



**PATENT THICKETS AND PRODUCT HOPS:  
HOW CONGRESS COULD REWARD LEGITIMATE  
INNOVATION WHILE FACILITATING MORE TIMELY  
GENERIC COMPETITION**

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Judiciary Committee  
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## Summary of major points

- Brand-name prescription drug manufacturers receive **time-limited government-granted rights** to sell their products free from direct generic competition, and generic firms can then enter the market once patent protection ends. This system is designed to reward innovation while ensuring that patients and payers ultimately benefit from access to low-cost therapies.
- Brand-name firms undermine this system by engaging in **strategies aimed at extending periods of market exclusivity** and delaying generic competition. Firms often obtain numerous patents not just on active pharmaceutical compounds but on peripheral features of their products such as formulations and delivery devices (establishing large **patent thickets**), and they make minor modifications to existing therapies that offer minimal or no clinical advantage (**product hops**).
- **Drug-device combinations** are particularly susceptible to patent thickets and product hops and represent a growing share of pharmaceutical spending. Recent research has found that inhalers for asthma and chronic obstructive pulmonary disease and glucagon-like peptide-1 (GLP-1) receptor agonists for diabetes and weight loss have been subject to especially problematic strategies aimed at limiting generic competition. More than half of all patents on these products, for example, are on the delivery devices, not the active ingredients.
- The Senate Judiciary Committee has recently moved **4 bipartisan bills** out of Committee that would help reduce barriers to generic entry. These bills would improve collaboration between the Food and Drug Administration (FDA) and US Patent and Trademark Office (USPTO), limit product hops, punish manufacturers for baseless citizen petitions, and strengthen the Federal Trade Commission's (FTC) authority to challenge pay-for-delay settlements.
- Several additional reforms would help advance the Committee's work aimed at facilitating timely generic competition. Congress should take the following steps:
  - Grant the FDA the **authority and resources to evaluate all patents submitted for listing in the Orange Book** to determine eligibility for inclusion.
  - Require that patents submitted to the FDA for listing in the Orange Book are also submitted to the USPTO for **re-examination**.
  - **Limit the number of patents that brand-name manufacturers can assert** to one patent per family when suing for infringement.
  - Grant the FDA **more resources and flexibility to approve generic drug-device combinations that differ slightly from brand-name reference products** (while still containing the same active ingredients) and require the FDA to ensure that **post-marketing surveillance studies** are conducted to confirm similar outcomes for patients receiving generic and brand-name versions.
  - **Increase the 180-day exclusivity periods** for the first generic firms to file paragraph IV certifications on complex products like drug-device combinations and **decrease the 30-month stays** awarded to brand-name firms that sue for infringement.

## **Chair Durbin, Ranking Member Graham, and Members of the Committee:**

My name is William Feldman. I am pulmonologist, ICU physician, and health policy researcher at Harvard Medical School and Brigham and Women's Hospital, where I have joint appointments in the Division of Pulmonary and Critical Care Medicine and the Division of Pharmacoepidemiology and Pharmacoeconomics. I am a faculty member in the Program On Regulation, Therapeutics, And Law (PORTAL), one of the largest non-industry-funded research centers in the US devoted to pharmaceutical use, costs, regulation, and outcomes. I also serve as co-chair of the Ethics Committee at Brigham and Women's Hospital, and I teach and mentor trainees from Harvard College, Harvard Medical School, and the residency and fellowship programs at the Harvard teaching hospitals.

I became interested in pharmaceutical pricing during my medical training when I observed firsthand how patients were often unable to afford their medications, leading to decreased adherence and worse outcomes. When I started my pulmonary fellowship in 2017, there was not a single generic inhaler for asthma or chronic obstructive pulmonary disease (COPD) on the US market out of dozens of brand-name versions that had been approved since 1956, when the first metered-dose inhalers entered the US market.<sup>1</sup> Over the past several years, I have embarked on a series of research studies with colleagues to understand how pharmaceutical firms have used the patent system to limit generic competition and preserve market exclusivity while keeping prices high.

I am honored to talk with you all today about this research and what we can do to improve competition for the benefit of patients. I will begin by providing a brief background of different strategies that manufacturers employ to delay generic competition. I will then discuss one type of pharmaceutical product that has proven especially vulnerable to patent abuses: drug-device combinations, which contain active pharmaceutical compounds sold together with their delivery devices.<sup>2</sup> My comments will focus on inhalers and glucagon-like peptide-1 (GLP-1) receptor agonists, two of the largest classes of drug-device combinations now sold in the US. I will then briefly turn to other pharmaceutical products (besides drug-device combinations) and will offer a set of policy reforms that could help facilitate generic entry for small-molecule drugs across the pharmaceutical system.

### **1. How brand-name firms seek to delay generic competition**

The US government grants time-limited rights for brand-name pharmaceutical firms to sell prescription drugs free from direct generic competition, and generic firms can then enter the market once patent protection ends. Such competition is, by far, the most important tool for lowering prescription drug prices in the US. Although approximately 80% of prescriptions are filled for generic drugs, these prescriptions account for just 20% of total spending.<sup>3</sup> As each

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<sup>1</sup> Stein SW, Thiel CG. The History of Therapeutic Aerosols: A Chronological Review. *J Aerosol Med Pulm Drug Deliv.* 2017 Feb;30(1):20-41.

<sup>2</sup> US Food and Drug Administration. Combination Products. Available online from: <https://www.fda.gov/combination-products>. Accessed May 17, 2024.

<sup>3</sup> US Department of Health and Human Services. Assistant Secretary for Planning and Evaluation. Trends in Prescription Drug Spending, 2016-2021. September 2022. Available from:

new generic competitor enters the US market, prices tend to drop and eventually approach the costs of production.<sup>4</sup> This system is designed to promote innovation while ensuring that patients and payers ultimately benefit from access to low-cost therapy.

Key to the function of our prescription drug market is *timely* generic competition. The government permits monopoly pricing *for a period* before allowing the free market to operate. Unfortunately, many brand-name firms undermine this system by engaging in strategies designed to extend periods of market exclusivity and delay generic competition. These strategies not only harm patients, but they raise health care costs for us all through higher insurance premiums and taxes that fund federal health programs like Medicare and Medicaid.

### Patent thickets

One key tactic that brand-name manufacturers employ to delay generic competition is erecting large thickets of patents.<sup>5</sup> Many of these patents do not cover active pharmaceutical compounds (otherwise known as primary patents) but cover peripheral features such as alternative formulations and methods of use (secondary patents) and delivery devices (tertiary patents).<sup>6</sup> They may also be continuations of earlier patents that disclose no new inventions; indeed, we have found that a majority of pharmaceutical patents now listed with the FDA are continuations and not original patents.<sup>7</sup> Brand-name firms augment large patent portfolios by adding numerous patents after FDA approval and, in many cases, timing these additions to create uncertainty for competitors just as FDA-granted “regulatory” exclusivities are set to expire.<sup>8</sup> Some of these strategies increase the *density* of patent portfolios (the number of patents on a given product) while others increase their *duration* (the time from approval until expiration of the last-to-expire patent).

For small-molecule drugs, which I’ll be focusing on today, companies list their key patents in the FDA’s *Approved Drug Products with Therapeutic Equivalence Evaluations* (Orange Book). Maximizing both the density and duration of patent portfolios on brand-name drugs can be effective for pharmaceutical companies, because the FDA cannot approve generic drugs for marketing until patents in the Orange Book on these drugs expire or are successfully challenged.<sup>9</sup> The FDA does not review what gets listed in the Orange Book but instead serves

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<https://aspe.hhs.gov/sites/default/files/documents/88c547c976e915fc31fe2c6903ac0bc9/sdp-trends-prescription-drug-spending.pdf>. Accessed May 17, 2024.

<sup>4</sup> Dave CV, Hartzema A, Kesselheim AS. Prices of Generic Drugs Associated with Numbers of Manufacturers. *N Engl J Med*. 2017 Dec 28;377(26):2597-2598.

<sup>5</sup> Feldman R. May your drug price be evergreen. *J Law Biosci*. 2018 Dec 7;5(3):590-647.

<sup>6</sup> Beall RF, Kesselheim AS. Tertiary patenting on drug-device combination products in the United States. *Nat Biotechnol*. 2018 Feb 6;36(2):142-145.

<sup>7</sup> Tu SS, Kesselheim AS, Wetherbee K, Feldman WB. Changes in the Number of Continuation Patents on Drugs Approved by the FDA. *JAMA*. 2023 Aug 1;330(5):469-470.

<sup>8</sup> Horrow C, Gabriele SME, Tu SS, Sarpatwari A, Kesselheim AS. Patent Portfolios Protecting 10 Top-Selling Prescription Drugs. *JAMA Intern Med*. 2024 May 13:e240836.

<sup>9</sup> US Food and Drug Administration. Patent Certifications and Suitability Petitions. Available from:

<https://www.fda.gov/drugs/abbreviated-new-drug-application-anda/patent-certifications-and-suitability-petitions>. Accessed May 17, 2024.

in a “purely ministerial” role, listing patents that manufacturers choose for submission.<sup>10</sup> When generic firms challenge FDA-listed patents (via what is known as paragraph IV certifications), brand-name firms that sue for infringement within 45 days can receive an automatic 30-month stay while litigation resolves. The large patent thickets created by brand-name pharmaceutical companies often tie up generic firms in costly legal battles and deter generic firms from challenging patents in the first place.

### Product hops

A second type of strategy that manufacturers employ to limit generic competition is developing new products that are closely related to originators (reformulations) yet sufficiently different to receive new patents. For example, manufacturers may move an active ingredient from one delivery device (e.g., an inhaler) to another with extended patent protection even if the new device offers minimal added clinical benefit to patients—or none at all. Pharmaceutical firms may combine two existing drugs into a single pill with new patent protection or release new strengths, salts, or esters (e.g., metoprolol tartrate rather than metoprolol succinate), or single enantiomers of racemic mixtures (e.g., esomeprazole rather than omeprazole).<sup>11</sup> These reformulations are considered hard product hops when the original drug is discontinued altogether and soft product hops when both versions remain on the market but the company seeks to move patients to newer products to reduce generic uptake of older versions.<sup>12</sup>

Although some product hops result in formulations that are more convenient for patients, many offer little to no meaningful clinical advantage over existing products. For example, in the largest systematic review to date of single enantiomer vs. racemic mixture drugs, the majority of randomized controlled trials found no differences in efficacy or safety between the two.<sup>13</sup> More importantly, the financial rewards of these small tweaks often far outstrip the benefits to patients, sometimes rivalling those bestowed on transformative new therapeutic breakthroughs.

### Incremental innovation

Manufacturers rely on these strategies—increasing the density and duration of patents and making small tweaks to existing products—to protect revenue streams. These strategies not only undermine the very rationale for time-limited, government-granted monopolies, but they divert resources away from investment in more meaningful therapeutic advances.

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<sup>10</sup> US Food and Drug Administration. The Listing of Patent Information in the Orange Book. Available from: <https://www.fda.gov/media/155200/download>. Accessed May 17, 2024.

<sup>11</sup> Darrow JJ, Chong JE, Kesselheim AS. Reconsidering the scope of US state laws allowing pharmacist substitution of generic drugs. *BMJ*. 2020 Jun 23;369:m2236.

<sup>12</sup> Gowda V, Beall RF, Kesselheim AS, Sarpatwari A. Identifying potential prescription drug product hopping. *Nat Biotechnol*. 2021 Apr;39(4):414-417.

<sup>13</sup> Long AS, Zhang AD, Meyer CE, Egilman AC, Ross JS, Wallach JD. Evaluation of Trials Comparing Single-Enantiomer Drugs to Their Racemic Precursors: A Systematic Review. *JAMA Netw Open*. 2021;4(5):e215731.

## 2. The particular challenges posed by drug-device combinations

Drug-device combinations, which include products like inhalers, insulin pens, GLP-1 receptor agonists, and epinephrine pens are especially susceptible to patent thickets and product hops.<sup>14</sup> They also represent a growing share of pharmaceutical spending. Of the 50 products with the highest 2022 gross Medicare Part D spending, 20 (40%) were drug-device combinations.<sup>15</sup> These include blockbuster drugs like Trelegy Ellipta (fluticasone-umeclidinium-vilanterol) and Symbicort (budesonide-formoterol) for asthma and COPD and Ozempic (semaglutide) and Lantus SoloStar (insulin glargine) for diabetes. Although manufacturers have engaged in harmful patenting behavior on a variety of products, I will focus on two of the largest classes of drug-device combinations—inhalers and GLP-1 receptor agonists—to illustrate key problems that threaten the function of our pharmaceutical system.

### Inhalers for asthma and COPD

More than 27 million people in the US have asthma<sup>16</sup> and nearly 12 million have COPD.<sup>17</sup> Patients with both conditions rely on maintenance inhalers for daily use and rescue inhalers to manage acute symptoms.<sup>18</sup> List prices for these products can run more than \$600 per month and, although payers negotiate rebates to lower costs for payers, net prices are still substantially higher than prices in other countries.<sup>19</sup> Because out-of-pocket costs are often tied to list prices and because those without insurance do not pay insurer-negotiated rates, high list prices can also threaten affordability for patients. For many years, spending on inhalers has represented approximately 3-5% of net spending on retail prescription drugs in Medicare.<sup>20</sup>

In research analyzing all 53 brand-name inhalers approved for asthma and COPD by the FDA from 1986 to 2020, we observed several worrisome features regarding the tactics employed by manufacturers to preserve market exclusivity.<sup>21</sup>

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<sup>14</sup> Sinha M., Costly Gadgets: Barriers to Market Entry and Price Competition for Generic Drug-Device Combinations in the United States. 23 Minn. J.L. Sci. & Tech. 293 (2022).

<sup>15</sup> Center for Medicare and Medicaid Services. Medicare Part D Spending by Drug. Available from: <https://data.cms.gov/summary-statistics-on-use-and-payments/medicare-medicaid-spending-by-drug/medicare-part-d-spending-by-drug>. Accessed May 17, 2024.

<sup>16</sup> Asthma and Allergy Foundation of America. Asthma Facts. Available from: <https://aafa.org/asthma/asthma-facts/>. Accessed May 17, 2024.

<sup>17</sup> American Lung Association. COPD Trends Brief: Prevalence. Available from: <https://www.lung.org/research/trends-in-lung-disease/copd-trends-brief/copd-prevalence>. Accessed May 17, 2024.

<sup>18</sup> Global Initiative for Chronic Obstructive Lung Disease (GOLD). 2024 GOLD Report. Available from: <https://goldcopd.org/2024-gold-report/>. Accessed May 17, 2024. Global Initiative for Asthma (GINA). 2023 GINA Report, Global Strategy for Asthma Management and Prevention. Available from: <https://ginasthma.org/2023-gina-main-report/>. Accessed May 17, 2024.

<sup>19</sup> NAVLIN database. Available online from: <https://data.navlin.com/alspc/>. Accessed May 17, 2024.

<sup>20</sup> Feldman WB, Gagne JJ, Kesselheim AS. Trends in Medicare Part D Inhaler Spending: 2012-2018. Ann Am Thorac Soc. 2021 Mar;18(3):548-550.

<sup>21</sup> Feldman WB, Bloomfield D, Beall RF, Kesselheim AS. Patents And Regulatory Exclusivities On Inhalers For Asthma And COPD, 1986-2020. Health Aff (Millwood). 2022 Jun;41(6):787-796. Demkowicz BJ, Tu SS, Kesselheim AS, Carrier MA, Feldman WB. Patenting Strategies on Inhaler Delivery Devices. Chest. 2023 Aug;164(2):450-460.



1. *New products in old classes*: Firms have not managed to find new therapeutic breakthroughs for inhaled medications to treat asthma and COPD. Instead, they have copied drugs in the same therapeutic classes. The last inhaler to reach the market with a new mechanism of action was Atrovent (ipratropium) in 1986. Since then, every inhaler to receive FDA approval has contained active ingredients with the same mechanisms of action already present in other inhaled products sold in the US.

2. *Large patent thickets*: Manufacturers have released inhalers with an increasing number of patents on their products. The median number of patents at the time of approval rose from 2 in the first decade of our study (with a median of 0 device patents) to 11 in the final decade (with a median of 7 device patents).

3. *Patents added after FDA approval*: Inhaler manufacturers filed patents after FDA approval for 25 (47%) products, including 12 cases in which the new patents extended periods of market exclusivity (by a median of 6 years).

4. *Numerous device patents*: Overall, device patents represented more than half of all patents listed on inhalers in the cohort. These device patents were on small plastic components of inhalers such as dose counters, filters, and nozzles. In some cases, the only patents listed on the product were on the delivery devices. Boehringer Ingelheim, for example, listed 25 patents on Combivent (albuterol-ipratropium) when the drug was approved in 2011, every single one of which was on the delivery device. This product, which contains albuterol (first approved in 1981) and ipratropium (first approved in 1986) still faces no generic competition.

5. *Features of device patents*: Many of these device patents were entirely disconnected from the drugs on which they were listed, making no mention of active pharmaceutical compounds, therapeutic classes, methods of use, or other features in their claims that might connect the patent to the drug. Companies are only permitted to list patents in the Orange Book that cover a drug (either a drug substance or drug product) or method of use.<sup>22</sup> A 2020 court case found that Sanofi had improperly listed a patent on the drive mechanism of an insulin injector pen because the patent made no mention (much less claimed) insulin or even the indication (diabetes).<sup>23</sup> In recent work, we applied a similar logic to analyze inhaler device patents and found that 77% made no mention of any active ingredients or molecular structures; 72% made no mention of any active ingredients, molecular structures, therapeutic classes, indications, device names, or the lungs.<sup>24</sup> Twenty-five inhalers had a device-only patent as the last-to-expire patent (with no mention of active ingredients), and these device-only patents extended periods of expected protection by a median of 8 years beyond other patents.

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<sup>22</sup> Congressional Research Service. Patent Listing in FDA's Orange Book. Available from: <https://crsreports.congress.gov/product/pdf/IF/IF12644>. Accessed May 17, 2024.

<sup>23</sup> *In re Lantus Direct Purchaser Antitrust Litig.*, 512 F. Supp. 3d 106 (D. Mass. 2020).

<sup>24</sup> Demkowicz BJ, Tu SS, Kesselheim AS, Carrier MA, Feldman WB. Patenting Strategies on Inhaler Delivery Devices. *Chest*. 2023 Aug;164(2):450-460.

The FTC has recently identified hundreds of patents that have been impermissibly listed in the Orange Book.<sup>25</sup> The *majority* of these patents are device-only patents listed on inhalers for asthma and COPD. These patents increase the density of patent portfolios, which make challenges more difficult, and increase the duration of protection, which make challenges necessary in the first place. Indeed, in an analysis of litigation following paragraph IV challenges on inhalers, we found that more than half of all litigated patents were on delivery devices.<sup>26</sup> Brand-name firms are not just listing device patents, but they are building litigation strategies around these patents to keep generic competitors off the market.

6. *Device hopping*: Inhaler manufacturers have also engaged in extensive device hopping—or shifting active ingredients from one delivery device to another with new patent protection. Manufacturers of 15 different originator inhalers in our study pursued this strategy, leading to 19 follow-ons. Some of these device hops were related to a ban on chlorofluorocarbons (CFC), which went into effect for pharmaceutical products from 2009 to 2013.<sup>27</sup> However, many of these device hops were unrelated to the ban. For example, GlaxoSmithKline released 5 different fluticasone products from 1996 to 2014: CFC-containing Flovent (1996) and then CFC-free Flovent Rotadisk (1988), Flovent Diskus (2000), Flovent HFA (2004), and Arnuity Ellipta (2014). Boehringer Ingelheim released two different CFC-free tiotropium inhalers: Spiriva HandiHaler (2004) and Spiriva Respimat (2014). By moving molecules to delivery devices with new patents, manufacturers can extend streams of revenue. The median duration of expected protection on products in our cohort with device hops was 28 years for the product lines, from approval of the first product to the last-to-expire patent listed for follow-ons.

These practices have been very lucrative for inhaler manufacturers. From 2000 to 2021, manufacturers earned more than \$178 billion on inhalers in the US, including \$67 billion (38%) when patents on active ingredients were active, and \$111 billion (62%) when these patents had expired.<sup>28</sup> Some of the biggest blockbuster inhalers have earned staggering sums when only secondary and tertiary patents were active: Advair: \$42 billion; Symbicort: \$16 billion; Flovent: \$12 billion; ProAir: \$8 billion; Spiriva: \$5 billion. In some cases, including AstraZeneca's Symbicort and Teva's ProAir, *all* manufacturer revenue accrued after primary patent expiration, as these patents had expired before product launch.

Without legislative reform, these practices are likely to continue. The Senate Committee on Health, Education, Labor, and Pensions launched an investigation in January 2024 examining

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<sup>25</sup> US Federal Trade Commission. FTC Challenges More Than 100 Patents as Improperly Listed in the FDA's Orange Book. Available from: <https://www.ftc.gov/news-events/news/press-releases/2023/11/ftc-challenges-more-100-patents-improperly-listed-fdas-orange-book>. Accessed May 17, 2024. US Federal Trade Commission. FTC Expands Patent Listing Challenges, Targeting More than 300 Junk Listings for Diabetes, Weight Loss, Asthma, and COPD Drugs. Available from: <https://www.ftc.gov/news-events/news/press-releases/2024/04/ftc-expands-patent-listing-challenges-targeting-more-300-junk-listings-diabetes-weight-loss-asthma>. Accessed May 17, 2024.

<sup>26</sup> Reddy S, Beall RF, Tu SS, Kesselheim AS, Feldman WB. Patent Challenges and Litigation on Inhalers for Asthma and COPD. *Health Aff (Millwood)*. 2023 Mar;42(3):398-406.

<sup>27</sup> Wouters OJ, Feldman WB, Tu SS. Product Hopping in the Drug Industry – Lessons from Albuterol. *N Engl J Med*. 2022 Sep 29;387(13):1153-1156.

<sup>28</sup> Feldman WB, Tu SS, Alhiary R, Kesselheim AS, Wouters OJ. Manufacturer Revenue on Inhalers After Expiration of Primary Patents, 2000-2021. *JAMA*. 2023 Jan 3;329(1):87-89.



potentially anticompetitive practices by inhaler manufacturers over the last several decades.<sup>29</sup> This work builds on important action taken by the FTC to crack down on impermissibly listed device patents on inhalers. In response, 3 of the 4 major inhaler manufacturers announced that they would voluntarily cap out-of-pocket costs at \$35.<sup>30</sup> While this is an important step for millions of Americans with asthma and COPD, it does not address the underlying problems that have limited generic competition, nor will it necessarily translate into less spending by payers as long as the same harmful patenting practices can continue.

### GLP-1 receptor agonists for diabetes, weight loss, cardiovascular disease

GLP-1 receptor agonists have shown remarkable promise for the treatment of diabetes, weight loss, and cardiovascular disease. But these drugs remain out of reach for many patients. List prices can run more than \$1,000 per month and, even with large manufacturer rebates for payers,<sup>31</sup> net prices are still substantially higher than in other countries,<sup>32</sup> raising alarms about looming unmanageable budgetary impacts for US payers, including Medicare.

GLP-1 manufacturers appear to be relying on a similar playbook as inhaler manufacturers—establishing large thickets of patents, many of which are centered on delivery devices. This should not be surprising, because the two largest GLP-1 manufacturers, Novo Nordisk and Eli Lilly, used the very same strategies on insulin pens over the last 3 decades. We found that half of all patents on insulin products approved from 1986 to 2019 were on the delivery devices of these products, and 85% of these patents made no mention of insulin in their claims.<sup>33</sup> The FTC has not targeted delivery device patents on insulin products because they are no longer listed in the Orange Book (they are now regulated as biologics rather than small-molecule drugs).

In other work, we identified several concerning trends on GLP-1s:<sup>34</sup>

*1. Large patent thickets:* Among 10 GLP-1 receptor agonists approved from 2005 to 2021, manufacturers listed a median of 20 patents per product, including a median of 17 before FDA approval and 2 added after FDA approval. The median period of expected protection on each product is more than 18 years. Because many of these products were recently approved, we

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<sup>29</sup> Tirrell M. Bernie Sanders, Senate Democrats open investigation into price of asthma inhalers. CNN. January 8, 2024. Available from: <https://www.cnn.com/2024/01/08/health/senate-democrats-investigate-price-of-asthma-inhalers/index.html>. Accessed May 17, 2024.

<sup>30</sup> Becker Z. GSK joins AstraZeneca, Boehringer in capping US out-of-pocket inhaler prices at \$35 per month. Fierce Pharma. March 21, 2024. Available online from: <https://www.fiercepharma.com/pharma/gsk-latest-inhaler-maker-commit-35-out-pocket-price-cap-us-following-peers-boehringer>. Accessed May 17, 2024.

<sup>31</sup> Hernandez I, Sullivan SD. Net prices of new antiobesity medications. *Obesity* (Silver Spring). 2024 Mar;32(3):472-475.

<sup>32</sup> NAVLIN database. Available online from: <https://data.navlin.com/alspc/>. Accessed May 17, 2024.

<sup>33</sup> Olsen A, Beall RF, Knox RP, Tu SS, Kesselheim AS, Feldman WB. Patents and regulatory exclusivities on FDA-approved insulin products: A longitudinal database study, 1986-2019. *PLoS Med*. 2023 Nov 16;20(11):e1004309.

<sup>34</sup> Alhiary R, Kesselheim AS, Gabriele S, Beall RF, Tu SS, Feldman WB. Patents and Regulatory Exclusivities on GLP-1 Receptor Agonists. *JAMA*. 2023 Aug 15;330(7):650-657. Alhiary R, Gabriele S, Kesselheim AS, Tu SS, Feldman WB. Delivery Device Patents on GLP-1 Receptor Agonists. *JAMA*. 2024 Mar 5;331(9):794-796.

are likely to see increasing numbers of patents added to the products in the coming years absent regulatory reform.

2. *Numerous device patents:* Manufacturers listed 188 patents on GLP-1 drug-device combinations, including 107 (57%) on the delivery devices.

3. *Features of device patents:* Not a single device patent on GLP-1 receptor agonists mentioned their active ingredients, molecular structures, therapeutic class, or device name. Only 1 patent (listed on 3 separate products) mentioned an indication (diabetes). In April of this year, the FTC announced a second round of improperly listed patents, including numerous device-only patents on GLP-1 receptor agonists.<sup>35</sup>

4. *Litigation strategies:* Although many GLP-1 receptor agonists have only recently been approved, we found that generic firms have already filed at least 30 paragraph IV challenges on 5 different products. Brand-name firms sued for infringement in these cases on 70 patents, 40 of which (57%) were device-only patents that should likely not have been listed in the Orange Book in the first place. As with inhalers, device patents form a core part of litigation strategies that brand-name firms employ to delay generic competition.

### 3. Other pharmaceutical products

Although drug-device combinations are perhaps the best exemplars of how pharmaceutical patenting practices have gone astray in the US health care system, brand-name firms employ similar strategies on other types of products. Research from our group has shown that the number of patents per new drug approval increased by more than two-thirds from 2000 to 2015.<sup>36</sup> Another study looking at drugs approved from 2005-2015 found that, among 106 top-selling drugs, manufacturers added patents after FDA approval that extended the duration of protection on 70% of products.<sup>37</sup> Recent research on 10 top-selling pharmaceuticals in 2021 found that approximately two-thirds of all issued patents on these products were filed after FDA approval and fewer than 20% had composition-of-matter claims.<sup>38</sup>

### 4. Proposals for Reform

Addressing the problems of patent thickets and product hops across the pharmaceutical system will require a multipronged strategy that includes the FDA, USPTO, and FTC. The Senate Judiciary Committee has recently moved 4 bipartisan bills out of Committee that, if enacted into law, would facilitate more timely generic competition.

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<sup>35</sup> US Federal Trade Commission. FTC Expands Patent Listing Challenges, Targeting More than 300 Junk Listings for Diabetes, Weight Loss, Asthma, and COPD Drugs. Available from: <https://www.ftc.gov/news-events/news/press-releases/2024/04/ftc-expands-patent-listing-challenges-targeting-more-300-junk-listings-diabetes-weight-loss-asthma>. Accessed May 17, 2024.

<sup>36</sup> Tu SS, Kesselheim AS, Wetherbee K, Feldman WB. Changes in the Number of Continuation Patents on Drugs Approved by the FDA. *JAMA*. 2023 Aug 1;330(5):469-470.

<sup>37</sup> Feldman R. May your drug price be evergreen. *J Law Biosci*. 2018 Dec 7;5(3):590-647.

<sup>38</sup> Horrow C, Gabriele SME, Tu SS, Sarpatwari A, Kesselheim AS. Patent Portfolios Protecting 10 Top-Selling Prescription Drugs. *JAMA Intern Med*. 2024 May 13:e240836.

## Senate Judiciary Committee bills

1. *Improving the quality of issued patents*: The Interagency Patent Coordination and Improvement Act 2023 (sponsored by Senator Durbin) would establish a formal task force to improve communication between the USPTO and FDA. Better communication could, among other things, help ensure that patentability standards are met at the USPTO and prevent invalid patents from being issued in the first place. Once issued, a patent is legally presumed to be valid and is therefore challenging to overturn in court, which emphasizes the importance of ensuring that the correct standards are applied in the first place.

2. *Limiting product hops*: The Affordable Prescriptions for Patients Act of 2023 (sponsored by Senator Cornyn) would authorize the FTC to enforce a prohibition on product hops that occur just after brand-name firms receive notification of generic drug applications up until 3 years after generic approval. Although product hops may occur well ahead of generic drug applications, this bill could help limit at least some forms of product hopping designed to stifle generic competition.

3. *Punishing brand-name firms for baseless citizen petitions*: The Stop Significant and Time-wasting Abuse Limiting Legitimate Innovation of New Generics (Stop STALLING) Act (sponsored by Senator Klobuchar) would fine firms that bring baseless citizen petitions up to \$50,000 each day that the FDA spends reviewing the petition. Prior research has shown that brand-name firms often file citizens petitions to delay FDA review of generic drug applications, and the vast majority of these petitions are denied.<sup>39</sup> By deterring frivolous citizen petitions, this bill could help the FDA approve generic drug applications in a more expeditious manner.

4. *Preventing pay-for-delay settlements*: The Preserve Access to Affordable Generic and Biosimilars Act (sponsored by Senator Klobuchar) would give the FTC more authority to challenge anticompetitive pay-for-delay settlement agreements. Preventing these types of reverse payment agreements could avoid the long delays that are now commonly seen between paragraph IV filings and generic entry.

## Other proposals

While all 4 bills offer meaningful improvements, several additional reforms could help further advance the Committee's work aimed at facilitating timely generic competition. I would encourage the Committee to consider the following:

1. *Orange Book listings*: Congress should require the FDA to release more comprehensive guidance on the types of patents that can be listed in the Orange Book and give the FDA the

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<sup>39</sup> Carrier MA, Wander D. Citizen Petitions: An Empirical Study, *Cardozo L Rev.* 2012;34:249-252. Carrier MA, Minniti C. Citizen Petitions: Long, Late-Filed, and At-Last Denied. *Am. U. L. Rev.* 66(2):305-352. Sachs R, Walentynowicz M, Frank RG, Adler L. The FDA Could do More to Promote Generic Competition: Here's How. June 14, 2022. Available from: <https://healthpolicy.usc.edu/research/the-fda-could-do-more-to-promote-generic-competition-heres-how/>. Accessed May 17, 2024.

resources and authority to review all submitted patents to determine eligibility for listing in the Orange Book. Although the FDA has expressed reluctance to take on this role given limited patent expertise and few resources to conduct the work,<sup>40</sup> an expanded role may be feasible with appropriate funding and close collaboration with the USPTO.

2. *Re-examination*: Congress could require manufacturers that submit patents for listing in the Orange Book to simultaneously submit these patents for re-examination by the USPTO. Given the stakes for the health care system of invalid patents, routine reexamination would help ensure that only truly patentable innovations appear in the Orange Book.<sup>41</sup>

3. *Litigation*: Congress should limit the number of patents that brand-name firms can assert when suing for infringement following patent challenges. One approach, for example, would limit litigation to one patent per family among patents joined by terminal disclaimers.<sup>42</sup>

4. *Generic approval standards*: Congress should grant the FDA more authority to approve complex generic drugs like drug-device combinations that differ in slight ways from brand-name reference products containing the same active pharmaceutical compounds. This would enable generic firms to more easily design products that avoid infringing brand-name patents. Congress should couple such a law with a requirement that the FDA review post-marketing data on outcomes to further ensure clinical comparability between the generic and brand-name drugs.

5. *Incentives for patent challenges*: To increase incentives for generic firms to bring paragraph IV certifications on complex drugs, Congress should increase the 180-day exclusivity period awarded to first-to-file generic firms. By the same token, to decrease the incentives for brand-name firms to file baseless litigation following paragraph IV certifications, Congress should reduce the length of automatic 30-month stays.

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<sup>40</sup> US Government Accountability Office. Generic Drugs: Stakeholder Views on FDA's Information on Patents. March 15, 2023. Available from: <https://www.gao.gov/products/gao-23-105477>. Accessed May 17, 2024.

<sup>41</sup> Tu SS. FDA Reexamination: Increased Communication between the FDA and USPTO to improve patent quality. Hous. L. Rev. 2022;60:403-465.

<sup>42</sup> Welsh, Braun, and Klobuchar Introduce Bipartisan Legislation to Streamline Drug Patent Litigation, Lower Cost of Prescription Drugs. January 12, 2024. Available from: <https://www.welch.senate.gov/welch-braun-and-klobuchar-introduce-bipartisan-legislation-to-streamline-drug-patent-litigation-lower-cost-of-prescription-drugs/>. Accessed May 17, 2024.