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THE MORE THINGS CHANGE: IN MEMORY OF DMITRY KARSHTEDT

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ABSTRACT—Policy debates at the intersection of patent law and pharmaceutical innovation have become increasingly polarized, often ending in a stalemate between seemingly incompatible goals of pharmaceutical innovation and access. Professor Karshtedt's body of work at this intersection navigates the partisan divide by carefully probing the assumptions and practices of patenting in pharmaceutical markets to identify opportunities for incremental improvement in both innovation and access. His Article *The More Things Change: Improvement Patents, Drug Modifications, and the FDA* exemplifies this approach, identifying an opportunity to nudge private sector incentives to innovate into closer alignment with public health gains through modest regulatory interventions.[1] In doing so, the Article offers a pathway through policy intransigence by offering a market-incentive based rationale for expanded agency authority, focusing on what should be a shared goal of improving the decision making of patients, prescribers and payors.

The impact of Professor Karshtedt's work stems not only from the insights in articles like *The More Things Change*, but also from the standards he set for himself as a scholar. Professor Karshtedt's work exemplifies the kind of thoughtfulness, analytical precision, and willingness to pursue a line of inquiry with patience, persistence, and intellectual intensity to which we should all aspire. His approach to patent law draws from both law and science, from experience working in a startup company, a law firm, working for a judge, and within a law school, and from the perspectives of a patent holder, a patent practitioner, and a patent scholar. Perhaps most importantly, both in his work and in his intellectual life Professor Karshtedt was always in thoughtful conversation with people and ideas around him. This essay is both a tribute to Professor Karshtedt's work and an invitation to draw lessons from his approach to scholarship and to building academic community that may serve well in navigating

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[1] Dmitry Karshtedt, *The More Things Change: Improvement Patents, Drug Modifications, and the FDA*, 104 IOWA L. REV. 1129 (2001).

contested terrains such as the current debates at the intersection of patent law and pharmaceutical policy.

I. INTRODUCTION

Policy debates over pharmaceutical regulation are often framed in terms of inevitable trade-offs between life-saving innovations on the one hand and regulatory measures to ensure product safety and effectiveness on the other. This simplified dichotomy is misleading. Not all drug innovations promote patient health—indeed, some innovations may cause harm.[2] Nor do all market based incentives encourage meaningful innovation.[3] Indeed, sometimes they can be used to impede it.[4] Not all regulatory measures designed to increase standards for safety and effectiveness have negative impacts on socially beneficial innovation.[5] Trying to parse out ways of harnessing the benefits of existing incentive structures for innovation, perhaps enhancing them, while curbing misuse, is a struggle that informs, or at least should inform, current pharmaceutical patent policy debates.[6]

Professor Karshtedt's body of work at the intersection of patent law and biomedical innovation carefully, rigorously, and creatively probes our underlying assumptions about patents and pharmaceutical markets. *The*

[2] *See, e.g.*, Robin Feldman et al., *Negative Innovation: When Patents are Bad for Patients*, 39 NATURE BIOTECH. 914 (2021).

[3] *See also* Kevin Richards & Kevin Hickey, *Drug Pricing and Pharmaceutical Patenting Practices*, CRS REP. (Feb. 11, 2022), https://sgp.fas.org/crs/misc/R46221.pdf [https://perma.cc/TN5A-C46G]; Christopher Buccafusco & Samuel Weinstein, *Anti-Social Innovation*, 58 GA. L. REV. 573 (2024).

[4] *See, e.g.*, Neilson Hobbs, *US FDA's Patent Concerns Include Product Hopping, and Evergreening*, THE PINK SHEET (Sept. 10, 2021), https://pink.pharmaintelligence.informa.com/PS144931/US-FDAs-Patent-Concerns-Include-Thickets-Product-Hopping-And-Evergreening [https://perma.cc/J7DA-P7XX].

[5] *See, e.g.*, Rena Conti et al., *Addressing the Tradeoff Between Lower Drug Prices and Incentives for Pharmaceutical Innovation*, BROOKINGS PAPER (Nov. 15, 2021), https://www.brookings.edu/articles/addressing-the-trade-off-between-lower-drug-prices-and-incentives-for-pharmaceutical-innovation/ [https://perma.cc/YS39-NKL8].

[6] *See id.*

More Things Change: Improvement Patents, Drug Modifications, and the FDA ("*The More Things Change*") exemplifies this approach.[7] It makes an important contribution to the contemporary debate over whether and when pharmaceutical patenting practices are helping or hindering the pursuit of public health. It contributes not only by offering a pragmatic response to the practice of "product hopping," but also by demonstrating the importance of examining the ways in which market structure, patent regulation, and the regulatory framework governing drug approvals interact. In doing so, the Article creates a space for scholars and policymakers on both sides of the debate to meet in the middle, offering arguments for expanded administrative regulation that are firmly grounded in market- based incentives and focused on what should be a shared goal of improving the decision making of patients, prescribers, and payors.

But on closer reading the Article also provides opportunities to depart from the middle ground. It introduces a pathway to regulatory change grounded in addressing information asymmetries and correcting misaligned incentives that can be taken as far as the reader wishes to go. While Professor Karshtedt adopts an incremental approach to change, one that shows optimism in the functioning of markets once improved information is made available, the Article opens the door to deeper interrogation of the costs of information failures and the dangers of misaligned market incentives for public health.

II. INCENTIVES TO INNOVATE OR IMPEDIMENTS TO COMPETITION?

The More Things Change begins with a pharmaceutical industry practice that has drawn the ire of policymakers, the courts, and the public, the practice of "product hopping." This practice involves replacing a prescription drug that is nearing the end of its regulatory exclusivities with a modified version of the drug to benefit from the extended market exclusivity arising from secondary patents covering the modification. The replacement occurs regardless of whether the modified version yields any improvement, and sometimes even when the modified version yields worse health outcomes.

The prevalence and anticompetitive effects of "product hopping" as a strategy for using patents to extend market power and impede competition in pharmaceutical markets has long been a subject of debate in policy circles.[8] Yet, the practice has persisted and efforts to address it remain hotly

[7] Karshtedt, *supra* note 1.

[8] *See, e.g.*, *FTC Files Amicus Brief Explaining that "Product Hopping" Can Violate the Antitrust Laws*, FED. TRADE COMM'N (Oct. 1, 2015), https://www.ftc.gov/news-events/news/press-releases/2015/10/ftc-files-amicus-brief-explaining-pharmaceutical-product-hopping-can-violate-

contested.[9] *The More Things Change* shines an analytical lens on the practices at the center of this debate, carefully distinguishing between efforts to make and patent improvements on existing products, which may be desirable, and "product hopping," which is undesirable from a social welfare perspective. Karshtedt explains, "[p]harmaceutical companies often replace prescription drugs that are already on the market with modified versions that have the same active pharmaceutical ingredient," sometimes for salutary reasons, but sometimes for strategic reasons.[10] "Product hopping" occurs when "firms . . . modify existing drugs not because new formulations would demonstrably improve health outcomes, but principally because so-called secondary patents covering the new version of the drug enable them to maintain some effective market power over the active ingredient for which the original, primary patent protection has expired."[11] The result of this practice is to delay competition, contributing to high drug prices, and in some cases forcing patients to switch to a less effective modification of the drug.

III. THE VALUE OF INFORMATION ABOUT COMPARATIVE EFFECTIVENESS

"[T]he strategy of product substitution seemingly for its own sake, with a new version exhibiting no proven clinical distinction from the original" creates problems for prescribers and for patients who are unable to ascertain the effectiveness of the new therapies.[12] Yet this problematic business strategy, one enabled by certain features of patent law, drug regulation under the FDA, and pharmaceutical markets, has proven to be a persistent feature of markets for many of the most profitable drugs.

One of the challenges of addressing product hopping lies in the fact that in some cases improvements to existing drugs are welfare-improving. They might address a problem with the current drug that was previously unsolvable, or introduce a new route of administering the drug. In other

antitrust-laws [https://perma.cc/5BR5-DL5A]; Michael A. Carrier & Steve D. Shadowen, *Product Hopping: A New Framework*, 92 NOTRE DAME L. REV. 167 (2017) (offering a framework for improving the antitrust analysis of product hopping); Arti Rai & Barak Richman, *A Preferable Path for Thwarting Pharmaceutical Product Hopping,* HEALTH AFFS. (May 22, 2018), https://www.healthaffairs.org/content/forefront/preferable-path-thwarting-pharmaceutical-product-hopping [https://perma.cc/X467-Z8YQ] (noting that the FDA is well placed to determine when product modifications lack genuine innovation and are being used primarily as deterrents to generic entry).

[9] *See, e.g.*, Peter Sullivan, *Drug Pricing Patent Bill Sets Off Tug of War*, AXIOS PRO (June 8, 2023), https://www.axios.com/pro/health-care-policy/2023/06/08/drug-pricing-patent-bill-battle [https://perma.cc/V3PM-LYGJ].

[10] Karshtedt, *supra* note 1, at 1129.

[11] *Id.* at 1129–30.

[12] *Id.* at 1136.

cases, however, the motivation for improvement is primarily, or even solely, monetary, and the improvements do not yield any significant health benefits. Information about the comparative benefits of a modification of a drug over the existing drug is essential to allow patients and prescribers to make informed decisions when determining whether to use the old drug or a generic equivalent, or switch to the new (and typically more expensive) modification. But this information is generally not available, making it difficult to sort between beneficial improvements and modifications that are no better and potentially even worse than the original drug.

One of the key insights that Professor Karshtedt offers is the importance that a lack of information about comparative drug value plays in allowing these practices to persist, and the value of targeting interventions towards inducing greater disclosure of comparative data. The information problem is allowed to persist because secondary patents can be obtained without any required showing of health benefit, and the FDA does not require any studies of comparative effectiveness of the modified drugs. Professor Karshtedt goes on to show how this is not only an information problem, but also a problem of inadequate interagency collaboration.

While the company seeking to product hop does need to satisfy both the U.S. Patent and Trademark Office (USPTO) requirements for patenting a modification of an existing product and FDA requirements for the modified product, it can do so without obtaining or disclosing any information about the comparative health benefits of the modified product. The patent system is tasked with determining whether a modification of an existing patented drug is patentable, and this requires an analysis of whether the modification is indeed novel and non-obvious in light of the existing drug. But the question of whether a modification is new and non-obvious is very different from the question of whether the modification offers any health benefits over the existing drug. So, the ability to obtain secondary patents tells us nothing about the comparative clinical benefits of the modification.

The modified drug must also undergo evaluation and approval by the FDA, but that process is confined to a determination of whether the modified drug is "safe[]" and "eff[ective]" according to the standards adopted by the FDA.[13] The FDA generally does not require the company seeking approval to "furnish any data suggestive of clinical distinctiveness between a drug's new form and its previous one, and such data is often completely unavailable when the new version enters the market."[14] It is not

[13] *Id.* at 1140.
[14] *Id.*

even clear whether the FDA has the authority to require such data to be produced.

And herein lies the problem. Companies are able to develop and patent a modification of their existing drug without showing that it offers health improvements and without testing whether it does. In fact, they may well have a disincentive to explore the comparative health value since doing so might yield evidence that it is actually worse for patients, or show that there is no benefit from having the modified drug enter the market. Without this information, patients and prescribers must rely on advertising by the company with the vested interest in encouraging the switch to the modified drug, and potential generic entrants face even more barriers to entering the market and securing market share for drugs that compete with the original drug.

IV. REGULATORS AS INFORMATION INTERMEDIARIES

The need for mechanisms that can sort strategic conduct from genuine innovation pervades much of drug policy, and product hopping is no exception. While difficult to implement, comparative effectiveness research offers a valuable tool in this fight. Although the FDA seems like the natural agency to require production of this data, it is limited by its existing statutory authority to require such information and its limited budget to develop this information on its own.

After showing how the persistence of product hopping relies upon information asymmetries about comparative product value in ways that limit competition, Professor Karshtedt goes on to propose ways in which the FDA could encourage product changes that improve patient care while deterring those changes that have little or no health benefit.[15] He proposes FDA "information-forcing" and "[information]-transferring" strategies that range in strength.[16] The first proposal is a mild requirement for the company seeking to market a modified drug to either provide comparative data or to have its decision not to provide such data included on the drug label. The FDA would request the company seeking approval for a modified drug to provide "comparative pre-market drug data that would be relevant to prescriber decisions."[17] If provided, this information would be vetted by the FDA and a summary of the information would be added to the drug package insert as part of the drug's required labeling. If the company did not provide such data, the FDA would require this deficit to

[15] *See id.* at 1142, 1191.

[16] *Id.* at 1144.

[17] *Id.*

be included on the drug label. The absence of information would thus serve as a reminder to patients, providers, and payors that the modified drug may offer no benefits and could even leave them worse off.

A stronger version of the proposal would increase the penalty for failing to provide the relevant comparative data by empowering the FDA with the authority to deny the company the ability to list patents covering the modified drug in the Orange Book. Since the benefits from product hopping lie primarily in delaying competition, removing the advantages that the Orange Book listings confer on the incumbent are likely to make product hopping less attractive for companies reluctant to produce pre-market comparative information.

In sum, Professor Karshtedt shows how product hopping emerges as the result of intersecting features of the patent system, drug regulation by the FDA, and market forces unique to pharmaceuticals. He focuses on the problem as one of information failure. A regulatory gap between USPTO patentability requirements and FDA drug approval requirements, neither of which require any showing of comparative effectiveness of old and new drugs, allows pharmaceutical companies to exploit information asymmetries in the marketplace in ways that extend monopoly power and keep drug prices high. The Article offers a creative way of addressing the disconnect by drawing on the potential of regulators to act as information intermediaries that operate within the existing confines of the marketplace to address the information asymmetries. By working within the existing system to align private incentives more closely with public health needs, Professor Karshtedt offers a way of navigating the partisan divide in pharmaceutical patent policy.

V. REFLECTIONS ON THE BROADER APPROACH TO ANALYZING PATENT LAW IN CONTEXT

In *The More Things Change,* Professor Karshtedt offers an approach to evaluating regulation that is multi-disciplinary, context rich, and attentive to the interactions of different regulatory regimes with the economic and political aspects of the marketplace. It highlights the need for a multi-disciplinary analysis of drug market policies and practices and offers us a framework for doing so. It employs the kind of approach that is essential to understanding the dynamics of pharmaceutical markets, bringing together an understanding of the science, intellectual property law, and health law and policy, as well as the perspective of someone who is

both a patent scholar and also a co-inventor on patents.[18] His measured, rigorous analysis of how to align profit incentives more closely with public health needs without radical change to the existing system offers an approach for pragmatic policymaking in a divided political arena. At a time when debates over drug policy are increasingly polarized, the approach embodied in this Article, and in Professor Karshtedt's work more broadly, is needed more than ever.

VI. IN REMEMBRANCE

In looking at *The More Things Change*, I conclude by noticing the long list of people that Professor Karshtedt mentions at the start. This reflects his central role in building and sustaining a robust intellectual and also very human community of intellectual property and health scholars. This communitarian role is also evident in the articles themselves. Professor Karshtedt's articles, at their core, are thoughtful conversations. During his framing of the problem and his analysis, he is in conversation with the other scholars, past and present, who write in the field. His work evolves in response to, though not always in agreement with, the existing universe of ideas. At its heart, the university is about building such a community– a universe of people interested in exploring ideas and addressing problems through critical exploration and debate. Professor Karshtedt exemplified the mind and soul of this community, and his presence will be missed.

[18] *See, e.g.*, Jason Rantanen, *Dmitry Karshtedt*, PATENTLYO BLOG (Oct. 31, 2022), https://patentlyo.com/patent/2022/10/dmitry-karshtedt.html [https://perma.cc/75CD-M3A4] ("Professor Karshtedt's work was wide-ranging. He is named as an inventor on 13 patents, is the first-named author on five scientific publications, and spoke at dozens of conferences and presentations.").