**UNITED STATES DISTRICT COURT**
**FOR THE DISTRICT OF COLUMBIA**

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| **MYLAN LABORATORIES LTD.; MYLAN PHARMACEUTICALS, INC.,**<br><br>**Plaintiffs,**<br><br>**v.**<br><br>**U.S. FOOD AND DRUG ADMINISTRATION, et al.,**<br><br>**Defendants,**<br><br>**and**<br><br>**RANBAXY LABORATORIES LIMITED,**<br><br>**Intervenor-Defendant.** | **Civil Action No. 12-1637 (JDB)** |

**MEMORANDUM OPINION**

On September 28, 2012, the Food and Drug Administration ("FDA") decided that Ranbaxy Laboratories Limited ("Ranbaxy") had not forfeited its eligibility for 180-day exclusivity to market generic valsartan tablets. Because of this decision, plaintiffs Mylan Laboratories Limited and Mylan Pharmaceuticals, Inc. ("Mylan") are blocked from marketing their generic valsartan tablets. Mylan brings this action challenging FDA's decision under the Administrative Procedure Act ("APA") and the Drug Price Competition and Patent Term Restoration Act of 1984 (the "Hatch-Waxman Act"), as amended by the Medicare Modernization Act of 2003. Before the Court are Mylan's motion for a preliminary injunction to set aside FDA's September 28, 2012 decision and to require FDA to grant final approval to Mylan's abbreviated new drug application, FDA's motion to dismiss under Federal Rule of Civil Procedure 12(b)(6),

or in the alternative, for summary judgment, and intervenor-defendant Ranbaxy's motion for summary judgment. Upon consideration of the parties' motions and accompanying memoranda, the motions hearing held on December 7, 2012, and the entire record herein, the Court will deny Mylan's motion for a preliminary injunction and grant FDA's and Ranbaxy's motions.

## BACKGROUND

### I. Statutory and Regulatory Background

This is a dispute about the right to 180-day marketing exclusivity under the Hatch-Waxman Act, codified at 21 U.S.C. § 355 and 35 U.S.C. §§ 156, 271, 282, as amended by the Medicare Modernization Act, Pub. L. No. 108-173, §§ 1101-23, 117 Stat. 2066 (2003).

To gain FDA approval to market a new drug, a pharmaceutical company must submit a new drug application ("NDA") that must include, among other things, information on the drug's chemical composition, clinical trial results showing the drug's safety and effectiveness, a description of the methods of manufacturing the drug, and proposed labeling for the drug. See 21 U.S.C. § 355(b)(1). An NDA must also include information on any patent that claims the drug or a method of using the drug. Id. FDA lists this patent information in Approved Drug Products with Therapeutic Equivalence Evaluations, a publication also known as the "Orange Book." See Mylan Pharm., Inc. v. Sebelius, 856 F. Supp. 2d 196, 200 (D.D.C. 2012); 21 C.F.R. § 314.53(e)-(f).

Pursuant to the Hatch-Waxman Act, a pharmaceutical company seeking to market a generic version of an approved drug is not required to submit an NDA and hence can avoid conducting costly and time-consuming clinical trials to show safety and effectiveness. See Mova Pharm. Corp. v. Shalala, 140 F.3d 1060, 1063 (D.C. Cir. 1998). Instead, it can submit an abbreviated new drug application ("ANDA") showing that the generic drug is "bioequivalent" to

the approved drug and meets certain chemistry and labeling requirements. See 21 U.S.C. § 355(j)(2)(A). One requirement for chemistry relates to a drug's strength, quality, and purity. "Monographs" setting forth test methods and drug specifications for determining strength, quality, and purity are published in an official compendium called the United States Pharmacopeia ("USP"), and if a USP monograph exists for an approved drug, an ANDA referencing that drug must meet the standards set forth in the monograph to gain FDA approval. See 21 U.S.C. §§ 321(j), 351(b).

In addition, an ANDA must contain one of four certifications as to each Orange Book-listed patent claiming the approved drug or a method of using the approved drug. The four certifications are: (I) that there is no patent information; (II) that the patent has expired; (III) that the patent is set to expire on a certain date ("paragraph III certification"); or (IV) that the patent is invalid or will not be infringed by the generic drug ("paragraph IV certification"). Id. § 355(j)(2)(A)(vii)(I)-(IV). If an ANDA applicant makes one of the first two certifications, FDA may approve the ANDA immediately. Id. § 355(j)(5)(B)(i). If an ANDA applicant makes a paragraph III certification, FDA may grant tentative approval of the ANDA, to be made effective on the date the patent expires. Id. § 355(j)(5)(B)(ii).

The effect of a paragraph IV certification is more complex. By statute, making a paragraph IV certification constitutes an act of patent infringement. See 35 U.S.C. § 271(e)(2)(A). An ANDA applicant that makes a paragraph IV certification must notify the patent holder of the certification, and the patent holder then has 45 days to bring a patent infringement suit against the ANDA applicant. See 21 U.S.C. § 355(j)(2)(B), (5)(B)(iii). If the patent holder does not bring suit within 45 days, FDA may approve the ANDA immediately. See id. § 355(j)(5)(B)(iii). But if the patent holder sues the ANDA applicant, then FDA must delay

approval for 30 months. See id.

To incentivize generic manufacturers to risk exposing themselves to patent infringement litigation, and thereby to bring lower-priced generic drugs to consumers faster, Congress provided that, for a given drug, the "first applicant" to file an ANDA containing a paragraph IV certification is eligible for a 180-day period of marketing exclusivity. 21 U.S.C. § 355(j)(5)(B)(iv). During this period, FDA may not approve any later-filed ANDAs, thus allowing the first applicant to sell its generic drug without competition from other generic manufacturers. See Mylan, 856 F. Supp. 2d at 201.

The 180-day exclusivity period may be forfeited, however. In the Medicare Modernization Act of 2003, Congress added to the Hatch-Waxman scheme six "forfeiture events"; if any one of these events occurs, a first applicant forfeits its entitlement to 180-day exclusivity. See 21 U.S.C. § 355(j)(5)(D)(i)-(ii); Teva Pharms. USA, Inc. v. Sebelius, 595 F.3d 1303, 1306 (D.C. Cir. 2010). One such forfeiture event, and the only one at issue here, is "[f]ailure to obtain tentative approval." See 21 U.S.C. § 355(j)(5)(D)(i)(IV). A first applicant forfeits exclusivity if it "fails to obtain tentative approval of the application within 30 months after the date on which the application is filed, unless the failure is caused by a change in or a review of the requirements for approval of the application imposed after the date on which the application is filed." Id. FDA has interpreted this forfeiture provision to establish a "bright-line rule" and has made clear that to invoke the exception to the rule, a first applicant cannot show merely that FDA changed or reviewed the requirements for approval but must also show that "one or more issues holding up tentative approval at the 30 month date [was] causally connected to the approval requirements that FDA reviewed or changed." Mem. from Martin Shimer, Branch Chief, Regulatory Support Branch, Office of Generic Drugs ("OGD"), on 180-Day

Exclusivity for Valsartan Tablets 1-2 (Sept. 28, 2012) [AR 1-12] ("Forfeiture Memo").

But-for causation is not required to meet this exception. Id. That is, "[i]f one of the causes of failure to get tentative approval by the 30-month forfeiture date was a change in or review of the requirements for approval imposed after the application was filed, an applicant will not forfeit eligibility even if there were other causes for failure to obtain tentative approval by the 30-month forfeiture date that were not caused by a change in or review of the requirements for approval." Id. Hence, "an applicant need only show that acceptability of one aspect of the ANDA (e.g., chemistry) was delayed due to a change in or review of the requirements for approval, irrespective of what other elements may also have been outstanding at the 30-month date." Id.

## II. Factual and Procedural Background

On December 28, 2004, Ranbaxy filed an ANDA to market a generic version of valsartan tablets (40 mg, 80 mg, 160 mg, and 320 mg), a hypertension drug currently marketed by Novartis Pharmaceuticals Corp. under the brand name Diovan. Id. at 3. Three patents for Diovan are listed in the Orange Book: U.S. Patent Nos. 5,399,578 (the '578 patent), 5,972,990 (the '990 patent), and 6,294,197 (the '197 patent). Ranbaxy's Mem. in Supp. of Mot. for Summ. J. [ECF 38] ("Ranbaxy MSJ") 11. Ranbaxy's ANDA contained a paragraph III certification as to the '578 patent, a paragraph IV certification as to the '197 patent, and, not relevant here, a "section viii statement" for the '990 patent. Id.[1] Because Ranbaxy's ANDA was the first to contain a paragraph IV certification as to a Diovan patent, Ranbaxy was a "first applicant" eligible for 180-

[1] See 21 U.S.C. § 355(j)(2)(A)(viii); Purepac Pharm. Co. v. Thompson, 354 F.3d 877, 880 (D.C. Cir. 2004) (explaining differences between paragraph IV certifications and section viii statements).

day exclusivity. See id.

Ranbaxy did not receive tentative approval within 30 months, however. As of June 28, 2007, 30 months after Ranbaxy's ANDA was filed, bioequivalence had been found acceptable, but the elements of chemistry and labeling remained outstanding. Forfeiture Memo 5. Between the filing of Ranbaxy's ANDA and the June 28, 2007 forfeiture date, there had been changes to the approval requirements for both labeling and chemistry. First, on November 22, 2006, FDA approved a labeling supplement for Diovan that consisted of changes to three sections of the drug's labeling. Id. at 7 & n.11. Second, on May 1, 2007 (about two months before the 30-month forfeiture date), a new USP monograph for valsartan became official. See id. at 4-5. Ranbaxy thereafter submitted, on June 26, 2007, a chemistry amendment to its ANDA proposing changes to its drug substance specifications and test methods to comply with the USP monograph. Id. at 5. During a telephone conference on July 2, 2007, FDA asked Ranbaxy to provide data showing equivalence between Ranbaxy's in-house test methods and the methods set forth in the new USP monograph. Id. at 6. Ranbaxy submitted another chemistry amendment on July 5, 2007. Id.

After reviewing Ranbaxy's chemistry amendments, FDA tentatively approved Ranbaxy's ANDA on October 25, 2007, nearly four months after the 30-month forfeiture date. Id. at 4, 6. On that date, FDA sent Ranbaxy a letter informing Ranbaxy that its ANDA was tentatively approved and stating: "This letter does not address issues related to the 180-day exclusivity provisions under section 505(j)(5)(B)(iv) of the [Federal Food, Drug, and Cosmetic] Act, except to note that for purposes of sections 505(j)(5)(B)(iv) and 505(j)(5)(D)(i)(IV), the agency regards the change in the USP monograph for Valsartan, published on May 1, 2007, in response to which you submitted an amendment on June 17, 2007, to be a change in the requirements for approval

imposed after the date on which your ANDA was filed." Letter from Gary Buehler, Dir., OGD, to Ranbaxy (Oct. 25, 2007) [AR 14-16]. In the letter, FDA made no determination on whether this change caused Ranbaxy's failure to obtain tentative approval by the 30-month forfeiture date. See id.[2]

About a year later, on September 15, 2008, Mylan filed an ANDA to market a generic version of valsartan tablets. Mylan's Mot. for Prelim. Inj. [ECF 17] ("Mylan PI Mot."), Declaration of Wayne Talton [ECF 17-5] ("Talton Decl.") ¶ 4. Like Ranbaxy's ANDA, Mylan's ANDA contained a paragraph III certification as to the '578 patent, a paragraph IV certification as to the '197 patent, and a section viii statement for the '990 patent. Id. ¶ 6. Because Mylan knew that Ranbaxy had not obtained tentative approval before the 30-month forfeiture date, and was "not aware of any change in or review of the relevant approval requirements," it "understood and believed" that its ANDA would be eligible for final approval on September 21, 2012, the date that the pediatric exclusivity period for '578 patent was set to expire. Id. ¶ 10. As such, Mylan sent three letters – on July 24, September 17, and September 21, 2012 – to FDA seeking confirmation that Ranbaxy had forfeited its exclusivity and asking FDA to grant final approval to Mylan's ANDA on September 21, 2012. Forfeiture Memo 7-8.

On September 21, 2012, FDA made public its October 25, 2007 tentative approval letter to Ranbaxy. Talton Decl. ¶ 19. Then on September 28, FDA took three actions related to Ranbaxy's and Mylan's ANDAs. First, as set forth in a 12-page memorandum, FDA determined that Ranbaxy had not forfeited its eligibility for 180-day exclusivity because its efforts to comply

[2] According to FDA, its general practice is "to forego forfeiture decisions until an applicant that is affected by the particular forfeiture determination is eligible for tentative or final approval." FDA's Mem. in Supp. of Mot. to Dismiss or, in the Alternative, for Summ. J. [ECF 37] ("FDA MTD") 11 n.9.

with the USP monograph, and FDA's review thereof, "were a cause of" Ranbaxy's failure to obtain tentative approval within 30 months. Forfeiture Memo 12. FDA therefore found it unnecessary to determine whether the November 22, 2006 labeling change was also a cause of the failure to obtain tentative approval. Id. at 7. Second, FDA tentatively approved Mylan's ANDA. Mylan PI Mot., Letter from Gregory P. Geba, Dir., OGD, to Mylan [ECF 17-10] 1 (Sept. 28, 2012). FDA explained that it was "unable at [that] time to grant final approval to [Mylan's] ANDA because another applicant [Ranbaxy] submitted an ANDA" before Mylan. Id. at 2. Hence, Ranbaxy's ANDA was "eligible for 180-day exclusivity" and Mylan's ANDA would be "eligible for final approval upon the expiration of [Ranbaxy's] 180-day exclusivity . . . or [upon] that exclusivity [being] otherwise resolved." Id. Third, FDA responded to Mylan's letters, stating:

> FDA has carefully considered the arguments set forth in Mylan's three letters in determining that the ANDA sponsor [Ranbaxy] that is eligible for 180-day exclusivity has not forfeited its eligibility. Due to the regulatory restriction on disclosure of information in an unapproved ANDA, however, we cannot provide you the basis on which the Agency determined that the first applicant for valsartan tablets has not forfeited its eligibility because that analysis rests on confidential information contained in that application. FDA appreciates the challenge this presents to you and other parties affected by a forfeiture analysis, but the Agency is nonetheless prohibited at this time from disclosing any additional information regarding the forfeiture decision.

Mylan PI Mot., Letter from Robert L. West, Deputy Dir., OGD, to William A. Rakoczy [ECF 17-10] 4 (Sept. 28, 2012) (footnote omitted).[3]

Mylan now stands ready to market its generic valsartan tablets but is prevented from doing so by Ranbaxy's continuing eligibility for 180-day exclusivity. Mylan filed an action in

[3] FDA did, however, address and reject Mylan's "more general argument" that FDA could not find that the publication of or a change in a USP monograph constituted "a change in or a review of the requirements for approval" supporting an exception to forfeiture.

this Court on October 2, 2012, and moved for a preliminary injunction two days later. FDA has moved to dismiss Mylan's complaint or, in the alternative, for summary judgment. Ranbaxy intervened as a defendant under Federal Rule of Civil Procedure 24(a)(2) and has also moved for summary judgment.

## STANDARD OF REVIEW

A plaintiff seeking a preliminary injunction must show (1) a likelihood of success on the merits, (2) a likelihood of irreparable harm in the absence of an injunction, (3) that the balance of equities tips in its favor, and (4) that an injunction is in the public interest. Winter v. Natural Res. Def. Council, Inc., 555 U.S. 7, 20 (2008). These four factors have historically been evaluated on a "sliding scale," such that "an unusually strong showing" on one factor could make up for a weaker showing on another factor. See Davis v. Pension Guar. Corp., 571 F.3d 1288, 1291-92 (D.C. Cir. 2009). The Supreme Court's decision in Winter, however, has called this "sliding scale" approach into question. See id. at 1296 (Kavanaugh, J., concurring); see also Sherley v. Sebelius, 644 F.3d 388, 393 (D.C. Cir. 2011). Regarding the first two factors in particular, the D.C. Circuit has read Winter "to suggest if not to hold 'that a likelihood of success is an independent, free-standing requirement for a preliminary injunction,'" Sherley, 644 F.3d at 393 (quoting Davis, 571 F.3d at 1296 (Kavanaugh, J., concurring)), and it has made clear that a showing of some irreparable harm is an "independent prerequisite" for a preliminary injunction, see Sierra Club v. Dep't of Energy, 825 F. Supp. 2d 142, 148 (D.D.C. 2011) (citing Chaplaincy of Full Gospel Churches v. England, 454 F.3d 290, 297 (D.C. Cir. 2006)). The Court need not now decide whether both a likelihood of success on the merits and a likelihood of irreparable harm must independently be shown, however, because it concludes that Mylan has not made a sufficient showing on either factor.

Ordinarily, a motion to dismiss under Federal Rule of Civil Procedure 12(b)(6) should be granted if the complaint does not contain "sufficient factual matter, accepted as true, to 'state a claim to relief that is plausible on its face.'" See Ashcroft v. Iqbal, 556 U.S. 662, 678 (2009) (quoting Bell Atlantic Corp. v. Twombly, 550 U.S. 544, 570 (2007)). And ordinarily, summary judgment is appropriate if the pleadings and evidence show that "there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." See Fed. R. Civ. P. 56(a).

In reviewing agency action under the APA, however, a district court "sits as an appellate tribunal" to decide questions of law based on the administrative record. See Marshall Cnty. Health Care Auth. v. Shalala, 988 F.2d 1221, 1222-23 (D.C. Cir. 1993). As a result, the usual standards do not apply, and in this context "the legal questions raised by a 12(b)(6) motion and a motion for summary judgment are the same." See id.; see also Hi-Tech Pharmacal Co. v. FDA ("Hi-Tech II"), 587 F. Supp. 2d 13, 18 (D.D.C. 2008). But cf. Marshall Cnty. Health Care Auth., 988 F.2d at 1226 n.5 ("It is probably the better practice for a district court always to convert to summary judgment . . . ."). "Under the APA, it is the role of the agency to resolve factual issues to arrive at a decision that is supported by the administrative record, whereas the function of the district court is to determine whether or not as a matter of law the evidence in the administrative record permitted the agency to make the decision it did." Hi-Tech II, 587 F. Supp. 2d at 18 (internal quotation marks omitted).

## DISCUSSION

### I. Mylan's Motion for a Preliminary Injunction

#### A. Likelihood of Success on the Merits

The probability of success on the merits is informed by the deferential standard of review

under the APA. FDA's no-forfeiture decision may be set aside if it is "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." See 5 U.S.C. § 706(2)(A). Arbitrary and capricious review is "fundamentally deferential," especially on "'matters relating to [an agency's] areas of technical expertise.'" Fox v. Clinton, 684 F.3d 67, 75 (D.C. Cir. 2012) (quoting Tripoli Rocketry Ass'n v. Bureau of Alcohol, Tobacco, Firearms, & Explosives, 437 F.3d 75, 77 (D.C. Cir. 2006)). But this deference is not absolute. An agency's decision "must be the product of reasoned decisionmaking." See id. at 74-75; see also Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co., 463 U.S. 29, 43 (1983). The APA does not require "a model of analytic precision" – "a decision of less than ideal clarity" may be upheld "if the agency's path may be reasonably discerned" – yet at a minimum, the agency's explanation must contain "a rational connection between the facts found and the choice made." See Dickson v. Sec'y of Def., 68 F.3d 1396, 1404 (D.C. Cir. 1995) (internal quotation marks omitted). Agency action may also be arbitrary and capricious if it is "inconsistent with the statutory mandate" or "frustrate[s] the policy that Congress sought to implement." See Beaty v. FDA, 853 F. Supp. 2d 30, 41 (D.D.C. 2012) (quoting FEC v. Democratic Senatorial Campaign Comm., 454 U.S. 27, 32 (1981) (internal quotation marks omitted)).[4]

1. Lack of reasoned decisionmaking

[4] To the extent that FDA's decision turned on its interpretation of the tentative approval forfeiture provision, this Court's review is governed by the familiar Chevron framework. See Chevron, U.S.A., Inc. v. Natural Res. Def. Council, Inc., 467 U.S. 837, 842-43 (1984); Mylan Labs., Inc. v. Thompson, 389 F.3d 1272, 1280 (D.C. Cir. 2004) (giving Chevron deference to FDA letter decision). But Mylan does not argue that FDA's interpretation of the forfeiture provision is incorrect. As discussed below, Mylan does not challenge FDA's determination that there was a change in the requirements for approval and apparently accepts FDA's seven-factor test for determining whether a failure to obtain tentative approval was "caused by" a change in USP requirements. Rather, Mylan's primary argument is that FDA has not given a rational or reasoned basis for its decision on causation.

FDA determined that (1) the May 1, 2007 publication of the USP monograph for valsartan constituted a change in the requirements for approval of Ranbaxy's ANDA, and (2) this change was a cause of Ranbaxy's failure to obtain tentative approval by the 30-month forfeiture date. Forfeiture Memo 6, 12. Mylan does not challenge the determination that there was a change in the requirements for approval; it challenges only the causation determination, and argues that FDA has given no rational or reasoned explanation for determining that publication of the USP monograph caused the delay in tentative approval. See 12/7/12 Tr. of Mot. Hr'g 27. Thus, the question for this Court is whether FDA's causation determination was based on reasoned decisionmaking. See Fox, 684 F.3d at 75.

In its September 28, 2012 decision, FDA explained that whether publication of or a change in a USP monograph has caused a failure to obtain tentative approval is "a very fact-specific question" involving "a number of potential factors." Forfeiture Memo 11. These factors include, but are not limited to: (1) "whether the monograph change is in a proposed or final monograph," (2) "the timing of any publication of or change in a monograph in relation to a particular 30-month forfeiture date," (3) "whether FDA requires compliance with the new/changed compendial standard [i.e., the USP]," (4) "whether the [FDCA] requires compliance with the new/changed compendial standard," (5) "the consistency of the new/changed monograph with pre-existing approval requirements," (6) "the nature and timing of the sponsor's efforts to comply with USP monographs," and (7) "[the nature and timing] of FDA's review of such efforts." Id.

FDA explained the basis for its decision that there was causation and hence no forfeiture as follows:

On May 1, 2007, approximately two months prior to the 30-month forfeiture date,

a new USP monograph for the drug substance, Valsartan, became official. In response, Ranbaxy submitted a chemistry amendment on June 26, 2007, two days before the 30-month forfeiture date, to revise its drug substance specifications and test methods to comply with the monograph. Specifically, Ranbaxy proposed the following changes to its drug substance specifications and test methods:

Changes in drug substance specifications:

- Requirement for identification test by IR test redefined to include USP reference standard
- Limits and requirements for Absorbance test revised as per USP monograph
- Changes in related compounds in line with USP monograph

    a. Criteria of 'Any other individual impurity' has been redefined to 'Any other individual impurity (Excluding Valsartan related compound A)'
    b. Limits of 'Isoleucine analog of Valsartan' and 'Any other individual impurity (Excluding Valsartan related compound A)' have been revised
    c. Chemical name of Valsartan related compound A, Valsartan related compound B and Valsartan related compound C has been updated in line with USP 30
    d. Additional note for 'In-house limits' incorporated for Valsartan related compound A and Any other individual impurity (Excluding Valsartan related compound A)

Changes in the drug substance test methods:

- Requirement for the IR test redefined and method for absorbance incorporated
- Method for 'Related Compound A' and 'Assay' updated in line with USP 30
- Parameter for sensitivity incorporated under the method for particle size
- Limit of quantification and the origin for Valsartan related compound A incorporated in line with validation.

Ranbaxy also provided copies of its revised drug substance specifications and test methods reflecting these changes. On July 2, 2007, FDA held a telephone conference with Ranbaxy, during which the Agency asked the firm to provide data to show equivalence between Ranbaxy's in-house test methods and the USP methods. Ranbaxy responded with a chemistry amendment on July 5, 2007. The amendment was reviewed and the ANDA was tentatively approved on October

> 25, 2007. As noted above, in the tentative approval letter, FDA stated that the USP monograph constituted a change in the requirements for approval, but the Agency did not make any determination as to whether the change caused Ranbaxy's failure to obtain tentative approval by the 30-month forfeiture date.
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> Upon the foregoing, FDA concludes that publication of the official USP drug substance monograph for valsartan with which Ranbaxy had to comply prior to approval constituted a change in the requirements for approval. FDA further concludes that Ranbaxy's effort to comply with this new requirement, and FDA's review of that effort, was a cause of Ranbaxy's failure to obtain tentative approval by the 30-month forfeiture date.

Id. at 5-6 (footnotes omitted).

Mylan contends that FDA's decision lacks any reasoned explanation and states only a bare conclusion. Mylan's Reply Mem. in Supp. of PI Mot. [ECF 44] ("Mylan Reply") 3-4. Mylan's chief complaint is that FDA did not apply the seven-factor test set forth in its own decision, and it focuses in particular on the lack of discussion of the fifth factor, "the consistency of the new/changed monograph with pre-existing approval requirements." See Mylan Reply 5-6; 12/7/12 Tr. 13.

Putting aside this factor for a moment, FDA's decision addressed the remaining six factors, albeit not in a formulaic recitation. First, FDA noted that the USP monograph was not merely proposed but became "official," i.e., final, on May 1, 2007 (factor 1). Second, FDA noted the timing of publication – "approximately two months prior to the 30-month forfeiture date" (factor 2). Third, FDA stated that Ranbaxy "had to" comply with the monograph, and indeed both FDA and the FDCA require compliance with official USP monographs (factors 3 and 4). See 21 U.S.C. §§ 321(j), 351(b); see also, e.g., Mylan's Supp'l Mem. in Supp. of PI Mot. [ECF 31] ("Mylan Supp'l Mem."), Letter [ECF 30-2] ("Doryx Letter") 8. Finally, FDA discussed the nature (proposed changes to Ranbaxy's drug substance specifications and test methods) and timing (two days before the 30-month forfeiture date) of Ranbaxy's efforts to comply with the

new USP monograph, and concluded that these efforts, and FDA's review thereof, caused the delay in tentative approval (factors 6 and 7). See Forfeiture Memo 5-6, 11.

Mylan argues, however, that the missing factor – the consistency of the USP monograph with pre-existing approval requirements – is the critical factor, and that FDA's failure to discuss it renders its no-forfeiture decision arbitrary and capricious. See 12/7/12 Tr. 10-11. FDA responds that this factor "isn't all that relevant" in this case, because before the May 1, 2007 publication of the USP monograph for valsartan, there were no standards set forth in a USP monograph or other official compendium. Id. at 35. Rather, as counsel for FDA represented at the motions hearing, the pre-existing approval requirements were "things that FDA and Ranbaxy had agreed upon," through a back-and-forth process, to show that Ranbaxy was making a drug that was sufficiently similar to Diovan. See id.;[5] see also id. at 44 (counsel for Ranbaxy discussing fact that in this case there was no pre-existing USP monograph so publication of the new monograph was necessarily a change in requirements).

The Court agrees with Mylan that this factor – the consistency of the monograph with

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[5] Counsel for FDA explained the pre-USP requirements as follows:

> And that's why – predominantly why that factor, the consistency of the new/changed monograph with pre-existing requirements is not – isn't all that relevant here. Because no matter what the pre-exising requirements were, they weren't set forth in any USP monograph. They were things that FDA and Ranbaxy had agreed upon. I mean, essentially, Your Honor, you go back to what does [the] ANDA have to show to get approval? Well, you have to show that you're making the same drug in many respects as the RLD, as the innovative drug.
>
> So until there's a USP monograph, that's being governed by the drug companies sort of doping out, "[H]ow do I make this drug? What are the tests? What are the specs?" Submitting it to the FDA. FDA is saying, "Well, you're close, but we'd like to see you do this test, do that test."
>
> Those were the pre-existing requirements.

12/7/12 Tr. 35.

pre-existing requirements – should be considered in the causation analysis. If this factor is not part of the analysis, and only the other factors need be considered, then the causation analysis approaches a bright-line test. Considering those factors alone, nearly any publication of a new, official USP monograph close to the 30-month forfeiture date would be sufficient to "cause" a delay in tentative approval. The Court will not give the forfeiture exception this interpretation. Causation in this context requires a showing of something more than just the fact and timing of a USP monograph publication.

Here, however, FDA's decision reveals that it was based on more than just the fact and timing of the monograph's publication. The Forfeiture Memo discusses Ranbaxy's efforts to comply with the monograph, listing the specific changes to drug substance specifications and test methods proposed by Ranbaxy. See Forfeiture Memo 5-6. It is true, as Mylan points out, that FDA's summary of these proposed changes repeats verbatim the language used by Ranbaxy in its June 26, 2007 amendment to its ANDA. See 12/7/12 Tr. 13; Letter from Sean M. Russell, Senior Regulatory Affairs Assoc., Ranbaxy, to OGD, FDA (June 26, 2007) [AR 18-21]. But the fact that FDA used Ranbaxy's own words to give an accurate description of the proposed changes does not mean that FDA failed to consider the substance of the changes in making its forfeiture determination. As noted in the Forfeiture Memo, upon review of Ranbaxy's amendment, FDA had a telephone conference with Ranbaxy, at which it asked Ranbaxy to provide data to show equivalence between its in-house test methods and the USP methods. Forfeiture Memo 6. Ranbaxy gave FDA the data it asked for, and more than three months later FDA tentatively approved Ranbaxy's ANDA. Id.

FDA's "path" to its conclusion on causation is not difficult to decipher. Compare, e.g., Transcon. Gas Pipe Line Corp. v. FERC, 518 F.3d 916, 922 (D.C. Cir. 2008) ("Here we can

discern the Commission's path . . . ."); with Dickson, 68 F.3d at 1405 (finding it "impossible to discern the Board's 'path'"). A new, final USP monograph was published; Ranbaxy made an initial effort to comply with the monograph; FDA then asked for more data; Ranbaxy gave FDA more data; and because FDA had to review Ranbaxy's amendments and the additional data to ensure that Ranbaxy's drug substance specifications and test methods met the standards set forth in the new monograph, tentative approval was delayed. This connection between the specific facts and FDA's conclusion is apparent from the face of the Forfeiture Memo and is both logical and rational. See Fox, 684 F.3d at 75; Dickson, 68 F.3d at 1404-05. And on this technical subject of drug substance specifications and test methods, such as "the [infrared] test" and "the method for particle size," the Court finds it particularly appropriate to defer to FDA's expertise. See Tripoli, 437 F.3d at 77; Forfeiture Memo 6.

Mylan, stressing the consistency-with-pre-existing-requirements factor, argues that a rational connection is lacking because FDA asked for data to show equivalence between Ranbaxy's in-house test methods and the USP methods. Hence, Mylan's argument goes, "[i]f whatever Ranbaxy was doing was the same as what the monograph did," it is unclear from FDA's decision how a change, if any, could have caused the delay in tentative approval. See 12/7/12 Tr. 14-15. But this misses the point that FDA and Ranbaxy have made. See 12/7/12 Tr. 34-35, 44. Before the USP monograph became official, Ranbaxy was not required to comply with any USP standards because none existed. After the monograph became official, Ranbaxy not only had to comply with the standards set forth in the USP monograph but also had to show FDA that it was in compliance. FDA would not have asked for data to show equivalence if it already had such data. So even if "whatever Ranbaxy was doing was the same as what the monograph did," FDA still had to verify that the methods were equivalent, and in this case that process delayed tentative

approval. Moreover, by focusing on Ranbaxy's July 5, 2007 submission of data showing equivalence, Mylan glosses over the fact that Ranbaxy's initial amendment proposed changes to bring its drug substance specifications and test methods into compliance with the USP monograph and was still pending on the 30-month forfeiture date. The consistency of the monograph with pre-existing approval requirements mattered to FDA's decision because (1) the monograph was new and set USP-specific requirements, and (2) the time that it took Ranbaxy to both make responsive changes and show that some of its existing methods met the new requirements, and for FDA to review these efforts, spanned a period of more than three months. It does not take guesswork to see that, regardless of any case-by-case standards that existed before the USP monograph became official, the imposition of USP standards for the first time, and the specific sequence of events that took place thereafter, led FDA to conclude that the publication of the monograph was a cause of the delay in tentative approval.

Finally, the Court rejects Mylan's contention that the May 1, 2007 publication of the USP monograph could not have caused the delay in tentative approval because a proposed monograph almost identical to the final one had been published in January-February 2006, some 14 months before the 30-month forfeiture date. According to Mylan, Ranbaxy knew that it would be required either to comply with the proposed monograph or to use an acceptable alternative method. Mylan Supp'l Mem. 6-7. To the contrary, however, Ranbaxy was not required to comply with the January-February 2006 proposed monograph. In general, the FDCA and FDA require ANDA applicants to comply with official, final USP monographs, but not with proposed USP monographs. See 21 U.S.C. §§ 321(j), 351(b); FDA MTD 20-21; Ranbaxy MSJ 20-24.[6] In

[6] Indeed, Mylan has itself previously recognized and relied on FDA's general practice of not requiring compliance with proposed USP monographs. See FDA MTD 20 & n.12 (citing

special cases, FDA may require or request an applicant to comply with a proposed monograph, but it did not do so here. See, e.g., Doryx Letter 9-10. In addition, the January-February 2006 proposed monograph was only the most recent of six proposed monographs for valsartan, the first of which was published in 1999, yet Mylan has not given any reason as to why Ranbaxy should have known that the January-February 2006 proposed monograph would become official in substantially the same form. See FDA MTD 23 n.14; Ranbaxy MSJ 25-27. Because Ranbaxy had no obligation to comply with the January-February 2006 proposed USP monograph, it was not a pre-existing requirement for purposes of the "consistency" factor discussed above, and consequently, the fact that FDA did not address the proposed monograph does not undermine its decision.

2. Contrary to congressional intent

Mylan also argues that FDA's decision was arbitrary and capricious because it frustrates the congressional policy underlying the Hatch-Waxman Act. See Mylan Reply 10-12 (citing Barnett v. Weinberger, 818 F.2d 953, 964 (D.C. Cir. 1987); Beaty, 853 F. Supp. 2d at 41). The Court is not persuaded.

Citing this Court's decision in Hi-Tech Pharmacal Co. v. FDA ("Hi-Tech I"), Mylan states that the goal of the forfeiture provisions is to "'ensure that the 180–day exclusivity period enjoyed by the first generic to challenge a patent cannot be used as a bottleneck to prevent additional generic competition.'" Mylan Supp'l Mem. 11 (quoting 587 F. Supp. 2d 1, 4 (D.D.C. 2008)); Mylan Reply 11 (same). Mylan argues that FDA's forfeiture decision frustrates this goal because it lets Ranbaxy "indefinitely bottleneck the entire generic valsartan market," and thereby also

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Mylan letters at AR 131, 147); Ranbaxy MSJ 22-23 (citing AR 147-48).

frustrates Hatch-Waxman's overarching goal of getting generic drugs to consumers. Mylan Reply 11-12.

Mylan is correct that in enacting the Hatch-Waxman Act Congress sought to promote generic competition. However, Congress created the 180-day exclusivity period for that very purpose and included in the statute an express exception to forfeiture for delays in tentative approval caused by changes in approval requirements beyond an ANDA applicant's control. Stripping Ranbaxy of exclusivity where, as FDA has determined, its failure to obtain tentative approval was caused by a change in approval requirements would contravene congressional intent as expressly stated in the exception. It also would deprive Ranbaxy of its anticipated reward for "stick[ing] out [its] neck[] (at the potential cost of a patent infringement suit)" by challenging Novartis's patent and, at least in theory, decrease the expected returns from future generic challenges to patents claiming brand drugs. See Teva, 595 F.3d at 1318.

Here, FDA has applied the tentative approval forfeiture provision and its exception to the facts of this case as it sees them. Considering the purposes of not only the forfeiture provision, as Mylan does, but also the exception and the exclusivity incentive created by Congress, the Court will not set aside FDA's decision on the ground that it frustrates the congressional policy underlying Hatch-Waxman.[7]

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[7] Mylan makes two additional arguments challenging FDA's causation determination, but neither is persuasive. First, Mylan argues that the publication of the USP monograph could not have caused the delay in approval because FDA has said that "unsolicited amendments to account for USP monograph updates . . . are 'routine or administrative in nature' and 'will not lengthen or impact the original [ANDA] review goal date' under the [Generic Drug User Fee Act] program." Mylan Supp'l Mem. 8-9 (first alteration in original). But the statement quoted was made in a different context relating to FDA's internal goals for reviewing ANDAs and was not intended to apply to fact-specific forfeiture determinations. See FDA MTD 25 & n.16. Moreover, it refers to unsolicited amendments to a pending ANDA that are "routine or administrative in nature and do not require scientific review (e.g., requests for final ANDA

3. Failure to actively pursue ANDA approval

Mylan's final argument in support of its likelihood of success on the merits is that Ranbaxy is "not actively pursuing approval" of its ANDA and hence FDA must grant immediate, final approval to Mylan's ANDA. See 21 C.F.R. § 314.107(c)(3).[8] The Court concludes, however, that Mylan has raised this argument too late.

"It is a hard and fast rule of administrative law, rooted in simple fairness, that issues not raised before an agency are waived and will not be considered by a court on review." Nuclear Energy Inst., Inc. v. EPA, 373 F.3d 1251, 1297 (D.C. Cir. 2004) (per curiam). Despite having sent three separate letters to FDA on the issue of Ranbaxy's eligibility for exclusivity, Mylan did not argue to FDA that Ranbaxy was not actively pursuing approval of its ANDA. Because FDA has not had a chance to consider this new argument, this Court will not consider it in the first

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approval, patent amendments, general correspondence, and USP monograph updates)," yet Ranbaxy's June 26, 2007 chemistry amendment did "require scientific review" and the USP monograph for valsartan was not "update[d]" but published for the first time. See id. at 24.

Second, Mylan argues that FDA's decision leads to absurd results. See Mylan Supp'l Mem. 9-11. Mylan tries to fault FDA for not mentioning that the USP monograph for valsartan was revised in May-June 2007, after it was published on May 1, and argues that FDA could not conclude that the May 1 publication, but not the later revision, "caused" Ranbaxy's failure to obtain tentative approval within 30 months. As Mylan well knows, however, but for causation is not required, so if the May 1 change was a cause of the delay, it would not matter whether a later change also contributed to the delay. See Forfeiture Memo 2. And FDA has not effectively rewarded Ranbaxy with exclusivity for "sitting on its hands until just two days before the [tentative approval] deadline." See Mylan Supp'l Mem. 10-11. As discussed above, Ranbaxy was not required to comply with the USP monograph until May 1, 2007, and Mylan has not argued that a responsive amendment submitted within two months of a change shows a lack of diligence.

[8] "[I]f FDA concludes that the applicant submitting the first application is not actively pursuing approval of its abbreviated application, FDA will make the approval of subsequent abbreviated applications immediately effective if they are otherwise eligible for an immediately effective approval." 21 C.F.R. § 314.107(c)(3).

instance.[9]

Also, Mylan raised this argument for the first time in this Court in its reply memorandum in support of its motion for a preliminary injunction and in opposition to FDA's and Ranbaxy's motions. Mylan did not so much as mention the pertinent regulation, 21 C.F.R. § 314.107(c)(3), in its complaint, its motion for a preliminary injunction, or its supplemental memorandum in support. Though Mylan tries to characterize its new argument as one raised "in opposition to a summary judgment and a dismissal motion" rather than as one raised in a reply, Mylan's memorandum presents Ranbaxy's alleged failure to actively pursue approval of its ANDA as an "additional, independent reason" that "Mylan has a strong likelihood of success on the merits," i.e., as an additional, independent reason in support of its affirmative claim for preliminary injunctive relief. See Mylan Reply 13, 17. For this reason as well, Mylan's new argument is waived. See Jones v. Mukasey, 565 F. Supp. 2d 68, 81 (D.D.C. 2008) (citing, inter alia, Am. Wildlands v. Kempthorne, 530 F.3d 991, 1001 (D.C. Cir. 2008)) (not considering arguments raised for first time in reply); see also Morrison v. Sec'y of Def., 802 F. Supp. 2d 6, 11 n.3

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[9] At the motions hearing, Mylan asserted that making its new argument to FDA would be futile because FDA "wrote six pages in [its] reply" rejecting the merits of that argument, and thus the futility exception to exhaustion should apply here. See 12/7/12 Tr. 22. But the futility exception is "quite restricted" and "limited to situations when resort to administrative remedies would be clearly useless." Tesoro Ref. Mktg. Co. v. FERC, 552 F.3d 868, 874 (D.C. Cir. 2009) (internal quotation marks and alteration omitted). Arguments made by an agency's counsel in a reply memorandum do not establish to a "certainty" that the agency would reject an argument presented to it in the first instance. See id. (internal quotation marks omitted). Hence, the Court will not invoke the futility exception and will not reach the merits of Mylan's argument that Ranbaxy has not actively pursued ANDA approval.

Here, moreover, even if judicial consideration were appropriate, Mylan would be hard-pressed to show that FDA acted arbitrarily and capriciously by not addressing an argument based on a regulation it has never enforced. See Advocates for Highway & Auto Safety v. Fed. Motor Carrier Safety Admin., 429 F.3d 1136, 1149-50 (D.C. Cir. 2005); Mylan, 856 F. Supp. 2d at 215; Buckingham v. Mabus, 772 F. Supp. 2d 295, 300 (D.D.C. 2011); see also 12/7/12 Tr. 38.

(D.D.C. 2011) (claim not raised in complaint waived); cf. Local Civ. R. 65.1(c) (requiring application for preliminary injunction to be "supported by all affidavits on which the plaintiff intends to rely" and allowing supplemental affidavits "only with permission of the court").

B. Likelihood of Irreparable Harm

To be entitled to preliminary injunctive relief, a plaintiff must show injury that is certain, great, actual, and imminent. See Wis. Gas. Co. v. FERC, 758 F.2d 669, 674 (D.C. Cir. 1985). In the D.C. Circuit, "mere economic loss" does not, in and of itself, constitute irreparable harm. Id. at 674-75 (internal quotation marks omitted). Monetary loss, even "irretrievable" monetary loss, may constitute irreparable harm only if it is "so severe as to cause extreme hardship to the business or threaten its very existence." Hi-Tech I, 587 F. Supp. 2d at 11 (internal quotation marks omitted); Gulf Oil Corp. v. Dep't of Energy, 514 F. Supp. 1019, 1026 (D.D.C. 1981); see also Wis. Gas., 758 F.2d at 675.

Mylan alleges that absent injunctive relief it will suffer substantial, "irretrievable" financial losses, including a loss in first-year sales of up to $44.55 million, or "perhaps more." Mylan PI Mot. 27-28. But this figure represents less than one percent of Mylan's annual revenues, forecasted to be close to $7 billion this year. See FDA MTD 34 (citing Mylan's Form 10-K Annual Report, available at http://investor.mylan.com/secfiling.cfm?filingID=1193125-12-70508). Hence, even if the losses alleged were certain, which they are not, they are not "so severe as to cause extreme hardship to [Mylan's] business or threaten its very existence." See Hi-Tech I, 587 F. Supp. 2d at 11 (internal quotation marks omitted).

Mylan also claims that the harm it will suffer is not "merely economic" because it has a "statutory entitlement" to immediate final approval of its ANDA. Mylan PI Mot. 26-27.

Although courts have held that a first applicant's loss of its statutory entitlement to the 180-day exclusivity period is irreparable because once lost "it cannot be recaptured," that is not what Mylan stands to lose here. See, e.g., Apotex, Inc. v. FDA, No. 06-627, 2006 WL 1030151, at *17 (D.D.C. Apr. 19, 2006); see also Mylan, 856 F. Supp. 2d at 216-17 ("Nor can Mylan's situation be compared to those of companies that stand to lose sole market exclusivity."). Mylan contends that it stands to lose the "flip side" of exclusivity – that is, its entitlement to final approval "because there is not exclusivity, because it's been forfeited." See 12/7/12 Tr. 24-25. But the so-called entitlement that Mylan claims here is not just the "flip side" of 180-day exclusivity. Congress provided for exclusivity to encourage and reward the first generics to challenge patents for brand-name drugs. See 21 U.S.C. § 355(j)(5)(B)(iv). Even though a runner-up like Mylan might happen to benefit from a first applicant's forfeiture of exclusivity, rewarding runners-up was not Congress's object. So the "statutory entitlement" Mylan claims, unlike generic exclusivity, is not one specifically intended by Congress. In addition, the harm Mylan says it will suffer is different in kind from the loss of exclusivity because exclusivity is unique and "cannot be recaptured" if lost. See Apotex, 2006 WL 1030151, at *17. Even if FDA approved Mylan's ANDA and Mylan launched its products immediately, it would not be guaranteed exclusivity and might have to share the market with Ranbaxy and/or Ivax Pharmaceuticals, whose valsartan ANDAs have been tentatively approved. This position, as one of just a few generics in the valsartan market, is one that Mylan might attain later even if it must wait until Ranbaxy's exclusivity expires.

In short, the harm Mylan alleges – loss of actual sales, sales opportunities, long-term contracts, and other market advantages – is really just economic, and given Mylan's status as a leading generic manufacturer and its already-large market presence, the potential financial impact

on Mylan's business is too small to support a finding of irreparable harm. Mylan's inability to show that it is likely to suffer irreparable harm in the absence of injunctive relief, then, is alone grounds for denying its motion for a preliminary injunction. See Sierra Club, 825 F. Supp. 2d at 148.

Because Mylan can show neither a likelihood of success on the merits nor a likelihood of irreparable harm, Mylan is not entitled to preliminary injunctive relief, and the Court need not address the two remaining factors. See Sherley, 644 F.3d at 393; Sierra Club, 825 F. Supp. 2d at 148.

II. FDA's and Ranbaxy's Motions for Summary Judgment

The administrative record on Ranbaxy's failure to obtain tentative approval within 30 months is complete. Both FDA and Ranbaxy have filed summary judgment motions that are fully briefed. For the reasons stated in Part I.A., the Court concludes that, as a matter of law, FDA's September 28, 2012 no-forfeiture decision is supported by the administrative record and is not "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." See 5 U.S.C. § 706(2)(A); Hi-Tech II, 587 F. Supp. 2d at 22. Hence, summary judgment in favor of FDA and Ranbaxy is appropriate and will be entered.

CONCLUSION

For the foregoing reasons, Mylan's motion for a preliminary injunction will be denied, and FDA's and Ranbaxy's motions for summary judgment will be granted. A separate order accompanies this memorandum opinion.

/s/
JOHN D. BATES
United States District Judge

Dated: December 27, 2012