UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

APOTEX, INC., *et al.*, Plaintiffs, v. KATHLEEN SEBELIUS, *et al.*, as Secretary of Health and Human Services, Defendants, and TEVA PHARMACEUTICALS USA, INC. Intervenor-Defendant.	Case Nos. 1:10-cv-00517-RMC 1:10-cv-00521-RMC

INTERVENOR-DEFENDANT TEVA PHARMACEUTICALS USA, INC.'S MEMORANDUM IN OPPOSITION TO PLAINTIFFS' MOTIONS FOR PRELIMINARY INJUNCTIVE RELIEF

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INTRODUCTION

FDA—albeit reluctantly—has finally learned the lesson that the D.C. Circuit now has taught it twice: There is "*not a single cogent reason* why Congress might have permitted … a scenario in which the brand maker can unilaterally deprive the generic of its exclusivity," *Teva Pharms. USA, Inc. v. Sebelius* ("*Teva v. Sebelius*"), 595 F.3d 1303, 1317 (D.C. Cir. 2010) (emphasis in original), nor any plausible "reason to conclude that the 2003 addition of forfeiture provisions meant to give the brand manufacturer a right to unilaterally vitiate a generic's exclusivity." *Id*. at 1318; *see also Ranbaxy Labs. Ltd. v. Leavitt*, 469 F.3d 120 (D.C. Cir. 2006). As FDA thus recognized in its March 26 letter decision, the arguments raised by Apotex in No. 1:10-cv-00517 and Roxane in No. 1:10-cv-00521 are squarely foreclosed by controlling D.C. Circuit precedent. *See* Losartan Letter Decision at 7, FDA Docket No. 2010-N-0134 (Mar. 26, 2010) ("[The D.C. Circuit's decision] appears to preclude a forfeiture of exclusivity on the basis of patent expiration where the expiration is in the control of the NDA holder.") (attached as Exh. A).

The fact that FDA has finally swallowed its medicine is the beginning and end of this litigation. As the Agency's letter decision frankly concedes, interpreting the Hatch-Waxman Act to let brand manufacturers do through the backdoor (by unilaterally failing to pay maintenance fees on a challenged patent) what the statute categorically forbids them from doing through the front door (by unilaterally delisting a challenged patent from FDA's Orange Book) plainly would not be "consistent with the Court of Appeals' reasoning in *Teva*." Losartan Letter Decision at 8. Neither Apotex nor Roxane offers any serious argument to the contrary, and there is none: Merck's decision to stop paying maintenance fees on the '075 patent was part and parcel of its antecedent decision to delist that patent in response to Teva's groundbreaking Paragraph IV

certification, not a separate event with independent significance for whether Teva can maintain its right to 180-day exclusivity after having *caused* Merck to effectively abandon that patent.

Incredibly, plaintiffs now take the position that FDA acted "arbitrarily and capriciously" when it followed the D.C. Circuit's decision in post-remand administrative proceedings. There is no basis in law or logic for that remarkable assertion. Federal agencies, no less than private parties, are bound by the law, and that is so regardless of whether the law is set forth in statutes or court cases interpreting those statutes (at *Chevron* step one). If it is arbitrary and capricious for FDA to account for the D.C. Circuit's teachings, then every agency stands condemned—and "'judicial review of agency action [would be transformed] into a ping-pong game,'" *George Hyman Constr. Co. v. Brooks*, 963 F.2d 1532, 1539 (D.C. Cir. 1992) (quoting *NLRB v. Wyman-Gordon Co.*, 394 U.S. 759, 766-67 n.6 (1969)), in which agencies are free simply to ignore every judicial decision with which they disagree. That is madness, and this Court should reject plaintiffs' invitation to Wonderland. Plaintiffs have no likelihood of success on the merits.[1]

The equitable factors relevant to the PI calculus likewise weigh decisively against the entry of injunctive relief. While Apotex and Roxane assert that they stand to lose a combined maximum of $38.6 million in generic losartan sales if Teva maintains its right to exclusivity in this case, Teva stands irretrievably to lose—as the D.C. Circuit recognized—"hundreds of millions of dollars" if other companies are approved and enter the market during Teva's 180-day exclusivity period beginning April 6. *Teva v. Sebelius*, 595 F.3d at 1314. Moreover, as the D.C.

[1] Teva also continues to maintain that the D.C. Circuit already considered and rejected the very claims plaintiffs seek to raise here, after FDA raised those arguments in post-judgment appellate proceedings. We recognize that this Court has disagreed with Teva on that point, and therefore will not burden the Court with further argument regarding the scope of the D.C. Circuit's mandate. Teva does, however, reserve the right to raise that argument in any future proceedings, and its decision not to seek re-reconsideration of this Court's ruling on the scope of the D.C. Circuit's mandate should not be construed as a waiver of its claim that these proceedings are beyond the scope of the appellate court's mandate.

Circuit recognized, Teva's injury "would not be remedied by … securing 180 days of exclusivity later on." *Teva v. Sebelius*, 595 F.3d at 1311. As a result, the harms to Teva from entering the requested relief dwarf those that Apotex and Roxane would suffer if such relief is denied.

Finally, the public interest sharply favors Teva and FDA in this case. As the D.C. Circuit recognized:

> The statute's grant of a 180-day delay in multiple generic competition for the first successful paragraph IV filer is a pro-consumer device. And it happens to be precisely the device Congress has chosen to induce challenges to patents claimed to support brand drugs. The statute thus deliberately sacrifices the benefits of full generic competition at the first chance allowed by the brand manufacturer's patents, in favor of the benefits of earlier generic competition, brought about by the promise of a reward for generics that stick out their necks (at the potential cost of a patent infringement suit) by claiming that patent law does not extend the brand maker's monopoly as long as the brand maker has asserted.

Id. at 1318. Divesting Teva of its exclusivity through the entry of injunctive relief thus would stall the engine that drives challenges to competition-blocking patents, in direct contravention of the Hatch-Waxman Act's pro-consumer goals.

At bottom, this is not a close case, and the approach FDA took in its letter decision only underscores how clear the matter is. While FDA's letter decision oozes with contempt for the D.C. Circuit's decision in this case, even FDA found itself compelled to side with Teva on the ground that unilateral patent delistings and unilateral patent terminations are both indistinguishable from each other and equally governed by the D.C. Circuit's *Chevron* step one analysis of the statute's incentive scheme. If there were a way to split the two sides of this single coin, the tenor of FDA's letter decision makes clear that the Agency would have found it. But FDA did not do so—because it could not do so—and this Court should now bring these proceedings to a close by rejecting plaintiffs' baseless challenge to Teva's hard-earned right to 180-day exclusivity for generic losartan potassium products.

BACKGROUND

A. The Hatch-Waxman Framework

As modified by the Drug Price Competition and Patent Restoration Act of 1984 (the "Hatch-Waxman Act") and the Medicare Modernization Act of 2003 ("MMA"), the Food, Drug, and Cosmetic Act (the "FDCA" or "statute") establishes the procedure for obtaining approval to market pharmaceutical products in the United States. *See* 21 U.S.C. § 355 *et seq*.[2] 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 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).

Generic drugs contain the same active ingredients and provide the same therapeutic benefits as their brand-name counterparts, but typically are sold at lower, more competitive prices. Prior to Hatch-Waxman's passage, generic manufacturers generally were required to complete a full NDA in order to obtain approval for a proposed generic drug. As a result, generic entry often was cost-prohibitive. In 1984, Congress enacted Hatch-Waxman to remove these barriers, increase the availability of generic drugs, and thereby reduce the cost of pharmaceuticals. *See, e.g.*, *Serono Labs., Inc. v. Shalala*, 158 F.3d 1313, 1326 (D.C. Cir. 1998) (citing, *inter alia*, H.R. Rep. No. 98-857, pt. 1, at 14 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2647, 2647)).

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[2] The FDCA has subsequently been amended by the Food and Drug Administration Amendments Act of 2007, but those amendments have no bearing on this case. All citations to statutes and regulations are to the current versions unless otherwise noted.

To accomplish those goals, Hatch-Waxman permits generic companies to obtain approval so long as they can show bioequivalence to a "listed" (or previously approved) drug that FDA already has deemed safe and effective. Generic applicants do so by submitting an Abbreviated New Drug Application ("ANDA") that includes, among other things, studies showing the proposed generic drug's bioequivalence to the previously approved drug. 21 U.S.C. § 355(j). If FDA accepts the applicant's bioequivalence studies, the generic applicant need not repeat the safety and efficacy studies that were conducted on the brand-name drug. *Id.* § 355(j)(2)(A); *see also Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1063 (D.C. Cir. 1998).

To balance the public's interest in prompt generic market entry against the intellectual-property rights of brand-name manufacturers, Congress requires each ANDA to include a "certification" for every patent the brand manufacturer has identified as claiming a previously approved drug. *Id.* § 355(j)(2)(A)(vii). To make this system work, the statute requires brand manufacturers to submit to FDA "the patent number and the expiration date of any patent which claims the[ir] drug … or … a method of using such drug," *id.* § 355(b)(1), and obligates FDA to "publish," "make available to the public," and regularly "revise" a list of the patent information submitted by brand manufacturers, *id.* § 355(j)(7)(a)(i)-(iii). FDA does so in a compilation known colloquially as "the Orange Book." *Purepac Pharm. Co. v. Thompson*, 354 F.3d 877, 880 (D.C. Cir. 2004); *Am. Bioscience, Inc. v. Thompson*, 243 F.3d 579, 580 (D.C. Cir. 2001).

Generic applicants can make one of four certifications to a listed patent: (1) that no patent information has been filed with respect to the pertinent brand-name drug ("Paragraph I certification"); (2) that a patent identified as claiming the brand-name drug has expired ("Paragraph II certification"); (3) that the generic drug will not be marketed until the date on which a patent identified as claiming the brand-name drug will expire ("Paragraph III

certification"); and (4) that a listed patent is invalid, unenforceable, and/or will not be infringed by the manufacture, use, or sale of the generic drug for which the ANDA is submitted ("Paragraph IV certification"). *See* 21 U.S.C. § 355(j)(2)(A)(vii).

Of these four possibilities, Paragraph IV certifications are the most important. Such certifications signal the generic manufacturer's intent to market its product prior to the natural expiration of one or more patents listed as claiming the brand-name drug (and thus that the applicant intends to provide consumers with expedited price relief through early market competition). *See, e.g.*, *Teva Pharms. USA, Inc. v. Leavitt* ("*Teva v. Leavitt*"), 548 F.3d 103, 106 (D.C. Cir. 2008) ("The legislative purpose underlying paragraph IV is to enhance competition by encouraging generic drug manufacturers to challenge the patent information provided by NDA holders in order to bring generic drugs to market earlier."); *Teva v. Sebelius*, 595 F.3d at 1305 ("Prospective generic competitors need not … take [brand makers'] lists as gospel. After a new drug hits the market, they can effectively challenge the brand maker's pronouncement by filing a certification that a proposed generic version of the brand drug would not run afoul of one (or more) of the putatively blocking patents, either because the patent is invalid or because the generic maker has found a way to design around it.").

But filing a Paragraph IV certification carries risks. The first generic drug company to challenge a patent by filing a Paragraph IV certification bears heavy research-and-development and legal costs in order to identify, design around, and/or mount a legal challenge to potentially vulnerable, competition-blocking brand-company patents. If those efforts succeed and the applicant attempts to break the patent logjam by filing a Paragraph IV certification, the very act of submitting that certification is a statutory act of patent infringement that could require the applicant to spend years defending itself in patent litigation. 35 U.S.C. § 271(e); *see also Teva v.*

Sebelius, 595 F.3d at 1305; *Eli Lilly & Co. v. Medtronic, Inc.*, 496 U.S. 661, 678 (1990). And if the brand manufacturer sues the applicant within 45 days of receiving notice of the applicant's Paragraph IV certification, FDA may not approve the applicant's ANDA for 30 months while the patent case unfolds. 21 U.S.C. § 355(j)(5)(B)(iii). This delay is known as the "30-month stay." *Eli Lilly & Co. v. Teva Pharms. USA, Inc.*, 557 F.3d 1346, 1348-49 (Fed. Cir. 2009).

By design, Hatch-Waxman encourages generic drug companies to file Paragraph IV certifications. To push generic makers to undertake the necessary investments and accept the risks of doing so, the statute 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 subsequent generic applicants. *E.g.*, *Teva v. Leavitt*, 548 F.3d at 104 ("Marketing exclusivity is valuable, designed to compensate manufacturers for research and development costs as well as the risk of litigation from patent holders."). Indeed, this reward can be worth "hundreds of millions of dollars to the regulated firm." *Teva v. Sebelius*, 595 F.3d at 1314.

As amended by the Medicare Modernization Act of 2003, the statute now provides that the first generic applicant can "forfeit" its entitlement to 180-day exclusivity after certain events occur. *See* 21 U.S.C. § 355(j)(5)(D)(i). Two of those events are relevant here. First, the statute provides that a generic applicant can forfeit its right to exclusivity if it fails to begin commercial marketing within certain periods of time following certain specified events. In particular, forfeiture under these "failure-to-market" provisions upon the *later* of two dates—one determined by the timing of FDA's actions with respect to the first applicant's ANDA, and the other determined by future contingencies related to potential litigation:

> (I) Failure to market.—The first applicant fails to market the drug by *the later of*—
>
> *(aa)* the earlier of the date that is—

> (AA) 75 days after the date on which the approval of the application of the first applicant is made effective under subparagraph (B)(iii); or
>
> (BB) 30 months after the date of submission of the application of the first applicant;
>
> *or*
>
> *(bb)* with respect to the first applicant or any other applicant (which other applicant has received tentative approval), the date that is 75 days after the date as of which, as to each of the patents with respect to which the first applicant submitted and lawfully maintained a [Paragraph IV certification], at least 1 of the following has occurred:
>
> > (AA) In an infringement action brought against that applicant with respect to the patent or in a declaratory judgment action brought by that applicant with respect to the patent, a court enters a final decision ... that the patent is invalid or not infringed.
> >
> > (BB) In an infringement action or a declaratory judgment action described in subitem (AA), a court signs a settlement order or consent decree that enters a final judgment that includes a finding that the patent is invalid or not infringed.
> >
> > (CC) The patent information submitted under subsection (b) or (c) of this section is withdrawn by the [brand manufacturer].

Id. (emphasis added).

Under these "failure-to-market" clauses, a first applicant's delay in launching thus can cause the applicant to forfeit exclusivity upon "the later of" two dates. The first date is either 75 days after FDA approves the applicant's ANDA or 30 months after the ANDA was submitted, whichever is first. 21 U.S.C. § 355(j)(5)(D)(i)(I)(aa). The second date is 75 days after the first applicant successfully removes patent barriers, through a court finding of invalidity or non-infringement; a settlement order including such a finding; or the withdrawal of a patent from the Orange Book (*i.e.*, the "delisting" of a previously listed patent). *Id*. § 355(j)(5)(D)(i)(I)(bb). In some cases, of course, there might not be such a court decision, settlement, or delisting. In those cases, FDA properly has held that the first applicant retains exclusivity despite its failure to

market. Granisetron Letter Decision, FDA Docket No. 2007N-0389 (Jan. 17, 2008) (attached as Exh. B). That is so because forfeiture occurs only on *the later of* (1) the date determined in the (aa) subsection ***or*** (2) the date determined in the (bb) subsection. If none of the events described in the (bb) subsection has occurred, it necessarily will be "the later of" the two possible dates, and the first applicant will not yet have failed to meet any condition set forth in that subsection.

In addition to the statute's "failure-to-market" provisions, the MMA added the forfeiture provision at issue in this litigation (including in proceedings before both the D.C. Circuit and D.C. District Court). Pursuant to this "patent expiration" forfeiture trigger, a first applicant may forfeit its exclusivity if "[a]ll of the patents as to which the applicant submitted a certification qualifying it for the 180-day exclusivity period have expired." 21 U.S.C. § 355(j)(5)(D)(i)(VI).

B. The Delisting Rule

Shortly after Congress passed the original Hatch-Waxman Act, brand manufacturers discovered a potential flaw in the Hatch-Waxman scheme: They realized that "delisting" a challenged patent from FDA's Orange Book—instead of defending that patent in litigation—could allow the brand manufacturer to eliminate the first challenger's exclusivity and thereby undercut the long-term incentive for generic companies to challenge brand patents in the first place. That was (and remains) so because generic applicants can only maintain a certification to patents listed in the Orange Book, and can only receive exclusivity if they maintain a Paragraph IV certification. *See* 21 U.S.C. § 355(j)(5)(B)(iv) (2002); 21 U.S.C. § 355(j)(5)(B)(iv)(II)(bb) (2003). FDA acquiesced in that manipulative practice, and brand companies routinely began to ward off patent challenges by delisting patents that were challenged and thereby reducing the potential reward for challenging their patents in the future.

Teva challenged this manipulative practice, and in *Ranbaxy Pharmaceuticals Ltd. v. Leavitt*, 469 F.3d 120 (D.C. Cir. 2006), the D.C. Circuit held that FDA's practice of permitting

brand manufacturers to "delist" challenged patents failed at *Chevron* step one. *Id.* at 126. As *Ranbaxy* explained, FDA's delisting policy effectively eviscerated the exclusivity incentive, because it allowed brand companies to strategically "reduce[e] the certainty of receiving a period of marketing exclusivity" and thereby "diminish[] the incentive for a [generic company] … to challenge a [listed] patent." *Id*. at 126. The D.C. Circuit thus declared FDA's delisting policy "inconsistent with the text and structure of the Act and, because it diminishes the incentive the Congress gave manufacturers of generic drugs, inconsistent with the purpose of the Act." *Id*.

Ranbaxy, however, was decided under the pre-MMA version of the statute. And seizing upon the statute's new "failure-to-market" forfeiture provision—which in certain circumstances provided for forfeiture when "patent information … is withdrawn by the" brand manufacturer, 21 U.S.C. § 355(j)(5)(D)(i)(I)(bb)(CC)—FDA soon announced that *Ranbaxy* did not survive the MMA amendments. *See Teva v. Sebelius*, 595 F.3d at 1306 ("FDA ruled that the 2003 amendments required a different outcome from the one *Ranbaxy* ordered under the old version of the law.") Instead, according to FDA, "[b]rand manufacturers [henceforth would be] free to delist challenged patents *whenever* they please—and any such delisting satisfies subsection (CC) of the 'failure to market' forfeiture section." *Id.* at 1315 (emphasis added).

C. Losartan Potassium Products

Losartan potassium is an angiotensin II receptor antagonist drug used primarily to treat hypertension. Merck holds two approved NDAs relating to losartan potassium: No. 02-0386 for losartan potassium tablets and No. 02-0387 for losartan potassium/hydrochlorothiazide tablets, which it commercially markets under the brand names Cozaar® and Hyzaar®, respectively.

When Merck obtained FDA approval for Cozaar® and Hyzaar®, it listed the same three patents[3] in the Orange Book for both drugs: U.S. Patent No. 5,138,069 ("the '069 patent"), which was scheduled to block generic competition through February 11, 2010; U.S. Patent No. 5,153,197 ("the '197 patent"), which was scheduled to block generic competition through April 6, 2010; and U.S. Patent No. 5,608,075 ("the '075 patent"), which was scheduled to block generic competition through September 4, 2014.[4]

On December 18, 2003, Teva submitted an ANDA seeking FDA approval to market a generic version of Cozaar® 25mg, 50mg and 100mg tablets. FDA accepted Teva's generic Cozaar® ANDA for filing on February 11, 2004 and docketed it as ANDA No. 07-6958. Teva's ANDA contained Paragraph III certifications to the '069 patent and the '197 patent, meaning that it would not seek to market its generic drug until the '197 patent expired on April 6, 2010. Importantly, Teva also submitted a Paragraph IV certification to Merck's '075 patent, claiming that that patent is invalid, unenforceable, and/or would not be infringed by Teva's generic drug product. Teva was the first generic applicant to submit a substantially complete ANDA for Cozaar® that contained a Paragraph IV certification to the '075 patent. *See Teva v. Sebelius*, 595 F.3d at 1307 ("Though the FDA does not formally announce which ANDA filer was the first to

[3] Merck also listed a fourth patent, U.S. Patent No. 5,210,079, in connection with its Cozaar® NDA, but that patent relates to a method of treatment for which Teva does not seek approval.

[4] Each patent actually expires six months before these dates. However, because Merck subsequently conducted studies of its losartan-potassium products' safety and effectiveness for children, it earned an additional six-month period of "pediatric exclusivity" which prevents FDA from approving generic applications for these drugs for six months after the expiration of each patent. *See* 21 U.S.C. § 335a. Accordingly, and in the absence of a Paragraph IV challenge, these three patents together would have blocked any generic competition in the losartan-potassium market until September 4, 2014, when the pediatric exclusivity period attached to the '075 patent would expire.

submit a paragraph IV certification … until the date on which generic sales can actually begin, Teva has every reason to believe that it was the first filer for both drugs at issue here.").

On May 24, 2004, Teva submitted an ANDA seeking FDA approval to market a generic version of Hyzaar® 50mg/12.5mg and 100mg/25mg tablets. FDA accepted Teva's generic Hyzaar® ANDA for filing on July 15, 2004 and docketed it as ANDA No. 07-7157. Teva's generic Hyzaar® ANDA contained the same patent certifications as its generic Cozaar® ANDA: Paragraph III certifications for the '069 and '197 patents, and a Paragraph IV certification for the '075 patent. Teva was also the first generic applicant to submit a substantially complete ANDA for Hyzaar® that contained a Paragraph IV certification to the '075 patent. On July 21, 2006, Teva amended its Hyzaar® ANDA to add an additional strength (100mg/12.5mg tablets) of the drug. The '075 patent is not listed in the Orange Book as claiming this strength.

Because Teva was the first generic applicant to submit substantially complete applications for generic Cozaar® and Hyzaar® that contained at least one Paragraph IV certification to at least one patent that Merck had listed in the Orange Book for those drugs, Teva became eligible for 180-day generic marketing exclusivity with respect to both drugs. *See* 21 U.S.C. § 355(j)(5)(B)(iv); *see also Teva v. Sebelius*, 595 F.3d at 1307.

As required by the FDCA, Teva notified Merck of its Paragraph IV certifications to the '075 patent on February 23, 2004 (for Cozaar®) and July 15, 2004 (for Hyzaar®). Teva alleged that certain claims of the '075 patent were invalid based on prior art and that Teva's generic losartan products did not infringe other claims of the patent under the doctrine of equivalents. Merck did not file a patent infringement claim against Teva. Instead, on March 18, 2005—*after* Teva submitted its exclusivity-qualifying Paragraph IV certifications to the '075 patent—"Merck asked the FDA to delist" the '075 patent from FDA's Orange Book, "which the agency did."

Teva v. Sebelius, 595 F.3d at 1307. In addition, Merck declined to list the '075 patent as claiming the 100mg/12.5mg strength of Hyzaar®, which was added after Teva filed its Paragraph IV certification. Then, *after* attempting to delist the '075 patent from the Orange Book, Merck stopped paying maintenance fees on that patent with the PTO. *See* 35 U.S.C. § 41(b) (patent maintenance fees are required); 37 C.F.R. § 1.362 (same).

By refusing to defend its patent in litigation and then abandoning it by asking FDA to delist it from the Orange Book, Merck conceded that Teva's challenges to the '075 patent were so strong that Merck could not reasonably assert the '075 patent against any generic applicant for Cozaar® or Hyzaar®, and thus that Merck could not lawfully maintain that patent in the Orange Book. Teva's Paragraph IV challenges to the '075 patent thus accomplished precisely what Congress sought to reward with 180-day exclusivity: Teva identified a vulnerable—but competition-blocking—patent, invested the resources necessary to challenge that patent, and successfully removed that patent as a barrier to generic market entry. Because of FDA's Delisting Rule, however, Teva—through no fault of its own—"had by the fall of 2008 *already* forfeited" any right to exclusivity because of Merck's unilateral decision to delist the '075 patent. *Teva v. Sebelius*, 595 F.3d at 1308 (emphasis in original).

D. The *Teva* Litigation

On June 17, 2009, Teva filed a complaint against Kathleen Sebelius, Margaret Hamburg, M.D., and the United States Food and Drug Administration (collectively, "FDA") in this Court. *See* Complaint, *Teva Pharmaceuticals USA, Inc. v. Sebelius*, No. 1:09-cv-01111-RMC, dkt. 1 (D.D.C.). Attacking the FDA's Delisting Rule as unlawful, Teva's complaint sought declaratory and injunctive relief to protect Teva's entitlement to 180-day exclusivity for its generic losartan potassium tablets. Teva also promptly moved for preliminary injunctive relief, explaining that it would be irreparably harmed in the absence of rapid judicial review.

FDA argued that Teva's suit was not yet ripe and that Teva lacked standing to bring suit. This Court rejected those jurisdictional arguments, but upheld the Delisting Rule as a reasonable interpretation of the FDCA. *See id.* at 1305 ("Despite protestations … that the matter was not ripe for review … the district court reached the merits of the claim—but ruled in the FDA's favor.").

Teva appealed, and though the D.C. Circuit agreed with this Court as to jurisdiction, it reversed on the merits. As to jurisdiction, the D.C. Circuit held that Teva had standing and that its claims were ripe. *See Teva v. Sebelius*, 595 F.3d at 1308-15. Of particular note, the D.C. Circuit held that "as of April 6, 2010, [Teva] will be entitled to start enjoying its exclusivity period and to continue doing so for 180 days before additional firms lawfully enter the market," and noted that if the court "refrained from adjudicating this dispute now, Teva would almost certainly face competition from Apotex on April 6—an injury that would not be remedied by Teva's securing 180 days of exclusivity later on." *Id.* at 1311 (internal citations omitted). The D.C. Circuit thus held that loss of Teva's "first-mover advantage" irreparably would harm the company. *Id.* (citing *Mova Pharm. Corp. v. Shalala*, 140 F.3d 1060, 1066 n.6 (D.C. Cir. 1998)).

On the merits, the D.C. Circuit held that *Ranbaxy*'s analysis of the statute's incentive structure remains good law, because there is "no reason to conclude that the 2003 addition of forfeiture provisions meant to give the brand manufacturer a right to unilaterally vitiate a generic's exclusivity." *Id.* at 1318; *see also id.* at 1317 ("The agency … *offers not a single cogent reason* why Congress might have … provided for a scenario in which the brand maker can unilaterally deprive the generic of its exclusivity.") (emphasis in original). Thus, the appellate court held, FDA's Delisting Rule "fails at *Chevron* step one." *Id.* at 1318; *see also id.* ("[N]othing in the 2003 amendments to the Food, Drug, and Cosmetic Act … changes the

structure of the statute such that brand companies should be newly able to delist challenged patents, thereby triggering a forfeiture event that deprives generic companies of the period of marketing exclusivity they otherwise deserve.").

The D.C. Circuit also made short work of FDA's curious claim that withholding Teva's exclusivity might somehow be in the public interest. Noting FDA's argument that allowing brand manufacturers to unilaterally deprive generic manufacturers somehow "benefits consumers by allowing full generic competition without a 180-day delay," the Court explained that FDA's analysis of the statute "betrays a misunderstanding of the exclusivity incentive." *Id.* at 1318. Exclusivity, the court explained, is not a burden on consumers but a blessing:

> The statute's grant of a 180-day delay in multiple generic competition for the first successful paragraph IV filer is a pro-consumer device. And it happens to be precisely the device Congress has chosen to induce challenges to patents claimed to support brand drugs. The statute thus deliberately sacrifices the benefits of full generic competition at the first chance allowed by the brand manufacturer's patents, in favor of the benefits of earlier generic competition, brought about by the promise of a reward for generics that stick out their necks (at the potential cost of a patent infringement suit) by claiming that patent law does not extend the brand maker's monopoly as long as the brand maker has asserted. As Congress deliberately created the 180-day exclusivity bonus, the FDA cannot justify its interpretation by proudly proclaiming that it has eviscerated that bonus.

Id. The appellate court then remanded the case to this Court "for further proceedings not inconsistent with this opinion," *id.* at 1319, but simultaneously entered a routine administrative order withholding issuance of the mandate until 7 days following the time within which FDA could seek panel rehearing and/or rehearing *en banc*. Order, *Teva Pharmaceuticals USA, Inc. v. Sebelius*, No. 09-5281 (D.C. Cir. Mar. 2, 2010).

E. Post-Judgment Proceedings In The D.C. Circuit

The appellate court's routine administrative order put Teva in a bind. *See* Emergency Motion To Issue Mandate Forthwith ¶¶ 4-7, *Teva Pharmaceuticals USA, Inc. v. Sebelius*, No. 09-5281 (filed Mar. 9, 2010). Because FDA has 45 days within which to seek rehearing, the earliest

date that the D.C. Circuit's mandate could have issued under that order was *April 23* (*i.e.*, 52 days from the appellate court's March 2 judgment). But, as the D.C. Circuit held, "Teva would almost certainly face competition from Apotex on *April 6*—an injury that would not be remedied by Teva's securing 180 days of exclusivity later on." *Teva v. Sebelius*, 595 F.3d at 1311 (emphasis added). Thus, if the D.C. Circuit's mandate were not promptly issued, this Court would not have been able to protect Teva's right to exclusivity before it was too late. Teva therefore moved that the mandate be issued forthwith.

On the same day Teva moved the D.C. Circuit to issue its mandate forthwith, Apotex apparently informed FDA that Merck's '075 patent may have prematurely expired in March 2009 due to Merck's failure to pay certain "maintenance fees" to the Patent and Trademark Office ("PTO"). On March 11, 2010, FDA solicited comments regarding "what effect, if any, a change in the patent expiration date for [the '075 patent] … would have on [Teva's] eligibility for 180-day exclusivity for losartan potassium tablets and losartan potassium-hydrochlorothiazide tablets." Solicitation of Comments, FDA Docket No. 2010-N-0134 (Mar. 11, 2010). Shortly thereafter, FDA opposed Teva's motion to issue the mandate forthwith on two grounds. *See* FDA Opp. to Teva Emergency Mot., *Teva Pharmaceuticals USA, Inc. v. Sebelius*, No. 09-5281 (filed Mar. 11, 2010). First, FDA claimed it needed 45 days to decide whether to seek *en banc* rehearing, *id.* at 4-5—even though waiting that long would guarantee irreparable harm to Teva. Second, and more significant for purposes here, FDA raised the exact claim that is the subject of the suits now pending before this Court, namely, that the '075 patent expired because Merck unilaterally failed to pay "maintenance fees" to PTO. *See id.* at 6-7 ("The expiration of the Merck '075 patent has important, and potentially dispositive,

consequences for this litigation.… [S]everal critical underpinnings of the panel majority's holdings are now, at a minimum, in considerable doubt.").

According to FDA, Merck's unilateral decision to stop paying maintenance fees on the '075 patent meant that "a forfeiture event other than the delisting of the '075 patent—namely, expiration of a patent that is the subject of a paragraph IV certification … has, in fact, occurred." *Id*. at 7 (citing 21 U.S.C. § 355(j)(5)(D)(i)(VI)). FDA, argued, moreover, that this patent expiry forfeiture trigger was of jurisdictional significance under the ripeness doctrine: Because "Teva has forfeited such exclusivity for a reason unrelated to that addressed in this preemptive litigation [*i.e.*, for a reason apart from the Delisting Rule], then Teva will suffer no harm, irreparable or otherwise" because of the Delisting Rule. *Id*. at 10.

Teva replied to FDA's submission the next day. *See* Reply in Support of Emergency Mot., *Teva Pharms. USA, Inc. v. Sebelius*, No. 09-5281 (filed Mar. 12, 2010). Teva noted FDA had had "ample opportunity" to raise the patent expiry issue ***before*** the D.C. Circuit's opinion was released, but that "in the laundry list of alternative forfeiture hypotheticals and other contingencies it presented …, FDA never once suggested there was any possibility that the '075 patent could or would 'expire' within the meaning of the Hatch-Waxman Act before April 6—much less that the '075 patent already had 'expired' within the meaning of the Hatch-Waxman Act before Teva filed this lawsuit last year." *Id*. at 4 & n.1 (emphasis omitted).

More important, Teva explained that the patent expiry issue raised by FDA was wholly derivative of Merck's unlawful attempt to delist the '075 patent, and so was squarely foreclosed by the D.C. Circuit's *Teva* opinion. In particular, Teva noted that "brand manufacturers routinely stop paying the fees on patents they have delisted (or at least attempted to delist) from the Orange Book" precisely because at that point such patents no longer have any value to the

brand manufacturers. *Id*. at 11 & n.2 (collecting examples). Accordingly, Teva argued, FDA's effort to divorce Merck's unlawful delisting request for the '075 patent from its subsequent failure to pay PTO maintenance fees on '075 patent "thus boils down to the absurd proposition that brand manufacturers somehow are allowed to achieve through the back door (by not paying maintenance fees on a challenged patent) precisely what [the D.C. Circuit's] decisions in both this case and *Ranbaxy* forbid them from doing through the front door (by delisting the challenged patent in the first place). As the [D.C. Circuit's] opinion recognized, however, there is 'not a single cogent reason why Congress might have permitted … a scenario in which the brand maker can unilaterally deprive the generic of its exclusivity,' and that judgment is controlling here." *Id*. at 11 (quoting *Teva v. Sebelius*, 595 F.3d at 1317).

After expressly considering the patent expiry issue, the D.C. Circuit agreed with Teva and entered an order directing the Clerk of Court to issue the mandate forthwith and thereby return the case to the D.C. District Court as expeditiously as possible. *See* 3/12/10 Order at 2, *Teva Pharms. USA, Inc. v. Sebelius*, No. 09-5281 ("Upon consideration of appellant Teva Pharmaceuticals' emergency motion to issue the mandate forthwith, *and the opposition thereto*; appellant Teva Pharmaceuticals' motion for leave to exceed the page limits, *and the lodged reply*, it is … ORDERED that the motion to issue the mandate forthwith be granted.") (emphases added).

F. The *Teva* Remand

This Court promptly held a status conference on March 15 to determine how to implement the D.C. Circuit's mandate. The next day, this Court declared that "Teva has not forfeited its right to 180-day marketing exclusivity for generic losartan potassium products under 21 U.S.C. § 355(j)(5)(D)(i)(I)" and enjoined FDA "from approving any [ANDA] for a generic version of [losartan potassium products] prior to the conclusion of Teva's 180-day period of

marketing exclusivity." Order, *Teva Pharmaceuticals USA, Inc. v. Sebelius*, No. 1:09-cv-01111-RMC, dkt. 28 (D.D.C. Mar. 16, 2010).

On March 19, FDA moved this Court to reconsider its March 16 Order, arguing that this Court had overread the D.C. Circuit's mandate. *See* FDA Mot. to Clarify or Alter or Amend Court's March 16 Order, *Teva Pharmaceuticals USA, Inc. v. Sebelius*, No. 1:09-cv-01111-RMC, dkt. 29, at 1-2 (filed Mar. 19, 2010). Teva opposed that motion, emphasizing that the mandate rule applies to all issues expressly or impliedly addressed by the appellate court—as Teva argued this issue was. *See* Teva Opp. to Defs. Mot. to Clarify or Alter or Amend Court's March 16 Order, *Teva Pharmaceuticals USA, Inc. v. Sebelius*, No. 1:09-cv-01111-RMC, dkt. 30, at 2-4 (filed Mar. 23, 2010). On March 24, this Court entered a minute order compelling FDA to file its letter decision on the patent expiry issue by 5PM on March 26. Order, *Teva Pharmaceuticals USA, Inc. v. Sebelius*, No. 1:09-cv-01111-RMC (filed Mar. 24, 2010). And on March 26, this Court granted FDA's motion over Teva's opposition, *see* Order, *Teva Pharmaceuticals USA, Inc. v. Sebelius*, No. 1:09-cv-01111-RMC, dkt. 33 (filed Mar. 26, 2010) (emphasis added), but noted that challenges to that decision could be brought "in a new lawsuit, filed as a case related to this one." *Id.* at 3 n.4.

G. FDA's Letter Decision

On March 26, FDA filed its letter decision in this Court's open docket in the *Teva* case, No. 1:09-cv-01111-RMC. Although the Agency's letter decision took issue with the D.C. Circuit's decision, the Agency nonetheless concluded that the appellate court's reasoning "appears to preclude a forfeiture of exclusivity on the basis of a patent expiration where the expiration is in the control of the NDA holder," Losartan Letter Decision at 7, and therefore declared that FDA "will not approve any other ANDA referencing Cozaar or Hyzaar until the

first applicant has received approval of its ANDA, begun commercial marketing, and the 180-day exclusivity period has expired." *Id*. at 8.

Plaintiffs now challenge that decision.

LEGAL STANDARD

The standard for obtaining preliminary injunctive relief is well-settled. "A plaintiff seeking a preliminary injunction must establish that he is likely to succeed on the merits, that he is likely to suffer irreparable harm in the absence of preliminary relief, that the balance of equities tips in his favor, and that an injunction is in the public interest." *Winter v. Natural Resources Defense Council, Inc.*, 129 S. Ct. 365, 374 (2008). Although "[t]hese 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), "a movant cannot obtain a preliminary injunction without showing *both* a likelihood of success *and* a likelihood of irreparable harm, among other things." *Davis v. Pension Ben. Guar. Corp.*, 571 F.3d 1288, 1296 (D.C. Cir. 2009) (Kavanaugh and Henderson, JJ., concurring) (emphasis in original). Moreover, where "substantial harm to the nonmovant is very high and the showing of irreparable harm to the movant very low, the movant must demonstrate a much greater likelihood of success." *Id.* at 1292.

ARGUMENT

I. PLAINTIFFS HAVE NO LIKELIHOOD OF SUCCESS ON THE MERITS.

FDA finally has gotten it right: The D.C. Circuit's "'*Chevron* step one'" interpretation of "the structure of the MMA exclusivity provisions … does not permit an NDA holder to 'unilaterally' deprive the generic applicant of its exclusivity," and that reasoning applies no less to Merck's unilateral attempt to deprive Teva of its exclusivity reward by abandoning the '075 patent through non-payment of maintenance fees than it does to Merck's unlawful attempt to

delist that patent in the first instance. Losartan Letter Decision at 7-8 (quoting *Teva v. Sebelius*, 595 F.3d at 1305, 1317); *see also Teva v. Sebelius*, 595 F.3d at 1317 ("The Agency, however, offers *not a single cogent reason* why Congress might have permitted … a scenario in which the brand maker can unilaterally deprive the generic of its exclusivity.") (emphasis in original); *id.* (holding that the statute "does *not* permit a brand manufacturer to vitiate a generic's exclusivity without the generic manufacturer's having had some say in the matter") (emphasis added); *id.* at 1318 (holding that there is "*no reason* to conclude that the 2003 addition of forfeiture provisions meant to give the brand manufacturer a right to unilaterally vitiate a generic's exclusivity") (emphasis added); *Ranbaxy Labs. Ltd. v. Leavitt*, 469 F.3d 120, 126 (D.C. Cir. 2006) ("FDA may not, however, change the incentive structure adopted by the Congress [by] allow[ing] an NDA holder … to deprive the generic applicant of a period of marketing exclusivity.").

Consistent with these clear instructions, FDA thus reached the only conclusion that the law allows: If Merck cannot unilaterally divest Teva of its exclusivity reward by delisting the '075 patent in response to Teva's Paragraph IV certification, then Merck cannot unilaterally divest Teva of its exclusivity reward by artificially pretermitting that patent's natural term after Teva's Paragraph IV certification *caused* Merck to effectively abandon its patent. Contrary to Apotex's remarkable assertions, *see, e.g.*, Apotex Br. at 9-11, there is nothing arbitrary or capricious about FDA's decision to conform its actions to what the D.C. Circuit held the statute's incentive structure *requires* at *Chevron* step one. And, indeed, the implications of Apotex's counterargument are staggering. By Apotex's reasoning, federal agencies not only are free to ignore judicial decisions with which they disagree, but are compelled to do so: "The agency may not reach a result that … *it itself* concludes is 'inconsistent with the plain language of the statute.' To do so is the very embodiment of an arbitrary and capricious decision." *Id.* at 11 (emphasis

added). That argument makes a mockery of judicial review and cannot be squared with the most fundamental tenet of our legal system: that it "is emphatically the province and duty of the judicial department to say what the law is." *Marbury v. Madison*, 5 U.S. (1 Cranch) 137, 177 (1803). Whether Apotex likes it or not, FDA is bound by the law of this Circuit, and while plaintiffs are free to echo FDA's disdain for the D.C. Circuit's *Chevron* step one analysis of the statute's incentive structure, they cannot sensibly fault FDA for following the law—or reasonably demand that FDA defy it. *See Cooper v. Aaron*, 358 U.S. 1, 18-20 (1958).

Plaintiffs next try to distinguish *Teva* on the ground that it merely addressed the delisting forfeiture trigger, 21 U.S.C. § 355(j)(5)(D)(i)(I)(bb)(CC), whereas this case involves the patent expiry forfeiture trigger, 21 U.S.C. § 355(j)(5)(D)(i)(VI). *See* Apotex Br. at 20-22; Roxane Br. at 13-17. Their arguments provide no basis for ignoring *Teva*'s sharply-worded instructions about the statute's incentive structure.

For its part, Roxane asserts that in contrast to patent delisting, which involves FDA's Orange Book, "patent expiration is a concept embedded in patent law and appropriately interpreted by the USPTO." Roxane Br. at 15. It then argues that "FDA and this Court's interpretation of 'expiration' should reflect the use of that term in patent law and by the USPTO," without reference to "the context of Hatch-Waxman." *Id*. But that is no way to read a statute. As the Supreme Court long has explained, statutes must be interpreted "by reference to the language itself, the specific context in which that language is used, and the broader context of the statute as a whole." *Robinson v. Shell Oil Co.*, 519 U.S. 337, 341 (1997) (citing *Estate of Cowart v. Nicklos Drilling Co.*, 505 U.S. 469, 477 (1992); *McCarthy v. Bronson*, 500 U.S. 136, 139 (1991)). Indeed, the Court repeatedly has emphasized a single word can—and, depending on its context, often must—have two different meanings even when it is used within a *single*

statute. *See, e.g., Gen. Dynamics Land Sys., Inc. v. Cline*, 540 U.S. 581, 595 & n.8 (2004) (quoting *Atl. Cleaners & Dyers v. United States*, 286 U.S. 427, 433 (1932) ("Most words have different shades of meaning, and consequently may be variously construed, not only when they occur in different statutes, but when used more than once in the same statute or even in the same section. Undoubtedly, there is a natural presumption that identical words used in different parts of the same act are intended to have the same meaning. But the presumption is not rigid and readily yields whenever there is such variation in the connection in which the words are used as reasonably to warrant the conclusion that they were employed in different parts of the act with different intent.")); *SEC v. Nat'l Secs., Inc.*, 393 U.S. 453, 466 (1969) ("The meaning of particular phrases must be determined in context…. Whatever these or similar words may mean in the numerous other contexts in which they appear in the securities laws, only this one narrow question is presented here.") (citing *SEC v. C.M. Joiner Leasing Corp.*, 320 U.S. 344, 350-351 (1943)).

That contextual approach is dispositive here, and even Roxane acknowledges it: "If the reasoning in *Teva* were to be applied to the patent expiration forfeiture provision, *FDA would be required, based on the incentive structure for 180-day exclusivity designed by Congress, to interpret the term expired in the forfeiture provision as not including expiration of a patent for failure to pay maintenance fees*. To do otherwise would allow the brand manufacturer to unilaterally deprive the generic manufacturer of 180-day exclusivity in contravention of the incentive structure." Roxane Br. at 16 (emphasis added); *see also Teva v. Sebelius*, 595 F.3d at 1317 ("The Agency, however, offers *not a single cogent reason* why Congress might have permitted … a scenario in which the brand maker can unilaterally deprive the generic of its exclusivity"); *id*. at 1318 (holding that there is "*no reason* to conclude that the 2003 addition of

forfeiture provisions meant to give the brand manufacturer a right to unilaterally vitiate a generic's exclusivity.") (emphasis added).

Roxane's only rationale for not applying *Teva*'s reasoning here is that "[i]n order to maintain consistency between the FFDCA and the patent code, Congress must have intended for the same meaning of expired to apply in both statutory schemes." Roxane Br. at 17. But that naked *ipse dixit* assumes precisely what it sets out to prove—that Congress was concerned with applying technical patent-law concepts when it passed the Hatch-Waxman Act, rather than in creating an incentive for generic applicants to challenge competition-blocking patents and thereby expedite the onset of market competition for prescription drugs. Needless to say, there is no support for the former proposition, and two decades of precedent supporting the latter. *See, e.g.*, *Teva. v. Sebelius*, 595 U.S. at 1318 ("The statute's grant of a 180-day delay in multiple generic competition for the first successful paragraph IV filer is a pro-consumer device. And it happens to be precisely the device Congress has chosen to induce challenges to patents claimed to support brand drugs. The statute thus deliberately sacrifices the benefits of full generic competition at the first chance allowed by the brand manufacturer's patents, in favor of the benefits of earlier generic competition, brought about by the promise of a reward for generics that stick out their necks (at the potential cost of a patent infringement suit) by claiming that patent law does not extend the brand maker's monopoly as long as the brand maker has asserted."); *Teva v. Leavitt*, 548 F.3d at 104 ("Marketing exclusivity is valuable, designed to compensate manufacturers for research and development costs as well as the risk of litigation from patent holders."); *Ranbaxy*, 469 F.3d at 126 ("By thus reducing the certainty of receiving a period of marketing exclusivity, the FDA's delisting policy [unlawfully] diminishes the incentive for a manufacturer of generic drugs to challenge a patent listed in the Orange Book.").

Moreover, as Teva repeatedly has explained in this case, there is another reason not to blindly apply technical patent-law doctrines in this context: Unlike patents that expire naturally, patents which PTO considers to have "expired" for non-payment of maintenance fees don't actually die. Instead, patents which lapse for non-payment of maintenance fees can be revived, and, indeed, in certain circumstances may be revived "at any time." *See* 35 U.S.C. § 41(c)(1) ("The Director may accept the payment of any maintenance fee required … within twenty-four months after the six-month grace period if the delay is shown to the satisfaction of the Director to have been unintentional, or at any time after the six-month grace period if the delay is shown to the satisfaction of the Director to have been unavoidable…. If the Director accepts payment of a maintenance fee after the six-month grace period, *the patent shall be considered as not having expired*.") (emphasis added).

Interpreting the statute to provide for forfeiture upon the brand manufacturer's unilateral failure to pay maintenance fees thus not only would allow brand manufacturers to *deliberately* strip the first patent challenger of its exclusivity reward in direct contravention of the D.C. Circuit's repeated instructions about the Hatch-Waxman Act's incentive structure, but also would allow brand manufacturers to *negligently* strip the first patent challenger of its exclusivity—with dire consequences for the first applicant and the statute's incentive structure. Following an inadvertent lapse in the payment of fees and consequent "forfeiture," FDA might approve all generic applicants immediately—leaving the first patent challenger with no conceivable recourse if and when the patent is revived by the brand manufacturer and becomes (as it always and continuously should have been) capable of grounding the first applicant's exclusivity period. *See Teva v. Sebelius*, 595 F.3d at 1311 (explaining that once a subsequent applicant is approved, the first filer suffers "an injury that would not be remedied by … securing

180 days of exclusivity later on"). Congress could not possibly have intended such a result, and there is no plausible basis for divesting the first patent challenger of its exclusivity when a supposedly "expired" patent can come back to life "at any time" and thereafter be "considered as *not* having expired." 35 U.S.C. § 41(c)(1) (emphasis added).

Roxane's alternative argument—that the statute contains no "exception … for patents that have expired due to non-payment of maintenance fees," such that "180-day exclusivity has been forfeited … if a patent has expired—for any reason," Roxane Br. at 12—should sound familiar. After all, FDA made the very same argument about the delisting trigger earlier in this case. *See Teva v. Sebelius*, 495 F.3d at 1315 ("The FDA, for its part, responds that 'the plain language of the statute contains no limitation on when delisting can occur.' Brand manufacturers are thus free to delist challenged patents whenever they please—and any such delisting satisfies [the delisting trigger].") (quoting FDA Br. at 44); *see also id.* at 1309 ("'[T]he plain language of subsection (CC) makes clear that the provision applies *whenever* a patent is withdrawn by the [brand manufacturer]'") (quoting FDA Br. at 42-43). The D.C. Circuit, however, rejected this very argument on the ground that such an interpretation of the delisting trigger cannot be reconciled with the statute's incentive structure, because it impermissibly would allow brand manufacturers to "rob the generic maker of earned exclusivity." *Id.* at 1317. Roxane's attempt to reprise that argument now fails for the same reasons it did the last time FDA took this tack.

And rightly so. Allowing brand manufacturers to divest the first generic patent challenger of its exclusivity reward through the simple artifice of ceasing to pay maintenance fees on a challenged patent would allow brand manufacturers to make an end-run around the statute's clear bar on exclusivity-divesting patent delistings—as Roxane forthrightly concedes. Roxane Br. at 17 ("A necessary bi-product of Congress's intent to maintain uniformity would

have been that a brand manufacturer, by not paying maintenance fees on his patents could unilaterally strip a generic manufacturer of 180-day exclusivity."). There is no reason why Congress would have intended to take from generics with one hand what it gave them with the other, and Roxane offers none.

For its part, Apotex at least tries to explain the inconsistency such a result would produce:

> Brand manufacturers, however, do not have the same incentives with respect to delisting as they do with respect to patent expiration. The D.C. Circuit in *Ranbaxy* accepted the proposition that a brand manufacturer might remove a patent from the Orange Book in order to interfere with a generic's 180-day exclusivity. A brand manufacturer that delisted a patent would give up the opportunity to delay the approval of ANDAs because it could no longer obtain a 30 month stay of approval in connection with the delisted patent. It may be conceivable that a brand manufacturer would give up that benefit to interfere with 180-day exclusivity because it would maintain the right to sue the generic for patent infringement once the generic product was on the market. Consequently it would still be able to enforce its patent. There are in fact cases in which a brand manufacturer chooses to sue a generic applicant not under Hatch Waxman but rather under traditional theories of patent infringement. *See, e.g.*, *Mylan v. Thompson*, 332 F. Supp. 2d 106 (D.D.C. 2004).
>
> That scenario is very different from one in which the patent is allowed to expire. When a patent expires, the brand manufacturer loses the right to enforce the patent. For the brand manufacturer, the choice to let a patent expire has far greater consequences, and the possibility that a brand manufacturer would give up a valid patent to interfere with an ANDA applicant's exclusivity is remote at best. Consequently, unlike a patent delisting, allowing a patent to expire is not a way in which brand manufacturers are likely to interfere with the incentive structure established by Congress.

Apotex Br. at 21-22.

Both ends of that argument are profoundly flawed. First, while it is certainly true that brand manufacturers occasionally bring suit on patents outside the Hatch-Waxman Act framework, brand manufacturers demonstrably cannot bring suit against a generic applicant for patent infringement after unilaterally delisting that patent in response to the applicant's Paragraph IV certification. As FDA itself has explained, "an NDA holder's request to delist a patent is implicitly an acknowledgment that the standard for patent listing set forth in section

505(b) and (c) of the Act—that a 'claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacturer, use, or sale of the drug'—could no longer be met." Risperidone Letter Decision at 9, FDA Docket No. 2007P-316 (Feb. 26, 2008) (attached as Exh. C). Accordingly, once a challenged patent has been unilaterally delisted from the Orange Book, applicants are "not … subject to any risk of patent infringement litigation." *Id*. The *Mylan* case cited by Apotex did not involve a lawsuit predicated on a unilaterally delisted patent, and to the best of Teva's knowledge, there is no case in the history of the Hatch-Waxman Act in which a brand manufacturer has attempted to sue a generic for infringing a patent the brand manufacturer unilaterally delisted after receiving the applicant's Paragraph IV certification. Apotex's assertion that a brand manufacturer which unilaterally delists a patent in response to a Paragraph IV certification somehow "would maintain the right to sue the generic for patent infringement," Apotex Br. at 22, thus is specious—as is its corollary effort to distinguish artificially induced patent expiration on the ground that patent expiry more conclusively extinguishes the brand manufacturer's patent rights than delisting.

Apotex's next assertion—that "the possibility that a brand manufacturer would give up *a valid patent* to interfere with an ANDA applicant's exclusivity is remote at best," *id*. (emphasis added)—is triply flawed. As a threshold matter, it rests on a faulty premise: The whole point of a Paragraph IV certification is that the challenged patent is *invalid*, and the concern with brand manipulation in both the delisting and patent-expiry contexts is that brand companies will punish generic applicants *not* for having challenged a *valid*, competition-blocking patent, but rather for having called the brand manufacturer's bluff and challenged a concededly *invalid* patent that—but for the generic applicant's challenge—nonetheless would have blocked competition. Moreover, Apotex's argument that brand companies are unlikely to engage in this kind of

strategic gamesmanship conflicts with the evidence in the record. As Teva repeatedly has noted (including to FDA during its administrative proceedings), brand manufacturers *routinely* cease paying maintenance fees on challenged patents—and quite often do so at the same time they seek to delist those patents from the Orange Book.[5] Finally, Apotex is simply wrong that the kind of artificial patent expiry at issue here decisively extinguishes the brand manufacturer's rights. As noted above, patents which lapse for non-payment of maintenance fees can be revived, and, indeed, in certain circumstances may be revived "at any time" such that they "shall be considered as *not* having expired." 35 U.S.C. § 41(c)(1) (emphasis added).

But even if Apotex were right that brand manufacturers could maintain a patent infringement action on a unilaterally delisted patent *and* that an artificial patent expiration represents a more decisive extinguishment of the brand manufacturer's patent rights than a delisting, its argument would run into another problem: A generic applicant's success in patent-infringement litigation against the brand manufacturer represents the most decisive extinguishment of the brand manufacturer's patent rights that can be imagined, yet FDA nonetheless retains the challenged patent in the Orange Book as a basis for exclusivity. The rationale for that approach is straightforward: removing such a patent as a basis for exclusivity would deprive the first applicant of the reward Congress intended it to have for having done precisely what Congress wanted it to do. *See, e.g.*, Abbreviated New Drug Application Regulations; Patent and Exclusivity Provisions, 59 Fed. Reg. 50,338, 50,348 (Oct. 3, 1994) ("If a

[5] In the brief window of time since FDA first raised this issue, we have identified no fewer than nine prior cases in which a brand manufacturer sought to delist a patent from the Orange Book and then ceased paying maintenance fees at the PTO, including U.S. Patent Nos. 6,248,741; 5,736,165; 5,667,794; 6,114,144; 6,113,920; 6,020,001; 6,368,627; 5,863,559; and 6,248,735—all of which were at one time listed in the Orange Book, but then allowed to lapse for non-payment of fees following the brand manufacturer's request that FDA delist the patent.

patent were removed from the list immediately upon a court decision that the patent is invalid or unenforceable, an applicant with a subsequently filed application might seek to certify that there is no relevant patent and seek an immediately effective approval. To ensure that this does not occur, the agency has required that a patent remain on the list after being declared invalid or unenforceable until the end of any applicable 180-day exclusivity period.").

Allowing brand manufacturers to strip the first applicant's exclusivity by unilaterally failing to pay maintenance fees not only is irreconcilable with that approach; it would render it a dead letter. After all, while FDA might (as it always has) maintain a challenged patent in the Orange Book following a generic applicant's victory in patent litigation precisely in order to preserve the first applicant's exclusivity reward, sanctioning the kind of conduct Merck engaged in here would allow brand manufacturers to evade that rule through the simple artifice of unilaterally ceasing to pay maintenance fees once it becomes clear that their patent case against a generic challenger is going poorly—thereby vitiating the first applicant's eventual exclusivity reward when the patent challenger eventually wins its case. If the patent expiration forfeiture trigger really means, as plaintiffs insist, that *any* kind of patent expiration counts, no matter the circumstances, then even winning a patent suit would not immunize the first applicant from the brand manufacturer's punitive manipulation. That, quite simply, cannot be the law, and there is no reason for construing the statute in that fashion.

Indeed, the rationale for divesting the first applicant of exclusivity upon natural patent expiry does not remotely apply in the circumstances at issue here. Long before the MMA added a forfeiture trigger based on patent expiry, FDA had interpreted the statute to preclude an award of exclusivity following a patent's natural expiration date. *See, e.g., Dr. Reddy's Labs., Inc. v. Thompson*, 302 F. Supp. 2d 340, 354-55 (D.N.J. 2003); *see also* FDA Letter Decision No. 99P-

1271/PSA1 and PSA 2 (cisplatin), at 4 (Aug. 2, 1999). The justification for that approach is straightforward. Paragraph IV certifications are intended to enable the early entry of generic drugs and thereby provide expedited price relief to consumers. *See, e.g.*, *Andrx Pharms., Inc. v. Biovail Corp. Int'l*, 256 F.3d 799, 809 (D.C. Cir. 2001) ("'Congress sought to get generic drugs into the hands of patients at reasonable prices—fast.'") (quoting *In re Barr Labs., Inc.*, 930 F.2d 72, 76 (D.C. Cir. 1991)). But where the first patent-challenging generic applicant is unable to (or simply does not) launch its product before the challenged patent expires naturally, the applicant's certification has accomplished virtually nothing. *Dr. Reddy's*, 302 F. Supp. 2d at 354 ("Once a listed patent expires, there is no longer a need to provide an incentive to challenge it in court."). That same rationale, of course, is why FDA does not otherwise allow an applicant to maintain a Paragraph IV certification if the applicant does not actually intend to launch its products prior to the challenged patent's scheduled expiration (and thus has accomplished nothing through its certification), and why FDA likewise does not award exclusivity where the first applicant loses its patent case (and thus has accomplished nothing through its certification).

By contrast, when a patent lapses not by the mere passage of time, but rather because the first applicant's Paragraph IV certification *caused* the patentee to cease paying its maintenance fees—as routinely happens—then the first applicant's Paragraph IV challenge will have accomplished *precisely* what the statute seeks to reward. It will have opened the market to competition years before consumers otherwise would obtain access to affordable generic medications, which is exactly what the exclusivity incentive is designed to reward. *See, e.g.*, *Teva v. Sebelius*, 595 F.3d at 1318 ("The statute's grant of a 180-day delay in multiple generic competition for the first successful paragraph IV filer is a pro-consumer device."); *Teva v. Leavitt*, 548 F.3d at 106 ("[P]aragraph IV [seeks] to enhance competition by encouraging generic

drug manufacturers to challenge the patent information provided by NDA holders."); *Andrx*, 256 F.3d at 809; *Serono Labs., Inc. v. Shalala*, 158 F.3d 1313, 1326 (D.C. Cir. 1998) ("The purpose of the Hatch-Waxman Amendments was, after all, to increase competition [and] make available more low cost generic drugs.").

Make no mistake: Teva thus earned its statutory reward here. The company made an enormous investment to develop legal challenges to the validity of the '075 patent's claims, and it deployed a team of scientists to engineer a non-infringing pathway around any claims not subject to legal challenge. Those investments paid off with a Paragraph IV certification so strong that Merck simply gave up—first by delisting that patent, and then by ceasing to pay maintenance fees on it. Teva's groundbreaking Paragraph IV certification thereby cleared the path for generic competition to begin more than four years earlier than it otherwise would have in the absence of Teva's Paragraph IV certification, and as a direct result of Teva's efforts, consumers now will save literally billions of dollars on losartan potassium products between April 6, 2010 and September 4, 2014, when the pediatric exclusivity period attached to the '075 patent would have expired in the absence of Teva's Paragraph IV certification. There is no basis for depriving Teva of its reward for generating those savings, and FDA quite properly applied the D.C. Circuit's decision in *Teva* to protect Teva's hard-earned rights in the face of Merck's manipulative conduct.

Two final points are in order. First, Roxane and Apotex both offer curious arguments regarding the interplay between Paragraph IV and Paragraph II certifications and their implications for this case. On one hand, Roxane argues that Teva's ANDAs "no longer contain[] a paragraph IV certification on which to base such exclusivity" because the '075 patent allegedly has expired. Roxane Br. at 11-12. And on the other hand, Roxane and Apotex both insist that

because they converted their own certifications to Paragraph II, Teva's exclusivity period does not block their approvals. Apotex Br. at 12-15, 19; Roxane Br. at 10-11. These arguments are purely question-begging. This case ultimately boils down to the question of whose certifications are valid: Teva's Paragraph IV certifications, or Apotex's and Roxane's Paragraph II certifications. If Teva and FDA are right that the '075 patent has not expired for purposes of the Hatch-Waxman Act, then Apotex and Roxane will be forced to re-certify to that patent under Paragraph IV. And if Apotex and Roxane are right that Merck lawfully vitiated Teva's exclusivity period by ceasing to pay maintenance fees on the '075 patent, then Teva will be forced to convert its Paragraph IV certifications to Paragraph IIs. *See Sandoz, Inc. v. FDA*, 439 F. Supp. 2d 26, 30-31 (D.D.C. 2006) (rejecting virtually identical arguments to the ones Apotex and Roxane are making here); *see also* 21 C.F.R. § 314.94(a)(12)(viii)(C)(1) ("[A]n applicant shall amend a submitted certification if, at any time before the effective date of the approval of the application, the applicant learns that the submitted certification is no longer accurate."). For all the ink Apotex and Roxane spill on these points, their arguments thus are collateral to the question that really matters in this case—Did FDA properly follow the D.C. Circuit's opinion in *Teva v. Sebelius*?—and carry no weight of their own.

Finally, plaintiffs cannot argue that FDA's "ministerial role" provides an excuse to let brand companies to manipulate the incentives for generic market entry in this fashion. After all, FDA tried to defend its (now unlawful) delisting policy in *Ranbaxy* on the basis of its supposedly "ministerial" role in the patent-listing process, and the D.C. Circuit nonetheless rejected FDA's enablement of the same kind of manipulation at issue here. *See* 469 F.3d at 125 (rejecting FDA's delisting policy despite claims that it "preserves the ministerial nature of the FDA's role in maintaining the patent listings in the Orange Book because, when an NDA holder asks it to

delist a patent, the agency need not determine whether the NDA holder is acting strategically to deny the generic applicant a period of marketing exclusivity or the patent actually does not cover the drug for which it was submitted—the interpretation of patent listings being outside the agency's expertise").

The "ministerial role" defense is no more availing here than it was in *Ranbaxy*. In fact, it is less so. The whole basis for FDA's "ministerial" role is the Agency's belief that it lacks the ability to carry out *a substantive review of patent claims* in order to ensure that only properly submitted patents are listed in the Orange Book:

> Several comments stated that parties, such as generic drug companies and even third parties, need a method for challenging patent listings or for de-listing patents in the Orange Book. Some comments explained that the lack of an administrative procedure for challenging patent listings either encouraged NDA applicants to submit inappropriate patent information, or did not deter the practice, to delay generic competition. A number of comments maintained that FDA has more than a ministerial role and should review patents to determine if they meet the requirements for listing. Several comments contend that we have the authority to determine the attributes of the approved drug and thus to determine the appropriate patent listings. Various administrative mechanisms were suggested through which FDA could conduct a review of patents. These suggestions ranged from hiring patent lawyers to review submitted patents to development of a full administrative hearing process….
>
> A fundamental assumption of the Hatch-Waxman Amendments is that the courts are the appropriate mechanism for the resolution of disputes about the scope and validity of patents. The courts have the experience, expertise, and authority to address complex and important issues of patent law…. In addition to the absence of any statutory basis for a substantive agency review of patents, we have long observed that we lack expertise in patent matters. An administrative process for reviewing patents, assessing patent challenges, and de-listing patents would involve patent law issues that are outside both our expertise and our authority.

Applications for FDA Approval to Market a New Drug, 68 Fed. Reg. 36,676, 36,683 (June 18, 2003).

Those concerns have no force here. Ensuring that an Orange Book patent listing reflects the listed patent's natural expiration date—as opposed to the date on which the brand manufacturer unilaterally sought to divest the first applicant of its exclusivity by ceasing to pay

maintenance fees to the PTO—does not require FDA to engage in a "substantive agency review of patents," "assess[] patent challenges," "review patents to determine if they meet the requirements for listing," "hir[e] patent lawyers to review submitted patents," or delve into "complex and important issues of patent law" in the context of "a full administrative hearing process." *Id.* It requires only that FDA ask brand manufacturers to supply the right information in the first instance, and where a given submission subsequently is challenged, that it ask the right follow-up question. FDA's "ministerial" role in policing the Orange Book thus provides no license for allowing Merck to unilaterally vitiate Teva's exclusivity in direct contravention of the D.C. Circuit's repeated instructions about the statute's incentive structure.

II. THE HARM TO TEVA FROM GRANTING INJUNCTIVE RELIEF VASTLY OUTWEIGHS THE HARM TO PLAINTIFFS FROM DENYING SUCH RELIEF.

The balance of hardships weighs heavily against injunctive relief. As the D.C. Circuit already recognized, Teva would be harmed irreparably if this Court enjoins FDA's decision and allows other applicants to enter the market during Teva's exclusivity period. *Teva v. Sebelius*, 595 F.3d at 1311 (noting that without relief, "Teva would almost certainly face competition from Apotex on April 6—*an injury that would not be remedied by Teva's securing 180 days of exclusivity later on*.") (emphasis added). Moreover, Teva would lose literally "hundreds of millions of dollars" from the entry of its competitors into the market. *Id*. at 1314. By contrast, Apotex and Roxane together stand to lose a combined maximum of $38.6 if Teva maintains its right to exclusivity in this case. Gettenberg (Apotex) Decl.. at ¶ 16; Roxane Br. at 18.

Numerous courts have recognized that such a gross disparity in the balance of hardships weighs sharply against the entry of injunctive relief, and that relatively small sums at stake for Apotex and Roxane are not sufficient to warrant injunctive relief. *See, e.g.*, *Apotex v. FDA*, No. Civ. A. 06-0627, 2006 WL 1030151, *17-*18 (D.D.C. April 19, 2006) (noting that while Apotex

stood to lose approximately $10 million if injunctive relief were denied, Teva and Ranbaxy stood "to lose a much greater sum if the launch of their generic products [was] delayed," and holding that "[i]n light of the considerable economic injury facing intervenor-defendants, and the less substantial injury to Apotex, the balance of hardships clearly tips against granting Apotex the emergency injunctive relief that it seeks."); *see also Davis*, 571 F.3d at 1296 (Kavanaugh and Henderson, JJ., concurring); *Am. Ass'n for Homecare v. Leavitt*, No. 08-0992, 2008 WL 2580217, at *4 (D.D.C. June 30, 2008) ("While this court has conceded that there is some appeal to the proposition that any damage, however slight, which cannot be made whole at a later time, should justify injunctive relief, nevertheless, some concept of magnitude of injury is implicit in the standard for issuing a preliminary injunction. Accordingly, a plaintiff seeking preliminary injunctive relief must show that it will suffer harm that is more than simply irretrievable. Harm that is merely economic in character is not sufficiently grave under this standard.") (internal citations and quotations omitted)..

Moreover, numerous courts addressing these issues in the Hatch-Waxman context have noted that the first applicant loses something far more important than money from the entry of injunctive relief under these circumstances: "[U]nlike the harm that Apotex allegedly faces, the potential injury that [Teva faces] is not 'merely economic.' Rather, [Teva] stand[s] to lose a statutory entitlement, which is a harm that has been recognized as sufficiently irreparable. Once the statutory entitlement has been lost, it cannot be recaptured." *Id.* at *17; *see also Teva v. Sebelius*, 595 F.3d at 1310, 1311 (noting that "Teva faces … a near-certain loss of the first-mover advantage," and that that "first-mover advantage" cannot be recovered once other generics launch); *Mova*, 140 F.3d at 1066-67 n.6 (holding that loss of the Hatch-Waxman Act's "officially sanctioned head start" is irreparable injury and rejecting FDA's argument that "the

public's interest in the rapid movement of generic drugs into the marketplace" outweighs the first applicant's right to exclusivity); *Sandoz*, 439 F. Supp. 2d at 31-32 (rejecting argument that plaintiff's potential loss of "millions of dollars, goodwill with its customers, and other significant tangible and intangible benefits" is sufficient to justify injunctive relief that effectively would strip the first filer of its exclusivity).

Accordingly, the balance of hardships sharply tilts against the entry of injunctive relief and in favor of allowing Teva to launch its products with exclusivity on April 6.

III. THE PUBLIC INTEREST WEIGHS DECISIVELY AGAINST THE ENTRY OF INJUNCTIVE RELIEF.

Whatever the balance of hardships between the parties, the public stands to lose the most if this Court enters an injunction that effectively—and irremediably—strips Teva of its exclusivity reward. If generic companies cannot be sure that the courts will protect their right to 180-day exclusivity when it matters most, 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. Because of Teva's extraordinary investments in this product and its successful elimination of the '075 patent as a barrier to approval, consumers who depend on losartan potassium products—which have a combined $1.5 billion in current annual sales—will literally save billions of dollars over the next four years. It would be hard to imagine a result more at odds with the public interest, or with the basic purpose of the statutory scheme, than depriving Teva of its reward for delivering those extraordinary savings to American consumers. *See Teva v. Sebelius*, 595 F.3d at 1318 ("The statute's grant of a 180-day delay in multiple generic competition for the first successful paragraph IV filer is a pro-consumer device [that] Congress has chosen to induce challenges to patents claimed to support brand drugs.").

CONCLUSION

For the foregoing reasons, Teva respectfully requests that this Court deny the motions for preliminary injunctive relief and enter judgment for FDA and Teva.

Dated: March 31, 2010

Respectfully submitted,

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CERTIFICATE OF SERVICE

The undersigned certifies that on this 31st day of March, 2010, he caused a copy of the foregoing **MEMORANDUM IN OPPOSITION TO PLAINTIFFS' MOTIONS FOR PRELIMINARY INJUNCTIVE RELIEF** to be served upon the following attorneys by electronic mail and through this Court's ECF filing system:

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