PHARMA’S STRATEGIES ON FIGHTING GENERICS AND HEALTHCARE REFORM

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The goal of current healthcare reform pushed through Congress is to tackle the problem of rising healthcare costs. One effective way to curb these rising costs is to introduce more cheap generic drugs. Though generics bring enormous cost savings to the consumers, they also dramatically erode the market monopolized by brand drugs. Because of this, the pharmaceutical industry, as the owner of brand drugs, uses several strategies to fight generics from invading the market. These strategies include delisting patents, layering patents, settling with generic makers, and authorizing generics. This article reviews and critiques these strategies.

This article first briefly reviews the “Drug Price Competition and Patent Term Restoration Act of 1984” (commonly referred as Hatch-Waxman Act, hereafter “Hatch-Waxman Act” or “the Act”). The Act authorizes a scheme to make it much easier to obtain marketing approval for generics, as well as gives incentives to generic makers to bring generics to the market. The article then discusses the four strategies and their future impacts on drug market. Lastly, to eliminate these impacts, it proposes two legislations to ensure cheap generics be more widely available in order to reduce the healthcare cost.

I. THE HATCH-WAXMAN ACT

A. Enactment of the Hatch-Waxman Act

Before 1984, it was costly and time consuming to get marketing approval for a generic drug from the U.S. Food and Drug Administration (“FDA”). Because Congress
had not authorized any special schemes for approving generic drugs, the FDA had to rely on the same one as approving brand drugs, i.e. the New Drug Application (“NDA”). The NDA process requires very expensive clinical trials to prove that the drug is safe and effective for human use. The cost of clinical trials is prohibitive for most generic makers. In order to ease some of the burden to generic makers, in 1980 the FDA announced a “paper” NDA for generic drug approval. This allows generic makers to omit the clinical trials if the safety and effectiveness data is publicly available.\(^1\) But the literature on most of the brand drugs is scarce and inadequate. The “paper” NDA applied to only a handful of generic drug applications,\(^2\) while most generic applications were still required to have data from expensive clinical trials.

Congress was determined to introduce more generic drugs into the market in order to bring down the healthcare cost. Generic drugs had only nineteen percent of the prescription drug market in 1983. One Congressional report found that there were 150 brand drugs that were off-patent in 1983, but no generic drugs were available for them.\(^3\) Lack of generics forced consumers to pay higher prices for the brand drug, which contributed to the high cost of healthcare. Congress believed that cheaper generic drugs could bring down the cost significantly.\(^4\) But against cheaper generic drugs was a competing interest in ensuring continuous development of innovative drugs by big

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\(^1\) Hutt and Merrill, *Food and Drug Law*, at 484-486, (Foundation Press, 2001) (brand drug owner may have published the clinical trial data on the brand drug).


\(^4\) *Id.* (Congress estimated that availability of generics for the brand drugs approved after 1962 could save consumers $920 million over 12 years).
pharmaceutical companies (“Pharma”) through investing in research and development. The Hatch-Waxman Act strikes a balance between bringing more generic drugs to the market and encouraging Pharma to develop more innovative drugs in the future.

The Hatch-Waxman Act contains two titles that are relevant to the pharmaceutical industry. Title I modifies the Food, Drug, and Cosmetic Act (“FDCA”) to set up a scheme to speed up the generic drug approval process. Title II amends the Patent Act by adding both a patent term restoration provision as an incentive to Pharma and a safe harbor provision that allows generic makers to prepare for the FDA marketing filing within the patent term of the brand drug.

B. Title I of the Hatch-Waxman Act

Title I adds several provisions to the FDCA. First, it defines the scheme of Abbreviated New Drug Application (“ANDA”) for getting generic drugs approved by the FDA. This reduces the amount of data that the generic maker needs to generate. The ANDA dramatically decreases the cost and time needed for generic drug approval. Furthermore, Title I also rewards the first generic maker who challenges the brand drug’s patents with a 180-day marketing exclusivity. More challenges may lead to invalidating weak patents and bringing the generic drug to the market earlier. On the other hand, Title I also provides protections to Pharma to encourage innovations. It protects the brand drug by ensuring that Pharma has an opportunity to fully adjudicate the challenged patents. Title I requires the FDA to stay the approval of an ANDA for thirty months if Pharma promptly defends the patents in courts. One incentive to Pharma by Title I is the exclusivity period to Pharma for innovative drugs which bars approval of any ANDA.

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5 The other title, Title III, is an amendment to “Textile Fiber Product Identification Act” and “the Wool Products Labeling Act of 1939.”
1. The data in ANDA

The ANDA is an abbreviated and streamlined version of the burdensome NDA process. In an ANDA, the generic maker must prove that the generic drug is bioequivalent to the brand drug. Most drugs contain two types of substances: active ingredients and inactive ingredients. ANDA demands that the active ingredients in the generic drug must be the same as the brand drug, which includes the chemical entity, dosage, route of administration, and condition of use. But for inactive ingredients, the requirement in ANDA is fairly low. The generic maker can make substitutions for inactive ingredients, as long as the substitutes are not “unsafe for use under the conditions prescribed, recommended, or suggested in the labeling proposed for the [generic] drug.”

The generic maker can rely on the mature technology of formulating drugs and select different inactive ingredients to differentiate from the brand drug, often to design around the formulation patent covering the brand drug. Once the generic maker submits adequate data proving that the generic drug and brand drug are bioequivalent, ANDA allows the applicant to use the brand drug’s clinical trial data (published or not) to establish safety and effectiveness for the generic drug. In other words, the clinical trials that prove that the brand drug is safe and effective also prove that the generic drug is safe and effective. ANDA thus relieves the generic maker of the burden of conducting the expensive clinical trials entirely.

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The ANDA process significantly reduces the cost of filing for approval of generic
drugs. Though the generic maker still needs to generate data to prove bioequivalence, the
cost is a small fraction of what is needed for conducting three-phase full clinical trials,\(^9\) which were required for generic drug approval before Hatch-Waxman Act. ANDA makes it much easier to apply for marketing approval for generic drugs.

2. Patent certifications

Title I requires the generic maker to certify the patent status of the targeted brand drug. The ANDA applicant needs to submit patent certifications to the FDA and the brand drug owner (mostly a big pharmaceutical company). There are four types of patent certifications: I) that patent information has not been filed with the FDA; II) that such patent has expired; III) that the patent will expire on the date which generic will be marketed, or IV) that such patent is invalid or will not be infringed by the generic drug for which the application is submitted.\(^{10}\) These certifications are referred to as Paragraph I to IV certifications respectively. The ANDA applicant must certify to the best of its knowledge that one of the four situations exists. The patent certifications represent the generic maker’s position regarding the patent at issue. Paragraph I to III certifications mean that there will be no confrontation with Pharma on the patent, while Paragraph IV certification indicates that the generic maker intends to directly challenge the patent protecting the brand drug.

To give generic makers notice of the patents covering any particular brand drug, Title I gives the FDA the responsibility of maintaining patent information in its Approved Drug Products with Therapeutic Equivalence Evaluations (commonly known as the

\(^9\) The clinical trial for drugs include Phase I for safety on healthy volunteers, Phase II for both safety and efficacy on patients, and Phase III for final study of efficacy on large patient populations.

“Orange Book”). The Orange Book has long been the authoritative reference for all the drugs the FDA has approved. After the enactment of the Hatch-Waxman Act, the FDA started listing patents protecting the brand drugs in the Orange Book. The generic maker can rely on the patents listed in the Orange Book to make the necessary patent certifications about the targeted brand drug.

3. 180-day marketing exclusivity

Besides making it easier to file for generic drug approval, Title I also provides a 180-day marketing exclusivity to encourage the generic maker to challenge the patent protecting the brand drug in order to bring the generic drug to the market earlier. Among the four types of patent certifications, only the Paragraph IV certification is for a direct challenge of the patent. So Title I grants the 180-day marketing exclusivity only to the first filer of an ANDA with a Paragraph IV certification. The exclusivity is automatically triggered by either the date of court’s favorable decision of the patent being invalid or noninfringed, or date of generic drug’s first commercial marketing, whichever is earlier. The marketing exclusivity functions by prohibiting the FDA from approving a second ANDA within that 180-day period.

However, this marketing exclusivity could be cut short if the challenged patent expires within the 180-day period. Upon the expiration of the patent, the patent status automatically changes from Paragraph IV certification to Paragraph II certification.

Because the 180-day exclusivity rests on the Paragraph IV certification, the exclusivity ends at the date when the patent expires and Paragraph IV certification becomes invalid.15

The FDA’s interpretation of “first applicant” of an ANDA with Paragraph IV certification changed in 1998. The FDA initially interpreted the “first applicant” of an ANDA as the one who filed an ANDA first and also successfully defended in the subsequent infringement action. The intent was to curb frivolous ANDA filings by generic makers. But a series of judicial decisions have concluded that the FDA’s interpretation was contrary to the plain language of the Act, which is “first applicant.”16

The FDA formally abandoned its interpretation in 1998 and now gives the first filer of an ANDA with Paragraph IV certification the right to the 180-day exclusivity, regardless of the outcome of the infringement lawsuit.17

The incentive of the 180-day exclusivity is very lucrative for the generic maker, who makes the bulk of its profits during the exclusivity period. For example, when generic maker Barr Laboratories enjoyed the exclusivity to market a generic version of Prozac, it had $311 million in sales for this one drug in the six months. After the exclusivity was over, “with multiple generic versions of Prozac on the market and the price in the basement,” Barr's annual sales of that drug had “dropped to less than $4 million.”18

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addition, the exclusivity also allows the generic maker to have the “first mover” advantage and establish its “brand” of generic drug. The later entered generic versions will have an uphill battle against the first one in capturing market share.

4. Thirty-month stay

The thirty-month stay of ANDA approval is a provision to protect the brand drug. The applicant of an ANDA must give notice of the patent certification to Pharma. This formally triggers the response period for Pharma if it’s a Paragraph IV certification. The response period is forty-five days after receiving the notice. Since the Hatch-Waxman Act treats the filing of an ANDA as constructive infringement, Title I gives Pharma the right to bring an infringement suit against the generic maker. When Pharma does bring an infringement suit within the response period, Title I requires the FDA to stay the approval of the ANDA for thirty months, which allows reasonable time for the parties to resolve the patent issues in a court. This provision prevents the generic maker from altering, or even destroying, the market for the brand drug before Pharma has the chance to resolve the disputes on the challenged patents.

Title I also gives a court the authority to modify the thirty-month stay in some circumstances. The first is that a court can shorten or lengthen the stay if Pharma or the generic maker fail to reasonably cooperate in expediting the action. The second circumstance is that once a district court decides that the patent is invalid or not infringed before the thirty months expires, the stay ends on the date of the court decision. Finally,

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if a district court decides that the patent is valid and infringed, the stay extends to the end of the patent term. In reality, the FDA always gives tentative approval to the ANDA during the stay. Once the stay is over, the approval immediately becomes official, which allows the marketing of the generic drug.

5. Pharma’s exclusivity

Title I also provides an incentive to Pharma for innovations, which is the right of exclusivity. The exclusivity period for an innovative brand drug is the period that no ANDA can be approved, regardless the status of the patent protecting the brand drug. So Pharma’s exclusivity is independent of, but runs in tandem with, patent protection. It guarantees certain minimal protection for the innovative brand drug, even if there is not patent protection, or the patent is invalid for some reasons.

The more innovative the brand drug is, the longer exclusivity Title I gives for the drug. There are two types of exclusivity in the Title: 1) for drugs with new chemical entity, the exclusivity period is five years; and 2) for drugs with approval of new use or new dosage that is based on additional clinical trials, the exclusivity is three years. Pharma’s exclusivity aims at stimulating innovations in drug development by providing extra protection for innovative drugs containing new chemical entity or requiring clinical trials.

C. Title II of the Hatch-Waxman Act

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Title II amends the Patent Act primarily in two ways. First, it gives an incentive to Pharma for investment in developing innovative new drugs. The patent term restoration provision awards Pharma half of the time spent on clinical trials and all the time for the FDA’s review of that brand drug. Second, in order to let generic makers file an ANDA earlier, Title II provides an exemption from patent infringement for the generic makers to make and use the patented drug for the FDA marketing approval purposes.

1. Patent term restoration

The patent term restoration provision provides Pharma the most valuable incentive to develop innovative drugs. The development of a new drug is a long and expensive process, which may take up to twelve years from identifying the active ingredient to getting the FDA approval for marketing, and cost around $1.3 billion.\(^\text{27}\) In reality, a large portion of the term for pharmaceutical patents lapses during the development process, which leaves Pharma little time to recoup the large investment in developing the new drug. To encourage Pharma to bring more innovative new drugs to consumers, Title II amends the Patent Act to restore half of the time Pharma spent in the clinical trials and all the time lost during the FDA’s regulatory review. The restored time is added back to the term of the patent protecting the new drug.\(^\text{28}\) The patent restoration provision in Title II is different from the patent term extension in the original Patent Act,\(^\text{29}\) which is for compensating the extra time that the U.S. Patent and Trademark Office (‘‘USPTO’’) takes to process the patent application.


\(^{28}\) 35 U.S.C. § 156.

To avoid abuse of the patent term restoration provision, Title II includes several limitations. One is that the maximum restoration to the patent term is five years. Another limitation is that, after the restoration, the total market monopoly period for a brand drug cannot exceed fourteen years.\textsuperscript{30} Pharma is required to exercise due diligence to facilitate the clinical trials and the FDA review. If Pharma fails to do so, the period lacking due diligence will be subtracted from the total restoration.\textsuperscript{31}

The patent term restoration provision is an effective way of encouraging Pharma to engage in the time consuming clinical trials and lengthy FDA regulatory review, which are essential and most burdensome for developing innovative drugs. Without the patent term restoration, coupled with earlier entry of generics, Pharma would not have enough time to recoup the cost of developing new drugs. The continuous inflow of innovative drugs may eventually die out.

2. Safe harbor for generic makers

To allow earlier filing of an ANDA, Title II carves out a safe harbor for the generic maker to make and use the patented drug for purposes “reasonably related” to the filing of the ANDA.\textsuperscript{32} Before the enactment of the Hatch-Waxman Act, the generic maker’s making and using the patented brand drug for generating data to satisfy the FDA’s regulatory requirements were considered infringement, as the Federal Circuit held that this was not “experimental use” because the use was not with an “insubstantial commercial purpose.”\textsuperscript{33} Since it usually takes three to four years for a generic maker to

\textsuperscript{30} 35 U.S.C. § 156.
\textsuperscript{31} 35 U.S.C. § 156(c)(1).
\textsuperscript{32} 35 U.S.C. § 271(e)(1).
generate the required data, the fact that the generic maker can only make and use the patented drug after the patent expires would effectively extend the brand drug’s market monopoly for that amount of time beyond the patent term.\(^{34}\)

Title II eliminates this delay by adding a safe harbor provision, which is also frequently referred to as “Bolar Exemption”. The safe harbor allows the generic maker to make the patented drug, use the drug to demonstrate the bioequivalence, and establish a safety profile for filing an ANDA with the FDA for permission to market the generic drug.\(^{35}\) The generic maker can finish all the preparation for the ANDA filing within the patent term and move up the date of filing the ANDA and the date of marketing the generic drug. Furthermore, the safe harbor allows the generic maker to prepare the ANDA to challenge the patent which still protects the brand drug.

D. The Hatch-Waxman Act and Generic Drugs

The Hatch-Waxman Act sets up a scheme for speedy introduction of generic drugs into the market. Under the Act, the first step for a generic maker is to select a brand drug from the Orange Book for which to file an ANDA. It should carefully evaluate the patent status of the brand drug. If no patents or the patents listed in the Orange Book with the drug have expired, the generic maker may file an ANDA and market a generic drug at any time. But if unexpired patents are listed in the Orange Book, the generic maker has the option of waiting until expiration of the patents (Paragraph III certification), or challenging the patents in order to market a generic drug earlier (Paragraph IV certification). The second step is making and testing the proposed generic drug to

\(^{34}\) \textit{Id} at 864. (The holding would “extend a pharmaceutical company’s monopoly for an indefinite and substantial period of time while the FDA considers whether to grant a pre-marketing clearance.”)

generate bioequivalence data. If the brand drug is still under patent protection, the generic maker can rely on the safe harbor provision to be exempted from patent infringement. The third step is filing the ANDA and patent certification, preferably Paragraph IV certification to get the 180-day marketing exclusivity. The fourth step, which occurs only if the generic maker files Paragraph IV certification to challenge the patent, is the infringement litigation. After Pharma brings an infringement lawsuit within forty-five days, the FDA will stay the ANDA approval for thirty months. The generic maker needs to defend that the patent is invalid or the drug described in ANDA does not infringe the patent. Once the court resolves the patent issues in the generic maker’s favor, or the thirty-month stay is over, the FDA will approve the ANDA immediately, which gives the generic maker the right to market the generic drug.

Since its enactment in 1984, the Hatch-Waxman Act has clearly achieved its intended purpose of introducing more generic drugs. The market share of generic has increased from nineteen percent in 1983 to near sixty percent in 2005. Furthermore, the generic drug industry expects ten to thirteen percent annual profit growth before 2010.36 This tremendous gain by generic makers comes at the loss of big pharmaceutical companies. For example, in the several years leading up to 2005, Pharma lost about $10 billion in sales to generic drugs each year.37 At the same time, Pharma is struggling in refilling its product pipelines, despite increasing R&D investment.38

Facing squeeze from both ends, Pharma spares no efforts in protecting its valuable assets and fighting back to delay generic drugs entering the market. Pharma has adopted four strategies to fend off generic pressures: (1) delisting patents from the Orange Book, (2) layering patents over a drug, (3) settling with generic makers, and (4) authorizing generics.

II. STRATEGY ONE: DELISTING PATENTS

A. Loophole in Hatch-Waxman Act that allows patent delisting

The FDA gives Pharma near complete control over patent listing in the Orange Book. The Act mandates the FDA to add patent information for drugs still under patent protection in its Orange Book. However, the statutory language is vague regarding what patents shall be included in the Orange Book.\(^{39}\) The FDA promulgated guidelines governing the type of patents the drug owner should submit to the Orange Book, but it lacks punishment provisions for violations.\(^{40}\) The Federal Circuit affirmed the FDA’s passive position regarding the patent listing process and “conclude[d] that the agency’s interpretation of the Act … is a reasonable one: that the Act does not require it to police the listing process.”\(^{41}\) Though the FDA did later issue tighter regulations on patent listing in 2003,\(^{42}\) it still refuses to create either an administrative process or an office to oversee


\(^{40}\) 21 C.F.R. §314.53(f). “Unless the application holder withdraws or amends its patent information… the agency will not change the patent information in the list, … despite any disagreement as to the correctness of the patent information.” The regulation has no provision for punishing violations of the regulations.

\(^{41}\) Apotex, Inc. v. Thompson, 347 F.3d 1335, 1349 (Fed. Cir. 2003). See also 21 C.F.R. §314.53(f).

the listing practice. As a consequence, Pharma can request the FDA to remove patents from the Orange Book if Pharma deems that the patents were listed improperly in the first place; or Pharma can add new patents to the Orange Book if it has reason to believe the patents are relevant to the drug.

These FDA regulations created a loophole in the Hatch-Waxman framework. The Act encourages generic makers to challenge the patents of brand drugs by filing Paragraph IV certifications alleging the patents are invalid or noninfringed. However, if there are no patents in the Orange Book for the brand drug on which Paragraph IV certifications may be filed, the generic maker is not entitled to the exclusivity. In other words, the awards of the Act do not reach brand drugs that have no patents on which Paragraph IV certifications can be filed. To exploit the loophole, Pharma adopts the strategy of delisting patents from the Orange Book and purposely making the drug fall into the loophole, therefore denying generic makers the biggest incentive under the Act: marketing exclusivity.

B. Early days of delisting patents strategy

Merck pioneered this strategy in its Zocor battle with Ranbaxy, an Indian generic maker. Zocor was Merck’s biggest drug with annual sale of $4.3 billion in 2005. There were initially three patents listed in the Orange Book for the hypercholesterol drug: active ingredient patent 4,444,784 (‘784 patent), reissued patent RE36,481 (‘481 patent), and reissued patent RE36,520 (‘520 patent). The latter two patents both claim compounds related to Zocor and their use in treating high cholesterol, but neither patents claim Zocor itself or its use.

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43 Id. 68 Fed. Reg. at 36683.
In December 2000, Ranbaxy filed an Abbreviated New Drug Application (ANDA) to market generic versions of Zocor, with Paragraph III certification on the ‘784 patent (promise to wait until patent expiration date on June 23, 2006) and Paragraph IV certifications on both the ‘481 patent and ‘520 patent (alleging both patents invalid or noninfringed by its generic drug). Surprising to many, in 2003, Merck requested the FDA to delist the ‘481 and ‘520 patents from the Orange Book. The FDA accepted Merck’s reason that these two patents were improperly listed in the first place and subsequently delisted them. Ranbaxy was left with no patents on which to base their Paragraph IV certifications, resulting in the loss of the 180-day exclusivity under the Act. Accordingly, the FDA then denied Ranbaxy’s right to the exclusivity.\(^45\) To revive its exclusivity right, in 2005, Ranbaxy filed a citizen petition to the FDA asking it to relist the two patents. The FDA denied the petition.

Ranbaxy next filed a lawsuit in the district court of the District of Columbia to force the FDA to relist the patents. Though the FDA’s ruling does have textual support in the Act, the court put great emphasis on the legislative intent and found the FDA violated the intent. The court held that “[t]he delisting practice … effectively eliminated Congress’s first commercial marketing trigger, in violation of the clear command of Congress.”\(^46\) The court thus concluded that the FDA improperly denied Ranbaxy’s citizen petitions.\(^47\)

The D.C Circuit affirmed this decision and agreed that “the FDA’s delisting policy diminish[es] the incentive for a manufacturer of generic drugs to challenge a patent listed

\(^{45}\) See FDA letter. Available at http://www.fda.gov/ohrms/dockets/dockets/05p0008/05p-0008-pdn0001-vol2.pdf.

\(^{46}\) Ranbaxy Lab. Ltd. v. Leavitt, 469 F. Supp. 2d 1, 10 (D.D.C 2006) (internal quotation marks omitted).

\(^{47}\) Id.
in the Orange Book.\textsuperscript{48} Denying Ranbaxy marketing exclusivity by delisting Merck’s patents was “inconsistent with the purpose of the Act.”\textsuperscript{49} To comply with the district court’s order, the FDA subsequently relisted the two patents in the Orange Book and gave Ranbaxy back the marketing exclusivity.\textsuperscript{50}

But in another patent delisting battle on Johnson and Johnson’s Risperdal, the D.C. Circuit sided with Pharma.\textsuperscript{51} In August 2001, generic maker Teva filed an ANDA with certifications on both patents listed with Risperdal in the Orange Book: patent 4,804,663 (‘663 patent) and patent 5,158,952 (‘952 patent). Here, the main patent, the ‘663 patent, covers Risperdal’s active ingredient and expired in December 2007. The secondary patent, the ‘952 patent, claims tablet formulation of the drug and expires in 2009. Teva chose to challenge the weak formulation patent (Paragraph IV certification on the ‘952 patent), but would delay generics until the expiration of the main patent (Paragraph III certification on the ‘663 patent). In October 2001, the FDA informed Teva that the ‘952 patent has been delisted from its Orange Book at the request of Johnson and Johnson.\textsuperscript{52} The FDA denied Teva’s citizen petition on relisting ‘952 patent, which was promptly challenged in the courts.

The D.C. Circuit first affirmed the FDA’s “purely ministerial role” on patent listing in the Orange Book.\textsuperscript{53} The court held that for the FDA to determine the relevance of a patent to a drug, “the patent’s actual scope is irrelevant. Rather, [the] FDA must base its

\textsuperscript{48} Ranbaxy Lab. Ltd. v. Leavitt, 469 F.3d 120, 126 (D.C. Cir. 2006).
\textsuperscript{49} Id.
\textsuperscript{50} See FDA’s letter to attorneys representing the parties. Available at http://www.fda.gov/ohrms/dockets/dockets/06p0258/06p-0258-let0001-vol1.pdf.
\textsuperscript{51} Teva Pharm. USA Inc. v. Leavitt, 548 F.3d 103 (D.C. Cir. 2008).
\textsuperscript{52} Teva Seeks Relisting of J&J’s Risperdal Patent, Orange Book Blog (January 7, 2008).
\textsuperscript{53} Teva, 548 F.3d at 106.
decision on what the NDA holder assert a patent claims."\textsuperscript{54} When Pharma requests delisting patents, the FDA must take Pharma’s assertion at face value and delist any patents from the Orange Book, unless that is in conflict with other provisions or intent of the Act.

The D.C. Circuit found no conflict between the FDA’s action and the legislative intent. A generic maker obtains vested right to marketing exclusivity only after a valid Paragraph IV certification has been submitted.\textsuperscript{55} If a patent has been delisted from the Orange Book before the Paragraph IV certification is submitted, “there can be no valid certification,”\textsuperscript{56} and the generic maker’s “right to a period of marketing exclusivity does not vest.”\textsuperscript{57} The ‘952 patent was delisted months before Teva attempted to submit a Paragraph IV certification.\textsuperscript{58} The patent delisting made Teva’s subsequent Paragraph IV certification invalid, which gave Teva no vested rights to marketing exclusivity. Since Teva’s exclusivity right never vested, the court held that there were no conflicts with Congressional intent.\textsuperscript{59}

The current view of the law is that if Pharma preemptively delist patents from the Orange Book in anticipation of potential ANDA filings, this strategy will achieve its intended purpose of denying generic makers the marketing exclusivity. However, once an ANDA has been filed and Paragraph IV certifications have been submitted, generic makers have vested rights to the marketing exclusivity. Pharma cannot then delist the

\textsuperscript{54} Teva, 548 F.3d at 107 (internal citations omitted).
\textsuperscript{55} Ranbaxy, 469 F.3d at 26.
\textsuperscript{56} Teva, 548 F.3d at 107
\textsuperscript{57} Id.
\textsuperscript{58} Teva, 548 F.3d at 108
\textsuperscript{59} Id.
patents, because it shows clear attempts to defeat generic maker’s efforts to secure the exclusivity, which is in conflict with the intent of the Act.

C. FDA no longer willing to fight Pharma’s battles

During the heat of Zocor and Risperdal court battles, the FDA repositioned itself and became unwilling to fight the battles for Pharma. In October of 2005, generic maker Hi-Tech filed an ANDA on Merck’s hypertension drug Cosopt, with Paragraph IV certifications to all three patents listed on the Orange Book: patent 4,797,413 (‘413 patent) that covers the active ingredient in Cosopt; patent 6,248,735 (‘735 patent); patent 6,316,443 (‘443 patent). The latter two patents cover the combination of Cosopt with other drugs. In response to the ANDA filing, Merck first filed statutory disclaimers with the USPTO on patents ‘735 and ‘443, effectively dedicating these two patents to the public.

Merck was unable to get the FDA to cooperate in delisting of the two patents. In April of 2006, Merck requested the FDA to delist these two patents from the Orange Book. But the FDA took no action, \(^{60}\) possibly not wanting to be involved in litigation to determine whether statutory disclaimers can void generic maker’s right to marketing exclusivity. This could be the beginning of the FDA’s unwillingness to engage in long court battles with generic makers on behalf of Pharma.

D. Pharma conceding defeat?

Recent developments indicate that Pharma may be ready to quit this strategy. For example, in preparing for potential filing of Paragraph IV certifications on its drug Cubicin, Cubist Pharmaceuticals (“Cubist”) requested the FDA to delist patent RE39071

\(^{60}\) See Dismissal of Invalidity Counterclaims Thwarts Apotex’s Attempt to Trigger 180-day Exclusivity on Cosopt, Orange Book Blog, (November 28, 2007).
(‘071 patent) from the Orange Book in September of 2007, citing an error in the patent.\textsuperscript{61} The ‘071 patent does not cover the drug’s active ingredient specifically, but rather covers composition of the active ingredient with two particular impurities often found in the drug. The FDA delisted the patent since no ANDA has been filed and no battle is on the horizon pursuing the Risperdal decision.\textsuperscript{62} However, one year later, Cubist voluntarily relisted the ‘071 patent in the Orange Book, claiming the error had been corrected by Certificate of Correction from USPTO in Jan, 2008.\textsuperscript{63}

Delisting the patent from the Orange Book does not seem necessary while requesting USPTO to correct an administrative error in the patent. One reason is that Cubist can easily and quickly correct the error while keeping the patent in the Orange Book. The Certificate of Correction process is quick and routine. More importantly, the ‘071 patent does not claim the active ingredient itself, instead it only claims composition of the active ingredient with two impurities. So the error is peripheral to the claims of the ‘071 patent. As a matter of fact, due to its peripheral nature, Cubist knew of the error for several years but did not bother to correct it until potential ANDA is on the horizon.\textsuperscript{64} It is thus likely that Cubist was contemplating the delisting strategy when requested the patent delisting, but it finally decided not to pursue it. This may be a signal of Pharma’s readiness to quit the patent delisting strategy.

E. The Future of Delisting Strategy

\textsuperscript{61} The error was that one of the 13 amino acids of the active ingredient was mistakenly marked L-form, in fact, it should be D-form.
\textsuperscript{62} See Teva, 548 F.3d 103.
Pharma uses this delisting strategy to hurt the generic makers by potentially denying them the 180-day marketing exclusivity. Without the exclusivity, generic markers have little incentive to challenge the patents of brand drugs. This strategy puts a realistic risk of not getting the exclusivity into generic maker’s calculations, and therefore may tip the balance in favor of Pharma. Pharma would be able to enjoy less generic pressures to its drugs in the future.

But this strategy is a double-edged sword and hurts Pharma as well. First, by delisting the patent, Pharma concedes that the delisted patents do not cover the drug and deprives itself the protection of these patents. Second, Pharma loses its own potential profit during the exclusive 180 days. This is because during the exclusivity period, generic drug sells at around twenty percent discount to brand name version. Pharma typically retains near half of the market share and still makes sizable profit. Denying generic makers the 180-day exclusivity means Pharma has to forfeit its own profit during the exclusivity period. In addition, the strategy gives Pharma bad publicity, as the public may very well perceive Pharma as manipulating the system to keep drug price high.

The patent delisting strategy is successful only in one narrow circumstance: before any ANDA filing with Paragraph IV certifications. Though the strategy can hurt generic makers badly and deter them from aggressively challenging drug patents in the future, because it hurts Pharma just as much. Pharma may be ready to abandon this strategy.

III. STRATEGY TWO: LAYERING PATENTS

A. Loophole in the Act that allows patent layering

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Pharma’s near complete control over patent listing in the Orange Book also created another loophole in the Hatch-Waxman framework allowing patent layering. Though the Act encourages generic markers to challenge the patents of brand drugs by filing Paragraph IV certifications, it also gives Pharma the opportunity of fully adjudicating the patents by staying the approval of ANDA for thirty months if Pharma engages prompt defense of the patents in courts.66 If Pharma could bring multiple infringing lawsuits on multiple patents covering the same drug, the Act gives multiple stays (one for each lawsuit). To exploit the loophole, Pharma adopted the strategy of layering later-issued patents over the drug in the Orange Book, which forces generic makers to submit a new Paragraph IV certification for each newly listed patent. The new certification is the basis for a new infringement lawsuit on the new patent, which leads to another automatic thirty-month stay of the ANDA approval. These multiple stays can significantly delay the introduction of generic drugs into the market, and extend the monopoly for the brand drug.

B. Pharma’s Patents on a Drug

Pharma often receives both a principle patent and multiple secondary patents for the same drug. During a typical process of drug development, Pharma first discovers the compound which would later become the active ingredient of the drug. After numerous experiments in the laboratories and lengthy clinical trials, Pharma identifies more features of the compound. In addition, Pharma has to determine the best ways to formulate, make, and use the drug before the FDA could approve it.67 Naturally, Pharma obtains the principle patent that covers the compound early in the drug development process. Years

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later, Pharma may obtain secondary patents on the new features of the compound or other aspects of the final product once they are discovered. For example, Glaxo discovered the active ingredient of Paxil in early seventies and filed a patent on it in 1974 (patent 4,000,196). As the drug went through the development process, more features were discovered about it. In 1986, Glaxo filed a secondary patent on a hemihydrate form of the drug (4,721,723). Later, Glaxo obtained four more secondary patents: patents 5,872,132 and 5,900,423 on new crystal forms in 1996 and 1997 respectively; patent 6,080,759 on a process of making the drug in 1997; and patent 6,113,944 on a tablet formulation in 1998.

Though the principle patent expired in 1992, the secondary patents effectively extend the monopoly of Paxil into 2018.

The principle patent usually stands well on the generic maker’s validity challenge and provides the much-needed protection for the drug. The chemical structure of the active ingredient is always unique, so the anticipation theory\textsuperscript{68} does not work for challenging the principle patent. In addition, the obviousness theory\textsuperscript{69} is very hard to substantiate by the challengers. The Federal Circuit has rejected the argument of obviousness based on modifying a prior art structure through routine methods to get the active ingredient in the patent.\textsuperscript{70} Another argument of obviousness based on generating the patented compound by combining a portion of one prior art structure with a portion of another prior art

\textsuperscript{68} 35 U.S.C. 102 (Single prior reference anticipate an invention where the reference contains every aspect (element) of the invention).

\textsuperscript{69} 35 U.S.C. 103 (Prior references make an invention obvious when a person with ordinary skills in the field, knowing the references, could obviously make the invention).

\textsuperscript{70} Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd., 492 F.3d 1350, (Fed. Cir. 2007). The court held that modifying the closest prior art compound, using steps of “homologation” or “ring-walking” is not reasonable basis to make the compound obvious, because nothing in prior art provided “reasonable expectation” that to pick the prior art compound and to achieve the “beneficial changes” by these steps.
structure was also rejected in *Yamanouchi*.\(^{71}\) A brief survey of Federal Circuit decisions on the patentability of chemical entity reveals only eight cases of challenging the principle patents since the enactment of the Act. Among the eight cases, the court found six principle patents valid and infringed;\(^{72}\) Pharma lost the other two cases on inequitable conduct grounds.\(^{73}\)

Secondary patents can also provide protection over the drug when the inventions are truly innovative and substantially related to the drug. For example, the Federal Circuit found the drug Prilosec’s formulation patent valid and infringed by the generic drug as described in the ANDA.\(^{74}\) The active ingredient of Prilosec degrades quickly in acidic gastric juices, which reduces the amount of the drug that can reach the acid-producing cells in the stomach lining where the drug inhibits acid production. The patented invention solved this problem by designing both a “subcoating” and an “outer layer” to protect the drug and allow the drug to reach the stomach lining without being degraded.\(^{75}\) This smart coating system is neither anticipated, nor obvious in light of prior art.\(^{76}\)

Furthermore, the coating system is essential for the drug’s effectiveness. The generic

\(^{71}\) *Yamanouchi Pharm. Co., Ltd. v. Danbury Pharmacal, Inc.*, 231 F.3d 1339, (Fed. Cir. 2000). The court held that a person with ordinary skills in the art lacks the “motivation to combine” due to poor predictability of the characteristics of chemicals.


\(^{73}\) *Pfizer, Inc. v. Apotex, Inc.*, 480 F.3d 1348, (Fed. Cir. 2007); *Aventis Pharma S. A. v. Amphastar Pharm., Inc.*, 525 F.3d 1334, (Fed. Cir. 2008).


\(^{75}\) Id. at 78.

\(^{76}\) Id. at 82-83. Holding prior art “provide[s] not motivation to add a subcoating.”
maker’s versions failed to design around it.\textsuperscript{77} Inventions such as this are essential to bring effective treatments to the patients and contribute to the public knowledge. Secondary patents on these inventions appropriately should extend the protection on the drugs after the principle patent expires.

C. Patent Layering

Pharma abuses this legitimate practice of obtaining secondary patents in its patent layering strategy. Pharma acquires a variety of secondary patents that cover a wide range of characteristics of the drug. Since it has complete control on listing patents in the Orange Book, Pharma layers the drug with secondary patents. Unfortunately, many of the inventions in these patents don’t reach the high level of innovation and relevance to the drug as the formulation of Prilosec. These secondary patents are often found invalid or noninfringed, therefore ultimately provide no legal protection for the drugs. However, they are effective in creating structural hurdles under the Hatch-Waxman Act for generic makers by obtaining multiple thirty-month stays.

1. Many secondary patents provide no legal protection

Many secondary patents aimed at layering over drugs in the Orange Book do not survive the generic maker’s challenges in courts. These patents are often found either not valid because anticipated/obvious in light of prior art, or non-infringed because the generic makers have designed their products around the patents. So the layering patents give no protection over the drug. There are five types of secondary patents commonly used by Pharma in patent layering strategy: a) formulation patents; b) metabolite patents; c) polymorph patents; d) process patents; e) use patents.

\textsuperscript{77} Id. at 83-84.
a. Patents on drug formulation

The formulation patents cover the inactive ingredients, which are used to improve the appearance, bioavailability, stability, and/or palatability of the drugs. The common inactive ingredients are divided into categories of coatings, artificial sweeteners, preservatives, coloring agents, fillers (such as sugars, lactose, starch), and salts.78 Throughout the history of modern medicine, the pharmaceutical industry has developed very mature technologies in formulating drugs. The rich prior art makes formulation patents very vulnerable in the face of obviousness challenges.79

Even if the formulation patent is valid, the generic maker can easily design around it. According to the Act, the generic maker can substitute the formulation (inactive ingredients) in the brand drug as long as the replacing formulation is not “unsafe for use under the conditions prescribed, recommended, or suggested in the labeling proposed for the [generic] drug.”80 Because of this loose statutory language, the drug formulation is readily changeable and replaceable.

b. Patents on metabolites


Drugs undergo metabolism, which breaks down the active ingredient into intermediates called metabolites. Though the metabolites do not exist in the drug, Pharma still lists patents on metabolites in the Orange Book to layer over the drug, such as metabolite patents for two drugs BuSpar and Prelosec.81 Because the generic drugs do not contain the metabolites, the courts found that generic makers did not infringe the two metabolite patents.82 In a later example of a metabolite patent on the popular allergy drug Claritin, the Federal Circuit went even further to declare the metabolite patent invalid as “inherently anticipated” by the patent on the active ingredient.83

c. Patents on polymorphs

When the active ingredient has different crystal/chiral forms, the Pharma will patent the new form once it is discovered. These are referred to as polymorph patents. Once again, the Federal Circuit has not treated these polymorph patents favorably. If the patent claims a new crystal form different from the one used in the drug, the generic drug containing the old crystal form does not infringe the patent.84 A more recent decision by the Federal Circuit put even more restrictions on the polymorph patents. If the claimed

82 Id.
83 Schering Corp. v Geneva Pharm., Inc., 339 F.3d 1373, 1379 (Fed. Cir. 2003). (Though a reference does not contain every element of the invention, the missing element is necessarily present in the reference, as recognized by person with ordinary skills).
84 Glaxo, Inc. v. Navapharm, Ltd., 110 F.3d 1562, 1566, (Fed. Cir. 1997). The court held that patent 4,521,431 claims a different crystal form of the active ingredient of drug Zantac is valid. But the generic drug based on the old crystal form does not infringe the patent, since patent holder failed to prove that the generic drug contains any new crystal form.
form exists in the drug as part of mixture with other forms, then the polymorph patent is obvious in light of the drug itself.\textsuperscript{85}

d. Patents on processes

Besides patenting the drugs, Pharma also obtains process patents on making or using the drugs. The Federal Circuit has invalidated these patents on several occasions. For example, the court found that the drug Prelosec’s 6,013,281 patent claiming the process of producing the coating of the drug was inherently anticipated by the patent on coating itself.\textsuperscript{86} Other examples are patents 5,641,803 and 5,670,537, directed to a process of three-hour administration of the drug Taxol to treat cancer patients. Both patents were found invalid as anticipated by prior art.\textsuperscript{87}

f. Patent on the use of drugs

The last category of common secondary patents are those claiming a new use for a drug. Pharma constantly tries to expand the market for its drug by finding new uses in additional diseases. But if generic makers market the drug for the old uses only, the patent on the new uses are not direct infringement.\textsuperscript{88} Otherwise, Pharma “would be able to maintain its exclusivity merely by regularly filing a new patents application claiming a

\textsuperscript{85} Aventis Pharma Deutschland GmbH, v. Lupin, Ltd., 499 F.3d 1293, 1302, (Fed. Cir. 2007). The court held that patent 5,061,722 claiming a purifier form of the drug Altrace: 5(S) stereoisomer is obvious based on prior art disclosed a mixture of different stereoisomers, including 5(S), because “separating” the 5(S) form from the mix “is a mainstay of the chemist’s art.”

\textsuperscript{86} In re Omeprazole Patent Litigation, 483 F.3d 1364, 1376, (Fed. Cir. 2007).

\textsuperscript{87} Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc., 246 F.3d 368, 1381 (Fed. Cir. 2001).

\textsuperscript{88} Warner-Lambert Co. v Apotex Corp., 316 F.3d 1348, 1355 (Fed. Cir. 2003). In addition, the use covered by the patent has not been “approved under the NDA.”
narrow method of use.” Pharma could then bar the generic markers from entering the market altogether.\textsuperscript{89}

In conclusion, the secondary patents layering over the drug in the Orange Book often cannot provide legal protection to the underlying drugs. The Federal Circuit invalidated them in many high profile cases involving blockbuster drugs. Scholars, as well as the Federal Trade Commision (“FTC”), have argued that these patents should not be allowed to be listed in the Orange Book.\textsuperscript{90} In particular, the metabolite patents and process patents have only dismal relevance to the drug itself, therefore it is inappropriate to include them in the Orange Book. The FTC even submitted a citizen petition to the FDA with requests of banning some of these patents in the Orange Book.\textsuperscript{91}

Social policy also demands invalidating these secondary patents. If these patents are allowed in the Orange Book, Pharma can extend the monopoly drastically by finding new, non-essential aspects of the drugs when the old patents are close to expiration. These new patents will keep the generic drugs out of the market for an extended period.

2. Secondary patents create multiple thirty-month stays

Though many secondary patents layering over a drug were eventually determined by the court to be either invalid or noninfringed by the generic drug, they are very effective in creating structural hurdles for the generic maker. By layering later-issued patents in the Orange Book, the generic challenger is forced to submit a new Paragraph IV certification

\textsuperscript{89} \textit{Id} at 1359.
\textsuperscript{91} FTC study, supra note 88, at appendix F.
each time a new patent is listed. Pharma can bring a new infringement lawsuit on the new certification, which leads to another automatic thirty-month stay of the ANDA approval, regardless the patent’s validity or relevance to the drug.92 By putting multiple layers of patents over a drug, Pharma can get multiple stays authorized by the Act, therefore significantly delay the introduction of generic drugs into the market.

A most noticeable example is that Glaxo was able to obtain five stays for a total of sixty-five months for its popular antidepressation drug Paxil.93 When the ANDA was filed in 1998 by generic maker Apotex, there were two patents listed in the Orange Book for Paxil: principle patent on the active ingredient, patent 4,000,196, which expired in 1992; patent 4,721,723 that covers the hemihydrate form of the drug until 2006 (formulation patent). Apotex’s ANDA contains Paragraph IV certification challenging the formulation patent, on which Glaxo promptly brought a lawsuit alleging infringement.94 This triggered the first thirty-month stay. In 1999, Glaxo obtained two more patents, 5,872,132 and 5,900,423, that cover new crystal forms of Paxil (polymorph patents). Both patents were subsequently listed in the Orange Book with Paxil. Apotex was forced to file additional Paragraph IV certifications on these two patents. In August 1999, Glaxo brought two more infringement suits against Apotex, which triggered two more thirty-month stays, fourteen months into the first stay.

In June 2000, Glaxo received two additional patents for Paxil. Patent 6,080,759 claims the process of making the drug (process patent) and patent 6,113,944 claims a tablet formulation (formulation patent). In two separate requests, Glaxo had FDA list

93 FTC study, supra note 31, at 51-52.
these two patents in the Orange Book. Apotex filed two more Paragraph IV certifications, on which Glaxo filed two more infringement lawsuits. Each lawsuit gave Glaxo one more thirty-month stay.

Glaxo layered a total of nine patents in the Orange Book on Paxil after the ANDA was filed. Glaxo brought infringement suits for four of the nine patents and was able to get five separate, but overlapping stays spanning 65 months. This extension was thirty-five months more than the stay of thirty months intended by the Congress. Because the annual sale of Paxil during these stays was about $1 billion, this patent layering strategy generated about $3 billion in sales for Glaxo.96

Glaxo is certainly not alone in using the patent layering strategy to get multiple stays for a single drug. The FTC study identified the following drugs had additional stays through layering later-issued patents over the drugs:97

- **Platinol**: later-issued secondary patents claim: formulation; total number of stays: 1; total length of stays: 30 months; Net sale in the year the second stay was issued: between $100 and $250 million.

- **Hytrin** (tablet): later-issued secondary patents claim: drug substance; total number of stays: 3; total length of stays: 70 months; Net sale in the year the second stay was issued: between $500 and $750 million.

- **Paxil**: later-issued secondary patents claim: drug substance, formulation, and method of use; total number of stays: 5; total length of stays: 65 months; Net sale in the year the second stay was issued: over $1 billion.

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95 FTC study, supra note 88, at 51.
96 Id., at 49.
97 Id.
• **Taxol**: *later-issued secondary patents claim*: formulation; *total number of stays*: 2; *total length of stays*: 60 months*; *Net sale in the year the second stay was issued*: between $750 million and $1 billion.

• **BuSpar**: *later-issued secondary patents claim*: method of use; *total number of stays*: 2; *total length of stays*: 30 months*; *Net sale in the year the second stay was issued*: between $500 and $750 million.

• **Neurontin** (capsule): *later-issued secondary patents claim*: formulation; *total number of stays*: 2; *total length of stays*: 53 months; *Net sale in the year the second stay was issued*: between $250 and $500 million

• **Neurontin** (tablet): *later-issued secondary patents claim*: formulation; *total number of stays*: 2; *total length of stays*: 37 months; *Net sale in the year the second stay was issued*: between $250 and $500 million

• **Tiazac**: *later-issued secondary patents claim*: formulation; *total number of stays*: 2; *total length of stays*: 60 months*; *Net sale in the year the second stay was issued*: between $100 and $250 million.

* The actual total length of the stays was shortened by court actions in these cases.

This patent layering strategy is very profitable for Pharma. During the period of multiple stays, these drugs had annual sales of at least $100 million, some even reached the $1 billion mark. Extra stays brought big profits for Pharma. Of course this profit came at the expense of consumers because they were forced to pay higher prices for the brand drugs during these stays. The delay of generic drugs has generated considerable public outcry. Both the FDA and the Congress were under tremendous pressure to stop this abuse of the Act.
D. Efforts to fix this loophole

There were two factors making the patent layering strategy possible. One was that the FDA gave the control over patent listing to Pharma, which allowed Pharma to layer questionable patents in the Orange Book. Many of these patents were either not valid, or had only a distant relationship with the drug. Another factor was that the Act did not limit the number of stays that could be granted for a single drug. Both the FDA and Congress took actions to close this loophole.

1. FDA’s new regulations governing patent listing

To curb listing questionable patents in the Orange Book, the FDA issued a new regulation in 2003 specifying the types of patents that could be submitted. The regulation excludes patents that are generally not relevant to the underlying drug: “[p]rocess patents, patents claiming packaging, patents claiming metabolites, and patents claiming intermediates.”

This regulation has only moderate effects on closing the loophole. First, though the FDA regulation categorically bans the listing of some types of questionable patents, it leaves the door open for other types of patents that are also subject to abuse by the Pharma, such as formulation patents, and methods of use patents. The FDA still gives Pharma complete discretion on listing of these latter patents in the Orange Book. More importantly, the FDA has no intention of reviewing the patents submitted by Pharma to make sure they follow the new guidelines. So this new FDA regulation is unlikely to stop the patent layering practice altogether.

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99 21 C.F.R. 314.53 (b).
100 See 68 Fed Reg. at 36683 (2003).

After the FTC released its study in 2002 on the widespread abuse of the Hatch-Waxman Act, Congress decided to follow the FTC’s recommendations\(^{101}\) to close the loophole of multiple-stays. Congress passed the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (“MMA”), which limits Pharma to only one thirty-month stay per drug.\(^{102}\) The MMA also relieves generic makers the obligations of certifying later listed patents after their ANDA was filed.\(^{103}\) This amendment eliminated the incentive for Pharma to layer patents in the Orange Book, which likely would put an end to the strategy of patent layering.

E. Future of Layering Strategy

The patent layering strategy was very success for Pharma to fight back the generics. By obtaining multiple stays, Pharma is able to enjoy extended monopoly and bring in hundreds of millions of dollars in revenue. The FDA’s new regulations on listing patents in the Orange Book categorically ban some of the most abused secondary patents. This will have some effects on restricting patent layering. More importantly, Congress enacted the MMA which allows only one thirty-month stay for each drug. This new provision takes away the biggest incentive of patent layering: multiple stays. The MMA will have a big impact on stopping the patent layering practice by Pharma. We are unlikely to see much of patent layering as a strategy to fight generics in the future.

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IV. STRATEGY THREE: SETTLING WITH GENERIC MARKERS

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\(^{101}\) FTC study, supra note 88, at ii-viii.

\(^{102}\) 21 U.S.C. §355(j)(2) and (5).

A. The loophole in the Act that allows settlement

To encourages generic markers to challenge the patents covering the brand drug, the Hatch-Waxman Act gives a lucrative 180-day marketing exclusivity to the first filer of an ANDA with a Paragraph IV certification.104 The Act treats filing of an ANDA as constructive infringement, which allows Pharma to, and it usually does, bring an infringement suit against the generic maker. The 180-day exclusivity automatically starts on (1) the date of court’s favorable decision of the patent invalidity or noninfringement by the generic drug, or (2) the date of the generic drug’s commercial marketing, whichever is earlier.105 Once a generic maker secures the right to exclusivity by being the first filer, if it settles the infringement suit with Pharma, the exclusivity can only be triggered by its own commercial marketing of the generic drug. The generic maker has this option because the exclusivity functions by prohibiting the FDA from approving another ANDA before the end the exclusivity.106 So after the settlement, the generic maker can hold off the entry of its generics and generics from any other generic makers as long as it wants without triggering the exclusivity. The power to control the generic market allows the generic maker to settle the infringement litigation and extract valuable considerations (usually a large payment) from Pharma in exchange of delaying the entry of generics (sometimes until right before challenged patents expire). This strategy benefits both sides: the generic maker gets payment and still has the lucrative exclusivity in the end, while Pharma enjoys extended monopoly. Such payments from the patent holder to the accused infringer are in the opposite direction of normal patent infringement

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105 Id.
106 Id.
suits, therefore are commonly referred as “reverse payment.” But the settlement strategy hurts consumers because they have to pay for the more expensive brand drugs when generics are delayed.

B. FTC trilogy

The FTC views settlements with reverse payment in the context of Hatch-Waxman Act with great suspicion. There are three alarming factors about these settlements from the antitrust point of view: (1) these settlements not only block the entry of the challenger’s generic drug, they also block the generic makers that are not parties of the settlement; (2) the flow of payment does not fit the pattern of normal patent infringement suits; and (3) the settlements potentially block even generic drugs that are not infringing the patent.\(^\text{107}\) To deter anti-competitive settlements, the FTC filed antitrust complaints on three such settlements in quick secessions: two in 2000 and one in 2001.

The first two complaints resulted in restraint orders from FTC, which were not contested by the parties.\(^\text{108}\) In the first case, Abbott’s hypertension and prostate drug Hytrin was challenged by generic maker Geneva, who was the first ANDA filer with a Paragraph IV certification. Geneva thus acquired the right to the 180-day exclusivity. In the subsequent patent infringement suit, the parties reached an agreement in April 1998 where Abbott agreed to pay Geneva $4.5 million per month in exchange for Geneva’s refraining from marketing the generic drug during the ongoing litigation. Geneva also promised not to waive its right to the 180-day exclusivity. In September 1998, the district court invalidated Abbott’s patent. But Geneva was content with the payment and did not


\(^{108}\) See *In re Abbott Labs.*, 2000 FTC LEXIS 15; *In re Hoechst Marion Rousel, Inc.*, 2000 FTC LEXIS 142.
bring its generic drug to the market.\footnote{In re Abbott Labs., 2000 FTC LEXIS 15.} The second complaint involved Hoechst’s brand drug Cardizem for hypertension and angina. The generic maker Andrx obtained the right to 180-day exclusivity through its ANDA filing. Hoechst settled the patent infringement suit with Andrx in July 1999. Under the settlement, Hoechst agreed to pay Andrx $10 million quarterly in exchange for Andrx’s refrain from marketing its generic drug or transferring its exclusivity right.\footnote{In re Hoechst Marion Rousel, Inc., 2000 FTC LEXIS 142.} In both cases, the settlement involved reverse cash payments from Pharma to a generic maker, who promised to delay the entry of generic drugs. The parties accepted the FTC’s orders to restrain from engaging in these and similar settlements.

The last complaint in the trilogy was factually the most complicated and vigorously contested by the parties.\footnote{In re Schering-Plough Corp., 2001 FTC LEXIS 39, reversed, Schering-Plough Corp. v. F.T.C., 402 F.3d 1056 (11th Cir. 2005), certiari denied, 126 S. Ct. 2929 (2006).} Schering-Plough’s brand drug K-Dur20 was a popular hypertension drug. The generic maker Upsher-Smith was the first to file an ANDA in August 1995 with a Paragraph IV certification to challenge Schering’s formulation patent (4,863,743 patent), which would expire on September 5, 2006. After Schering-Plough promptly brought a patent infringement suit against Upsher-Smith, the parties settled in 1997 under the terms that Upsher-Smith agreed not to market any generic versions of K-Dur20 until September 2001 in exchange for payment of $60 million; in addition, Schering-Plough received licenses to five unrelated products from Upsher-Smith. A second generic maker ESI-Lederle filed its ANDA in December 1995. Schering-Plough also brought patent infringement suit, which was settled in 1998. Though ESI-Lederle
had no right to exclusivity, it agreed not to market any generic version of K-Dur20 until 2004, and not to market more than one such generic for an additional two years. In return, Schering-Plough paid $5 million for ESI-Lederle’s legal fees and up to $10 million contingent upon the FDA’s approval of its ANDA. Schering-Plough also agreed to pay $15 million for licenses to seven unrelated ESI-Lederle products.  

According to the FTC, Schering-Plough’s settlements with Upsher-Smith and ESI-Lederle violated antitrust law. Schering-Plough’s payments exceeded the fair market value of the cross-licensed products from each generic maker, so the payment constituted reverse payments. Both generic makers promised to delay the marketing of generic drugs: Upsher-Smith not to market any generics in four years and ESI-Lederle not to market any in six years. In evaluating whether the entry date in the settlements violated the antitrust law, the FTC used the hypothetical “entry dates that might have been agreed upon in absence of payments” as a benchmark. If the agreed entry date was later than the hypothetical date and accompanied by reverse payments, the FTC automatically draws the presumption that the payments are for delaying the generic’s entry, which violated antitrust law. The FTC puts a heavy burden on the parties of the settlements to rebut the presumption. Here, the FTC held that the parties failed to offer convincing evidence to rebut the presumption of anti-competition. The FTC “concluded that the quid pro quo for the payment was an agreement to defer the entry date, and that such delay would injure competition and consumers.”

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112 Schering-Plough Corp. v. F.T.C., 402 F.3d 1056, 1060-61 (11th Cir. 2005).
113 Id., at 1070.
114 Id., at 1062 (internal quotation marks omitted).
115 Id., at 1062.
The FTC issued an order to the parties to “cease and desist from being parties to any [such] agreement.” Essentially, the FTC required the parties to settle on the terms most favorable to the consumers based on its benchmark entry date. Given the FTC’s mission to prevent anticompetitive activities to protect consumers, it was understandable that the FTC treated these settlements as highly suspicious, if not per se illegal.

C. Court of Appeals’ Policy Concerns

The court took a broader view of these settlements that went beyond the antitrust ground. When Schering-Plough appealed the FTC’s restraint order to the Eleventh Circuit, the court applied a three-prong test to determine the legality of the settlement: “(1) the scope of the exclusionary potential of the patent; (2) the extent to which the agreements exceed that scope; and (3) the resulting anticompetitive effects.”

Specifically, the court advanced two other policies besides deterring anticompetitive activities. They were the policy of patent protection which gives the patent owner the exclusionary power and the policy of favoring settlements over costly litigation.

The court put great emphasis on the patent’s exclusive nature. The court “reversed [the FTC order] for a rather simple reason: one of the parties owned a patent.” The patent law rewards innovation by granting inventors the right to exclude competition. So the “anticompetitive effect” existed already, which was the “context of patent litigation.” The FTC’s benchmark for analyzing anticompetitive effects, the hypothetical entry date without reverse payment, completely ignored the patent’s

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116 Id., at 1058.
117 Id., at 1066.
118 Id., at 1064.
119 Id.
exclusionary nature. The right benchmark, announced by the court, was the patent’s “exclusionary potential,” in other words, the full patent term. If “the exclusionary effects of the agreement fall within the scope of the patent’s protection,” the public was not substantially injured. Here, the court found that “the terms of the settlement to be within the patent’s exclusionary power,” therefore the settlement was neither anticompetitive nor violating antitrust law.  

The court advanced another policy to reverse the FTC’s order, which was the public policy of favoring settlement over litigation, even in the context of antitrust law. “Patent owners should not be in a worse position, by virtue of the patent right, to negotiate and settle surrounding lawsuit.” The adverse effects of litigations have been well documented, such as overcrowding the court dockets, high cost for both parties, causing uncertainty to the business, and hindering market activities. So the courts are reluctant to invalidate settlements absent reasons that they are illegal.

When the court balanced and reconciled the three competing policy: antitrust, patent law, and favoring settlement, it found the settlements were not illegal. The exclusionary potential of the patent outweighed the antitrust effects of the later-entry settlements. The long-standing public policy of favoring settlement also puts significant weight on the side of upholding the settlements. While the FTC found the reverse payment distasteful, the

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120 Id., at 1076.
121 Id., at 1072.
122 Schering, 402 F.3d, at 1072, (citing Standard Oil Corp. v. U.S. 283 U.S. 163, 170-71 n.5 (1931) (noting the interchange of rights and royalties in a settlement agreement “may promote rather than restrain competition”)).
123 Id.
court merely treated it as byproduct of the Hatch-Waxman Act. Overall, the court found the FTC’s restraint order without evidential support, and vacated it.\(^\text{124}\)

The Eleventh Circuit was also troubled by the FTC’s hostile view of pharmaceutical patents. The presumption of patent validity is stated expressly in the Patent Act,\(^\text{125}\) which can only be overcome by “clear and convincing” evidence of invalidity. But the FTC ignored this presumption by reasoning that “a large reverse payment was an acknowledgement of the patent’s weakness.”\(^\text{126}\) Then the remaining life of the patent should be adjusted shorter proportionally to reflect that weakness.\(^\text{127}\) In addition, the FTC observed that many challenged pharmaceutical patents were invalidated by courts. It concluded that every pharmaceutical patent should be assumed to be at risk of invalidity.\(^\text{128}\) The Circuit Court held that the FTC’s view conflicts with the fundamental principle of patent law: presumption of validity. It found no legal basis for the FTC’s hostile view of pharmaceutical patents.

The presence of reverse payments in a settlement does not necessarily make it illegal in the context of the Hatch-Waxman Act. Though the FTC put great emphasis on the reverse payments, the Circuit Court found that the Act “essentially redistribute[d] the relative risk” between the parties.\(^\text{129}\) The Act gave the generic maker “considerable leverage in patent litigation: the exposure to liability amounted to litigation costs, but

\(^{124}\) Id., at 1076.


\(^{127}\) Id.

\(^{128}\) Petition for a Writ of Certiorari, FTC v. Schering-Plough, 126 S. Ct. 544 (No. 05-273) at 14-15.

\(^{129}\) *Schering*, 402 F.3d, at 1074.
paled in comparison to the immense volume of generic sales and profits.”

But Pharma’s risk was much bigger as potentially losing a blockbuster product and a large profit at stake. “Even a patentee confident in the validity of its patent might pay a potential infringer a substantial sum in settlement.” The imbalance of risks between the parties mandated “consideration flows from the patent holder to the alleged infringer.”

The court concluded that “reverse payments were a natural by-product of the Hatch-Waxman process.” So the FTC’s emphasis on the reverse payment in analyzing the antitrust issue was misplaced.

There seems to be an emerging trend in favor of the principle articulated by the Eleventh Circuit in the Schering case. For example, the Second Circuit agreed that “simply because a brand-name pharmaceutical company holding a patent paid its generic competitor money cannot be the sole basis for a violation of the antitrust law unless the exclusionary effects of that agreement exceed the scope of the patent protection.” The exception was the Sixth Circuit which held that the settlement with a reverse payment was per se illegal.

130 Id.
131 Id., at 1075, (citation marks omitted).
132 Id., at 1074, (citation marks omitted).
133 Id., (citation marks omitted).
135 In re Tamoxifen Citrate Antitrust Litigation, 429 F.3d 370, 396, (2d Cir. 2005).
D. Efforts to deter settlements

The settlements with restriction on generic entry increased from five in 2004 to twenty-five in 2007. One of the premises of these settlements was that the generic maker who secured the right to the 180-day exclusivity could delay the commercial marketing of the generic drug in exchange for reverse payments and still keep the lucrative exclusivity. If the generic maker might risk of losing the exclusivity, it would be more reluctant to settle with Pharma. The Congress enacted MMA that aims at deterring these settlements in two ways. One is the forfeiture provision which gives the FDA authority to take away the generic maker’s right to exclusivity. The provision is triggered if the generic maker failed to market the generic drug within seventy-five days after (1) it “received FDA approval or thirty months after ANDA submission, whichever is earlier;” (2) a “non-appealed favorable district court or favorable Federal Circuit decision has been rendered;” (3) “favorable settlement has been entered;” or (4) the “patent expires or is withdrawn.” In addition, the 180-day exclusivity may also be forfeited if the ANDA applicant entered into a settlement with Pharma, which was found to violate the antitrust law by the FTC or an appeals court. The risk of losing the exclusivity should make the generic maker more cautious in settling with Pharma.

Another way to deter settlement is by the FTC filing provision in the MMA. It requires that certain types of agreements between generic makers and Pharma must be filed with the FTC and Department of Justice within ten days of execution of the

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agreement. These include any agreements related to 1) the “manufacture, marketing or sale” of the brand drug or its generic equivalent; or 2) the 180-day exclusivity of the generic drug.\textsuperscript{140} Having the FTC and Department of Justice reviewing the settlements may also deter generic makers from entering anticompetitive settlements.

E. Future of settlement strategy

In 2007, there were thirty-three final settlement agreements between Pharma and generic makers filed with FTC pursuant to the MMA. Twenty-five of them had restrictions on generic entry. Among the twenty-five settlements, eleven had no payment to the generic maker; another eleven settlements involved the generic maker receiving Pharma’s promise not to launch authorized generics during the exclusivity; and only three involved the generic maker receiving payments as part of a side-deal.\textsuperscript{141} There seems a new trend of using authorized generics as a consideration in negotiating settlement with generic makers. The settlement strategy will likely continue to play an important role in Pharma’s fight against generics.

V. STRATEGY FOUR: AUTHORIZING GENERICS

A. Definition of authorized generics

Pharma, as the owner of a brand drug, may license a third party to market a generic version of its own brand drug, typical during the 180-day exclusivity period. Since Pharma authorized its marketing, this generic version is called authorized generics (“AG”). AG is identical to the brand drug, except it is packaged under a generic label.

\textsuperscript{140} MMA § 1112(a).

\textsuperscript{141} Agreements at FTC, supra note 135, at 2-3.
Because the legality of AG rests on the NDA which gives approval to the brand drug, it does not require a separate marketing approval from the FDA.

Because AG directly competes with the generic version marketed by the ANDA applicant, AG represents a great threat to the generic maker who has the right to exclusivity. When there are two generic versions of the brand drug, instead of one, during the exclusivity period, the generic maker would make significantly less profit during that period. For example, generic maker Apotex had the right of 180-day exclusivity for generic Paxil. Apotex initially expected the generic drug to generate sales between $530 million to $575 million during the exclusivity period. However, because the owner of Paxil introduced an AG, Apotex only had sales of approximately $150 million to $200 million.\textsuperscript{142} The reduction of profit was due to both loss of about half of the generic market and selling at lower price during the exclusivity. Because the generic makers receive the bulk of their profits during the exclusivity period, they feel a great threat from the AG.\textsuperscript{143}

But an AG allows Pharma to recoup some of the loss that will occur during the exclusivity period. An AG competes with the generic version from the first ANDA applicant and recoups near half of sales in generic drug market. Because the monopoly of brand drug is lost anyway when the exclusivity period starts, the strategy of authorizing generics to make up the loss after monopoly is over is a natural defense for Pharma.

B. Lack of Authority in Statutes to Prohibit AG

When Pfizer and Proctor & Gamble introduced their respective AGs into the market during the 180-day exclusivity period, the generic makers Teva and Mylan launched

\textsuperscript{142} See Greene article.
\textsuperscript{143} Id.
vigorous challenges to the legality of AGs. The generic makers argued that Congress had
a clear intent in the Hatch-Waxman Act to “grant the first ANDA filer complete
exclusivity in the generic market for 180 days.”\textsuperscript{144} They charged that exclusivity shared
with an AG was not exclusivity. The AG violated the Act because, the generic maker
contended, it was contrary to the legislative intent. The two generic makers submitted
citizen petitions separately to ask the FDA to “prohibit the marketing and distribution of
authorized generic versions of brand name products until after the expiration” of the
exclusivity period.\textsuperscript{145} The FDA denied both petitions in a single letter, concluding that the
statute “does not contemplating or countenance delaying the marketing of authorized
generics.”\textsuperscript{146} The FDA found no authority under the statutes to regulate when Pharma
could introduce, or license a third party to introduce, an authorized generic version of its
brand drug into the market.\textsuperscript{147}

On review of the FDA’s ruling, both the Fourth Circuit and the D.C circuit agreed
that the FDA simply did not have “the power to prohibit the marketing of authorized
generics during the 180-day exclusivity period.”\textsuperscript{148} First, there was no textual support of
alleged authority from the statutes. The courts found no support from the original FDCA
that “prohibits NDA holders from introducing a brand generic drug in the market during
the ANDA’s exclusivity period.”\textsuperscript{149} In addition, the Hatch-Waxman Act gives the generic

\textsuperscript{144} Teva Pharm. Indus. Ltd. v. Crawford, 410 F.3d 51, 53 (D.C. Cir. 2005).
\textsuperscript{145} Id., at 52.
\textsuperscript{146} FDA letter re: Docket No. 2004P-0075 & 2004p-0261 (Feb 7, 2004), at 3, available at
www.fda.gov/ohrms/dockets/dailys/04/july04/070704/04p-0075-pdn0001.pdf, (Hereinafter “FDA letter to
Teva and Mylan”).
\textsuperscript{147} Id.
\textsuperscript{148} Mylan Pharm., Inc. v. F.D.A., 454 F.3d 270, 271, (4th Cir. 2006); See also Teva, 410 F.3d 51.
maker the right to exclusivity in a provision that functions by prohibiting the FDA from approving other later-filing ANDA during the exclusivity period. The provision “says nothing about how the holder of an approved NDA may market its drug.”

Second, the court did not agree with the generic makers’ asserted legislative intent. The generic makers argued that the legislative intent behind the Hatch-Waxman Act was creating “the 180-day exclusivity period … to encourage generic companies to file Paragraph IV challenges to brand drug patents.” Since an AG would “reduce the revenues” for the ANDA applicant, the practice was against the legislature intent. The court found this argument unconvincing. One reason was that the plain language meaning of the Act was clear. There was “not textual ambiguity of the sort that would ordinarily lead us to” consult the legislative intent. In addition, more importantly, though Congress had intended to create an incentive for the generic makers, it did not follow that Congress was “solely concerned with making generic drugs available more speedily.” Congress clearly also had a “countervailing interest” in protecting “the intellectual property rights of pioneer drug companies,” who had the rights “to make ordinarily licensing agreements with third parties.” Therefore, Pharma is “free to license generic versions of [its] pioneer drugs at anytime.”

151 Teva, 410 F.3d at 53.
152 Id., at 54.
153 Id.
154 Mylan, 454 F.3d at 275.
155 Id.
156 Id., at 275-76.
157 Id., at 276.
In conclusion, the courts agreed that “the statute does not grant the FDA the power to prohibit the marketing of authorized generics during the 180-day exclusivity period.”\textsuperscript{158} The FDA did not act arbitrarily or capriciously in denying the generic makers’ citizen petitions.

C. Anti-competitive effects

The generic makers advanced another argument that AGs reduced competition between generics and brand drugs, which would harm the consumers. The alleged anti-competitive effects can be analyzed separately during the 180-day exclusivity period and in the long term.

1. Anti-competitive effects during the exclusivity

Neither the FDA nor the FTC believed that an AG was anti-competitive during the exclusivity period. The FDA stated that competition between an AG and a generic maker’s generic version “enhance[d] competition overall among drug products,” which lead to “lower prices during the exclusivity period.”\textsuperscript{159} The FTC also long held the position that “authorized generic agreements are pro-consumer because they allow multiple generic entrants sooner.”\textsuperscript{160}

There is some evidence that suggests that an AG increases price competition among the competing generic versions. One independent study found that AGs lead to lower prices for the generics and greater market penetration by the generics during the

\textsuperscript{158} Id., at 271.

\textsuperscript{159} FDA letter to Teva and Mylan, at 12.

\textsuperscript{160} Britol/Teva “Authorized generic agreement approved by FTC, the pink sheet at 7, (May 31, 2004).
exclusivity period.\textsuperscript{161} It is quite clear that during the exclusivity period the AG promotes competition and reduces the price of generic drugs.

2. Anti-competitive effects in the long term

The generic maker further claimed that an AG would hurt competition in the long term. The generic maker alleged that it needed the incentive of 180-day exclusivity to justify taking the risk of challenging Pharma’s patents. An AG would give the generic maker “significantly less profit during the period of 180-day exclusivity than if the [generic maker] had no authorized generic competition.”\textsuperscript{162} With reduced profit during exclusivity, the generic makers would be less willing to challenge the patents. It would eventually result in less generic drugs, less competition, therefore hurt the consumers in the future.\textsuperscript{163}

The FDA was not convinced. It found that the generic makers “offer[ed] no evidence that generic companies would stop submitting ANDAs just because they faced the prospect of making less money during the 180-day exclusivity period.”\textsuperscript{164} The FDA believes that “the incentives created by 180-day exclusivity remain[ed] adequate” for the generic makers to challenge the patents, even with competition from AG.\textsuperscript{165}

\textsuperscript{161} Ernst Berndt et al., Authorized generic drugs, price competition, and consumers’ welfare, 26 Health Affairs 790 (2007). See also Leila Abboud, Drug makers use new tactic to ding generic-drug firms, Wall Street Journal at B2 (Jan. 27, 2004), (Hereinafter “Abboud article”) (The generic maker Barr’s CEO commenting about the AG: “The authorized generic drove down prices and cut into sales of the Barr drug [during the exclusivity period]”).

\textsuperscript{162} Mylan, 454 F.3d at 273.

\textsuperscript{163} See Greene article.

\textsuperscript{164} FDA letter to Teva and Mylan, at 13

\textsuperscript{165} Id.
Some commentators also argued that an AG would not deter generic makers from challenging the patents because the profits from the exclusivity still far outweighs the costs of filing an ANDA.\textsuperscript{166} For example, Apotex spent five years and $13 million researching its copy of Paxil and mounting a successful challenge in court.\textsuperscript{167} But the generic Paxil still brought over $150 million revenue for Apotex even with an AG. The incentive for generic makers to challenge the patents seems to be adequate, given the profit margin of near 1000 percent even with an AG during the exclusivity period.\textsuperscript{168}

D. Investigation of authorized generics

The FTC has not publicly taken a position on the issue of AG’s long term effects on competition and consumers. A group of law makers including Waxman (one of the two authors of Hatch-Waxman Act) were concerned that “authorized generics could have a negative impact on competition… Consequently… it is possible that fewer generic drugs would come to market and the prices for certain drugs would remain high for consumers.”\textsuperscript{169} At their request, the FTC in 2006 proposed a study on “the use, and likely short- and long-term competitive effects, of authorized generics in the prescription drug marketplace.”\textsuperscript{170} The final report of this study has not been released yet. The report, once released, could prompt Congress to amend the Hatch-Waxman Act to limit the practice of AGs in the future, particularly if the study finds significant negative impact of AGs on competition between brand drugs and generics.

\textsuperscript{166} See Greene article.
\textsuperscript{167} See Abboud article.
\textsuperscript{168} See Greene article.
\textsuperscript{169} Grassley, Leahy, Rockefeller Request Study on Impact of “Authorized” Generics, (May 12, 2005), available at \url{http://leahy.senate.gov/press/200505/051205b.html}.
\textsuperscript{170} See \textit{FTC Proposes Study of Competitive Impacts of Authorized Generic Drugs}, \url{http://www.ftc.gov/opa/2006/03/authgenerics.shtm}. 
E. Future of Authorized Generics Strategy

Authorizing generics seems to be a favorite strategy for Pharma. Since the late 2003, “the launch of every Paragraph IV generic expected to be a blockbuster has been met with the availability of an AG,” such as Neurotin, Paxil, OxyContin, and Macrobid.\footnote{Narinder Banait, \textit{Authorized Generics: Antitrust issues and the Hatch-Waxman Act}, available at www.fenwick.com/docstore/Publications/IP/Authorized_Generics.pdf.} The FDA maintains a list of authorized generic drugs at its website.\footnote{http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm126391.htm.} The list was last updated on July 21, 2009, which contains 530 entries. There is also a new trend that Pharma uses AGs as a consideration in settling infringement litigations with generic makers, as discussed above.

So far, the generic makers get little sympathy from the FDA and the courts. The reason may very well be the generic makers’ huge profits during the 180-day exclusivity period relative to the small investment in filing an ANDA and litigating the patents. In addition, the large profit is disproportional to the modest risk, since the Hatch-Waxman Act shields most of the risk off the generic makers in challenging the patents. Even if AGs cuts the market in half, the exclusivity is still a large windfall on the generic makers by any measure.

VI. Proposed Legislations

The four strategies used by Pharma to fight back generic drugs have differing impacts on the drug market. The patent delisting strategy is successful only in narrow circumstances: before any ANDA filing with Paragraph IV certifications. It is a double edged sword and Pharma feels the pain as well. This strategy will have little effects on

\footnote{172 http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm126391.htm.}
future drug prices. Congress thus has no pressing need to address it in the current healthcare reform.

The patent layering strategy contributed significantly to delay the generics entry and keep the drug prices high. Congress addressed the problem by enacting the MMA in 2003, which allows only one thirty-month stay for each drug. Since the MMA takes away the main incentive of patent layering, Pharma may not use this strategy with the same enthusiasm in the future. But to stop Pharma completely, Congress should require the FDA to strictly enforce the patent listing guidelines. The FDA should demand Pharma to list only patents that are truly relevant to the drug product, instead of any patents remotely related. More importantly, Congress should require FDA to review the patents Pharma submits to the Orange Book to determine the relevance and refuse inappropriate listings. For any intentionally misleading or misrepresentation of patent listing, the FDA should impose hefty penalties. Only if the FDA gets serious about its guidelines, will Pharma be entirely deterred from using patent layering to delay the entry of generics.

For both settling with generic makers and authorizing generics strategies, the courts have been reluctant to interfere under the current anti-trust law. The new trend is for Pharma to use AGs as bargaining power to settle with generic makers in securing delayed generic entrants. This combined use of the two strategies will significantly hinder consumers’ access to cheap generic drugs. Congress can address both strategies in a single scheme: limiting Pharma’s use of AGs.

Though the FDA and the courts agree on AG’s legality and its short term benefit on reducing drug prices, the long term impacts have not been adequately addressed. The fact that Pharma actively introduces AGs leads one to reasonably conclude that AGs are
intended to reduce competition in the long run. The Hatch-Waxman Act gives incentives to the generic makers to introduce more cheap drugs early. While AGs almost assuredly reduce incentives for the generic makers, the critical question is whether AGs reduce the incentives to such a level that generic makers will stop filing ANDAs and introducing generics altogether.

The FTC’s proposed study on AGs’ long term impacts may take years to finish. We should address the AG problem now, best in the context of the current healthcare reform. The proponent of AGs often argues that for drugs with annual sales over $1 billion, the generic maker is expected to make over $100 million even with an AG. The profit is thus an adequate incentive for relatively small risk and investment. But even if the incentive is sufficient for blockbuster drugs, the picture is more complex for drugs with smaller annual sales (less than $300 million), which account for the majority of the brand drugs in the market.\(^{173}\)

There are many drugs with annual sales so small that generic makers would not take the risk and invest the resources to market the generics if AGs will be introduced. Because AGs cut the generic makers’ profit at least in half during the exclusivity period, the generic makers would be pushed into smaller profit not justified by the risk and investment in filing an ANDA. AGs will undoubtedly diminish the incentive for the generic makers to bring generics of these smaller brand drugs to consumers. The public thus has to bear the higher cost for these drugs.

In light of this, Congress should pass legislation to regulate AGs with a reference to the annual sales of the brand drug. This will ensure that consumers have access to cheap

\(^{173}\) See MedAdNews 200 - World's Best-Selling Medicines, MedAdNews, July 2007. Of the thousands of brand drugs, there are only 105 drugs with worldwide sale over $1 billion in 2006. Their annual sales in the U.S. are even less. Vast majority of them have annual worldwide sale below $300 million.
generics for drugs big and small. Congress should create a series of annual sales bracket for the brand drugs and regulate AGs differently according to the sales bracket the brand drug falls within. For the highest sales bracket (blockbuster drugs with sales over $1 billion), AGs should be unlimited. For the lowest sales bracket (drugs with sales around $100 million or below), AGs should be forbidden. For middle brackets, the Congress should delay the AGs increasingly as the annual sales bracket decreases.

This annual sales based regulation scheme is nothing new. The FDA itself already regulates food labeling according to the annual sale of food products. This food regulation exempts any nutrition labeling for food product with annual sales less than $50,000.174 Similarly, the Environmental Protection Agency (“EPA”) also has a scheme to regulate volatile organic compounds emissions to comply with the national ambient air quality standard for ozone. The EPA employs a complex model that takes into account of annual sales of the product.175 The higher the annual sale the product has, the stricter the limitation is.

This new scheme for regulating AGs is in accordance with the legislative intent of the Hatch-Waxman Act. It will give adequate incentives to the generic makers to bring generics to the market for drugs in any annual sales range. This will make a significant contribution to control the healthcare as part of the current healthcare reform.

VII. CONCLUSION

The Hatch-Waxman Act is a very successful legislation in bringing more generic drugs into the market. The market share of generic drugs has increased from nineteen

175 Section 183(e)(2)(B) of the Clean Air Act. See also http://www.epa.gov/EPA-AIR/1995/March/Day-23/pr-503.html
percent in 1983 to near sixty percent in 2005. This tremendous gain by generic makers comes at the loss of big Pharma. To protect its valuable assets, the Pharma has used four main strategies in fighting back the generic drugs: patent delisting, patent layering, settlement with generic maker, and authorizing generics.

The strategies of patent delisting and patent layering are having quickly diminishing value for Pharma. The patent delisting strategy is successful only in narrow circumstances: before any ANDA filing with Paragraph IV certifications. The patent layering strategy was a favorite for Pharma. But Congress partially closed the loophole by enacting the MMA in 2003, which allows only one thirty-month stay for each drug. The latter two strategies are still likely to play big roles in Pharma’s fight against generics. The settlement strategy has evolved into a new form: instead of cash payments to generic makers, Pharma uses the threats of authorized generics to gain concessions from generic makers. Courts have found no objections to this new trend so far.

This article proposes two legislations to reduce the prescription drug cost. The first is to mandate FDA to aggressively enforce the patent listing guidelines and punish any violations. This will completely deter Pharma from layering patents in the Orange Book. The second is a scheme to regulate AGs in reference to the annual sales of the brand drugs. The aim is to ensure the generics are more widely available for drugs big and small. Both approaches will contribute to lower the cost of healthcare and should be considered as part of the current healthcare reform.