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Re: Comments at the Listening Session on Joint USPTO-FDA Collaborative Initiatives

My comments at the Listening Session on the Joint USPTO-FDA Collaborative Initiatives, hosted at the U.S. Patent & Trademark Office on January 19, 2023, will present the empirical findings on patent data discrepancies in *Unreliable Data Have Infected the Policy Debates Over Drug Patents* along with the central claim of this policy brief about the key importance of evidence-based policymaking in the patent system. The policy brief is attached.

Best regards,

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POLICY MEMO

Unreliable Data Have Infected the Policy Debates Over Drug Patents

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The COVID-19 pandemic has vividly brought to the public's attention the key role of medical innovation in saving lives and increasing the quality of daily life. The pandemic has also precipitated an international debate over the role of patents and other intellectual property rights in the discovery, manufacture, and distribution of drugs and vaccines to patients. Even before COVID-19, there has been an ongoing policy debate in Washington, D.C., over drug prices and patents with congressional hearings, proposed legislation, and antitrust enforcement actions. The pandemic has thus made apparent what reliable data have already shown: poorly crafted legislation or antitrust enforcement actions could have a tremendous negative impact on the innovation economy in general and on healthcare specifically by undermining the incentives that drive the billions invested annually in the research and development of life-saving drugs and other medical treatments. Congress and regulators should engage in evidence-based policymaking on these important issues, which have far-reaching implications for economic growth and quality of life. This policy memo identifies a serious concern about the data in these discussions.

The Rise of I-MAK Data in the "Evergreening" Patent Policy Debates

The policy debate over patents and drug prices was first prompted by allegations by commentators and generic drug companies that innovators of new drugs abuse the patent system and extend their property rights beyond the original patent terms—a practice these critics brand as "evergreening." Drug innovators, they argue, obtain additional patent protections on new uses or new versions of breakthrough drugs to continue their market exclusivity and thereby prevent competition from generic drug manufacturers. In sum, drug innovators are accused of gaming the patent system in order to extend exclusive protections over drugs, causing drug prices to remain high for a longer time. Ergo, the complaints

about "high drug prices" as a symptom of a "broken patent system."

The rhetoric of "evergreening" has been strongly contested in both law and policy, and thus this policy memo will not review this well-trodden ground concerning the soundness of these arguments and whether this term is sufficiently precise or empirically grounded to guide evidence-based decision-making by courts or Congress.[1] Rather, the focus here is on an equally important part of the policy debate that has not yet received the attention it deserves: the nature and reliability of the data invoked in the "evergreening" arguments.

From the beginning of the "evergreening" debate, there has been a paucity of data on the total number of patents and of patent applications covering innovations in new medical treatments in these discussions. In recent years, Initiative for Medicines, Access & Knowledge (I-MAK) has become a principal, go-to source for this requisite factual information that ensures that policy claims are not merely political rhetoric. I-MAK is neither an academic center nor a think tank producing peer-reviewed research published in economic or scientific journals. It is a policy advocacy organization advancing its view that "a root cause of the high cost of medicines is an outdated patent system" that creates "unjust patent monopolies."[2] Consistent with its policy position, I-MAK publishes white papers and reports criticizing the role of patents in healthcare innovation.[3] I-MAK also files legal claims against drug patents; it was the first policy organization to file a petition in the Patent Trial and Appeal Board seeking to cancel a pharmaceutical patent—in that case, on a revolutionary drug to treat hepatitis C.[4]

To support its policy and legal activities, I-MAK created a database of patents and patent applications covering therapeutic products and processes created by biopharmaceutical companies and used by patients in the healthcare market.[5] On its website and in its white papers, such as the oft-cited *Overpatented, Overpriced* (2018) and *America's Bestselling Drugs of 2019*,[6] I-MAK reports the total number of patents covering drugs. For example, I-MAK asserts that 68 patents cover Lyrica, a drug produced by Pfizer to treat pain caused by nerve damage from diabetes, shingles, or other injuries.[7] Aside from whether this number is correct or not (the next section details evidence indicating why this and other patent numbers are unreliable), I-MAK's actual data (the patents, what the patents cover, etc.) and the coding variables used in its database are not available to the public or to other researchers.

I-MAK claims to be *the* authoritative source on the number of patents covering drugs and drug treatments, and its numbers have been accepted uncritically and relied upon by academics, witnesses at congressional hearings, and policymakers.[8] A recent example is an investigative report on drug pricing issued on December 10, 2021, by the House Committee on Oversight and Reform, in which I-MAK's patent numbers are authoritatively cited as factual support for the report's argument that excessive numbers of patents are a cause of high drug prices.[9] I-MAK's patent numbers are increasingly used by scholars and others arguing in law journal articles that patents are a principal cause of drug prices allegedly being too high, a problem to which they propose solutions among a myriad of antitrust enforcement actions or changes in patent law.[10] The ubiquity of I-MAK's numbers is understandable, if only because it has published the most wide-ranging and seemingly complete listing of total numbers of patents and patent applications in its various white papers and op-eds.

Questions of Unreliability in I-MAK's Patent Dataset

Unfortunately, the ubiquity of I-MAK's drug patent numbers in policy discussions and in the academic literature does not correlate with the proven reliability of its underlying dataset. It is unclear why there are discrepancies between the numbers of total patents reported in government sources,

such as by the Food and Drug Administration (FDA) or in court documents, and the drug patent numbers that I-MAK reports in the infographics, tables, and charts in its white papers. These could potentially be the result of differing definitions of "patents"; for instance, I-MAK's total patent numbers included in often-cited reports like *Overpatented, Overpriced* could include patent applications, patents issued by different countries, or both. Unfortunately, without access to the underlying dataset and coding variables I-MAK uses in producing its conclusions (the final numbers it publishes), confirming this is impossible.

A "spot check" of some of I-MAK's patent numbers highlights these concerns about the reliability and accuracy of its data. For example, as noted earlier, in its 2018 *Overpatented, Overpriced* report, I-MAK asserts that Lyrica has 68 patents covering it.[11] A different story is told by the Orange Book published by the FDA, which lists the drugs approved by the FDA for use by patients.

Before we continue, I must explain briefly what the Orange Book is and why its listing of patents is relevant in considering I-MAK's reported total patent numbers. The official title of this governmental report is "Approved Drug Products with Therapeutic Equivalence Evaluations," but it is known simply as the "Orange Book."[12] The FDA requires that drug innovators submit information on all patents for which a claim of infringement could reasonably be asserted against another person for making, using, or selling a drug or method of using such a drug without authorization.[13] The FDA lists these patents in the Orange Book. As such, the Orange Book definitively identifies all relevant patents covering a drug for any company seeking to make a generic version of this drug.

For Lyrica, the Orange Book identifies 4 patents covering this drug, but in actuality there are only 3 original patents. One of these 4 patents is a "reissue" patent, which is a patent reissued by the U.S. Patent and Trademark Office that corrects a mistake in form in a previously issued patent.[14] Since it merely corrects a formal defect, a reissue patent neither adds substantive protections beyond the original patent nor extends the time of the original patent.[15] A reissue patent simply replaces the original patent. Thus, in actuality, only 3 patents cover Lyrica.

This discrepancy in patent numbers is a surprisingly large—I-MAK asserts that 68 patents cover Lyrica and the FDA identifies only 3 patents covering Lyrica.[16] Perhaps I-MAK has some explanation for this vast discrepancy in patent numbers. Unfortunately, I-MAK's 2018 report provides no such explanation and simply lists 68 total patents as covering Lyrica.

This is not the only discrepancy found in I-MAK's claims about Lyrica. On the basis of its undisclosed data, I-MAK's 2018 report also asserts that Pfizer will retain exclusive rights over Lyrica until 2038—a whopping 20 years from the date of I-MAK's 2018 report and far beyond the 2027 expiration date of the patents listed in the Orange Book for Lyrica CR. Similar to the unexplained discrepancies concerning the total number of patents covering Lyrica, there are also discrepancies between I-MAK's reports and public sources concerning this period of exclusivity for Lyrica.

I-MAK's claim that Pfizer has exclusivity in Lyrica until 2038 means that no generic versions of Lyrica can be made until 2038. But the "main" patent for Lyrica (i.e., the original patent covering the drug's active ingredient) expired in December 2018, as confirmed by the FDA's approval of 9 generic versions of Lyrica in 2019 and the well-publicized 2019 entry into the market of a generic competitor of Lyrica. The generic drug manufacturer, Amneal Pharmaceuticals, announced in July 2019 that it had "received approval for, and launched, its generic version of Lyrica."[17] One media outlet reported in July 2019 that, for Pfizer's Lyrica, "its patent cliff is here."[18] (The "patent cliff" refers to the end of the patent term for a drug and other companies can then make, use, or sell the drug once they receive approval to do so by the FDA.)

As with its numbers of total patents, I-MAK offers no explanation for how it derived the 2038 date so that we can understand the almost 20-year discrepancy between I-MAK's claim of exclusivity for Lyrica until 2038 and the actual entry of a generic drug into the healthcare market in 2019. Instead, I-MAK simply states the conclusion. There may be a reasonable explanation, such as a definition of "exclusivity" in its coding of the data that differs from that used by lawyers and governmental officials to identify when the FDA approves a generic company to compete with a "branded drug" (a patented drug produced by a biopharmaceutical innovator and made available to patients). Unfortunately, it is impossible to determine if this discrepancy is merely an accidental error, a byproduct of differing classifications in identifying patents and patent terms, or something more.

Another example of unexplained factual discrepancies is in I-MAK's claims about the total patents covering Eliquis, a drug produced by Bristol Myers Squibb and Pfizer that reduces the risk of life-threatening blood clots caused by irregular heartbeats following surgery. In its 2018 report, I-MAK states that 27 issued patents and another 48 patent applications cover Eliquis. In its 2019 report issued the following year, I-MAK increases these numbers to 31 issued patents covering Eliquis with 49 total patent applications.

Again, it is unclear what these issued patents and patent application numbers represent and what explains the differences between 2018 and 2019 when I-MAK increased issued patents by 4 and increased patent applications by 1. There are many unanswered questions. Were the new patents and patent applications in the 2019 report merely mistakenly not counted in the report published in 2018? Are they entirely new patent applications or merely newly published applications (patent applications are published 18 months after filing if they are not yet issued as patents)? Were these US or foreign patent applications or patents? Also, what does it mean to say that there are 27 issued patents covering a single drug?

All of these questions about the reliability of I-MAK's numbers are concerning, and it is doubly concerning in the case of Eliquis. Similar to Lyrica, there is a surprising and stark contrast between the number of patents listed in the FDA's Orange Book and the patent numbers that I-MAK asserts in its reports. The FDA's Orange Book lists 3 patents covering Eliquis and its uses, not the 27 patents or 31 patents reported by I-MAK in 2018 and 2019, respectively.

Furthermore, Eliquis was the subject of patent litigation in the US, and the resulting court opinion provides an additional contrast in the number of patents identified by the court and the number of patents asserted by I-MAK covering this drug and its uses. In this lawsuit, Bristol Myers Squibb and Pfizer, the owners of the patents covering Eliquis and its uses, sued several generic companies for patent infringement of several of the patents listed in the Orange Book patents.[19] In August 2020, a federal district court ruled in favor of Bristol Myers Squibb and Pfizer; the court rejected the arguments by the defendants that the patents were invalid and concluded that the patents were infringed by the defendants.[20] The defendants appealed this decision, and the U.S. Court of Appeals for the Federal Circuit affirmed the district court's decision in September 2021.[21]

If there were 27 or 31 patents covering Eliquis, as claimed by I-MAK in its 2018 and 2019 reports, respectively, then Bristol Myers Squibb and Pfizer would have asserted in their lawsuit far more than the several patents listed in the Orange Book. The "evergreening" theory predicts that this must happen. According to it, the sole reason for a drug innovator to obtain numerous patents covering a single drug is to swamp a generic drug company with excessively high business expenses in its efforts to avoid liability or even higher legal costs in defending itself in court if formally accused of patent infringement. According to evergreening theory, the only way to impose these high litigation costs on generic drug companies would be to sue them for infringement of the 27

or 31 patents, and not limit a lawsuit to the few patents listed in the Orange Book. Moreover, if a drug innovator would not assert the 27 or more patents against an infringer, then there would be no viable threat that it would impose high litigation costs on future generic drug companies to prevent them from making and selling the drug. Beyond evergreening theory, it is well established in patent law that a patent owner will always assert all relevant patents against an accused infringer to ensure that its lawsuit will succeed even if the defendant successfully invalidates some of the patents (as the defendants attempted to do with the few patents covering Eliquis that were asserted against them by Bristol Myers Squibb and Pfizer).

In their patent infringement lawsuit, Bristol Myers Squibb and Pfizer relied on the few patents listed in the Orange Book for Eliquis, and not the 27 or 31 patents identified by I-MAK as covering Eliquis. These vast discrepancies raise legitimate questions about the reliability of the underlying I-MAK dataset. One possible explanation for these discrepancies is that they might result from I-MAK's inclusion of some patents not relevant to generics or biosimilars in its total patent counts. But this is only a guess. These and other questions are impossible to answer without knowing exactly how I-MAK collected its data on patents and how it classified ("coded" in the language of researchers) this data to produce its final tally of total patent numbers. But what is clear and undeniable is the consistency of the inconsistencies—and the vast differences in numbers—between I-MAK's numbers of total patents covering specific drugs and the numbers of patents covering these same drugs in official, publicly available sources such as the FDA's Orange Book and in federal court decisions.

This spot check of I-MAK's patent numbers produced other examples of discrepancies between I-MAK's patent numbers and the patent numbers listed in official, public sources. Xarelto, for example, is a drug produced by Janssen Pharmaceuticals to treat blood clots, and I-MAK reported in 2018 that 30 issued patents cover Xarelto with an additional 49 pending patent applications covering this same drug. In its 2019 report issued the following year, I-MAK increased the number of issued patents covering Xarelto to 32 and increased the number of pending patent applications to 51. I-MAK gave no explanation for the basis for these higher numbers. As with the two previously discussed drugs, Lyrica and Eliquis, there is a vast discrepancy between I-MAK's numbers and the listing of all relevant patents covering Xarelto in the FDA's Orange Book. Whereas I-MAK identifies 32 total patents covering Xarelto, the FDA's Orange Book identifies only 6 patents covering Xarelto and its uses by patients.[22]

Ultimately, there may be explanations for such repeated, vast discrepancies between the total numbers of patents and exclusivity periods reported by I-MAK and the official data on the patents covering these drugs that are found in governmental sources such as the FDA's Orange Book or court opinions. Still, these are *substantial discrepancies* in total numbers of patents—the differences are on the scale of an order of magnitude in some cases. In light of these factual discrepancies, I-MAK's empirical claims in the "evergreening" policy debate are an unreliable foundation for policymaking.

Conclusion

Policy advocacy organizations can and should contribute both empirical evidence and theoretical arguments to robust policy debates on important topics like medical innovation, the patent system, drug prices, and antitrust law. However, all data should be reliable in both form and substance in order to ensure "evidence-based policymaking, and not policy-based evidence-making."[23] With this in mind, I-MAK's reported numbers of issued patents, patent applications, and exclusivity periods for drugs are infected with serious questions of reliability and accuracy. There are repeated and vast discrepancies between I-MAK's numbers and the numbers found in official, publicly available governmental

sources like the FDA's Orange Book and court opinions. Until these questions are resolved according to rigorous norms of empirical research accompanied with reasonably clear explanations, the I-MAK data on total patent numbers and exclusivity periods should not be relied upon by scholars or policymakers.

Endnotes

1 *See, e.g.*, Erika Lietzan, *The Evergreening Myth*, Regulation (Washington, DC: Cato Institute, Fall 2020), https://www.cato.org/sites/cato.org/files/2020-09/regulation-v43n3-4.pdf; Joanna M. Shepherd, *The Legal and Industry Framework of Pharmaceutical Product Hopping and Considerations for Future Legislation* (Arlington, VA: Center for the Protection of Intellectual Property, Dec. 2020), https://cip2.gmu.edu/wp-content/uploads/sites/31/2020/12/Shepherd-Product-Hopping.pdf; Adam Mossoff, *Does Congress Really Want to Stop Medical Innovation?*, RealClearHealth (May 21, 2021), https://www.realclearhealth.com/articles/2021/05/21/does_congress_really_want_to_stop_medical_innovation_111212.html.

2 "Drug Pricing Crisis," https://www.i-mak.org/health-equity/#pricing (accessed June 20, 2021).

3 *See Overpatented, Overpriced: How Excessive Pharmaceutical Patenting Is Extending Monopolies and Driving Up Prices* (New York: I-MAK, 2018), http://www.i-mak.org/wp-content/uploads/2018/08/I-MAK-Overpatented-Overpriced-Report.pdf.

4 *See First-Ever U.S. Patent Challenges Dispute Gilead's Monopoly on Hepatitis C Drugs that Blocks Millions from Treatment* (New York: I-MAK, Oct. 25, 2017), https://www.i-mak.org/2017/10/25/first-ever-us-patent-challenges-gilead-hepatitis-c/.

5 *See* I-MAK Data, https://www.i-mak.org/data/ (accessed June 20, 2021).

6 *See America's Bestselling Drugs of 2019*, https://www.i-mak.org/2019-bestselling/ (accessed Jan. 2, 2022); *Overpatented, Overpriced*, http://www.i-mak.org/wp-content/uploads/2018/08/I-MAK-Overpatented-Overpriced-Report.pdf (accessed June 20, 2021). The specific numbers, but not the underlying dataset itself, is available at https://www.i-mak.org/overpatented-data/.

7 *See* https://www.i-mak.org/overpatented-data/. As of May 2020, I-MAK claimed 64 patents had been issued and 118 patent applications covered Lyrica. *See* https://www.i-mak.org/lyrica/.

8 *See, e.g.*, Kevin J. Hickey, Erin H. Ward, & Wen S. Shen, *Drug Pricing and Intellectual Property Law: A Legal Overview for the 116th Congress* (Congressional Research Service, Apr. 4, 2019), https://fas.org/sgp/crs/misc/R45666.pdf; *Durbin, Cassidy Introduce REMEDY Act To Lower Drug Prices By Curbing Patent Manipulation, Promoting Generic Competition* (Apr. 11, 2019), https://www.durbin.senate.gov/newsroom/press-releases/durbin-cassidy-introduce-remedy-act-to-lower-drug-prices-by-curbing-patent-manipulation-promoting-generic-competition; Michael A. Carrier, Response to Senator Grassley's Questions for the Record: Sen. Jud. Comm. Hearing on "IP and the Price of Prescription Drugs: Balancing Innovation and Competition" (May 28, 2019), https://www.judiciary.senate.gov/imo/media/doc/Carrier%20Responses%20to%20QFRs.pdf.

9 *See Drug Pricing Investigation*, Staff of House of Representatives Committee on Oversight and Reform, 117th Cong. (2021), 91, https://oversight.house.gov/sites/democrats.oversight.house.gov/files/DRUG%20PRICING%20REPORT%20WITH%20APPENDIX%20v3.pdf.

10 *See Drug Pricing Investigation*; *see also* Uri Y. Hacohen, *Evergreening at Risk*, 33 Harv. J. L. & Tech. 479 (2020) (citing I-MAK reports numerous times to support factual claims about patents covering drugs and proposing changes in patent law to stop "evergreening" practices); Ana Santos Rutschman, *Regulatory Malfunctions in the Drug Patent Ecosystem*, 70 Emory L.J. 347, 387 (2020) (citing I-MAK report for support of factual claim that "an average of 125 patent applications are filed per drug and an average of 71 patents are granted per drug" for the "12 top-grossing drugs in the United States in 2017").

11 *See supra* note 8, and accompanying text.

12 *See* Orange Book Preface, https://www.fda.gov/drugs/development-approval-process-drugs/orange-book-preface (accessed Jan. 11, 2022). Apparently, it was given an orange cover and became known as the "Orange Book" given that it was first published in October 1980, and the color was selected given the proximity to Halloween. *See* Jennifer Gershman, "4 Interesting Facts About the Orange Book," *Pharmacy Times* (March 13, 2018), https://www.pharmacytimes.com/view/4-interesting-facts-about-the-orange-book.

13 *See* 21 U.S.C. 355(b)(1).

14 Since the early nineteenth century, an inventor has been able to obtain a reissue patent to correct any formal defects in a patent that inadvertently undermined the substantive protections afforded by this patent. It has been a longstanding rule since the inception of reissue patents that a patent owner is prohibited from using a reissue patent to expand the scope of protections of the original patent. *See* Adam Mossoff, *Institutional Design in Patent Law: Private Property Rights or Regulatory Entitlements*, 92 Iowa

L. Rev. 921, 935-36 (2019) (discussing the nature and function of reissue patents).

15 *See* Manufacturing Co. v. Ladd, 102 U.S. 408, 411 (1880) ("The real object and design of a reissue of a patent have been abused and subverted" when it is used to expand the scope of the original patent.).

16 Even if one includes the additional patents listed in the Orange Book for Lyrica CR, this adds only 3 patents. Thus, this would bring the total number of patents covering both Lyrica and Lyrica CR to 6 patents.

17 Amneal Announces Launch of Generic Lyrica® (July 22, 2019), https://investors.amneal.com/news/press-releases/press-release-details/2019/Amneal-Announces-Launch-of-Generic-Lyrica/default.aspx.

18 Eric Sagonowsky, *Lyrica generics roll: Pfizer blockbuster finally hits patent cliff*, Fierce Pharma (July 22, 2019), https://www.fiercepharma.com/pharma/lyrica-generics-roll-pfizer-finally-hits-patent-cliff-for-nerve-pain-and-fibromyalgia.

19 This lawsuit was filed pursuant to a regime expressly created by Congress in the Hatch-Waxman Act in 1984 to promote faster entry by generic companies in selling drugs in the healthcare market.

20 *See* Bristol-MyersSquibb Co. v. Aurobindo Pharma USA Inc., 477 F. Supp. 3d 306 (D. Del. 2020), *aff'd*, Bristol-Meyers Squibb Co. v. Sigmapharm Labs., LLC, 858 Fed. Appx. 359 (Fed. Cir. 2021).

21 Bristol-MyersSquibb Co. v. Aurobindo Pharma USA Inc.

22 As of today, the Orange Book lists only 4 patents for Xarelto.

23 Alan Marco, *Why the patent system should look more like Indiana and less like Kentucky*, TEDxTysons (Aug. 3, 2017), https://youtu.be/HJhSD8ABt3s?t=759. Alan Marco is the former Chief Economist of the U.S. Patent and Trademark Office.

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Adam Mossoff is a senior fellow at Hudson Institute and chairs Hudson's Forum for Intellectual Property. He is also professor of law at Antonin Scalia Law School, George Mason University, where he teaches courses in intellectual property, property, and internet law. He is a Visiting Intellectual Property Fellow at the Heritage Foundation, and is a former Chair and current member of the Executive Committee of the Intellectual Property Practice Group of the Federalist Society. He is Chair of the Intellectual Property Working Group of the Regulatory Transparency Project at the Federalist Society. He also is a member of the Intellectual Property Rights Policy Committee of ANSI, the Intellectual Property Committee of the IEEE-USA, and the Academic Advisory Committee of the Copyright Alliance.

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