Minor Advances, Major Consequences: Hatch-Waxman Administers Exclusivity for Drug Delivery Devices

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MINOR ADVANCES, MAJOR CONSEQUENCES: HATCH-WAXMAN ADMINISTERS EXCLUSIVITY FOR DRUG DELIVERY DEVICES

Taylor Stemler*

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I. INTRODUCTION

When pharmaceutical companies create a new drug, they can usually receive a patent, which allows them to operate with patent exclusivity for the life of the patent. This exclusive period allows drug companies to recoup their massive research and development expenses and eventually become profitable. Without some amount of patent exclusivity, it becomes economically irrational for a biotechnology company to invest the huge amounts of time and money required for the development of a drug. More recently, costs for pharmaceutical research and development have skyrocketed as traditional methods of small molecule drug development are starting to appear more “tapped out.” As a result, drug companies are forced to turn to more cutting-edge and expensive methods of development.

After a pharmaceutical company’s period of patent exclusivity elapses, generic companies can enter the market and offer essentially the same drug for a fraction of the price. Before obtaining the approval of the U.S. Food and Drug Administration (FDA), a generic company must certify that the branded drug: (1) has not been patented, (2) the applicable patents have expired, (3) the patents will expire on a given date and the generic will not be marketed before that date, or (4) the listed patents are not infringed or invalid.

Generic companies do not have the same up-front research costs that branded companies face. Additionally, since the introduction of the Drug Price Competition and Patent Term Restoration Act of 1984 (“Hatch-Waxman Act”), generic drug companies may undergo a shortened FDA

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2 Id. at 573.

3 Id. at 572.

4 Id. at 573.

5 Id.


approval process.\textsuperscript{8} Studies show that due to these limited upfront expenditures, generic drug companies may undercut the prices of branded drugs, thereby dropping the branded drug price as much as ninety percent within the first 2.5 years of generic entry.\textsuperscript{9}

To combat these extreme price drops, some branded pharmaceutical companies may choose to raise the price on branded drugs while they are still patented to get the greatest value from their patent protection period.\textsuperscript{10} Others have developed strategies to achieve a greater period of patent exclusivity.\textsuperscript{11} These strategies effectively extend the patent protection for the products, which may minimize the damage from the drastic generic entry price drop or prevent generic entry to the market altogether.\textsuperscript{12} Tactics such as developing new formulations, creating new routes of administration, making changes to molecular structures, and finding new uses for products have all been used in some ways by branded pharmaceutical companies.\textsuperscript{13}

One new strategy that this article will examine in depth relates to patents on combination medicine and delivery device products.\textsuperscript{14} Frequently used combination products include pulmonary inhalers, injection systems, or infusion systems.\textsuperscript{15} This strategy presents a new set of challenges for lawmakers to navigate, since drug companies can attain patent protection on both the device and the underlying drug. After examining the ways in which this strategy is employed, this article will explore impacts of this strategy on patients and regulatory solutions that can mitigate its negative effects.\textsuperscript{16} Lastly, one mitigation scheme will be identified as the best regulatory pathway for future legislation in the United States.\textsuperscript{17}

\begin{itemize}
\item \textsuperscript{10} Robin Feldman, \textit{May Your Drug Price Be Evergreen}, 5 J. L. BIOSCIENCE 590, 594 (2018).
\item \textsuperscript{11} Id. at 596.
\item \textsuperscript{12} Id. at 602.
\item \textsuperscript{13} See Gupta et al., supra note 7, at 4–6.
\item \textsuperscript{14} See infra Part IV.
\item \textsuperscript{16} See infra Sections IV.C–D.
\item \textsuperscript{17} See infra Section IV.D.
\end{itemize}
II. BACKGROUND

Before exploring new patent extension strategies, it is helpful to provide an overview of the drug development process along with a discussion of pharmaceutical patenting and the Hatch-Waxman Act. An understanding of these concepts is useful when discussing how lawmakers have structured the regulatory pathway for new drugs in response to gamesmanship in the Hatch-Waxman and pharmaceutical patent system.

A. New Drug Development and Approval Overview

Developing and obtaining FDA approval for a new drug typically takes around twelve years and costs about $1.44 billion. The process begins when pharmaceutical companies supply grants to professors conducting basic research in universities to understand the mechanisms behind the diseases they hope to cure. After identifying some target mechanism for the potential treatment to attack, researchers employed by the pharmaceutical company will look into natural components from plants, animals, fungi, or other organisms to build a list of potential therapy candidates. This list may start with as many as 10,000 compounds, which are then narrowed down to around ten or twenty most likely to cure the disease.

Once the final list of candidates is created, the compounds will be tested to ensure that they are safe and effective. Before the compounds are used on humans, they may be tested using computer models, cells, and animals. This process will typically narrow down the list to between five and ten remaining compounds.

After this laboratory testing phase, the potential drugs are then moved into clinical trials. There are three main pre-approval phases of clinical trials. Phase one trials are typically small and aim to determine the

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* Id.
* Id.
* Id.
* Id.

* Id.
tolerance, side effects, and coping effects of the drug. Phase two trials go on to determine how well the new treatment works, how to best manage the side effects, and the subtype of disease that the therapy works best on. Lastly, phase three trials test a much larger group of patients and determine how the treatment affects one’s quality of life compared to alternative therapies.

After the successful completion of the clinical trials, which, in some circumstances, may be even more extensive than what is outlined above, the drug may be submitted for FDA approval. Submissions also require the completion of a New Drug Application (NDA). When submitting an NDA, the pharmaceutical company must list all of the patents relevant to its new drug for publication in the FDA’s Orange Book. Upon submission, the FDA’s Center for Drug Evaluation and Research (CDER) evaluates the drugs by weighing evidence from the clinical trials. This independent and unbiased review process is meant to determine whether the drug is safe and effective, whether the labeling and packaging are appropriate, and what manufacturing methods are appropriate for safe production.

B. Pharmaceutical Patenting

Patents help advance innovation in the pharmaceutical industry by allowing inventors to recoup their costs and see a return on their research and development investment. Branded companies typically patent new compounds very early in the drug research process to protect their intellectual property from other drug developers. Since the FDA’s drug approval process can take an extremely long time, once a new drug finally

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26 Id.
27 Id.
28 Id.
29 Id.
30 Id.
31 See ROBIN FELDMAN, RETHINKING PATENT LAW 178 (2012).
32 Feldman, supra note 10, at 598.
makes it to the market, often, a considerable amount of the life of the patent has elapsed. Patents granted by the United States Patent and Trademark Office last for twenty years. However, estimates for the average life of patent protection remaining once a drug finally reaches the market show that the patent usually has only about twelve years left.

Pharmaceutical companies strive to extend the patent protection period of their products by covering them under multiple patents, which allows the companies to protect different aspects of an invention so that the product cannot be copied after the primary patent elapses. This practice may fall within what has been nicknamed “patent evergreening.” Patent evergreening is loosely defined as obtaining a secondary patent that extends a product’s exclusivity period without a proportionate benefit of any sort. In the healthcare context, the definition of evergreening has been modified slightly to include secondary patents that extend a product’s exclusivity period without a proportionate therapeutic benefit.

Provisions of the Hatch-Waxman Act, which will be discussed in greater detail in Section II.C., allow a patent holder to file for a patent-term extension. The length of the extension is based on the amount of time the drug spent in the clinical testing and regulatory review phases of the drug approval process. As long as the patent was issued prior to clinical testing, the patent term can be extended for one half of the clinical testing period, plus the full length of the regulatory review period. However, this extension may be reduced if the patent holder did not act reasonably diligently during clinical testing and regulatory review. The patent extension period may not exceed five years, and the total, extended patent life cannot exceed fourteen years upon approval.

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* Feldman, supra note 10, at 599.
* Id.
* Id.
* Id. The calculation of the length of the extension period varies depending on the type of product for which an extension is sought. Id.
* Id.
C. The Hatch-Waxman Act

To understand the methods and effects of pharmaceutical evergreening, it is important to be familiar with the provisions of the Drug Price Competition and Patent Term Restoration Act of 1984—the Hatch-Waxman Act. This act was intended to provide an accelerated path for generic entry while maintaining patent protection for branded pharmaceutical companies. Rather than requiring generic drug companies to go through the entire new-drug approval process, the Hatch-Waxman Act permits them to file an abbreviated new drug application (“ANDA”) and establish bioequivalence with the approved branded drug. This abbreviated process was meant to make more low-cost generic drugs available to the public.

After the branded drug manufacturer receives approval of their NDA by the FDA, the new drug is added to the FDA’s Orange Book. When a generic drug company seeks FDA approval of its product, it must show not only bioequivalence but also that:

1. the active ingredient of the generic drug is the same as that of the pioneer drug;
2. the generic drug has the same route of administration, dosage form and strength as the pioneer drug; and
3. the generic drug’s labeling must be same as the labeling of the pioneer drug.

Additionally, a generic drug company must certify that the patents listed in the Orange Book by the named brand:

- (i) have not been filed,
- (ii) are expired,
- (iii) will expire by a given date, or
- (iv) are invalid or will not be infringed by the manufacture, use, or sale of the new generic drug.

If the generic drug applicant wishes to proceed under paragraph IV, it must

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48 Id.
provide notice to the patent holder and the NDA applicant with a detailed explanation of why the patent is not infringed or should be declared invalid. If the NDA holder then brings a patent infringement lawsuit within forty-five days of this notice, the FDA is barred from granting approval to the ANDA holder for thirty months. Otherwise, if no lawsuit is filed within the forty-five-day period, or if the ANDA declares only Paragraph I or II certifications, the FDA must approve the ANDA, provided that all other approval requirements are satisfied.

As an incentive for generic companies to enter the market, the Hatch-Waxman Act allows the first generic ANDA applicant to enter the market with a 180-day exclusivity period, during which no other generic companies may be granted FDA approval. This effectively allows the generic and branded companies to share FDA exclusivity for a period of time. The idea behind this is to “encourage generic companies to challenge questionably weak or invalid patents.”

Although the Hatch-Waxman Act seems to give generic manufacturers many advantages throughout the path to market approval, there are provisions within it that serve branded NDA holders as well. An NDA holder may list additional patents in the Orange Book after an ANDA is submitted, and if they do so, “the ANDA applicant must make additional certifications within 30 days of the listing of the new patent.” Further, Hatch-Waxman creates additional FDA exclusivity periods for NDA holders that prohibit generic manufacturers from submitting an ANDA for three to five years after approval of the NDA. NDA holders are entitled to this exclusivity period regardless of whether the underlying patents on the

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“Id. § 355(g)(2)(B)(iv)(I).
“See id. § 355(g)(2)(B)(vi).
“Id. § 355(g)(2)(B)(vi).
“Id. § 355(g)(2)(B)(vi).
“Id.
“Kelly, supra note 51, at 420 (citing Natalie M. Derzko, The Impact of Recent Reforms of the Hatch-Waxman Scheme on Orange Book Strategic Behavior and Pharmaceutical Innovation, 45 IDEA J.L. & TECH. 164, 174 (2004)).
“Id.
drug are expired. Problems arising from these statutory provisions are explained in the following section.

D. Evergreening Using the Hatch-Waxman Act

Although specific evergreening strategies will be discussed in more detail in Parts III–IV below, the Hatch-Waxman Act provides a general framework that drug companies can leverage to extend the length of their patent and FDA exclusivity periods and block generic competitors. For example, branded manufacturer, Marion Merrell Dow, took advantage of the thirty-month stay provision for a secondary patent on their Seldane product. After Baker Norton filed an ANDA claiming paragraph IV non-infringement, Marion sued for infringement even though, “[s]imply stated, Baker Norton’s proposed activity [was] outside the scope of the . . . patent.” However, in this case, the FDA still initiated the thirty-month stay. Thus, although Baker Norton was granted summary judgment on the infringement issue, Marion was able to take advantage of the entire thirty-month stay period of exclusivity.

The FDA requires only patents related to drug substance, drug formulation, and method of use to be submitted to the Orange Book. This rule also explicitly prohibits patents related to the “packaging, metabolites, or intermediates” from being included with the NDA. Interestingly, however, the FDA does not have any “regulatory mechanisms for reviewing patent listings” made by NDA holders. In fact, the FDA has expressed that it does not even conduct a “review of submitted patent information to determine, at least on a very general basis, applicability to the particular NDA in question.” Accordingly, in the interest of preventing competitors
from entering the market, NDA holders often take wide latitudes when determining the types of patents to list in the Orange Book.\footnote{Kelly, supra note 51, at 438 (citing Terry G. Mahn, Patenting Drug Products: Anticipating Hatch-Waxman Issues During the Claims Drafting Process, 54 FOOD & DRUG L.J. 245, 250 (1999)).}

NDA holders may also “late-list” patents that were not included in the original NDA.\footnote{21 C.F.R. § 314.53(d)(3) (2019).} If an NDA holder lists a patent in the Orange Book after a generic company files an ANDA, the ANDA applicant must still make a certification regarding the newly listed patent.\footnote{21 C.F.R. §§ 314.50(i)(4) & (6), 314.94(a)(12)(vi) & (viii) (2019).} Although the 2003 amendments to the Hatch-Waxman Act do not allow for the NDA holder to obtain a second thirty-month stay against an ANDA applicant, a Paragraph IV certification may result in patent infringement litigation between the NDA holder and the ANDA applicant, the costs of which may ultimately deter an ANDA applicant from entering the market.\footnote{Applications for FDA Approval to Market a New Drug, 68 Fed. Reg. at 36676.}

III. HISTORICAL PHARMACEUTICAL EVERGREENING STRATEGIES AND RESPONSES

Pharmaceutical evergreening often involves obtaining secondary patents on features of a drug other than the main active ingredient. Secondary patents may cover aspects of the product, such as a tablet’s coating, alternate crystalline structures of the drug, or methods of use.\footnote{Tahir Amin & Aaron S. Kesselheim, Secondary Patenting of Branded Pharmaceuticals: A Case Study of How Patents on Two HIV Drugs Could Be Extended for Decades, 31 HEALTH AFF. 2286 (2012).} These secondary patents are often weaker than the original patent on the drug itself; however, they may still be used to either delay a generic drug’s market approval or make market entry prohibitively expensive.\footnote{Id. at 2286–87.}

A. New Uses

1. Overview and Examples

New uses for a drug currently on the market will sometimes allow a drug developer to obtain new method-of-use patents.\footnote{Rebecca S. Eisenberg, The Problem of New Uses, 5 YALE J. HEALTH POL’Y L. & ETHICS 717, 720 (2005).} Thus, developing
new uses for a patented drug may help the patent holder maximize research dollars and prolong the commercial life of the drug.\textsuperscript{77}

Several pharmaceutical companies have successfully deployed this new method-of-use patenting strategy.\textsuperscript{78} One example of this is Merck’s patents for its branded versions of the drug Finasteride.\textsuperscript{79} Finasteride is the active ingredient in Proscar, a drug first patented by Merck in 1992 for treating enlarged prostates with a five-milligram tablet.\textsuperscript{80} When Proscar came off patent in 2006, the FDA approved Merck’s competitors to begin manufacturing and selling generic versions of Proscar.\textsuperscript{81}

However, in 1997, Merck received a second patent on Finasteride when it proved that a lower one-milligram dose of the drug could help treat male pattern baldness.\textsuperscript{82} Using the protection from this patent, Merck continued marketing Finasteride as a one-milligram pill under the brand name Propecia for treating baldness at a price twenty-six times greater than it could have with Proscar.\textsuperscript{83}

Some criticize “use patents” that pharmaceutical companies obtain and attempt to deploy as unfair evergreening.\textsuperscript{84} Supporting this viewpoint is the fact that method-of-use patents have allowed branded competition to extend their patent exclusivity in the United States for an average of 7.4 years.\textsuperscript{85} However, as traditional methods for discovering new drugs become less successful and more expensive, the idea of discovering new uses for old drugs is gaining in popularity.\textsuperscript{86}

One example illustrates just how important use patents can be to society. Although originally created and marketed as a potential treatment for cancer, azidothymidine was later found to be an effective treatment for...
helping patients with HIV. It is unlikely that, without the patent incentive for this new use of the drug, azidothymidine would have been worth the additional research and development investment to find new uses and gain new approvals.

2. Skinny Labeling

More recently, patents on new uses have become less valuable due to the FDA now allowing generic drugs to engage in a practice known as “skinny labeling.” As stated before, generic companies are allowed to manufacture and sell an off-patent drug for an off-patent use once their ANDA is approved by the FDA. When marketing the generic version of the drug, the ANDA applicant may only list the off-patent uses on the drug’s label. However, if the branded company receives a patent and FDA approval for a new use of the drug, physicians may still prescribe the generic skinny-labeled version for this patented new use. Thus, a branded drug company can invest heavily in clinical trials and regulatory submissions to have an alternative use approved, only to be immediately undercut by physicians prescribing skinny-labeled generic drugs in place of the branded drug marketed and labeled for that use.

The Federal Circuit has validated this practice by holding that mere knowledge by a generic company that its product is being used to infringe patent rights is insufficient to show induced infringement. Rather, the Federal Circuit requires the generic company to have actually marketed the product for the infringing use. Thus, by merely selling the drugs that physicians prescribe for a patented use, generic manufacturers do not infringe the branded drug patents.

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88 Id.

89 Rai & Rice, supra note 84.

90 See supra notes 78–83 and accompanying text (discussing the off-patent use of Proscar).

91 Id.

92 Id.

93 Id.


95 Id. at 1365.
3. Branded Response to Skinny Labeling

a. Use Codes

To prevent generic skinny labeling, brand-name companies have also submitted overly broad use code claims to the FDA Orange Book to artificially increase the scope of their patented uses, thereby limiting the ability of generic companies to identify and list an unprotected use on their labels. This practice can be effective because, as mentioned before, the FDA plays a very limited role in screening out overly broad Orange Book submissions.

However, in Caraco, the United States Supreme Court determined that overly broad use codes submitted to the FDA’s Orange Book could be challenged by generic companies. In Caraco, Novo Nordisk’s only unexpired patent covered a fairly narrow use—treating non-insulin-dependent diabetes through a combination of its drug, repaglinide, and another drug, metformin. In contrast, the Orange Book use code that was claimed by Novo Nordisk attempted to cover every method of “improving glycemic control in adults with type 2 diabetes.” This much broader claim effectively prevented generic companies from skinny labeling the drug and marketing it for any use. In its opinion, the Court held that the 2003 amendments to the Hatch-Waxman Act allowed generic companies to file a counterclaim to correct an overly broad use code listed in the Orange Book. Absent the ability to do so, a generic drug company would be unable to market its product for any non-infringing uses.

The Caraco decision seems to follow both the statutory language and legislative intent behind the 2003 Hatch-Waxman amendments. The practices employed by Novo Nordisk had been thoroughly documented by the Federal Trade Commission (FTC) and served as an impetus for the new legislation. However, as noted in Justice Sotomayor’s concurrence, the
2003 amendments are suboptimal for generic companies.\textsuperscript{106} To correct an overly broad use-listing in the Orange Book, a generic company must first provoke the branded company into suing it for patent infringement by filing a paragraph IV invalidity or noninfringement certification.\textsuperscript{107}

Justice Sotomayor noted two potential problems with this requirement. First, it undoubtedly requires the generic company to incur significant expenses in litigation and further delays generic entry.\textsuperscript{108} Second, the statute is silent on what would happen if the branded company did not launch a lawsuit against the generic paragraph IV applicant.\textsuperscript{109} The FDA might still approve the ANDA.\textsuperscript{110} If, however, the generic company was approved, the generic company would be forced into marketing the product with a label identical to the branded manufacturer’s.\textsuperscript{111} In this case, the generic company would likely then be liable to the branded company for induced infringement of the underlying patent.\textsuperscript{112} Either way, the generic company is placed in a tough position.

\textit{b. Rescue Drugs}

In certain situations, good faith patenting on legitimate secondary uses may still allow branded drug companies to prevent themselves from being immediately undercut by physicians prescribing skinny-labeled generic drugs. These situations involve drugs that went through the clinical trial stage, were determined to be safe for use in humans, but were ultimately abandoned due to lack of efficacy.\textsuperscript{113} Often, these abandoned drugs are old, and the original patent on their chemical composition expired.

Rediscovering, repurposing, and patenting these drugs for a different use than that originally intended can help deliver new therapies to patients while still allowing drug companies to see a return on their investments. These “rescue drug” method-of-use patents allow companies to maintain patent protection just as they would with a composition-of-matter patent.\textsuperscript{114} Because there is no FDA approved, off-patent use for the rescue drugs, there is no way for generic companies to skinny label around the branded

\textsuperscript{106} Caraco, 566 U.S. at 426 (Sotomayor, J., concurring).
\textsuperscript{107} Id.
\textsuperscript{108} Id.
\textsuperscript{109} Id.
\textsuperscript{110} Id. (citing 21 U.S.C. § 355(j)(5)(B)(iii)) (“[W]ithout prejudice to infringement claims the patent owner might assert when the ANDA applicant produces or markets the generic drug.”).
\textsuperscript{111} Id.
\textsuperscript{112} Id. at 428.
\textsuperscript{113} Rai & Rice, supra note 84.
\textsuperscript{114} Id.
drugs. Without this type of patent protection, there would be no financial incentive for a company to investigate or work to approve new uses for already developed drugs. Therefore, patients would stand to lose out on many therapies that could otherwise be available.

One of the more famous examples of utilizing a method-of-use patent for an initially failed drug is the erectile dysfunction (ED) drug, Viagra. Although Viagra was ineffective and abandoned for treating hypertension, it was found to be useful for treating ED. After obtaining a method-of-use patent in 1994, the patent was successfully upheld and asserted in an infringement action in the U.S. District Court for the Eastern District of Virginia.

B. New Formulations

1. Overview and Examples

A pharmaceutical company may also choose to patent a new formulation of a drug to extend its patented life. Often, these new formulations may involve new strengths and dosage forms of the previous product. These new formulations may be protected by additional patents and may receive a three-year period of exclusivity for “new clinical investigation” under the Hatch-Waxman Act. Studies have shown that the practice of introducing new pharmaceutical formulations may be so prevalent that about half of the new small-molecule drugs approved in 2002 have introduced new formulation products, usually within five years of launching the original product.

In one illustrative example, a new formulation allowed the branded manufacturer to maintain several additional years of patent protection after

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115 Id.
116 Id.
117 Id.
119 Id.
123 Beall et al., supra note 121, at 219.
generic companies entered the market.\textsuperscript{124} Otsuka developed an aripiprazole that is used to treat mental conditions such as schizophrenia, bipolar mania, and major depressive disorder.\textsuperscript{125} After generic companies entered the market and began competing with Otsuka with the original tablet form of the medication, Otsuka developed an injectable, extended-release formulation of the product that allowed them to maintain a monopoly over the extended-release form.\textsuperscript{126} The injectable formulation had some benefits, such as less frequent administration, which was likely to benefit certain patients in need.\textsuperscript{127} This new formulation is an example of a pharmaceutical innovation for which patients were willing to pay a premium price.

At its core, new formulations of drugs certainly do have some positive effects. New formulations are typically introduced shortly after approval of the original product.\textsuperscript{128} If a drug company wants to extend the length of its patent protection with new formulations, it may be more inclined to wait until its original patents are about to expire before obtaining additional patents on new formulations. The fact that this is generally not the case indicates that, rather than solely trying to extend the life of their patent protection, some drug companies are attempting to provide greater choices to patients who are unable to use the original formulation of the product.\textsuperscript{129} This practice further suggests that at least some manufacturers are merely being diligent by continuously improving their products and striving to add value for a larger patient base.\textsuperscript{130}

Additionally, since the scope of these secondary patents is narrower, they achieve the dual purpose of creating an incentive to research new therapeutic benefits of a product without blocking access to the drug itself.\textsuperscript{131} The new formulation patents do not extend the term of the original patent on the chemical compound.\textsuperscript{132} Accordingly, after the original composition

\textsuperscript{124} Id. at 222.
\textsuperscript{126} Id.
\textsuperscript{127} Id.
\textsuperscript{128} Id.
\textsuperscript{129} Id.
\textsuperscript{130} Id.
\textsuperscript{131} Id.
of the matter patent expires, there is no patent-based restriction on the
generic companies entering the market and competing with branded
products.  

Some say that unless this secondary patent covers a valuable new
advancement that consumers are willing to pay for, it will essentially be
worthless and not have any impact on the market for the original drug. In
theory, this is because consumers, who see the much more expensive
patented drug, will be able to determine that the value of the patented
advancement is not proportional to the increased cost. In that case, the
consumer will instead opt for the cheaper generic version of the original off-patent product. Indeed, a leading patent expert, Judge Giles Rich of the
U.S. Court of Appeals for the Federal Circuit, has expressed, “A monopoly
on something nobody wants is pretty much . . . a nullity. That is one of the
beauties of the patent system. The reward is measured automatically by the
popularity of the contribution.”

Unfortunately, however, the pharmaceutical industry does not always
work so neatly. The pharmaceutical market requires the doctor to select the
drug for the patient. Because the doctor does not bear the cost of the
prescription, often they will not even know or consider the price of the drug,
and patients have minimal say in selecting a cheaper alternative. In this
way, the pharmaceutical market does not function like a free market
economy, and, as a result, Judge Rich’s theory breaks down. Certain
tactics, such as the product hop, show how these unique aspects of the
pharmaceutical industry permit gamesmanship of the patent system and the
Hatch-Waxman Act by pharmaceutical companies.

2. The Product Hop

One strategy that patent holders often employ is the product hop. Although product hopping can be used with other secondary patenting
methods, it is useful to include in this section on new formulations because
the most popular examples of product hopping have featured patents on

pharmaceutical products, but without removing older and less expensive variants from the
market.”).  

Id.

133 Id. at 137–38.

134 Id. at 138.

135 Id. (quoting Giles S. Rich, Principles of Patentability, 28 GEO. WASH. L. REV. 393, 402 (1960)).


137 Id.

138 Id.; see also Rich, supra note 136.
new formulations. As illustrated in the following cases, product hopping involves using provisions within the Hatch-Waxman Act, patent laws, and drug substitution laws to block generic competition and ensure that patients continue to purchase monopolized products. The tactic has been combated with mixed success using antitrust laws.

C. New York v. Actavis PLC (Namenda)

Actavis developed a patented drug called Namenda IR for treating Alzheimer’s patients. However, as the Namenda IR patents were set to expire in 2015, generic companies began preparing to rush into the market with low-cost alternatives. Shortly before the IR patent’s expiration, Actavis went on to announce a newly patented, extended-release formulation, Namenda XR, which would not come off patent until 2029. The XR formulation only required drug administration once per day, rather than the twice-a-day IR formulation. To transfer patients to its newly patent-protected product, Actavis began promoting the XR formulation to doctors, pharmacists, and caregivers while temporarily lowering the price of the XR below that of the IR version. Months before the release of generic Namenda IR, Actavis announced that they would discontinue selling Namenda IR. Since the branded IR formulation was no longer on the market, drug substitution laws did not allow prescriptions to be substituted for the generic formulation.

In response to Actavis’s actions, the State of New York filed a complaint seeking to block Actavis’s product hop, alleging that Actavis was

140 See Namenda, 787 F.3d at 645–46 (involving a product hop to a new extended release formulation of the drug); see also Mylan Pharm. Inc. v. Warner Chilcott Pub. Ltd. Co. (Doryx), 838 F.3d 421, 429 (3d Cir. 2016) (involving product hops to various new tablet formulations).
141 See Namenda, 787 F.3d at 655–58 (holding that introducing a new patented formulation while simultaneously pulling the soon-to-be off-patent formulation from the market violated provisions of the Sherman Anti-Trust Act); Doryx, 838 F.3d at 438–39 (finding that defendants actions were not anticompetitive because plaintiff was advantaged by its 180-day exclusivity period and other substitute drug options remained available for consumers).
142 Karshtedt, supra note 8, at 1168.
143 Namenda, 787 F.3d at 643–46.
144 Id. at 647.
146 Namenda, 787 F.3d at 648.
147 Id.
148 Id.
violating provisions of the Sherman Antitrust Act. To show that Actavis was violating the law, New York had to prove “(1) that the defendant ha[d] engaged in predatory or anticompetitive conduct with (2) a specific intent to monopolize and (3) a dangerous probability of achieving monopoly power.”

The Second Circuit found that by introducing the new XR formulation while simultaneously withdrawing the IR formulation, patients were forced into switching prescriptions, which impeded generic competition and amounted to anticompetitive conduct under the Sherman Antitrust Act. In reaching this conclusion, the court examined both the consumer coercion effects and the likely impediment to competition. Lastly, a “dangerous probability” of monopoly power was present because of the unique characteristics of the Alzheimer’s pharmaceutical market and the way the product-hopping scheme could circumvent drug substitution laws.

D. Mylan Pharmaceuticals Inc. v. Warner Chilcott Public Co. (Doryx)

To receive approval of an ANDA, a generic company must first show that its product is bioequivalent and therapeutically equivalent to the branded product. If the generic company both proves measures of equivalence and earns an AB rating, state laws permit pharmacists to substitute the generic for the branded prescription. To achieve an AB rating for drug tablets, most state laws require generic companies to demonstrate that their tablets are identical in size and scoring to the branded drug.

Doryx, an off-patent doxycycline hyclate capsule used for treating acne, was approved by the FDA in 1985. After facing unsuccessful sales on the capsule product, Mayne, the drug manufacturer, and Warner, the

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149 Id. at 649; see also 15 U.S.C. §§ 1–2 (2018).
150 Namenda, 787 F.3d at 651 (quoting Spectrum Sports, Inc. v. McQuillan, 506 U.S. 447, 456 (1993)).
151 Id. at 654.
152 Id. at 654–58.
153 Id. at 655.
155 Generally, multisource drug products with identical active ingredients, strength, dosage forms, and routes of administration are coded as AB if the data demonstrate bioequivalence. Orange Book Preface, FDA, supra note 50 (citation omitted). AB-rated drugs are drugs that meet the necessary bioequivalence standards established by the Food and Drug Administration. What is an AB-Rated Drug (Non-AB-Rated Drug), TAKERx, www.takerx.com/abrated.html [https://perma.cc/XBY9-4C37] (last visited Mar. 27, 2020).
157 Id. at 429.
distributor (collectively “Mayne”), decided to develop a new extended-release tablet formulation of the drug.158 After receiving FDA approval for the tablet, Mayne stopped selling the capsule formulation.159

Later, Mayne proceeded to implement a sequence of changes to the capsule size and scoring, each of which would require generic manufacturers to file a new ANDA and await regulatory approval before returning to market and benefiting from drug substitution laws.160 To compete with Mayne, Mylan developed each iteration and obtained ANDA approval for each of the four changes before subsequently being shut out of the market when Mayne pulled its previous designs from the shelves.161

Although the Third Circuit Court of Appeals found that Mayne indeed changed its tablets primarily to delay generic market entry, the court found that the conduct did not create a dangerous possibility of monopoly power.162 To reach this conclusion, the court noted that the relevant market should include more than just Doryx and, accordingly, examined all oral tetracyclines used to treat acne.163 When viewed from this broader perspective, Mayne held only eighteen percent of the market.164 Consequently, the court held that Mayne’s conduct did not rise to the level prohibited by the Sherman Antitrust Act.165

E. Reconciling Namenda and Doryx

In both Namenda and Doryx, courts found that discontinuing a product on its own does not amount to exclusionary conduct.166 Under an antitrust analysis, courts must find some additional coercive conduct by the branded company that forces consumers to purchase their products.167 This question can be especially complicated and nuanced for judges and juries who are unfamiliar with the complexities of the pharmaceutical industry to make an informed decision.168 It involves a combination of analyzing complicated antitrust law, patent law, the Hatch-Waxman Act, and state law.
drug substitution laws. Accordingly, the antitrust analysis is especially prone to deliver inconsistent and ill-informed results. Indeed, courts have acknowledged that they are ill-equipped to handle these types of decisions.

F. Chiral Switches

1. Chirality Explained

Two-thirds of the drugs currently on the market contain chiral molecules. Simply put, a chiral molecule lacks symmetry within its molecular structure. As a result, chiral molecules have counterparts called enantiomers that are mirror images of the chiral molecules. A mix of two different enantiomers is known as a racemic mixture.

The body typically interacts with different enantiomers in different ways. Usually, one enantiomer—the eutomer—will have more desired bioactive effects, while the other enantiomer—the distomer—is biologically inactive or even toxic to humans. Originally, drugs were primarily racemic mixtures. However, in the 1980s, scientists began purifying these mixtures into just their therapeutically beneficial enantiomers. In some cases, when purified, the drugs may be taken in smaller doses or have fewer associated side effects.
2. Overview and Examples

When developing a new drug, the FDA gives developers some leeway to choose their own stereochemistry as long as they demonstrate an understanding of the effects of the different enantiomers. As a result, strategic thinking about patent protection for the new drug may play a role in decisions regarding the stereochemistry of the drug. In particular, companies may first opt to patent a slightly less effective racemic mixture and later obtain a patent on the eutomer once the patent term is close to expiration. This chiral switch has been estimated to extend the patent life for an additional five years. Interestingly, at least one study has found that many blockbuster single enantiomer drugs show no evidence of superiority to their older racemic mixture counterparts.

An example of the chiral-switch patent extension method can be seen with Nexium, developed by AstraZeneca. AstraZeneca originally obtained a patent and FDA approval for the racemic Prilosec to treat acid reflux. By 2000, Prilosec was the best-selling medicine in the world and was earning $5 billion a year in the United States alone. By 2003, when the Prilosec patent expired, the company was already actively advertising a newly patented enantiomer version of Nexium. Because Prilosec had no major side effects, switching from the racemic mixture to the enantiomer provided no significant clinical benefits to patients. AstraZeneca also was successful in switching Prilosec and its generic counterparts onto the over-the-counter market while maintaining a prescription status for Nexium. By doing this, the company was able to further thwart generic competition by creating the illusion that the new prescription Nexium was the stronger product.

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180 Id. at 755.
181 Id.
184 Id.
185 Id. at 755.
186 Joffe, supra note 80.
187 Goozner, supra note 185, at 83.
188 Id. at 84.
IV. DRUG-DEVICE COMBINATION AS A PATENT EXTENSION STRATEGY

A. Drug-Device Combination Products Explained

According to the Code of Federal Regulations, a combination product is “[a] product comprised of two or more regulated components, i.e., drug/device, biologic/device, drug/biologic, or drug/device/biologic, that are physically, chemically, or otherwise combined or mixed and produced as a single entity.” As technological advances continue to blur the lines between product types, the FDA expects to receive more and more combination products for review. Currently, the most common types of drug-device combination products include pulmonary inhalers, injection systems, and infusion systems. Other frequently seen combination products include nasal sprays, creams, eye drops, ear drops, drug-eluting stents, and transdermal patches. Many conditions, such as asthma, diabetes, and allergic reactions, are often treated using a medicine paired with a specific device.

B. Overview and Examples

Medicines and devices that are used together are typically patentable separately from one another. By patenting the medicine and the device, companies can prolong their patent exclusivity since the various device patents can typically outlast those for the medicine itself. Additionally, section 3038 of the 21st Century Cures Act of 2016 creates an expedited regulatory pathway for patenting combination products with an already approved constituent part and allows drug-device combination patents, also referred to as tertiary patents, to be listed in the Orange Book. By listing these patents in the Orange Book, drug-device

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189 21 C.F.R. § 3.2 (2019).
191 Featherstone, supra note 15, at 22.
192 Id.
193 Id.
194 Id.
195 Reed F. Beall & Aaron S. Kesselheim, Tertiary Patenting on Drug-Device Combination Products in the United States, 36 Nature Biotechnology, 142, 142 (2018) (explaining that device patents typically outlast the patents on the drug itself because device patents can be updated and patented incrementally).
combination product manufacturers are better able to prevent generic entry by requiring generics to either await the expiration of the patents or make a paragraph IV certification and risk being sued for infringement. While the FDA explicitly prohibits listing patents related to the packaging of drugs, interestingly, the agency is silent on whether drug delivery patents that do not claim the drug itself should be placed in the Orange Book. However, by not rejecting listings after several pharmaceutical companies have explicitly notified the agency about listing these patents, it seems that the FDA has acquiesced to this practice.

Because medical devices are typically developed (and patented) after the drug itself, the younger device patent normally outlives the patent on its associated drug. Also, the mechanical drug-delivery devices are generally easier to modify and patent than the drugs with which they are used in combination. Accordingly, where the patents on drugs expire and potential modifications are limited, device patents can be extended much longer and provide increased patent protection. By allowing drug-device patents to be listed in the Orange Book, the FDA has permitted pharmaceutical companies claiming a delivery device to benefit for an additional 4.7 years of patent protection on average.

A recent study has found that the practice of obtaining and listing patents on the drug delivery device has increased in the past twenty years. In 2000, forty-two drug-device combination products existed on the market with twenty-nine associated device patents. In 2016, however, 127 drug-device combination products existed on the market with twenty-nine associated device patents.
device combination products were on the market, and 478 device patents were associated with them.\footnote{Id. at 142.}

This increase in device patenting can likely be attributed to three main causes. First, device patenting is playing a larger role in combination products’ patent portfolio.\footnote{Beall et al., supra note 39, at 2.} This is largely due to the tendency of device patenting to extend the life of a product’s patent protection longer than the patent for the drug itself.\footnote{Id.} In fact, in 2016, thirty-two drug products were covered exclusively by tertiary device patents.\footnote{Beall & Kesselheim, supra note 195, at 143.} Second, more combination products now list a larger number of device patents related to the product.\footnote{Id.; see also Beall et al., supra note 39, at 3.} Studies have found that, on average, drug-device products list two patents on the drug itself and three patents on the delivery device, while thirteen percent listed ten or more patents for the delivery device.\footnote{Beall et al., supra note 39, at 3; see also Beall & Kesselheim, supra note 195, at 143.} Third, companies accrued device patents more frequently than other patents relating to the product.\footnote{Beall & Kesselheim, supra note 195, at 143 (stating that in seventy percent of the study’s sample size, device patents were the last to expire).} Again, this is likely because mechanical modifications to the delivery device are more readily updated and patented than their pharmaceutical counterparts.

It has been suggested that drugs with a more niche, specialized market typically experience fewer paragraph IV patent challenges than those with larger scale consumer bases.\footnote{Henry G. Grabowski & Margaret Kyle, Generic Competition and Market Exclusivity Periods in Pharmaceuticals, 28 MANAGERIAL & DECISION ECON. 491, 491 (2007).} One likely reason for this could be that the smaller market for more niche drugs is not sufficient to make up for the expenses incurred by a generic company following patent litigation after the paragraph IV challenge. As many drug-device combination products serve these types of specialized markets, more of the delivery device patents may go unchallenged, thus further delaying generic market entry and incentivizing companies to list patents further unrelated to their associated medicine.\footnote{Beall & Kesselheim, supra note 195, at 143.}

While some have criticized the FDA’s practice of allowing patents on associated delivery devices to be listed in the Orange Book, in a draft guidance report, the FDA has clarified its position on why it considers mechanical aspects of delivery systems as part of the “drug product,” making

\begin{itemize}
  \item \textit{Id.} at 142.
  \item Beall et al., \textit{supra} note 39, at 2.
  \item \textit{Id.}
  \item Beall & Kesselheim, \textit{supra} note 195, at 143.
  \item \textit{Id.; see also} Beall et al., \textit{supra} note 39, at 3.
  \item Beall et al., \textit{supra} note 39, at 3; \textit{see also} Beall & Kesselheim, \textit{supra} note 195, at 143.
  \item Beall & Kesselheim, \textit{supra} note 195, at 143 (stating that in seventy percent of the study’s sample size, device patents were the last to expire).
  \item Beall & Kesselheim, \textit{supra} note 195, at 143.
\end{itemize}
them listable.\footnote{Terry G. Mahn, Michael A. Siem & Elizabeth M. Flanagan, Orange Book Listing Opportunities for Drug-Device Combinations, BLOOMBERG L. (Nov. 18, 2011), https://news.bloomberglaw.com/pharma-and-life-sciences/orange-book-listing-opportunities-for-drug-device-combinations [https://perma.cc/8Y9M-G9E7].} As noted in the report, since the mechanical components of the delivery system are thought to work in concert with the drug system, they are deemed “integral” to the drug product.\footnote{Id. (citing FDA, DRAFT GUIDANCE FOR INDUSTRY: METERED DOSE INHALER (MDI) AND DRY POWDER INHALER (DPI) DRUG PRODUCTS 60 (2003)).} Because these components are designed to dispense extremely accurate amounts of a drug, any changes in a component could lead to a change in the dose of the drug administered to the patient. Therefore, the FDA seems to believe patents on delivery devices are necessary for review and listing in the Orange Book.\footnote{Id.}

Yet, recent litigation in the First Circuit suggests otherwise and points to the FDA’s statements that “[t]he key factor is whether the patent being submitted claims the finished dosage form of the approved drug product.”\footnote{Cesar Castillo, Inc. v. Sanofi-Aventis U.S., LLC (In re Lantus Direct Purchaser Antitrust Litig.), 950 F.3d 1, 8 (1st Cir. 2020) (citing Applications for FDA Approval to Market a New Drug Patent Submission and Listing Requirements and Application of 30-Month Stay on Approval of Abbreviated New Drug Applications Certifying That a Patent Claiming a Drug Is Invalid or Will Not Be Infringed 68 Fed. Reg. 36,680 (June 18, 2003) (to be codified at 21 C.F.R. pt. 314)).} Thus, the First Circuit concluded that components of the drug device that do not claim the drug itself are ineligible for listing in the Orange Book.\footnote{Id. at 9.}

The First Circuit decision comes at a time where the FDA is “unable to reach a decision [on the matter] . . . due to the need to address other Agency priorities.”\footnote{Id. at 10.} It seems likely that in the absence of clear FDA guidance, courts will continue to fill in and create their own rules for how delivery device Orange Book listings ought to be handled.\footnote{See Sara Koblitz, If FDA Won’t Regulate, Maybe the Courts Will: First Circuit Opines on Listing Device Patents in the Orange Book, HYMAN, PHELPS, & McNAMARA: FDA L. BLOG (Mar. 16, 2020), http://www.fdalawblog.net/2020/03/if-frd-wont-regulate-maybe-the-courts-will-first-circuit-opines-on-listing-device-patents-in-the-orange-book/ [https://perma.cc/U7WL-TRZV].}

C. Effects on Population

Permitting companies to list drug-device patents in the Orange Book, thereby impeding generic competition, has several potential effects on patients who use them. The epinephrine autoinjector, known as the EpiPen,
is used for treating severe allergic reactions.\textsuperscript{221} Although epinephrine, the active ingredient in the EpiPen, was first isolated over 100 years ago, the product saw price increases of over 400\% from 2016 to 2018.\textsuperscript{222} The primary cause of this price increase was the patents on the drug delivery device.\textsuperscript{223} In 2015, an estimated 3.6 million Americans were prescribed an EpiPen.\textsuperscript{224} Although Mylan, the drug manufacturer, has now released a cheaper generic version, at its peak, the EpiPen cost consumers over $700. With an expiration date of only eighteen months from the date of manufacture, American consumers were spending an estimated $1.8 billion per year on EpiPens.\textsuperscript{225} After the generic version of the EpiPen was released, the price dropped to as low as $150.\textsuperscript{226} Collectively, this could mean that the device patents on the EpiPen costed Americans as much as $1.4 billion more for essentially the same products.

In addition to the EpiPen, another commonly patented drug delivery product is the inhaler, used for delivering medication into the body through one’s lungs. In 2008, the FDA instituted regulations requiring all inhalers to stop using ozone-depleting chlorofluorocarbon propellants (CFCs).\textsuperscript{227} This led many companies to develop new inhaler designs that were intended to work with new, less environmentally harmful, propellants.\textsuperscript{228} In turn, many of these companies began patenting features of these new inhaler designs. This caused many off-patent medications to be newly marketed with on-patent inhalers at double or triple the price of their earlier CFC inhaler counterparts.

Permitting companies to extend the patent protection on a drug through incremental advances in the delivery system of devices may have some potential to increase the medication’s therapeutic value by

\textsuperscript{221} See Beall & Kesselheim, supra note 195.
\textsuperscript{222} Id.
\textsuperscript{223} Id.
\textsuperscript{228} Beall et al., supra note 39, at 2.
incentivizing the development of a more effective delivery system. However, this therapeutic value must be evaluated against its other negative effects. In addition to raising costs for medications, increased modifications to mechanical aspects of the delivery device may also “increase the risk of product recalls, manufacturing errors, and device failures,” while requiring physicians to continuously retrain on how the modified device works. Although not explicitly linked to patent incentives, several drug delivery devices have undergone large-scale recalls in the last three years alone. Continuing to make trivial modifications on these devices may increase the likelihood of issues in the device design or manufacturing process. Such events show the seriousness of the situation and the potentially dangerous effects of the abuse of the patent system when it comes to pharmaceuticals.

D. Proposed Solutions

Before taking action to prevent drug companies from engaging in this tertiary form of evergreening, it is important to properly define what conduct actually constitutes evergreening and should be prohibited. A general definition of patent evergreening would include any secondary or tertiary patent that extends the exclusivity period of the product without providing any proportionate benefit. Under this definition, many patents covering improvements to device-delivery systems could still be patented and used to extend the product’s exclusivity period.

Another possibility could be to define evergreening in a more health-specific way. Under the health-specific definition, any secondary or tertiary patent that extends the product’s exclusivity period without a proportionate therapeutic benefit would qualify. As an example, the patented inhalers developed following the FDA’s prohibition on CFC inhalers did benefit society by preventing harmful emission of CFCs even though they did not produce any health-related benefits to the users. Under the definitions above, these types of modifications would fall under the health-specific definition but would not be considered evergreening under the general definition.

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230 Beall & Kesselheim, supra note 195, at 143.
231 Id.
232 Id. at 143–44.
233 Id.
234 Beall et al., supra note 39.
235 Id.
236 Id.
1. The Indian Approach

In 2005, India adopted this health-specific definition and took a major step against all types of secondary and tertiary patent evergreening by requiring new patent applicants to show that their inventions result in enhanced therapeutic efficacy compared to a known compound.\(^{237}\) To make this showing, Indian patent applicants must now demonstrate therapeutic improvement by way of sufficient clinical evidence.\(^{238}\) Unfortunately, at least one study suggests that actions taken by the Indian government have not done much to curb secondary patenting and that seventy-two percent of secondary patents on drugs were allegedly incorrectly granted to applicants.\(^{239}\) According to this study, conditional exceptions to the anti-evergreening therapeutic efficacy statute allowed drug companies to circumvent its restrictions and obtain patents despite failing to show therapeutic improvements.\(^{240}\)

The United States could amend its laws in several ways to combat tertiary pharmaceutical patent evergreening. First, one option could be to adopt a similar prohibition as India against advances that do not provide enhanced therapeutic efficacy. However, should the United States adopt similar legislation, lawmakers should look to achievements and shortcomings in the Indian anti-evergreening statutes to ensure that U.S. laws will serve their intended purpose and be fairly enforced. One option for doing so could be to permit generic companies to show that the proposed advance does not lead to a significant increase in therapeutic efficacy over traditional therapies and allow such evidence to invalidate a patent. However, such regulations would likely dramatically increase the expense of pharmaceutical patent litigation, as each side would probably end up having to fund clinical studies to demonstrate therapeutic efficacy and spend additional time and money litigating the merits of each study. Because branded companies have much higher profit margins and likely greater resources to spend in such a fight against a generic competitor, it is

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\(^{238}\) Id.


\(^{240}\) Id. at 24.
unlikely that this proposed solution would cause generic companies to fare much better than in the Indian system.\footnote{See Curt D. Furberg, Bengt D. Furberg & Larry D. Sasich, Knowing Your Medications: A Guide to Becoming an Informed Patient 56 (2010), https://www.express-scripts.com/art/pdf/kap17Medications.pdf [https://perma.cc/3H39-8JM8].}

2. The Skinny Labeling Approach

A second solution could be for the FDA to allow generic companies to follow a similar methodology as that for skinny labeling discussed in Section III.A. In skinny labeling, generics are permitted to list an off-patented use of the drug on its label, which doctors can then prescribe to patients for an on-patent use.\footnote{Rai & Rice, supra note 84.} Likewise, if the FDA permitted generic companies to market the drug using an off-patent, previously approved version of a delivery device, generic companies could enter the market and offer cheaper alternatives. Branded companies would still have the opportunity to compete with generics by making patented, beneficial developments to the device design; however, consumers would have more power to determine whether the improvement is worth paying the higher cost of the branded drug.

Such a solution may require modifications to the Hatch-Waxman Act and the Orange Book. In the current state, if a generic drug company wanted to market a drug using an off-patent delivery device, it would still have to make a paragraph IV certification that they are not infringing the newer, on-patent device improvements listed in the Orange Book.\footnote{21 U.S.C. § 355(j)(2)(B)(iv)(II) (2018).} As discussed in Section II.D. and illustrated by the Seldane example, such a certification could expose the company to expensive patent litigation and a thirty-month stay of FDA approval, even though they are in no way infringing the device patent.\footnote{21 U.S.C. § 355(j)(5)(B)(iii) (2018).}

To prevent this problem, the FDA could introduce a different segment in the Orange Book, where certain other broader categories of device patents could be listed.\footnote{Beall et al., supra note 39, at 12.} Additionally, if the Hatch-Waxman Act is revised so that generic companies would not have to make a paragraph IV certification and be subject to litigation when designing around these broader device patents, generic companies may be much more likely to
enter markets for off-patent drugs that are only currently protected by device patents.\textsuperscript{246}

In this case, if generic companies were infringing the patents for the drug-delivery device, the patent holder could certainly still sue them for patent infringement, as would be the case in almost any other industry. Here, however, the Hatch-Waxman Act would not impose an automatic thirty-month stay or otherwise prevent approval of the generic by the FDA. Thus, patients in need of the drugs could still have access to these low-cost generic alternatives while the branded and generic companies litigate the patent infringement suit.

The Orange Book would still perform its function of informing generic companies that wish to enter a particular pharmaceutical market of the relevant patents without imposing Hatch-Waxman restrictions that block them from entering the market.\textsuperscript{247} However, under this model, there would be a need to decide which patents should be listed in which section of the Orange Book, as branded companies would be unlikely to voluntarily list their patents in the less enforceable section. If this solution were to be adopted, it could be left to manufacturers to comply with the FDA guidelines in good faith, or risk facing anti-trust liability, as was expressed by the First Circuit.\textsuperscript{248} Alternatively, it may fall to the FDA—as the regulatory agency in charge of the Orange Book—to take a more hands-on approach to determine what patents should be listed in which section.\textsuperscript{249}

Although the FDA has made it clear that the agency does not want to be in the business of policing Orange Book listings for fear of directing litigation toward itself, it may be time for the FDA to get involved.\textsuperscript{250} The current system shifts the social expenses of Hatch-Waxman gamesmanship to the patients paying for and relying on the drugs at issue.\textsuperscript{251} Though the Hatch-Waxman Act is intended to expedite generic market entry, by

\textsuperscript{246} This is because various provisions within the Hatch-Waxman Act serve to deter generics from entering the market. See 21 U.S.C. § 355(j)(2)(B)(vi)(I)(II) (2018).

\textsuperscript{247} Orange Book Preface, supra note 50 (“The Addendum to this publication identifies drugs that have qualified under the FD&C Act for periods of exclusivity and provides patent information concerning the approved drug products in the Orange Book.”).

\textsuperscript{248} Cesar Castillo, Inc. v. Sanofi-Aventis U.S., LLC (In re Lantus Direct Purchaser Antitrust Litig.), 950 F.3d 1, 13 (1st Cir. 2020) (holding that the absence of good faith adherence by a branded manufacturer supports a finding of anti-trust liability).

\textsuperscript{249} Id.


\textsuperscript{251} See supra Section IV.C.
designing a system where generics have to wait on FDA approval and litigate with branded companies every time branded companies abuse the rules, the legislation may have the opposite effect.

The FDA maintains that it does not have the expertise to determine whether patents in the Orange Book apply to the product and purports to push the question downstream for courts to determine during Hatch-Waxman litigation. However, as Orange Book patents become less and less related to their corresponding products, perhaps it is time that the FDA develops this expertise. Creating some sort of pre-litigation administrative pathway for settling listing disputes between branded companies and the FDA could help filter out some of the feared claims. Settling these disputes before generics attempt to enter the market would likely promote faster access to low-cost medication.

A foreseeable issue with the skinny labeling approach could be that it would incentivize branded companies to recreate the model of the rescue drug, as described in Section III.A.3. Similar to how branded companies created uses for drugs that had not yet been approved for any use, branded companies may attempt to patent devices to be used with medications that have never previously been approved for use with a device. Such a tactic could have the effect of unnecessarily increasing the number of devices used in combination with pharmaceutical products on the market as branded companies would be incentivized to pair devices with drugs not for therapeutic improvements but for extending the life of their patent protection. If the branded company were to accompany this new device pairing with a product hop away from non-device treatment, they may be successful in blocking out the generic competition that seeks only to sell the pharmaceutical product. However, this issue could likely be avoided if the FDA also permits generic companies to market the pharmaceutical when an off-patent, previously approved version of the drug exists without a device.

3. The All-Up-Front Approach

Third, in addition to, or in place of, creating an additional segment within the Orange Book, the FDA could also mandate that branded

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252 Examining Issues Related to Competition in the Pharmaceutical Marketplace, supra note 250, at 64–65 (indicating that the courts should be assessing the validity of the listed patents because the FDA does not have the expertise).

253 Id. at 64.

254 See supra Section III.A.3.

255 This is because there would be no earlier-version off-patent device that could be substituted for the new patented device. See supra Section III.B.2.
companies list all device-related patents in the Orange Book when the drug is first placed on the market. This would allow branded companies to enjoy the same protections afforded by the Hatch-Waxman Act for a limited period and simultaneously prevent them from listing new device-improvement patents after the cutoff date. Again, doing so would allow branded companies to sue generics outside of the Hatch-Waxman framework, but there would be less motivation to do so because of the unavailability of the thirty-month stay provision.

However, a foreseeable problem of this proposed solution is that generics might be less well informed on existing patents related to the device, as branded companies may no longer have to publicly list patents obtained after the market date in the Orange Book. This could result in generic companies unknowingly infringing on patented products or being forced to incur additional costs of conducting extensive freedom-to-operate research prior to marketing new products.

In light of the above discussion, the best solution is likely the second, "skinny labeling" option with corresponding amendments to the Hatch-Waxman Act. This solution seems to best allow branded companies to benefit from making genuinely beneficial device improvements to therapies while preserving the public’s access to greatly needed pharmaceutical products. Moreover, this option does not have the same inherent issues of leaving generic companies uninformed about branded patents, as seen in option three, or having the potential to dramatically increase the costs of the pharmaceutical patent system, as seen in option one.

V. CONCLUSION

Due in part to the provisions of the Hatch-Waxman Act, pharmaceutical patent evergreening has become extremely profitable for branded drug companies seeking to prevent generic companies from entering the market. Although not a new phenomenon, branded companies have continued to explore and use new methods to delay or prevent generic entry into the market, at which point the price of their drugs may decrease as much as ninety percent. While courts and lawmakers have been successful in preventing some abuse of the system by amending provisions of the Hatch-Waxman Act and applying antitrust law, companies have recently begun to use patents on medical devices related to the drug product to restrict generic competition.

256 Beall & Kesselheim, supra note 195, at 143.
257 See supra Section IV.D.3.
258 See supra Section IV.D.1.
259 See IMS INST. FOR HEALTHCARE INFORMATICS, supra note 9.
This new method of achieving patent exclusivity may have serious consequences for patients using the product, as can be seen in recent price increases with the EpiPen and inhaler products. Additionally, increased modifications could increase the likelihood of product defects or recalls, further injuring patients. To combat abuse of the Hatch-Waxman Act through device patenting, lawmakers should consider amending the Orange Book regulations and the Hatch-Waxman Act to reflect what has been allowed by skinny labeling. In this way, the United States might prevent minimal incremental advances in delivery devices from blocking generic entry and the public’s access to much needed pharmaceuticals.
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