UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

TEVA PHARMACEUTICALS USA, Inc.

Plaintiff,

v.

MICHAEL O. LEAVITT, in his official capacity as Secretary of Health and Human Services;

ANDREW C. VON ESCHENBACH, M.D., in his official capacity as Commissioner of Food and Drugs;

UNITED STATES FOOD AND DRUG ADMINISTRATION,

Defendants.

Case: 1:08-cv-00395
Assigned To : Lamberth, Royce C.
Assign. Date : 3/4/2008
Description: TRO/PI

PLAINTIFF'S MOTION FOR EXPEDITED PRELIMINARY INJUNCTIVE RELIEF

Plaintiff Teva Pharmaceuticals USA, Inc. ("Teva") respectfully submits this emergency application for expedited preliminary injunctive relief enjoining Defendants, Michael O. Leavitt, in his official capacity as Secretary of Health and Human Services, Andrew C. von Eschenbach, in his official capacity as Commissioner of Food and Drugs, and the United States Food and Drug Administration (collectively, "FDA"), from taking any action to issue an approval of any Abbreviated New Drug Application for risperidone tablet products other than Teva's pending the expiration of Teva's 180-day generic exclusivity period for such products.

The grounds for the present application are fully set forth in the accompanying Memorandum in Support of Teva's Motion for Preliminary Injunction and Declaration of David Marshall.

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Dated: March 4, 2008

Respectfully submitted,

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UNITED STATES DISTRICT COURT
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TEVA PHARMACEUTICALS USA, Inc. Plaintiff, v. MICHAEL O. LEAVITT, in his official capacity as Secretary of Health and Human Services; ANDREW C. VON ESCHENBACH, M.D., in his official capacity as Commissioner of Food and Drugs; UNITED STATES FOOD AND DRUG ADMINISTRATION, Defendants.	Case No. _____

TEVA PHARMACEUTICALS USA, INC.'S MEMORANDUM IN SUPPORT OF ITS MOTION FOR A PRELIMINARY INJUNCTION

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March 3, 2008

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INTRODUCTION

In August 2001, Teva filed the first Abbreviated New Drug Application ("ANDA") seeking FDA approval to market a generic version of Risperdal® (risperidone) tablets—an antipsychotic medication with more than $2.5 billion in annual sales. As it was required to do by the Hatch-Waxman Act and FDA's own regulations, Teva filed certifications regarding each of the two patents that at that time were listed as claiming Risperdal® in FDA's official patent register, *Approved Drug Products with Therapeutic Equivalence Evaluations* (commonly known as the "Orange Book"). Specifically, Teva certified that it would not market its generic risperidone tablets until one of those patents expired (a "Paragraph III certification"), but that the other officially listed patent—U.S. Patent No. 5,158,952 ("the '952 patent")—was invalid and otherwise would not be infringed by Teva's generic risperidone tablets, and thus that Teva intended to bring its product to market and provide price relief to consumers before that patent expired (a "Paragraph IV certification"). As the first generic company that invested the resources necessary to identify a vulnerable patent; engineer a non-infringing pathway around that patent; and then challenge that officially listed patent by filing a Paragraph IV certification, Teva subjected itself to the risk of patent infringement litigation but simultaneously secured eligibility for a 180-day marketing exclusivity period during which no other generic risperidone product could be approved.

FDA's decision in this case now threatens to deprive Teva of its statutory exclusivity period by sanctioning the "delisting" of an officially listed Orange Book patent ***after*** Teva undertook the very investments and risks that 180-day marketing exclusivity is designed to reward. Two months after Teva submitted its ANDA, FDA asserted that it had "delisted," or removed, the '952 patent from the Orange Book ***before*** Teva submitted its ANDA. That was a curious assertion: On the date Teva submitted its Paragraph IV ANDA to FDA in August 2001,

the '952 patent not only appeared in the 2001 annual edition of the Orange Book, but FDA's then-current monthly Cumulative Supplement to the Orange Book indicated that there had been no subsequent changes to the patent listing information for Risperdal®, and thus, that the '952 patent continued to be officially listed as claiming Risperdal® tablets. Indeed, FDA's monthly Cumulative Supplements continued to reflect that there had been no changes to the official patent listing information for Risperdal® tablets for some four months ***after*** Teva submitted its Paragraph IV ANDA. FDA nonetheless informed Teva that it would not accept Teva's ANDA for filing unless and until Teva withdrew its Paragraph IV certification to the '952 patent—effectively divesting Teva of the exclusivity it had earned by identifying weaknesses in the Risperdal® patents, developing a non-infringing, generic form of Risperdal® tablets, and assuming the risk that it would be sued for patent infringement by submitting the first Paragraph IV certification for a Risperdal®-claiming patent.

As it did the last time FDA delisted a patent and thereby deprived Teva of its exclusivity, *see Ranbaxy Labs. Ltd. v. Leavitt*, 469 F.3d 120 (D.C. Cir. 2006), Teva petitioned the Agency for relief. *See* Citizen Petition No. 2007P-0316 (filed Aug. 8, 2007) (attached as Ex. 1). And again, as it did the last time FDA delisted a patent and thereby deprived Teva of its exclusivity, the Agency now has refused to relist the '952 patent and restore Teva's exclusivity. *See* FDA Letter Decision (dated Feb. 26, 2008) (attached as Ex. 2). The problem here is that the D.C. Circuit's decision last time around ***rejected*** FDA's approach to patent delisting, and the Agency's refusal to follow that decision by relisting the '952 patent and restoring Teva's exclusivity is no less inconsistent with the plain language and structure of the Hatch-Waxman Act than its refusal to relist the patents at issue in *Ranbaxy*. As the D.C. Circuit explained in *Ranbaxy*, FDA simply may not effectuate the delisting of a patent where doing so would have the effect of depriving a

generic manufacturer of its marketing exclusivity, because effectuating the delisting of a patent after a manufacturer has made the investments necessary to challenge that patent and assumed the risk of infringement litigation fundamentally undermines the incentive scheme Congress designed to encourage Paragraph IV challenges and speed the advent of generic competition.

Make no mistake: that is exactly what FDA's decision does in this case. When Teva decided to develop generic risperidone tablets, it reviewed the annual Orange Book and the then-current monthly Cumulative Supplement to the Orange Book; identified weaknesses in an officially listed patent; invested in the development of a non-infringing alternative; and undertook the risk of costly and protracted patent infringement litigation by submitting a Paragraph IV challenge to the '952 patent—only to have the Agency turn around and strip Teva of its statutory reward ***after*** Teva did precisely what Congress sought to encourage. As both this Court and the D.C. Circuit recognized in *Ranbaxy*, FDA's actions violate the Hatch-Waxman Act.

It is no answer that FDA purports to have delisted the '952 patent before Teva submitted its Paragraph IV challenge to that patent. That assertion is belied both by the fact that the '952 patent remained physically "listed" in the 2001 Orange Book at the time Teva submitted its Paragraph IV certification, and by the fact that FDA's then-current monthly Cumulative Supplement indicated that there had been no changes to the Risperdal® patent-listing information at the time Teva submitted its ANDA. Indeed, FDA's monthly Cumulative Supplements to the Orange Book continued to reflect that there had been no changes to the Risperdal® patent-listing information for some four months after Teva submitted its Paragraph IV certification.

FDA now tries to get around those key facts—which it does not dispute—by asserting that FDA also maintained an electronic version of the Orange Book on its website, and alleging that Teva would have discovered that the '952 patent had been delisted if Teva had searched that database before submitting its Paragraph IV certification. That argument fares no better. Setting aside that FDA has not produced any actual evidence of what appeared on its website in August 2001—but instead must rely on a putative reconstruction of the website and, indeed, cannot even identify the date on which it allegedly updated the Risperdal® patent-listing information on that website—the Agency's claims about the website's alleged content are irrelevant as a matter of law. FDA's own regulations at that time directed applicants to consult the Agency's printed monthly Cumulative Supplement to the Orange Book—***not*** the electronic Orange Book or any other part of the Agency's website—in order to obtain the latest patent listing information for approved drugs like Risperdal®, and so did the 2001 Orange Book itself, as FDA grudgingly concedes in its response to Teva's Petition.

And while FDA makes much of the fact that the 2001 Orange Book and monthly Cumulative Supplements to the 2001 Orange Book referenced the availability of an "Electronic Orange Book Query" feature on FDA's website, neither the annual Orange Book nor the monthly Cumulative Supplements so much as hint that that "Query" feature might have contained any information apart from what appeared in the Agency's monthly Cumulative Supplements. To the contrary, the key passage on which FDA's pins its response to the Petition stated only that the electronic Orange Book Query data was "updated ***concurrently*** with the publication of the annual edition or monthly cumulative supplements," FDA Letter Decision at 6 (quotation omitted; emphasis added)—not that the electronic Orange Book Query data was updated ***between*** printings of the monthly Cumulative Supplement. As a result, the Cumulative

Supplement's reference to the electronic Orange Book Query feature merely informed readers that that feature would provide ***the same*** data that was published in the most current monthly Cumulative Supplement to the Orange Book.

Teva, in short, was legally entitled to rely on the 2001 Orange Book listing and monthly Cumulative Supplement to the Orange Book in effect at the time it submitted its Paragraph IV certification to the '952 patent. FDA's attempt to deprive Teva of its statutory reward now thus is inconsistent with the plain text and structure of Hatch-Waxman (as *Ranbaxy* makes clear), and cannot be reconciled with FDA's own regulations or the Orange Book itself. Injunctive relief thus is appropriate to prevent FDA from unlawfully and unfairly depriving Teva of its 180-day exclusivity period.

Indeed, such relief is especially appropriate here because Teva would suffer truly irreparable harms if this Court does not promptly act to protect Teva's rights. On June 29, 2008, Janssen's pediatric exclusivity for Risperdal® tablets will expire and FDA will be free to begin approving ANDAs for generic risperidone tablets. If FDA at that point approves ANDAs other than Teva's—and thereby divests Teva of its generic marketing exclusivity—there would be no way for Teva to recover losses attributable to sales that it could have made during its statutory head-start on the competition. Pharmaceutical companies simply cannot "make up" for sales lost to competitors during a would-be exclusivity period; prescriptions are filled only once and patients take their medicine daily, so Teva could not turn back the clock on July 1 and replace medication provided by another company on June 29 and consumed by patients on June 30. Far more important, marketing exclusivity typically permits the first generic company to enter into long-term sales contracts and secure additional market share over the long-run. But once other companies are allowed to enter the market, that officially sanctioned head-start permanently

disappears because all companies are free to enter into such arrangements. These harms would be especially pronounced in this case, because FDA's immunity from monetary damages precludes Teva from recovering even a penny of the significant sales revenue it stands to lose as a result of the Agency's official actions.

Finally, it bears note that time is of the essence. It takes months to plan and prepare an exclusive generic launch for a product with more than $2.5 billion in current annual sales. Indeed, in this case, planning for such a launch would require immediate worldwide shifts in Teva's production, testing, packaging, and shipping schedules. Every day that goes by thus makes it less likely that Teva will be able to launch generic risperidone tablets on June 29 and reap the full benefits of its exclusivity. As a result, the public interest strongly favors an immediate resolution of this case which faithfully reflects Congress's unmistakable intent to speed the advent of generic competition.

BACKGROUND

A. Statutory Framework

The Food, Drug, and Cosmetic Act (the "FDCA" or "statute"), as modified by the Drug Price Competition and Patent Restoration Act of 1984 (the "Hatch-Waxman Act"), establishes the procedure for obtaining approval to market pharmaceutical products in the United States. *See* 21 U.S.C. § 355 (2002).[1] The FDCA requires the manufacturer of a pioneer or brand-name (*i.e.*, non-generic) drug to file a complete New Drug Application ("NDA") that contains, among

[1] The FDCA has subsequently been amended by the Medicare Modernization Act of 2003 ("MMA") and the Food and Drug Administration Amendments Act of 2007 ("FDAAA"). Because Teva filed its ANDA prior to the passage of either of these amendments, however, the substantive aspects of this case relating to the listing and delisting of patents in the Orange Book and Teva's eligibility for 180-day marketing exclusivity are governed by the Hatch-Waxman version of the FDCA. All references to the FDCA and relevant FDA regulations in this brief refer to the pre-2003 versions of the laws unless otherwise noted.

other things, extensive scientific and clinical data demonstrating the safety and effectiveness of the proposed new drug. *See id.* § 355(b)(1). The NDA must also include information about each patent the applicant asserts as claiming that drug. *See id.* § 355(b)(2); *see also* 21 C.F.R. § 314.50(h); *id.* § 314.53(b).

Prior to the passage of the Hatch-Waxman Act, generic manufacturers generally were required to complete a full NDA in order to obtain approval for a proposed generic drug product—even though generic drugs contain the same active ingredients, and provide the same therapeutic value, as their brand-name counterparts. As a result, generic market entry often was cost-prohibitive, and patients lacked widespread access to generic medicines that typically are sold at lower, more competitive prices to consumers, private insurers, and public insurers. In 1984, Congress enacted Hatch-Waxman to remove those barriers to entry, increase the availability of generic drugs, and thereby reduce the average cost of pharmaceuticals. *See* Drug Price Competition and Patent Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984).

To accomplish those goals, Hatch-Waxman permits generic companies to obtain marketing approval so long as they can show that a proposed generic drug product is bioequivalent to a "listed drug" that FDA has already deemed safe and effective. Generic applicants do so by submitting an Abbreviated New Drug Application ("ANDA") that, among other things, establishes the proposed generic product's bioequivalence to the listed (or previously approved) drug. *See* 21 U.S.C. § 355(j). Provided that bioequivalence is fully established in the ANDA, the generic applicant need not repeat the safety and efficacy studies that were conducted on the listed drug. *See id.* § 355(j)(2)(A).

In an effort to balance the interest in speedy generic market entry against the intellectual property rights of brand-name manufacturers, Congress required each ANDA to include a

certification regarding every patent that the brand manufacturer has identified as claiming a previously approved drug. *See id.* § 355(j)(2)(A)(vii). Four types of certifications are available:

> (I) that patent information has not been filed with respect to the previously approved drug [a "Paragraph I certification"],
>
> (II) that the patent identified as claiming the previously approved drug has expired [a "Paragraph II certification"],
>
> (III) that the generic drug will not be marketed until the date on which the patent identified as claiming the previously approved drug will expire [a "Paragraph III certification"], or
>
> (IV) that the patent identified as claiming the previously approved drug is invalid or will not be infringed by the manufacture, use, or sale of the generic drug for which the ANDA is submitted [a "Paragraph IV certification"]

See id.

The most important of these is the Paragraph IV certification. Such certifications signal the generic applicant's intent to market its product prior to the expiration of a competition-blocking patent on the brand-name drug, introducing market competition at an earlier date and lowering prices for consumers. But filing a Paragraph IV certification carries significant risks for the applicant. Paragraph IV applicants must invest significant resources in order to identify weaknesses in a competition-blocking patent, develop a non-infringing alternative to the branded product, and/or craft a legal challenge to the validity or applicability of the listed patent. And if those efforts prove successful and the applicant follows through on its efforts to break the patent logjam, the very act of submitting a Paragraph IV challenge to FDA constitutes a "highly artificial" act of patent infringement that can give rise to a lawsuit by the brand manufacturer and require the generic applicant to spend years defending itself in costly patent litigation. *See* 35 U.S.C. § 271(e); *see also Eli Lilly and Co. v. Medtronic, Inc.*, 496 U.S. 661, 678 (1990).

To encourage manufacturers to undertake those investments and accept those risks, Hatch-Waxman offers a significant reward to the first Paragraph IV challenger: a 180-day period during which it is entitled to market its generic product without competition from other generic applicants. *See, e.g.*, *Purepac Pharm. Co. v. Thompson*, 354 F.3d 877, 879 (D.C. Cir. 2004); *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1064 (D.C. Cir. 1998); *Sandoz, Inc. v. FDA*, 439 F. Supp. 2d 26, 29 (D.D.C. 2006); *see also* 21 U.S.C. § 355(j)(5)(B)(iv) ("180-day exclusivity period"). This 180-day exclusivity period runs from either the date on which a court decides that the challenged patent is invalid or not infringed (if litigation results from the Paragraph IV certification), or the date on which the first Paragraph IV applicant commercially markets its generic drug product. *Id.* § 355(j)(5)(B)(iv).

To make this system work, Hatch-Waxman requires FDA to publish an official list containing every patent that a brand manufacturer has identified as claiming any previously approved drug product. *See* 21 U.S.C. § 355(b)(1), (c)(2), (j)(2)(A)(vii); *see also* 21 C.F.R. § 314.53(b). FDA fulfills that mandate by publishing the Orange Book, which (among other things) lists every approved drug product and its indications; every patent identified as claiming each drug product; the expiration date of each such patent; and any additional exclusivity period to which the brand manufacturer is entitled. *See, e.g.*, Orange Book (21st ed. 2001) ("2001 Orange Book") (excerpt attached as Ex. 3). At the time Teva was preparing its risperidone ANDA, FDA printed an annual edition of the Orange Book at the beginning of every calendar year, and then supplemented the annual edition with official, printed monthly Cumulative Supplements that were designed to provide notice of any changes in the official patent information for approved drug products. *See, e.g.*, Orange Book 21st ed. Cumulative Supplement 8 (Aug. 2001), at iii (the "August 2001 Supplement") (attached as Ex. 4).

These Cumulative Supplements were legally binding. FDA's own regulations required the Agency to update the Orange Book's patent-listing information by publishing the monthly Cumulative Supplements, 21 C.F.R. § 314.53(e) ("Patent information submitted by the last working day of a month ***will be published in that month's supplement to the list***.") (emphasis added), and the 2001 Orange Book and monthly Cumulative Supplements themselves each directed ANDA applicants to consult "the most current Cumulative Supplement" to ascertain up-to-date patent information before submitting certifications "[b]ecause all parts of the [annual Orange Book] are subject to changes, additions, or deletions." *See, e.g.*, August 2001 Supplement at iii. As a result, each "Cumulative Supplement provides [the] updated patent and exclusivity data ... required by the [Hatch-Waxman Act]." *Id*. at iii.

While FDA printed the annual Orange Book and monthly Cumulative Supplements at the time Teva submitted its risperidone ANDA, the Agency never played more than a "ministerial" role in maintaining the patent listings included in those official publications. Because FDA has no expertise in patent law, it does not evaluate the validity of patents before listing them in the Orange Book. *See, e.g.*, *aaiPharma v. Thompson*, 296 F.3d 227, 238-40 (4th Cir. 2002); *American Bioscience Inc. v. Thompson*, 269 F.3d 1077, 1084-85 (Fed. Cir. 2001); *Alphapharm Pty Ltd. v. Thompson*, 330 F. Supp. 2d 1, 8-9 (D.D.C. 2004). Rather, once a brand manufacturer submits patent information on a reference listed product, the statute always has provided that FDA "***shall*** publish it." 21 U.S.C. § 355(c)(2) (emphasis added); *see also id.* § 355(b)(1). As a result, ANDA applicants routinely relied on the printed Orange Book and printed Cumulative Supplements at the time Teva submitted its risperidone ANDA in order to obtain the most current information about which patents have been identified as claiming a particular listed

drug—and, thus, which patents they must certify to in connection with the submission of an ANDA.

Indeed, generic applicants ***must*** follow the official Orange Book listing, as reflected in the latest Cumulative Supplement, regardless of whether they believe the information in the Orange Book or Cumulative Supplement to be accurate. FDA's own regulations state that "an abbreviated new drug application under section 505(j) of the act submitted for a drug that is claimed by a patent for which information has been submitted ***must***, despite any disagreement as to the correctness of the patent information, contain an appropriate certification ***for each listed patent***." 21 CFR § 314.53(f) (emphasis added). And courts, including this Court, have continually reaffirmed that ANDA applicants thus are required to submit a certification for ***each*** patent listed in the Orange Book as claiming the branded product, regardless of the applicant's belief that the patent information is not (or may not be) correct. *See, e.g.*, *Sandoz v. FDA*, 439 F. Supp. 2d 26, 31 (D.D.C. 2006); *Apotex v. Thompson*, 347 F.3d 1335, 1349-50 (Fed. Cir. 2003) (same).

B. Factual Background

Janssen Pharmaceutica ("Janssen") holds the approved NDA for risperidone tablets, No. 20-272, an atypical antipsychotic medication that it commercially markets under the brand name Risperdal®. Janssen submitted two patents to FDA as claiming Risperdal® tablets: U.S. Patent No. 4,804,663 ("the '663 patent") and the '952 patent, and FDA therefore listed both of those patents in the Orange Book. *See* 2001 Orange Book at ADA 57. The '663 patent expired on December 29, 2007, but Janssen received an additional six months of exclusivity beyond the patent's expiration as a reward for studying Risperdal®'s effectiveness in children and prevailing in patent litigation regarding the validity of that patent. *See* 21 U.S.C. § 355a. That "pediatric exclusivity" period runs to June 29, 2007. The '952 patent is set to expire on October 27, 2009.

Throughout 2001, Teva invested significant resources to develop both a generic risperidone tablet product that would not infringe the '952 patent and a strong legal challenge to the '952 patent's validity and applicability. On August 28, 2001, after successfully engineering a non-infringing product and developing a legal challenge to the '952 patent, Teva submitted its risperidone ANDA to FDA and sought approval to market generic risperidone tablets in 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, and 4 mg strengths. On the date Teva submitted its ANDA, the 2001 Orange Book continued to list both the '663 and '952 patents as claiming Risperdal®, *see* 2001 Orange Book at ADA 57, and FDA's then-current official Cumulative Supplement reflected no change to the official patent information listing for Risperdal® tablets. *See* August 2001 Supplement at A-14. Thus, in accordance with 21 U.S.C. § 355(j)(2)(A)(vii) and FDA's own regulations, Teva submitted certifications regarding both of those patents with its ANDA—a Paragraph III certification to the '663 patent, and a Paragraph IV certification to the '952 patent. *See* FDA Letter Decision at 5. As the first Paragraph IV challenger to the '952 patent, Teva became eligible for a 180-day marketing exclusivity period for generic risperidone tablets that would vest either if Teva was not sued for patent infringement at all, or if the '952 patent was later held to be invalid or not infringed by Teva's generic risperidone tablets in litigation. *See* 21 U.S.C. § 355(j)(5)(B)(iv); *see also Ranbaxy*, 469 F.3d at 125.

On October 12, 2001, however, FDA asserted that it had removed, or "delisted," the '952 patent from the Orange Book prior to the submission of Teva's ANDA. *See* FDA Letter Decision at 5. FDA made that assertion despite the fact that the 2001 Orange Book continued to list the '952 patent as claiming Risperdal® tablets, *see* 2001 Orange Book at ADA 57, and notwithstanding the fact that the monthly Cumulative Supplement in effect at the time Teva filed its ANDA reflected no change to the official patent listing information for Risperdal® tablets.

See August 2001 Supplement at A-14. Indeed, at the time FDA notified Teva of the '952 patent's putative delisting in October, the then-current Cumulative Supplement continued to reflect no change to the official patent listing information for Risperdal® tablets, *see* Orange Book 21st ed. Cumulative Supplement 10 (Oct. 2001), at A-19 (the "October 2001 Supplement") (excerpt attached as Ex. 5), and no change appeared in the November or December Cumulative Supplements. *See* Orange Book 21st ed. Cumulative Supplement 11 (Nov. 2001), at A-21 (the "November 2001 Supplement") (excerpt attached as Ex. 6); Orange Book 21st ed. Cumulative Supplement 12 (Dec. 2001), at A-24 (the "December 2001 Supplement") (excerpt attached as Ex. 7). FDA's official Orange Book did not reflect the delisting of the '952 patent until its 2002 annual edition was released in January of that year—more than four months after Teva submitted its ANDA. *See* Orange Book (22nd ed. 2002), at ADA 65 ("2002 Orange Book") (excerpt attached as Ex. 8).

FDA nonetheless informed Teva that it would not accept Teva's ANDA for filing unless and until Teva withdrew its Paragraph IV certification in order to reflect FDA's assertion that the '952 patent had been delisted. *See* FDA Letter Decision at 5 (explaining that FDA made its determination that the '952 patent had been delisted "[d]uring a filing review of the ANDA to determine whether it was sufficiently complete to permit a substantive review," and refused to send an "acknowledgement letter to Teva indicating that Teva's ANDA for risperidone tablets had been received for substantive review" until Teva withdrew its Paragraph IV certification). Thus, despite the fact that the 2001 Orange Book continued to list the '952 patent as claiming Risperdal® tablets; despite the fact that the then-current monthly Cumulative Supplement to the Orange Book reflected no change to the official patent-listing information for Risperdal® tablets; and despite Teva's significant investments in the development of a non-infringing pathway and

legal challenge to the '952 patent, Teva was given no choice but to follow the Agency's directive and amend its ANDA in order to ensure that FDA would commence its regulatory review of Teva's file and put Teva's proposed generic risperidone tablets on the path to approval. *See id.*

After Teva successfully challenged FDA's delisting practices in the *Ranbaxy* case, Teva (like several other manufacturers) undertook a comprehensive review of its portfolio of pending ANDAs to determine whether FDA's unlawful delisting practices had deprived Teva of its entitlement to 180-day generic exclusivity for any other products. On August 3, 2007, Teva petitioned FDA to relist the '952 patent in the Orange Book for Risperdal® tablets; confirm that Teva's right to 180-day exclusivity for risperidone tablets has not been affected by FDA's unlawful delisting of the '952 patent; and refrain from granting final approval to any other ANDAs for 0.25 mg, 0.5 mg, 1 mg, 2 mg, 3 mg, and 4 mg risperidone tablets until Teva's 180-day exclusivity period expires. *See generally* Teva Citizen Petition.

FDA denied the Citizen Petition on February 26, 2008, and this suit follows.

LEGAL STANDARD

The legal standard governing motions for temporary injunctive relief is well-settled. To secure relief, the plaintiff must show that (1) there is a substantial likelihood of success on the merits; (2) the plaintiff would suffer irreparable injury if the requested injunction is denied; (3) an injunction will not substantially injure the opposing party or other third parties; and (4) the public interest will be furthered by the issuance of the injunction. *See Mova Pharm.*, 140 F.3d at 1066. "These factors interrelate on a sliding scale and must be balanced against each other," *Davenport v. Int'l Bd. of Teamsters, AFL-CIO*, 166 F.3d 356, 360-61 (D.C. Cir. 1999), so that "[a]n injunction may be justified … where there is a particularly strong likelihood of success on the merits even if there is a relatively slight showing of irreparable injury." *CityFed Fin. Corp.*

v. OTS, 58 F.3d 738, 747 (D.C. Cir. 1995); *see also Mova Pharm. Corp. v. Shalala*, 955 F. Supp. 128, 131 (D.D.C. 1997). Teva readily meets all four prongs of this standard.

ARGUMENT

I. Teva Is Likely To Succeed On The Merits.

The plain language of the FDCA entitles Teva to a 180-day period of marketing exclusivity for generic risperidone tablets. Teva was the first generic manufacturer to file an ANDA for generic risperidone tablets that contained a Paragraph IV certification to the '952 patent. Under 21 U.S.C. § 355(j)(5)(B)(iv), the earliest any subsequently-filed Paragraph IV ANDA can be approved is "one hundred and eighty days after" Teva first commercially markets its generic risperidone tablets or the date of a court decision holding the '952 patent to be invalid or not infringed. *Id*. To date, neither of these events has occurred—there has been no litigation concerning the '952 patent, and Teva will not begin to market its generic risperidone tablets until Janssen's pediatric exclusivity expires on June 29, 2008. At that time, and upon launching its generic risperidone tablets into the market, Teva will be entitled to 180 days of sole marketing exclusivity under the plain terms of § 355(j)(5)(B)(iv); no other manufacturer that has submitted an ANDA for generic risperidone tablets may be approved until the conclusion of Teva's exclusivity period.[2]

FDA's refusal to relist the '952 patent and honor Teva's right to 180-day exclusivity as the first Paragraph IV filer fundamentally undermines the Hatch-Waxman regime and flatly contradicts the D.C. Circuit's recent decision in *Ranbaxy Labs. Ltd. v. Leavitt*, 469 F.3d 120

[2] Because the '663 patent has been held to be valid and enforceable, *see Janssen Pharmaceutica N.V. v. Mylan Pharms Inc.*, No. 03-6220, 2006 WL 3231459 (D.N.J. Nov. 8, 2006), *aff'd* 223 Fed. App'x 999 (Fed. Cir. 2007) (per curiam), no manufacturer is entitled to exclusivity based on its first-to-file status with respect to that patent. Teva alone is eligible for marketing exclusivity.

(D.C. Cir. 2006). In that case, NDA-holder Merck initially listed three patents in the Orange Book as claiming its blockbuster drug Zocor® (simvastatin). *Id.* at 123. Two generic manufacturers, Ranbaxy and IVAX (which since has been acquired by Teva, and for ease of reference will be referred to as Teva), filed ANDAs seeking approval to market generic simvastatin products in different dosages. Both ANDAs contained Paragraph III certifications to one of the simvastatin patents and Paragraph IV certifications to each of the other two simvastatin patents listed in the official Orange Book at the time the applicants submitted their ANDAs to the Agency. *Id.* Because the Teva and Ranbaxy ANDAs concerned different dosages of simvastatin, Teva and Ranbaxy each were entitled to 180-day exclusivity for their respective simvastatin dosages as the first generic companies to file Paragraph IV challenges to patents officially listed as claiming simvastatin.

Before Teva or Ranbaxy could take advantage of their respective exclusivities, however, Merck asked FDA to delist the two Paragraph IV patents from the Orange Book. FDA claimed that it was exercising its ministerial role in maintaining the Orange Book, acceded to Merck's request, and required Teva and Ranbaxy to delete the Paragraph IV certifications from their ANDAs. *Id.* Left undisturbed, that action would have divested Teva and Ranbaxy of their respective exclusivities for generic simvastatin: exclusivity, after all, depends on having a Paragraph IV certification, so once FDA forces an applicant to withdraw its exclusivity-qualifying Paragraph IV certification, the jig is up. *Id.* Both companies challenged FDA's delisting by filing citizen petitions demanding that FDA restore the delisted patents to the Orange Book and enforce the companies' right to exclusivity against subsequent ANDA filers. *Id.* As here, however, FDA denied the companies' petitions, reasoning that delisting was appropriate

because neither company had been sued by Merck for patent infringement and thus allegedly had not incurred the risks Congress sought to encourage when it designed the exclusivity reward. *Id*.

Teva and Ranbaxy filed suit against FDA in this Court. This Court soundly rejected FDA's arguments, *Ranbaxy Labs., Ltd. v. Leavitt*, 459 F. Supp. 2d 1 (D.D.C. 2006), and the D.C. Circuit affirmed. *Ranbaxy*, 469 F.3d at 126. As that court explained, FDA's delisting practices violated both the plain text and structure of the Hatch-Waxman Act by fundamentally "chang[ing] the incentive structure adopted by the Congress." *Id*. at 125. That was so, the D.C. Circuit reasoned, because allowing FDA to delist a challenged patent ***after*** an ANDA applicant has made the investments necessary to prepare its Paragraph IV challenge and incurred the risk of infringement litigation would "reduce the certainty of receiving a period of marketing exclusivity" at the time applicants must choose whether or not to make those investments—"diminish[ing] the incentive for a manufacturer of generic drugs to challenge a patent listed in the Orange Book" and making it less likely that generic companies will challenge competition-blocking patents in the future. *Id*. Because FDA's actions thus directly undermined the statute's key incentive, the D.C. Circuit invalidated FDA's delisting practices and required FDA both to relist the improperly removed simvastatin patents and honor the exclusivity periods earned by first-filers Teva and Ranbaxy. *Id*.

This case falls squarely within *Ranbaxy*'s holding. Put simply, FDA's attempt to strip Teva's 180-day exclusivity by effectuating the delisting of the '952 patent ***after*** Teva invested in the development of non-infringing generic risperidone tablets and assumed the risk of patent infringement litigation by filing its Paragraph IV challenge to the '952 patent fundamentally altered Hatch-Waxman's incentive scheme in the same way FDA's actions did in *Ranbaxy*: by undermining the statutory incentive to challenge competition-blocking drug patents in the future.

Nonetheless, FDA now seeks to distinguish *Ranbaxy* from this case by claiming that the Agency actually delisted the '952 patent from the Orange Book at some point ***before*** Teva filed its ANDA—though, to be sure, it can't quite say when. FDA Letter Decision at 8. The problems with that assertion are obvious. FDA does not, and cannot possibly, deny that the '952 patent remained listed in FDA's 2001 Orange Book at the time Teva submitted its Paragraph IV certification on August 28, 2001. *See* 2001 Orange Book at ADA 57. FDA does not, and cannot possibly, deny that the August 2001 Cumulative Supplement to the Orange Book failed to reflect that there had been any change in the official patent listing information for Risperdal® tablets at any point during the eight months after the 2001 Orange Book first was released. *See* August 2001 Supplement at A-14. And FDA does not, and cannot possibly, deny that each of the four Cumulative Supplements that followed Teva's Paragraph IV certification likewise failed to reflect any change to the official patent listing information for Risperdal® tablets. *See* Orange Book 21st ed. Cumulative Supplement 9 (Sept. 2001), at A-19 (excerpt attached as Ex. 9); October 2001 Supplement at A-19; November 2001 Supplement at A-21; December 2001 Supplement at A-24.

Teva thus was required to include a certification to '952 patent its ANDA. Indeed, the plain language of the statute, FDA's own regulations, the 2001 Orange Book, and the Cumulative Supplements hardly could be more clear on this point. By statute, every NDA applicant is required to "file with the [NDA] the patent number and the expiration date of any patent ***which claims the drug*** for which the applicant submitted the application or which claims a method of using such drug." 21 U.S.C. § 355(b)(1) (emphasis added). Once the NDA is approved, FDA is obligated to "***publish*** information submitted under [that requirement]." *Id.* (emphasis added). And every generic ANDA applicant must thereafter submit "a certification …

with respect to each patent ***which claims the listed drug***." 21 U.S.C. § 355(j)(2)(A)(vii) (emphasis added). Together, then, these provisions unambiguously require ANDA applicants to make a certification with respect to any patent that FDA has "publish[ed]" pursuant to its statutory reporting duty.

In the roughly 15 years between Hatch-Waxman's enactment and the submission of Teva's risperidone ANDA, there was never a shred of doubt that FDA formally discharged that duty by printing the annual Orange Book and its issuing its printed Cumulative Supplements to the Orange Book. *See, e.g.*, *Purepac Pharm. Co. v. Thompson*, 354 F.3d 877, 880 (D.C. Cir. 2004) ("In order to determine what patents cover existing brand-name drugs and hence whether any paragraph IV certifications … are needed, applicants look in the 'Orange Book,' an FDA publication that includes all patent information that companies have submitted to the agency."); *Apotex, Inc. v. Thompson*, 347 F.3d 1335, 1338 (Fed. Cir. 2003) ("The statute directs the FDA to list the disclosed patents, which the FDA does in a publication entitled 'Approved Drug Products With Therapeutic Equivalence Evaluations,' more commonly known as the 'Orange Book.'"); *Andrx Pharms., Inc. v. Biovail Corp. Int'l*, 256 F.3d 799, 802 (D.C. Cir. 2001) ("The FDA maintains a record of [patent] information in its publication entitled *Approved Drug Products with Therapeutic Equivalence*, commonly known as the Orange Book."); *American Bioscience, Inc. v. Thompson*, 243 F.3d 579, 580 (D.C. Cir. 2001) ("The FDA keeps all [patent] information in a publication officially titled *Approved Drug Products with Therapeutic Equivalence*, commonly called the Orange Book.").

It thus should come as no surprise that, time and again, the courts made clear that ANDA applicants must submit a certification for every drug-related patent that appeared in the Orange Book (or whose listing was reflected in the Agency's current official Cumulative Supplement to

the Orange Book) at the time they filed an ANDA. *See, e.g.*, *Ranbaxy*, 469 F.3d at 122 ("Each ANDA … must contain: 'a certification ... with respect to each patent which claims [a drug or a method of using a drug listed in the Orange Book].'") (quoting 21 U.S.C. § 355(j)(2)(A)(vii); alteration in original); *Apotex*, 347 F.3d at 1350 ("The statutory language shows a clear congressional intention to require certification whenever an ANDA applicant seeks approval of a drug that is claimed by a patent that is listed in the Orange Book."); *Andrx*, 256 F.3d at 802 ("For each patent … listed in the Orange Book, an ANDA applicant must certify whether the proposed generic drug would infringe that patent and, if not, why not."); *see also Apotex Inc. v. FDA*, 414 F. Supp. 2d 61, 64 (D.D.C. 2006) ("An ANDA-applicant seeking to market its drug before the NDA-drug's patent has expired must make a paragraph IV certification with respect to the 'listed patents' (*i.e.*, the patents that are listed in the Orange Book when the ANDA is filed), as well as those that are placed in the Orange Book subsequently (*i.e.*, 'later-listed patents')."). That, of course, is precisely what Teva did when it submitted its Paragraph IV certification to the '952 patent—and FDA's claim that Teva's certification to that patent was "neither necessary nor permitted," Letter Decision at 7, is both unprecedented and unsupportable.

FDA nonetheless seeks to evade all of this by asserting that, in addition to its annual Orange Book and monthly Cumulative Supplements to the Orange Book, the Agency also maintained an "electronic Orange Book" at the time Teva submitted its risperidone ANDA, Letter Decision at 6, and alleging that "[a]n applicant searching the electronic Orange Book shortly after June 29, 2001, and no later than July 20, 2001, would have found that only the '663 patent was listed for Risperdal tablets." *Id*. at 7. Whether or not that is true, FDA's speculative assertions about what may have appeared in the electronic Orange Book in June (or maybe

July?) 2001 are legally immaterial to the question of whether Teva was legally required to submit, and thus properly did submit, a Paragraph IV certification to the '952 patent.

As a matter of law—set forth in FDA's own regulations, and unambiguously confirmed by the 2001 Orange Book and FDA's monthly Cumulative Supplements to the 2001 Orange Book—the only relevant sources of patent-listing information at the time Teva submitted its ANDA for generic risperidone tablets were the 2001 Orange Book and FDA's monthly Cumulative Supplements to the 2001 Orange Book. Pursuant to the statutory mandate that FDA "publish" a list of all patents that claim an approved drug product, 21 U.S.C. § 355(b)(1), the Agency always has provided for the "public disclosure of patent information" by obligating itself to "publish … the patent number and expiration date of each patent that is required to be, and is, submitted to FDA by an [NDA] applicant." 21 C.F.R. § 314.53(e). FDA's implementing regulations in effect at the time of Teva's certification to the '952 patent informed applicants that in the event of any change to the official patent information, all new "[p]atent information submitted by the last working day of a month ***will be published in that month's supplement to the list***." *Id*. (emphasis added). And at no point in 2001 did those regulations refer to the existence, maintenance, or availability of an electronic Orange Book—much less suggest that it would provide any data other than what was published in the monthly Cumulative Supplements.

To the extent there is any doubt that the 2001 Orange Book and monthly Cumulative Supplements to Orange Book represented the Agency's official efforts to fulfill its statutory and regulatory disclosure obligations at the time Teva submitted its ANDA, those publications themselves conclusively resolve the matter. For its part, the introduction to the 2001 Orange Book's Patent and Exclusivity Information Addendum explained that

> [Hatch-Waxman] requires that patent information must now be filed with all newly submitted section 505 drug applications, and that no NDA may be

> approved after September 24, 1984, without the submission of pertinent patent information to the Agency. ***The patent numbers and the expiration dates of appropriate patents claiming drug products that are the subject of approved applications will be published in this*** **Addendum** ***or in the monthly Cumulative Supplement to this publication***.

2001 Orange Book at AD-2 (emphasis added). In turn, each printed Cumulative Supplement that issued during the 2001 calendar year underscored that it was intended to "provide[], among other things, information on newly approved drugs and, if necessary, revised therapeutic equivalence evaluations and ***updated patent and exclusivity data***." *See, e.g.*, August 2001 Cumulative Supplement at iii (emphasis added).

But these publications do more than simply make clear that the official 2001 Orange Book and FDA's official monthly Cumulative Supplements to the 2001 Orange Book were the legally operative publications for purposes of the statute and regulations at the time Teva submitted its ANDA for generic risperidone tablets. They expressly directed applicants to rely on the monthly Cumulative Supplements in order to verify that patent listings printed in the annual Orange Book remained correct—and, specifically, to ensure that relevant patent listings (like the '952 patent in this case) had not been ***deleted*** since they first appeared in the annual Orange Book. As both the 2001 Orange Book and each 2001 Cumulative Supplement put the point, "[s]ince all parts of this publication are subject to changes, additions, ***or deletions***, the Addendum must be used in conjunction with ***the most current Cumulative Supplement***." *Id*.; *see also* August 2001 Cumulative Supplement at iii ("Because all parts of the [annual Orange Book] are subject to changes, additions, ***or deletions***, the [annual Orange Book] must be used in conjunction with the ***most current Cumulative Supplement***."). The only possible interpretation of those directives is that applicants were obligated to consult the "most current Cumulative Supplement" in order to determine whether there had been any "deletions" that would have affected the patent-listing information published in the 2001 annual Orange Book. And given

those express directives, FDA's attempt to divest Teva of its exclusivity for relying on the most current Cumulative Supplement at the time it filed its ANDA epitomizes arbitrary and capricious Agency decisionmaking.

Faced with all of this, FDA claims that its electronic Orange Book nonetheless controlled in the event of a conflict with the annual Orange Book and then-current Cumulative Supplement because the inside cover of the 2001 Orange Book—in the section which listed the Library of Congress classification data for the publication—"prominently" noted that the book is "[u]pdated by monthly cumulative supplements [and] on the Internet," Letter Decision at 7, and because the official Cumulative Supplements themselves "describe[] the availability of the electronic Orange Book." Letter Decision at 6. But those claims are entirely irrelevant. Whether or not an "electronic Orange Book" was available "on the Internet," and regardless of what information it may have contained, there is not a single word in the statute, the regulations, the 2001 Orange Book, or any of the monthly Cumulative Supplements to the 2001 Orange Book that directed applicants to consult the electronic Orange Book—or even offered the slightest hint that the electronic Orange Book's patent-listing information was any different than the information contained in the current monthly Cumulative Supplement.

To the contrary, the key passage on which FDA bases its response to the Petition actually indicates that precisely the opposite was true: "'The data [in the Electronic Orange Book Query feature] is updated ***concurrently*** with the publication of the annual edition [of the Orange Book] or monthly cumulative supplements.'" FDA Letter at 6 (quoting January 2001 Supplement at v) (emphasis added). The only conceivable interpretation of that statement is that the electronic Orange Book would have contained ***the same*** information as the current Cumulative Supplement: outside the writings of George Orwell, a government agency's pronouncement that

it "concurrently" is updating two parallel databases that contain the same legally required data leaves no room for the possibility that it might be using two different data sources to update those databases—and that in the event of any conflict, the only database that matters is the one the agency ***has not*** expressly directed citizens to consult and which ***is not*** referenced in the agency's regulations, rather than the one the agency ***has*** expressly directed citizens to consult and which ***is*** referenced in the agency's regulations.

To summarize: the statute requires FDA to maintain a published list of drug-related patents; FDA's regulations and the 2001 Orange Book itself made clear that the Orange Book was designed to discharge that responsibility, and further obligated the Agency to keep the Orange Book current by publishing monthly Cumulative Supplements (but not to maintain an online version of the Orange Book); and both the 2001 Orange Book and 2001 Cumulative Supplements expressly directed applicants to consult the current official Cumulative Supplement (but not the electronic Orange Book) before filing an ANDA in order to obtain the most current patent-listing information. Given the plain language and structure of the statute, FDA's own regulations, and the Orange Book's express directives, then, generic applicants were not only ***entitled*** to rely on the 2001 Orange Book and 2001 Cumulative Supplements for up-to-date patent information at the time Teva submitted its risperidone ANDA; they ***had to*** rely on the 2001 Orange Book and then-current Cumulative and ***had to*** submit a certification with respect to every patent listed in the 2001 Orange Book, as confirmed by the then-current monthly Cumulative Supplement, at the time Teva submitted its risperidone ANDA.

That is exactly what Teva did here, and Teva thus is entitled to 180-day exclusivity for generic risperidone tablets. At all times during the preparation of its ANDA, and on the date Teva submitted that ANDA to FDA, the '663 and '952 patents were listed in the official Orange

Book, 2001 Orange Book at ADA 57, and the then-current official monthly Cumulative Supplement to the Orange Book reflected no additions, changes, or deletions to the patent listing information for Risperdal® tablets. August 2001 Supplement at A-14. As a result, Teva made significant investments in (a) identifying vulnerabilities in the patent listings for risperidone, (b) designing a generic risperidone product that would not infringe the '952 patents, and (c) formulating a strong legal challenge to the '952 patent in case Janssen later attempted to assert the '952 patent against Teva. And once Teva developed its non-infringing product and crafted a successful challenge to the '952 patent, it deliberately exposed itself to the risk of patent litigation by submitting a paragraph IV certification to the officially listed '952 patent in its original ANDA. *See* 35 U.S.C. § 271(e)(2).

180-day exclusivity is designed to encourage and reward precisely those actions—and the risks Teva assumed by undertaking them—and FDA's delisting of the '952 patent without legally required notice, and subsequent refusal to relist that patent in the Orange Book, honor Teva's Paragraph IV certification to that patent, and effectuate Teva's exclusivity contradict the plain text, structure, and purposes of the Hatch-Waxman Act. On this point, then, Teva has a strong likelihood of proving is entitlement to judgment as a matter of law—and this Court should require FDA to relist the '952 patent, honor Teva's Paragraph IV certification, and enjoin FDA from approving any subsequently filed ANDAs pending the expiration of Teva's exclusivity, or otherwise preliminarily enjoin FDA from approving any risperidone ANDAs other than Teva's pending the entry of a final judgment on the merits.

One final point is in order here. In a last-ditch effort to justify its denial of Teva's petition, FDA asserts that the '952 patent should not be relisted and that Teva should not be accorded exclusivity for its generic risperidone tablets, because Teva never notified Janssen or

the owner of the '952 patent that it had submitted a Paragraph IV certification with respect to the '952 patent. FDA Letter Decision at 1-2 ("Teva did not provide the required notice of such certification to the holder of the NDA for [Risperdal®] and each owner of the listed patent."); *id*. at 9 ("Teva withdrew its paragraph IV certification and never notified the NDA holder and patent owner that it believed the '952 patent to be invalid, unenforceable, or not infringed.").

That claim is utterly frivolous. As FDA well knows—because FDA acknowledges as much in its Letter Decision—generic applicants are ***not*** required to send the NDA holder or patentee notice of a Paragraph IV certification until "receipt of an acknowledgement letter from the Office of Generic Drugs (OGD) advising that the application is sufficiently complete to permit a substantive review and has been received by OGD." *Id*. at 3 (citing 21 C.F.R. § 314.95(b)). Of course, the basic problem in this case is that FDA ***refused*** to send Teva such an acknowledgement letter after receiving Teva's Paragraph IV certification, because the Agency unlawfully forced Teva to withdraw its Paragraph IV certification before accepting Teva's ANDA for filing. *See id*. at 5-6 & n.11 (explaining that FDA made its determination that the '952 patent had been delisted "[d]uring a filing review of the ANDA to determine whether it was sufficiently complete to permit a substantive review"; that FDA subsequently ordered Teva withdraw its Paragraph IV certification to the '952 patent and refused to send an "acknowledgement letter to Teva indicating that Teva's ANDA for risperidone tablets had been received for substantive review" until Teva withdrew its Paragraph IV certification; and that OGD never issued Teva a "paragraph IV acknowledgement letter which describes … an ANDA applicant's obligations to provide the required notice to the NDA holder and each patent owner … because [Teva's] ANDA did not contain a paragraph IV certification to a listed patent when received for substantive review by OGD").

Needless to say, FDA cannot possibly defend its actions by asserting that Teva somehow should have notified Janssen or anyone else about its Paragraph IV certification when FDA alone is responsible for Teva's failure to do so. Teva, in short, did not choose to leave Janssen in the dark; it was FDA that refused to accept Teva's Paragraph IV certification; FDA that refused to accept Teva's ANDA for filing; FDA that refused to acknowledge its receipt of Teva's ANDA; and FDA that, by its own actions, failed to trigger the statutory notification requirement. The principles that "[n]o one shall be permitted to profit by his own fraud, or to take advantage of his own wrong, or to found any claim upon his own iniquity" are older than the Republic itself, *see Riggs v. Palmer*, 115 N.Y. 506, 511-15 (1889) (collecting historical sources), and FDA's shameless suggestion that the Agency lawfully may deprive Teva of its exclusivity based on the Agency's own unlawful conduct is wholly bereft of merit. If and when this Court holds that FDA unlawfully effectuated the delisting of the '952 patent after it received Teva's Paragraph IV certification, and orders the FDA to relist that patent in the Orange Book, accept Teva's Paragraph IV certification, and honor Teva's claim to exclusivity as the first Paragraph IV filer, Teva is fully committed to providing Janssen with the requisite patent certification. In the meantime, however, Teva's failure to provide a Paragraph IV notification to Janssen offers no support for FDA's position in this case.

II. Teva Will Suffer Irreparable Harm Absent Preliminary Relief.

Teva will be irreparably harmed unless this Court takes prompt action to relist the '952 patent and restore Teva's exclusivity. Janssen's pediatric exclusivity expires on June 29, 2008. Barring injunctive relief, FDA will be free to approve other ANDAs for generic risperidone tablets at that time. Should FDA do so, the principal benefits of exclusivity will be lost to Teva forever. 180-day generic marketing "exclusivity typically gives the first generic entrant a permanent advantage over subsequent entrants, because that officially sanctioned 'head start'

permits first entrants to secure distribution channels and access to customers; enter into long-term sales agreements; increase sales across all of its product lines; and retain greater market share in the long-run." Declaration of David Marshall ¶ 11 (attached as Ex. 10). Loss of that "head start," however, would "impair[] [Teva's] access to customers for generic risperidone tablets, decreas[e] its opportunities to strengthen market position on other product lines, and diminish[] Teva's ability to establish and retain long-term market share for generic risperidone products." *Id*. ¶ 13.

Regrettably, there is no way to remedy these losses. "Because a given prescription can be filled only once, it is impossible to 'make up' for a lost sale by filling a subsequent prescription." *Id*. ¶ 15. And since the defendants in this case are immune from money damages, there is no way to recoup the substantial lost revenue opportunities Teva would incur from losing its exclusivity. *See, e.g.*, *Brendsel v. Office of Fed. Hous. Enter. Oversight*, 339 F. Supp. 2d 52, 66 (D.D.C. 2004); *see also Entergy Ark., Inc. v. Nebraska*, 210 F.3d 887, 899 (8th Cir. 2000); *cf. CSX Transp. v. Williams*, 406 F.3d 667, 674 n.7 (D.C. Cir. 2005). It thus should come as no surprise that courts have repeatedly recognized that lost generic marketing exclusivity is a form of irreparable injury sufficient to ground preliminary injunctive relief against FDA. *See, e.g.*, *Mova Pharm. Corp. v. Shalala*, 140 F.3d at 1066 n.6; *Sandoz, Inc. v. FDA*, 439 F. Supp. 2d 26, 32 (D.D.C. 2006) (citing *Apotex, Inc. v. FDA*, No. Civ.A. 06-0627-JDB, 2006 WL 1030151, *17 (D.D.C. Apr. 19, 2006)); *Torpharm, Inc. v. Shalala*, No. 97-1925, 1997 WL 33472411 (D.D.C. Sept. 15, 1997).

In this case, the harm to Teva from a loss of exclusivity would be significant. In 2007, Janssen sold 556 million doses of risperidone with a reported market value exceeding $2.5 ***billion*** dollars. Marshall Decl. ¶ 4. As the Unredacted Marshall Declaration details, Teva stands

to lose a significant portion of both its anticipated first-year market share and anticipated annual risperidone revenues in the event it is deprived of its exclusivity. *Id*. ¶ 14. Only a preliminary injunction can prevent Teva from suffering these massive, irreparable harms.

Finally, it bears emphasis that Teva must make significant production and staffing changes ***now*** if it is to prepare for an exclusive launch. These changes—which include shifting manufacturing priorities, rescheduling the production of other products, transferring additional manpower, and ordering additional ingredients from its suppliers—will take months to complete. *Id*. ¶ 16-17. In short, the question whether Teva will enjoy 180 days of exclusivity beginning in June 2008 will have a substantial, immediate impact on the planning and production process, and must be resolved now in order to ensure that launch-ready quantities of risperidone are available for immediate commercial marketing upon the expiration of Janssen's pediatric exclusivity period. *Id*. ¶ 18.

III. The Balance Of Hardships And Public Interest Favor Granting Relief.

The final equitable factors—the balance of hardships and public interest—likewise favor granting immediate injunctive relief. With respect to the former, FDA is a federal agency and cannot seriously claim that it would be harmed by an injunction requiring it to apply Hatch-Waxman Act in a manner consistent with Congress's intent, the D.C. Circuit's decision in *Ranbaxy*, and its own regulations. Nor will any private parties suffer significant harm from the entry of an injunction. Janssen will not be harmed, because it will face generic competition on June 29 regardless of the outcome here. And while injunctive relief will prevent FDA from approving other generic applicants for 180 days, any harm to those companies would be vastly outweighed by the harm that Teva would suffer without injunctive relief. After all, Teva claims the exclusive right to market generic risperidone tablets starting June 29, 2008, while those companies merely could seek the right to be one of many companies to enter the market at that

time. As a result, the costs of denying injunctive relief will be borne singularly by Teva, while any costs to the subsequent applicants from the entry of an injunction would be shared across the industry. Finally, it bears note that the generic drug industry as a whole ultimately stands to benefit from the entry of an injunction preserving exclusivity here, because each of them is likely to be a first-filer on one or more future products and thus would benefit from a decision that fully preserves the value of exclusivity for those who undertake the significant risks inherent in submitting the first Paragraph IV certification.

But make no mistake: it is the public that stands to lose the most if this Court declines to enter injunctive relief. If generic companies cannot be sure that FDA and the courts will protect their right to 180-day exclusivity, they will be less likely to challenge patents by filing Paragraph IV certifications in the future—slowing the onset of generic competition, and ultimately increasing prices for patients and insurers. That result would directly undermine the basic purpose of the Hatch-Waxman Act, which is to "'get generic drugs into the hands of patients at reasonable prices—fast.'" *Andrx Pharms., Inc. v. Biovail Corp. Int'l*, 256 F.3d 799, 809 (D.C. Cir. 2001) (quoting *In re Barr Labs., Inc.*, 930 F.2d 72, 76 (D.C. Cir. 1991)). Injunctive relief would foster that basic goal by preserving the incentive scheme Congress established in the Hatch-Waxman Act, and this Court should act quickly to restore the integrity of the Hatch-Waxman regime.

CONCLUSION

For the foregoing reasons, Teva respectfully requests that this Court grant its motion for a preliminary injunction.

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Respectfully submitted,

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