prescription

period where the approved generic is the only generic available. This creates a strong incentive for a generic manufacturer to file as quickly as possible and encourages patent challenges. After this exclusive time period, the remaining approved generics may enter the market, typically at a lower price as they compete amongst one another for market share, creating a low margin business environment.

Large molecule medicines, known as biologics, do not have the same dynamics of competition at the end of their period of patent protections and regulatory exclusivity. A biosimilar is not necessarily therapeutically interchangeable, so the prescriptions are not automatically switched from a brand to a biosimilar. In addition, health plans or pharmacy benefit manufacturers may retain preferred placement for a branded biologic medicine in an effort to retain the rebates or put in utilization management for a biosimilar.[12] As a result, the branded biologic retains a larger market share relative to an off-patent branded small molecule medicine.[13] However, there is an FDA approval process for biosimilars seeking to be deemed interchangeable with the branded medicine, while states permit automatic substitution of biosimilars.

MISPERCEPTIONS ABOUT BIOPHARMACEUTICAL INTELLECTUAL PROPERTY PROTECTION

PATENT THICKETS:

Critics use the term "patent thicket" to refer to a product with so many patents that they believe there is an impenetrable wall of intellectual property protection deterring competition. There is no evidence that patent thickets exist in biopharmaceuticals where there are typically fewer patents relative to complex technologies such as smart phones.[14] The proliferation of generic medicines and 48 FDA approved biosimilars, and the average market exclusivity period of 13 to 14 years for small molecule branded medicines is evidence of a largely well-functioning system. [15,16]

PATENTS STOP COMPETITION:

While there are some medicines with no generic or biosimilar competition after 14 years, it is uncommon particularly for small molecules. Lack of generic or biosimilar uptake or entry can occur for myriad reasons not just patent protection, including contracting agreements

12 Yu, T., Jin, S., Li, C. et al. Factors Associated with Biosimilar Exclusions and Step Therapy Restrictions Among US Commercial Health Plans. BioDrugs 37, 531–540 (2023). https://doi.org/10.1007/s40259-023-00593-7

13 IQVIA, "Insights Into the 2023 U.S. Pharmaceutical Market", July 2023

14 USPTO Economic Working Paper No. 2018-01 February 2018

15 Grabowski H, Long G, Mortimer R, Bilginsoy M. Continuing trends in U.S. brand-name and generic drug competition. J Med Econ. 2021 Jan-Dec;24(1):908-917

16 FDA Biosimilar product information website lists 48 approved accessed https://www.fda.gov/drugs/biosimilars/biosimilar-product-information

with payers that deter entry or lack of interest from a generic company in launching a competitor (typically for small market products with high manufacturing costs). There is competition between different brands in the same therapeutic area. Over 90% of all prescriptions in the U.S. are dispensed as a generic demonstrating that the vast majority of the time patent protections expire, or do not apply, and allow for generic competition.[2]

GENERIC BLOCKED BY MULTIPLE PATENTS:

Generics companies may, and often do, challenge patents and receive approval prior to the expiration of certain patent protections. In fact, more than half of drugs receive a challenge from a generic manufacturer before the patent term expires.[17] As an example, an innovator could invent an extended-release formulation that is covered by a patent and a generic develops an extended-release formulation that meets the FDA generic approval requirements but is different enough that it does not infringe the patent. Many of these challenges are successful in having a generic enter the market prior to the expiration of the patent protection.

CLINICAL TRIALS ARE CONDUCTED TO EXTEND PATENTS:

A medicine approved for one indication may expand its use to other types of conditions by demonstrating it is a safe and effective treatment for that disease. New indications can also be used for different patient populations with the same disease or different stages of a disease. This is typically done through human clinical trials, most drugs are studied after the first indication is approved, and often patent holders seek approval in more than one indication.[18] This type of development for an additional indication can expand the profitability of an existing drug by expanding its use into a new population. Moreover, the additional indications can often be demonstrated with fewer clinical studies relative to the first approval.[19]

17 Kannappan S, Darrow JJ, Kesselheim AS, Beall RF. The timing of 30-month stay expirations and generic entry: A cohort study of first generics, 2013-2020. Clin Transl Sci. 2021;14(5):1917-1923. doi:10.1111/cts.13046

18 Skydel JJ, Luxkaranayagam AT, Dhruva SS, Ross JS, Wallach JD. Analysis of Postapproval Clinical Trials of Therapeutics Approved by the US Food and Drug Administration Without Clinical Postmarketing Requirements or Commitments. JAMA Netw Open. 2019;2(5):e193410. Published 2019 May 3. doi:10.1001/jamanetworkopen.2019.3410

19 Dhodapkar M, Zhang AD, Puthumana J, Downing NS, Shah ND, Ross JS. Characteristics of Clinical Studies Used for US Food and Drug Administration Supplemental Indication Approvals of Drugs and Biologics, 2017 to 2019. JAMA Netw Open. 2021;4(6):e2113224. doi:10.1001/jamanetworkopen.2021.13224

POLICY THAT ERODES INTELLECTUAL PROPERTY PENALIZES RESEARCHERS AND ACADEMIC CENTERS

One approach suggested as a means to reduce the time a medicine is protected by exclusive intellectual property rights is to exercise the use of 'march-in' rights by the federal government. 'March-in' rights were included in the Bayh-Dole Act, which was intended to create a uniform framework across the federal government that would encourage technology transfer between public and private sectors. The Act allowed for the federal government to "march-in" in limited circumstances when specific statutory requirements were not met. Essentially if all patents covering a commercialized product involved research funded by the federal government, the government could grant the right to a third-party company to manufacture and/or sell the product.

This approach has also been suggested as a way to reduce the price of a medicine. Initially, consideration of price as a basis for exercising march-in is not included in the Bayh-Dole Act and the drafters of the bill have stated that price was intentionally omitted from the march-in analysis. In reality, however, very few medicines are eligible for march-in if the statutory criteria were met. Most clinical research is funded by private industry, and even when there is government funding for foundational research, the medicine is typically also covered by other patents that were not funded by government research.

Moreover, Bayh-Dole patents are predominately held by universities, not biopharmaceutical companies. Universities take government funding and use their own funds to conduct primarily early-stage research. When an invention shows promise for human health a drug company may license the patent from the university, which creates an income stream for the academic institution. Expansion of the use of march-in rights would make this type of research significantly less valuable to the private sector and reduce royalties to universities for the rights to those patents.[20,21,22]

CONCLUSION

Intellectual property protections for medicines in the U.S. have created a system that encourages investment in clinical development, even for higher risk research or conditions where there is a low expectation of profitability. These protections expire and generic or biosimilar medicines lower costs leveraging the innovators' investment in

20 Jack Corrigan and Sara Abdulla. "Bayh-Dole Patent Trends" (Center for Security and Emerging Technology, August 2023). https://doi.org/10.51593/20230012

21 Oulette and Sampat, "THE FEASIBILITY OF USING BAYH-DOLE MARCH-IN RIGHTS TO LOWER DRUG PRICES: AN UPDATE", NBER Working Paper 32217, 2024

22 Bayh-Dole: Birch Bayh, Bob Dole, "Our Law Helps Patients Get Drugs Sooner," Wash. P. (April 11, 2002)

clinical study. While there is a significant amount of rhetoric about abuses of the patent system, in reality the evidence does not support that assertion. The vast majority of all prescriptions for drugs in the U.S. are filled with a generic or biosimilar medicines. Intellectual property protections for medicines are the foundation of a well-functioning research and development ecosystem that supports academic centers, private institutions and health.

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