UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

AMNEAL PHARMACEUTICALS LLC, *Plaintiff*, v. FOOD AND DRUG ADMINISTRATION, *et al.*, *Defendants*, and LUPIN PHARMACEUTICALS, INC., *et al.*, *Intervenor-Defendants*.	Civil Action No. 17-180 (RDM)

MEMORANDUM OPINION

The Federal Food, Drug, and Cosmetic Act ("FDCA"), as amended by the Drug Price Competition and Patent Restoration Act of 1984 ("Hatch-Waxman Act") and the Medicare Prescription Drug Improvement and Modernization Act of 2003 ("Medicare Modernization Act"), grants 180 days of market exclusivity to the first generic manufacturer to file an abbreviated new drug application ("ANDA") that challenges a patent covering the brand-name version of the drug. But that right is not absolute and is subject to various statutorily defined "forfeiture events." As relevant here, an applicant who fails "to obtain tentative approval of [its ANDA] within 30 months after the date on which the [ANDA] is filed" forfeits its right to the 180 days of market exclusivity, "unless th[at] 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." 21 U.S.C. § 355(j)(5)(D)(i)(IV).

The plaintiff in this case, Amneal Pharmaceuticals LLC ("Amneal"), was the first manufacturer to file an ANDA to market a generic version of Namenda XR (memantine hydrochloride extended release capsules), and its ANDA challenged a patent held by the manufacturer of the brand-name version of the drug. Amneal did not, however, obtain tentative approval for its ANDA within the 30-month window. As a result, Amneal's eligibility for the 180 days of generic market exclusivity turns on whether its failure to obtain timely approval was "caused by a change in or a review of the requirements for approval of the" ANDA. In proceedings before the Food and Drug Administration ("FDA"), Amneal argued (1) that the delay was caused by the FDA's demand for data from a commercial-scale batch of the drug and (2) that this demand constituted a change in a requirement for approval of the ANDA. The FDA disagreed on both counts. Amneal, in response, brought the present action pursuant to the Administrative Procedure Act ("APA"), 5 U.S.C. § 701 *et seq.*, challenging the FDA's decision.

The case is now before the Court on Amneal's motions for summary judgment, Dkt. 25, and for a preliminary injunction or, in the alternative, a temporary restraining order, Dkt. 62, and the cross-motions for summary judgment filed by the FDA, Dkt. 34, and intervenor-defendant Lupin Pharmaceuticals ("Lupin"), Dkt. 30. Although Amneal raises a host of other issues, the heart of the dispute is whether the FDA's request that Amneal supplement its ANDA with data from a commercial-scale batch, as opposed to data from the pilot-scale batches that Amneal originally submitted, constituted a "change in . . . the requirements for approval of" Amneal's ANDA—or, more precisely, whether the FDA's decision that the request did not was contrary to law or otherwise unreasonable. As explained below, the Court concludes that the FDA acted within its authority and reasonably in rejecting Amneal's claim to market exclusivity. The Court will, accordingly, deny Amneal's motion for summary judgment, Dkt. 25, and will grant the

FDA's and Lupin's cross-motions for summary judgment, Dkt. 30; Dkt. 34. Moreover, having resolved the case on the merits, the Court will deny Amneal's motion for a preliminary injunction or, the alternative, a temporary restraining order, Dkt. 62, as moot.

I. BACKGROUND

A. Statutory and Regulatory Background

To obtain approval to market a new drug, the innovator-manufacturer must submit a new drug application ("NDA") to the FDA that contains extensive information and data, including "full reports of investigations which have been made to show" that the new drug is safe and effective, "a full statement of the composition" of the new drug, "a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packaging" of the new drug, and proposed labeling for the new drug. 21 U.S.C. § 355(b)(1). In addition, the NDA must include "the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the [NDA] or which claims a method of using [the new] drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug." *Id.* The FDA then lists this patent information in the "*Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations*," or, as it is commonly known, simply the "Orange Book."[1] *See also Mylan Labs. Ltd. v. FDA*, 910 F. Supp. 2d 299, 301 (D.D.C. 2012).

In 1984, Congress enacted the Drug Price Competition and Patent Term Restoration Act, Pub. L. No. 98-417, 98 Stat. 1585 (1984), popularly known as the "Hatch-Waxman Act." The Act sought, among other things, to encourage the development of generic drugs to increase market competition and to lower prices for consumers. *See Mead Johnson Pharm. Grp., Mead*

[1] Available at https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm.

Johnson & Co. v. Bowen, 838 F.2d 1332, 1333 (D.C. Cir. 1988). To that end, the Hatch-Waxman Act streamlined the process for bringing new generic drugs to market by creating the abbreviated new drug application—or "ANDA"—process, under which a manufacturer can "piggyback[] on the original manufacturer's evidence of safety and efficacy." *Teva Pharm., USA, Inc. v. Leavitt*, 548 F.3d 103, 104 (D.C. Cir. 2008). To obtain FDA approval for a generic drug, the ANDA applicant must demonstrate (1) that it is "bioequivalent" to the brand-name drug (also referred to as the "listed drug"); (2) that the prescribed conditions of use have been approved for the listed drug, 21 U.S.C § 355(j)(2)(A); (3) that the generic drug satisfies certain chemistry and labeling requirements; (4) and that the proposed manufacturing and packaging processes and controls are adequate to "preserve its identity, strength, quality, and purity," *id.* § 355(j)(4)(A).

Although the Hatch-Waxman Act streamlined the process for bringing generic drugs to market, obtaining FDA approval for an ANDA remains a prolonged task. The process begins with the submission of an application, which must comply with FDA requirements for receipt. If an application is not "substantially complete," 21 C.F.R. § 314.101(b)(1), the FDA will issue a "refuse-to-receive decision" in which it rejects the ANDA without evaluating the substance of the application, *id.* § 314.101(b)(3). In response, an applicant may resubmit the ANDA with the required data or may withdraw the ANDA. *Id.* Only after the FDA has determined that the ANDA meets the receipt requirements does the agency begin to evaluate whether the applicant's product is bioequivalent, manufactured in an appropriate manner, and properly labeled. During this substantive review, there is "inevitably and invariably back and forth" between the agency and the applicant, *see* Dkt. 69 at 8 (Tr. 8:7), in which the agency generally requests additional

data or information to determine whether the ANDA meets the requirements for approval, *see* 21 C.F.R. § 314.127. This process can take years to complete.

An ANDA must also include one of four certifications with respect to each of the Orange Book patents that claims the listed drug. 21 U.S.C. § 355(j)(2)(A)(vii)(I)-(IV). The four certifications are identified by the paragraph in which they appear: A "paragraph I" certification attests that, to the best of the applicant's knowledge, no such patent information has been filed. *Id.* § 355(j)(2)(A)(vii)(I). A "paragraph II" certification attests that any such patent has expired. *Id.* § 355(j)(2)(A)(vii)(II). A "paragraph III" certification identifies the date on which any such patent will expire. *Id.* § 355(j)(2)(A)(vii)(III). And, most importantly for present purposes, a "paragraph IV" certification asserts that any such patent is invalid or will not be infringed by the generic drug. *Id.* § 355(j)(2)(A)(vii)(IV). "If an ANDA applicant makes one of the first two certifications, [the] FDA may approve the ANDA immediately," and, if the "applicant makes a paragraph III certification, [the] FDA may grant tentative approval of the ANDA, to be made effective on the date the patent expires." *Mylan Labs.*, 910 F. Supp. 2d at 301. The consequences of making a paragraph IV certification, however, are different in kind. Most significantly, a paragraph IV certification is treated as an act of patent infringement. 35 U.S.C. § 271(e)(2)(A). If the patent holder brings an infringement action within 45 days of receiving notice of the certification, moreover, the FDA's approval of the ANDA will not take effect for a period of 30 months, unless otherwise ordered by the district court in which the patent litigation is pending. *Id.* § 355(j)(5)(B)(iii).

Would-be generic drug manufacturers thus risk costly patent infringement litigation if they seek FDA approval before the brand-name drug's patent has expired or is invalidated—a risk that Congress feared would discourage market competition and delay bringing lower-priced

generic drugs to market. *See Teva Pharm. USA, Inc. v. Sebelius*, 595 F.3d 1303, 1305 (D.C. Cir. 2010). To "compensate [generic] manufacturers for research and development costs as well as the risk of litigation from patent holders," *Teva Pharm.*, 548 F.3d at 104, Congress enacted an incentive for generic drug manufacturers to submit ANDAs and, if necessary, to engage in patent litigation: the "first applicant" to file an ANDA containing a paragraph IV certification is eligible for 180 days of market exclusivity, "during which the FDA may not approve for sale any competing generic version of the drug at issue." *Teva Pharm.*, 595 F.3d at 1305; *see also* 21 U.S.C. 355(j)(5)(B)(iv); *Mylan Labs.*, 910 F. Supp. 2d at 302.

The first-filer's entitlement to the exclusivity period is not absolute, however, and may be forfeited under certain conditions. As relevant here, the exclusivity period is forfeited if the "first applicant fails to obtain tentative approval of [its ANDA] within 30 months after the date on which the [ANDA] is filed." 21 U.S.C. § 355(j)(5)(D)(i)(IV). Congress added this forfeiture rule to the statute as part of the Medicare Modernization Act of 2003, Pub. L. No. 108-173, 117 Stat. 2066 (2003), to "ensure that the 180-day exclusivity period enjoyed by the first generic to challenge a patent [could not] be used as a bottleneck to prevent additional generic competition." *Hi-Tech Pharmacal Co. v. U.S. Food & Drug Admin.*, 587 F. Supp. 2d 1, 4 (D.D.C. 2008) (quoting 149 Cong. Rec. S15746 (daily ed. Nov. 24, 2003) (statement of Sen. Schumer)).

Congress created one exception to the 30-month forfeiture rule: the 180-day market exclusivity is not forfeited if the applicant's failure to obtain tentative approval within 30 months was "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." 21 U.S.C. § 355(j)(5)(D)(i)(IV). This exception was included to ensure that ANDA applicants are not penalized "for delays in tentative approval caused by changes in approval requirements beyond [the] ANDA applicant's control."

Mylan, 910 F. Supp. 2d at 311. If an applicant fails to obtain tentative approval within 30 months and the failure is not excused under the exception, however, the FDA may approve other ANDAs for the same generic drug product. *See id.*

B. Factual Background

On June 10, 2013, Amneal submitted an ANDA seeking approval to market a generic version of Namenda XR—a medication intended to treat moderate to severe dementia of the Alzheimer's type. AR 153, 160.[2] Namenda XR is a memantine hydrochloride capsule designed to facilitate an "extended release" of the drug. AR 1059. The FDA had previously approved an NDA submitted by Forest Laboratories LLC ("Forest") to market Namenda XR in four dosage levels: 7 mg, 14 mg, 21 mg, and 28 mg. AR 160. Amneal's ANDA included all four dosage levels; it was the first filed; and it included a paragraph IV certification for at least one of the patents listed in the Orange Book. AR 1041, 1043–44.

Amneal's ANDA proposed to achieve Namenda XR's extended-release effect by manufacturing capsules containing tiny "beads" of the active ingredient that would dissolve into the body at different rates. AR 182. Unlike the brand-name version of Namenda XR, which includes a single type of bead, Dkt. 33 at 13 & n.5, each capsule of Amneal's proposed product would contain both immediate release beads ("IRs") and extended release beads ("ERs") [redacted], AR 185. Consistent with the FDA's Guidance on ANDA Submissions—Refuse-to-Receive Standards, AR 240, 252, Amneal submitted data from three "pilot batches" of 150,000 capsules for each of the four dosage strengths in its ANDA, AR 198–

[2] The seven-part Administrative Record ("AR") can be found at Dkt. 46 (pages 1–140), Dkt. 46-1 (pages 141–239), Dkt. 46-2 (pages 240–406), Dkt. 46-3 (pages 418–544), Dkt. 46-4 (pages 545–637), Dkt. 46-5 (pages 638–753), and Dkt. 46-6 (pages 754–1063). For ease of reference, the Court will cite to the AR page numbers.

99. These pilot batches produced the capsules by combining [redacted] to create the extended release effect. AR 437. For purposes of commercial sales, however, Amneal proposed to produce much larger batches of 1,000,000 capsules and, in doing so, to blend up to six different lots of ER beads with two different lots of IR beads. AR 199, 437.

On November 5, 2013, the FDA sent Amneal a letter refusing to receive Amneal's ANDA because it was "not sufficiently complete to merit a critical technical review." AR 63. Specifically, the FDA explained that Amneal had "failed to produce accelerated stability data which encompasses at least 84 days in the accelerated stability chamber for the 30 and 500 counts for all strengths." *Id.* Amneal responded a month later by clarifying that the required data had, in fact, been included—it only appeared insufficient because a "typographical error" indicated the wrong date on which the stability testing began. AR 67. After confirming that the date in the ANDA was indeed a typographical error, the FDA rescinded its "Refuse to Receive" letter and treated the date of Amneal's original submission as the date of the application. AR 109. Although the record does not reflect when other generic manufacturers filed their ANDAs, there is no dispute that, using Amneal's original date of submission, Amneal qualified as the "first applicant" to submit an ANDA for Namenda XR containing a paragraph IV certification, making it eligible for 180 days of generic exclusivity if approved within 30 months, *i.e.*, by December 10, 2015. AR 1016.

On September 10, 2014, the FDA sent Amneal a letter identifying a number of substantive deficiencies with Amneal's ANDA. *See* AR 230–39. As relevant here, the FDA wrote:

> The proposed combination of multiple ER and IR lots for commercial production, combined with the deficiencies observed in the information submitted for the exhibit lots, requires the review of the resulting data from the manufacture of a commercial size lot before application approval. In this regard, please submit all

> the required [chemistry, manufacturing, and controls] information for the production of a 7 mg and 28 mg Memantine HCl lot of the size intended for commercial distribution.

AR 233. As the FDA further explained in its chemistry review, this deficiency was based on several factors. In particular: (1) Amneal's product required a specific ratio of IR beads to ER beads in each capsule [redacted] to ensure the desired rate of release, AR 189, 222–23; (2) the pilot batches used in the ANDA involved mixing [redacted] of IR beads, while Amneal proposed to market a product produced in commercial batches made by mixing "six different ER batches with two IR lots," AR 199; (3) Amneal's pilot batches had deficiencies such as overfilled capsules, AR 224; and (4) the "in-process controls" that Amneal proposed to use for the commercial manufacture of the drug were "regular controls used for simpler encapsulated drugs[,] which [might] not be sufficient to . . . monitor the quality of" a product made by combining "different types of . . . beads," AR 203. Overall, the FDA reviewers concluded that, "[d]ue to the complexity of the proposed process, combined with the deficiencies noted in the review," and because "mixing multiple lots of ER and IR beads could induce additional deviations not observed during the manufacture of the [pilot] lots that may require additional control," Amneal "should submit a scale up batch before approval." AR 199; *see also* AR 233 (requesting that Amneal "please submit all the required . . . information for" commercial lot sizes).

Complying with the FDA's request required considerable time and effort on Amneal's part. Amneal needed to "acquire commercial-scale quantities of source materials, ramp up production to manufacture commercial-size lots, conduct comprehensive analytical testing on the finished product, evaluate the resulting data, and resubmit its ANDA"—a process that took eight months to complete. AR 654. But, upon review of the additional data, the FDA noted several

issues. Most problematically, Amneal's proposed IR-to-ER bead ratio "was not followed in the newly submitted batches" and, while "some latitude in this ratio [was] required[,] . . . the deviation . . . was not justified." AR 460.

Amneal submitted a lengthy response to the FDA's review, which, among other things, highlighted the differences in processes used in producing the pilot-scale and commercial-scale batches. AR 437–44. As Amneal explained, "[i]n the ANDA exhibit batches, [redacted] were used to manufacture the intermediate blend; whereas for manufacturing of future commercial scale batches, multiple batches of IR pellets and ER pellets will be used." AR 437. Acknowledging that combining multiple lots of IR and ER beads introduced additional "complexity" into the production process, which "may result in calculation errors," Amneal proposed an "additional control . . . to ensure [that the] accurate dose of the drug product is administered to the patients." AR 444. The FDA, however, concluded that the additional control was "not acceptable," and it, accordingly, "recommend[ed]" that Amneal "scale down the proposed commercial batch size[] to a size with a constant, reproducible capsule filling weight as well as a constant bead type composition." AR 483. Amneal accepted the FDA's recommendation to scale down the proposed commercial-scale batches—from 1,000,000 capsules to 150,000 capsules—thus resolving the issue and clearing the way for approval of its ANDA. AR 488–89.

In the meantime, however, Amneal experienced a further delay: an "Import Alert" was issued on October 15, 2015, to the supplier of Amneal's active pharmaceutical ingredient ("API"). AR 486, 490, 527. As the FDA has explained, an Import Alert signals that an "imported product will be detained because it appears to be in violation of the FDCA or its implementing regulations." Dkt. 34 at 16 n.10. In light of this development, Amneal sought

approval to use a different API supplier, AR 486, 490, 527, and sought to amend its ANDA to substitute the new supplier in place of the one that was previously identified, AR 495. Amneal's troubles continued, however, and, on December 7, 2015, the FDA notified Amneal that its proposal to change its source of API was "not acceptable" because Amneal had yet to demonstrate bioequivalence. AR 740. Amneal provided the missing data demonstrating bioequivalence using the new source of API on February 25, 2016, but FDA chemistry reviewers raised additional deficiencies in Amneal's product, which were not addressed until August 11, 2016 and September 15, 2016. AR 1037. Finally, on September 28, 2016, the FDA tentatively approved Amneal's ANDA. *Id.* By that time, however, the 30-month period for approval had run.

C. FDA's Determination

On December 2, 2015, Amneal requested that the FDA "confirm . . . that Amneal's Memantine XR ANDA will remain eligible for 180-day generic marketing exclusivity regardless of whether the [a]gency grants tentative approval . . . or final approval to that ANDA on or before December 10, 2015." AR 640. In support of that request, Amneal raised a variety of arguments, but only one is relevant for present purposes. That argument posited, as Amneal argues in this proceeding, that its failure to obtain approval within 30 months of June 10, 2013—the date that the FDA treated as the date of filing—was caused by the FDA's "post-filing review of and change in the requirements for approval." AR 651. Amneal asserted that, prior to the date on which it filed its ANDA, the FDA "long . . . permitted applicants to submit ANDAs . . . based on the production of, and presentation of date regarding, pilot-size test batches." *Id.* It was only after the ANDA was filed, Amneal argued, that the FDA changed "the pertinent approval requirements" and required "that [it] scale up and complete 'the production of a 7 mg

and 28 mg Memantine HCl lot of the size intended for commercial distribution' and then 'submit all the required . . . information' in order to enable FDA 'review of the resulting data from the manufacture of a commercial size lot before application approval.'" *Id.* (emphasis omitted). Finally, Amneal asserted that it was unaware "of any other ANDA for which the [a]gency ha[d] ever required the production and analysis of . . . data from a commercial-size lot as a condition of approval," and, indeed, despite having obtained 95 ANDA approvals, it had "never previously been required to produce" such data in support of an ANDA. AR 652 (emphasis omitted).

On September 28, 2016, the same day the FDA tentatively approved Amneal's ANDA, the agency issued a 17-page letter decision concluding that Amneal had forfeited the 180-day period of exclusivity. AR 1041–57. In that letter, the FDA explained that its request that Amneal provide commercial-scale data was not a "change" in "requirements for approval" that would trigger the exception. AR 1055. The "approval requirement" at issue was not, according to the FDA, the submission of commercial-scale data; rather, the relevant requirement was that the applicant "demonstrate that the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of the drug are adequate to assure and preserve its identity, strength, quality, and purity." *Id.* The FDA wrote: "That statutory requirement has not changed, nor has [the] FDA's specific requirements for certain complex products like Amneal's proposed memantine hydrochloride ER capsules to meet it." *Id.*

The FDA's letter decision further explained that its request for commercial-scale data was nothing new. To the contrary, although limited in its ability to disclose proprietary information regarding other applications, AR 1055 n.43, the FDA represented that it has, "[s]ince at least 2010," requested commercial-scale data for "certain complex drug products and/or a complex manufacturing process." AR 1055. The decision whether that information is

"necessary," however, is case-specific "and is made during the substantive review of the ANDA by the chemistry reviewers." *Id.* "Merely having a complex process," the FDA continued, "is not, by itself, typically sufficient to warrant a request for the manufacture of commercial batches pre-approval," but:

> [I]f the applicant does not demonstrate a good understanding of its product and manufacturing process and have appropriate in-process controls, [the] FDA will have concerns about the ability of the applicant to successfully produce scaled-up commercial lots of the drug product upon approval. In that situation, [the] FDA typically would request that an applicant manufacture a commercial scale batch and submit information on that batch to the Agency for review prior to approving the ANDA. If, as is the case here, the applicant then revises its proposed commercial batch size to match the size of its exhibit batches, this would address the [a]gency's concern, as the applicant would no longer be seeking to produce a scaled-up commercial batch.

Id. Accordingly, the FDA reasoned, because neither statutory requirements nor agency policy had changed, the exception to the 30-month rule did not apply. AR 1056.

As an alternative basis for its decision, the FDA also concluded that the FDA's request for data from a commercial-scale batch, even if a change in a requirement for approval, did not *cause* Amneal to miss the 30-month mark. AR 1054–55. It premised that conclusion on two points: First, the FDA's request for commercial scale data was resolved before the forfeiture date and, therefore, could not have "preclude[d] tentative approval or approval at that time." AR 1055. Second, Amneal did not "demonstrate[] that the [FDA's] request" that Amneal provide the commercial-scale data "caused it to fail to obtain tentative approval or approval by [the relevant date]." *Id.*

D. Procedural History

Four months after receiving the FDA's adverse determination, Amneal filed this APA action, alleging that the FDA's decision was arbitrary and capricious and contrary to law. Dkt. 1. Two other pharmaceutical manufacturers with tentatively approved ANDAs for generic versions

of Namenda XR—Lupin Pharmaceuticals, Inc. and Lupin Limited (collectively, "Lupin"), and Par Pharmaceutical, Inc. ("Par")—moved to intervene in support of the FDA, Dkt. 20; Dkt. 52, and the Court granted those motions, Minute Order (Mar. 6, 2017); Minute Order (Nov. 8, 2017). In addition, Amneal filed a motion for summary judgment, Dkt. 25, and the FDA and Lupin responded with their own cross-motions for summary judgment, Dkt. 30; Dkt. 34.

While the events described above were unfolding, another generic manufacturer, Teva Pharmaceuticals USA ("Teva"), filed its own ANDA seeking approval to market a generic version of Namenda XR, and Teva's ANDA included a paragraph IV certification asserting that six of the associated patents were invalid or would not be infringed by its product. *Forest Labs., Inc. v. Teva Pharm. USA, Inc.*, Nos. 14-121, 14-200, 14-508, 14-686, 14-1058, 14-1271, 2016 WL 54910 (D. Del. Jan. 5, 2016). Forest then filed an infringement action against Teva in the U.S. District Court for the District of Delaware, which ultimately entered a judgment of invalidity on the ground of indefiniteness. *Id.* On December 11, 2017, the Federal Circuit affirmed that decision. *Forest Labs, Inc. v. Teva Pharm. USA, Inc.*, Nos. 2016-2550, 2016-2553, 2017 WL 6311688 (Fed. Cir. Dec. 11, 2017). Although the Federal Circuit's mandate has yet to issue, and a petition for rehearing is pending, a final affirmance in the *Teva* case would open the door for generic manufacturers with approved ANDAs to market their products. Dkt. 63 at 11–12. Given that prospect, and the prospect that other holders of approved ANDAs might imminently enter the market, Amneal filed a motion for a preliminary injunction or, in the alternative, for a temporary restraining order on December 14, 2017. Dkt. 62.

The following day, the Court held a status conference to address how best to proceed in light of these developments. To promote efficiency, the Court proposed—and the parties agreed—that the Court would issue a decision on the fully briefed cross-motions for summary

judgment on an expedited basis, and, at the request of the FDA—and with no objection from Amneal—the Court agreed to stay the time for Defendants to respond to Amneal's motion for a preliminary injunction or, in the alternative, a temporary restraining order. Dkt. 67 at 7 (Tr. 7:12–14). On January 10, 2018, Court heard oral argument on the pending cross-motions for summary judgment. *See* Dkt. 69.

II. LEGAL STANDARD

Under Federal Rule of Civil Procedure 56, summary judgment is ordinarily available if the movant demonstrates "that there is no genuine dispute as to any material fact and" that, based on the uncontested facts, "the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a). In the unique context of a case brought under the APA, however, the district court "sit[s] as an appellate tribunal," *Marshall Cty. Health Care Auth. v. Shalala*, 988 F.2d 1221, 1222–23 (D.C. Cir. 1993), to decide "as a matter of law [whether] the agency action is supported by the administrative record and is otherwise consistent with the APA standard of review," *Coal. for Common Sense in Gov't Procurement v. United States*, 821 F. Supp. 2d 275, 280 (D.D.C. 2011); *see also Citizens to Preserve Overton Park, Inc. v. Volpe*, 401 U.S. 402, 415 (1971); *Sw. Merch. Corp. v. NLRB*, 53 F.3d 1334, 1341 (D.C. Cir. 1995). In short, it is the role of the administrative agency to "resolve factual issues" and "to arrive at a decision that is supported by the administrative record," while it is the role of the district court "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 Pharmacal*, 587 F. Supp. 2d at 18.

III. ANALYSIS

All parties agree that this case is governed by the two-step framework established in *Chevron U.S.A. v. Natural Resources Defense Council*, 467 U.S. 837 (1984), as well as the

APA's arbitrary and capricious standard, 5 U.S.C. § 706(2)(A). Under *Chevron*'s first step, the Court must consider "whether Congress has directly spoken to the precise question at issue." 467 U.S. at 842. If so, the Court must "give effect to the unambiguously expressed intent of Congress." *Id.* at 843. But, if the Court concludes that Congress has left an ambiguity or "gap" to fill on the "precise question at issue," the Court proceeds to the second step of *Chevron*. 467 U.S. at 842–43. Under the second step, the Court asks whether the agency's construction of the statute is a "permissible" one. *Id.* at 843. If it is, the Court must defer to that construction.

The APA also precludes agency action that is "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A). An agency's decision, accordingly, must be the product of "reasoned decisionmaking." *Motor Vehicle Mfrs. Ass'n of U.S. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 52 (1983). An agency action will normally be set aside as "arbitrary and capricious" if the agency "has relied on factors which Congress has not intended it to consider, entirely failed to consider an important aspect of the problem, offered an explanation for its decision that runs counter to the evidence before the agency, or is so implausible that it could not be ascribed to a difference in view or the product of agency expertise." *Id.* at 43.

As this Court has previously observed, "[t]hese standards overlap and are, at times, intertwined." *Amarin Pharm. Ireland Ltd. v. Food & Drug Admin.*, 106 F. Supp. 3d 196, 206 (D.D.C. 2015). Because *Chevron*'s second step asks whether an agency's interpretation is "arbitrary or capricious in substance," *Judulang v. Holder*, 565 U.S. 42, 52 n.7 (2011) (citing *Mayo Found. for Med. Educ. & Research v. United States*, 562 U.S. 44, 53 (2011)), "the analysis required pursuant to *Chevron* [s]tep [t]wo, and that required under the arbitrary and capricious standard enunciated in *State Farm*" overlap, *EchoStar Satellite L.L.C. v. FCC*, 704 F.3d 992,

1001–02 (D.C. Cir. 2013) (citation omitted). "Ultimately, under either standard of review, the relevant question is whether the FDA's decision represents the result of a reasonable exercise of its authority." *Amarin Pharm.*, 106 F. Supp. 3d at 206. This means that, under either standard, judicial review is "fundamentally deferential—especially with respect to 'matters relating to [an agency's] areas of technical expertise.'" *Fox v. Clinton*, 684 F.3d 67, 75 (D.C. Cir. 2012) (citation omitted). It does not mean, however, that courts must "simply accept whatever conclusion an agency proffers." *Tripoli Rocketry Ass'n v. Bureau of Alcohol, Tobacco, Firearms & Explosives*, 437 F.3d 75, 77 (D.C. Cir. 2006). In short, it is the Court's role to decide whether the agency acted "within the scope of its lawful authority," and whether it engaged in "reasoned decisionmaking," *id.*, but not to second guess an agency's reasonable exercise of the authority that Congress gave it.

In determining that Amneal forfeited the 180-day period of generic exclusivity, the FDA concluded (1) that Amneal failed "to obtain tentative approval of" its ANDA "within 30 months after the date on which the application [was] filed," *see* 21 U.S.C. § 355(j)(5)(D)(i)(IV), and (2) that its failure to do so was not "caused by a change in or a review of the requirements for approval of the application imposed after the date on which the application [was] filed," *see id.*; *see also* AR 1055–56. Amneal does not dispute the first conclusion, but it contends that the second is flawed on multiple levels. Most significantly, Amneal disagrees with the FDA's conclusion that the agency's "demand for commercial-scale data" did not constitute a "change in a requirement for approval of the application." Dkt. 25 at 29. It also argues that the FDA erred in failing "even [to] consider whether the delay in receipt [of Amneal's ANDA due to the typographical error] resulted from a change in or review of approval requirements," *id.*, and erred in failing to treat "all of the activity regarding whether the [a]gency would receive the

application" as a "'change in or [a] review of' . . . a 'requirement[] for approval of the application,'" *id.* at 42 (quoting 21 U.S.C. § 355(j)(5)(D)(i)(IV)). Finally, Amneal devotes the lion's share of its brief to arguing that the FDA erred in concluding, in the alternative, that even if either of these regulatory actions constituted a change in a requirement for approval of the ANDA, neither action "caused" Amneal to miss the 30-month deadline. Dkt. 25 at 23–38.

As explained below, the Court holds that the FDA did not violate the plain terms of the statute or act unreasonably in deciding that neither of the regulatory steps identified by Amneal constituted "a change in or review of [a] requirement[] for approval of" Amneal's ANDA. The Court, in contrast, does have significant doubts about the FDA's conclusion that the delay occasioned by its request for the commercial-scale data was not *a* cause of Amneal's failure to meet the deadline. But, even if Amneal were correct about that portion of the FDA's decision, it would not save Amneal's claim; Amneal can prevail only if it can show that the FDA erred in declining to treat one or both of the identified regulatory steps as a change in or review of a requirement for approval *and* that the FDA's causation analysis was flawed. Because Amneal fails to clear the first of these hurdles, the Court need not decide whether it has cleared the second.

A. Request for Commercial-Scale Data

The principal dispute between the parties turns on whether the FDA's request that Amneal supplement its ANDA by submitting data from a commercial-scale batch constituted "a change in . . . the requirements for approval of" Amneal's ANDA. Although one might think that it would be relatively straightforward to identify "the requirements for approval of the application" to market a generic version of a drug, all agree that more is required than simply flipping through the statute, regulations, and policies. To be sure, a change in the statute,

regulations, or policies would generally be sufficient to trigger the proviso. But the FDA acknowledges that other steps can alter "the requirements for approval of" ANDAs. An ANDA applicant, for example, must demonstrate that the labeling it proposes to use is the same as the labeling for the listed drug, and, accordingly, if the label of the listed drug changes, the FDA will typically require that ANDA applicants submit new, proposed labels. Dkt. 33 at 25. FDA concedes that such a scenario represents a change in "the requirements for approval." Similarly, when the FDA changes or reviews the types of study designs that it recommends to establish bioequivalence, that process may delay ANDA applicants who rely on that guidance. *Id.* Again, FDA concedes that such a change would trigger the proviso.

What all of these circumstances have in common, according to the FDA, is that the rule, guidance, or practice at issue applies generally to other similarly-situated ANDA applicants. That is, according to the FDA, "requirements for approval" are those steps or efforts that the "FDA would demand from *any and all* applicants submitting an ANDA for the drug at issue." *Id.* at 22. The FDA does not, in contrast, construe the phrase "requirements for approval" to encompass occasions when the FDA requests additional data or information from a specific applicant to address a specific deficiency noted in the course of the agency's scientific review of the ANDA. *Id.*

Amneal, for its part, takes a broader view of what it means to change a "requirement[] for approval of" an ANDA. It agrees that the types of changes of general applicability identified by the FDA meet the terms of the proviso. But it would also include what it characterizes as "changes applied to particular applications." Dkt. 25 at 43. Amneal concedes, as it must, that this does not mean that every request for additional data or information that emerges as part of the FDA review process constitutes a change in the relevant requirements; all agree that the

review process is an iterative one "in which there is inevitably and invariably back and forth" requiring applicants to provide additional information. Dkt. 69 at 8 (Tr. 8:6–7). What separates this case from those garden-variety requests for additional information, according to Amneal, is that the FDA's request in this case for data from a commercial-scale batch was *different in kind* from the request for pilot-scale batch data that the FDA required at the time Amneal filed its ANDA. Dkt. 25 at 40. The FDA may not have changed "what" Amneal was required to demonstrate—that the production methods "are adequate to assure and preserve [the drug's] identity, strength, quality, and purity," AR 1055; *see also* 21 U.S.C. § 355(b)(1)(D), (j)(2)(A)(vi)—but it changed "how" Amneal was required to show that it satisfied that standard—by using a commercial-scale batch as opposed to pilot-scale batches. Dkt. 38 at 11; Dkt. 69 at 15 (Tr. 15:16–22), *id.* at 26 (Tr. 26:11–15).

Understanding what Amneal means by this, however, requires consideration of what, if anything, actually changed from when Amneal filed its ANDA and when the FDA approved it. Amneal asserts that, before it submitted its ANDA, the FDA had "stated [that] it [would] generally *receive* and *approve* applications containing only pilot-scale data," Dkt. 25 at 40 (emphasis added), and that "[i]t is undisputed that [the] FDA's public policies required only the submission of pilot-scale data," Dkt. 38 at 12. In support of this contention, Amneal cites to five FDA guidance documents. *See* Dkt. 25 at 17 & n.2; Dkt. 38 at 12; Dkt. 68 at 32 (Tr. 32:8–9). Although each of those documents supports Amneal's contention that the FDA generally requires only pilot-batch data for purposes of *receipt* of an ANDA as "substantially complete"

under 21 C.F.R. § 314.101(b), none of them supports Amneal's further contention that the FDA has stated that pilot-batch data is sufficient to support *approval* of an ANDA.[3]

The Court does not doubt that the type of information required for the FDA to receive an ANDA will often mirror the type of information required to approve it. But, the receipt of a "substantially complete" application only begins the process, which inevitably requires the submission of additional information. *See* Dkt. 69 at 8 (Tr. 8:7). As the FDA put it in its decision letter, the "Agency's requirements in 21 C.F.R. [§] 314.101 as to whether an ANDA is sufficiently complete to permit substantive review, and thus may be received by the Agency, are distinct from the question as to whether the application meets the requirements for approval set forth in 21 C.F.R. § 314.127." AR 1055 n.44. And, the approval "requirements" make clear that the FDA will "refuse to *approve* an ANDA" if "[t]he methods used in, . . . and controls used for, the manufacture, processing, and packaging of the drug product are inadequate to ensure and [to] preserve its identity, strength, quality, and purity." 21 C.F.R. § 314.127(a)(1) (emphasis added).

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[3] *See* ANDA Submissions – Refuse-to-Receive Standards 1 (May 2015), AR 243 (stating that the guidance "highlights deficiencies that may cause FDA to *refuse to receive* an ANDA" (emphasis added)); Guidance on the Packaging of Test Batches 1, 5 (Sept. 2012), AR 44, 48 [hereinafter Guidance: Test Batches] (noting that "[t]he *minimum amount* to be packaged is 100,000 units" and explaining that "[i]t is critical that all testing be conducted on samples that represent the entire batch and *mimic the product which will be marketed post-approval*" (emphasis added)); Q1A(R2) Stability Testing of New Drug Substances and Products 8 (Nov. 2003), https://www.fda.gov/downloads/drugs/guidances/ucm073369.pdf [hereinafter Guidance: Stability Testing] (noting that "two of the three batches *should be at least* pilot scale batches" and also that "[t]he manufacturing process used for primary batches *should simulate that to be applied to production batches*"); ANDAs: Stability Testing of Drug Substances and Products, Questions and Answers 3, 8 (May 2014), https://www.fda.gov/downloads/drugs/guidances/ucm366082.pdf (indicating what data "should [be] submit[ted]," with the application); ANDAs: Stability Testing of Drug Substances and Products 2 (June 2013), https://www.fda.gov/downloads/drugs/guidances/ucm320590.pdf (explaining what data "should be provided" with the application).

The same guidance documents that Amneal cites, moreover, inform ANDA applicants that "[i]t is critical that all testing be conducted on samples that represent the entire batch and *mimic the product which will be marketed post-approval*." Guidance: Test Batches at 1 (emphasis added); *see also* Guidance: Stability Testing at 8 ("The manufacturing process used for primary batches should simulate that to be applied to production batches and should provide product of the same quality and meeting the same specification as that intended for marketing"); *id.* at 18 (defining "pilot scale batch" as "[a] batch of drug product manufactured by a procedure fully representative of and simulating that to be applied to a full production scale batch"). That admonition is apt here because Amneal proposed using a significantly different manufacturing process for "the product which [would] be marketed post-approval" than it used for the pilot batches that it submitted with its ANDA. Amneal's pilot batches, as explained above, were produced by combining [redacted] of IR (that is, immediate release) beads with [redacted] of ER (that is, extended release) beads, yielding 150,000 capsules. For commercial purposes, however, Amneal proposed producing batches of 1,000,000 capsules by combining up to two lots of IR beads with up to six lots of ER beads. It was this difference in production techniques that, at least in substantial part, prompted the FDA to request data from a commercial-scale batch to address concerns about the [redacted] required to achieve the desired rate of release of the drug.

Against this backdrop, Amneal's proposed reading of the statute must be clarified as follows: A change in the requirements for approval occurs when the FDA allows for the receipt of an ANDA that contains a certain type of information—here, data from pilot-scale batches—and, then, in the course of its technical review of the application, the FDA concludes that a different type of information—here, data from a commercial-scale batch—is necessary for it to

approve the ANDA. To this, Amneal adds that the change here was a significant one, requiring, for example, substantially larger quantities of the active ingredient, AR 654, and that "across a portfolio of 95 approved ANDAs, Amneal ha[d] never previously been asked to produce a commercial-scale lot as a condition of approval," AR 1056. With this clarification in mind, the Court turns to the *Chevron* framework.

1. Chevron *Step One*

Under *Chevron* step one, the Court must consider "whether Congress has directly spoken to the precise question at issue." 467 U.S. at 842. If so, the Court "must give effect to the unambiguously expressed intent of Congress." *Id.* at 843. In making this determination, the Court applies the "traditional tools of statutory construction," *id.* at 843 n.9, including looking to "the text, structure, and the overall statutory scheme, as well as the problem Congress sought to solve," *Financial Planning Assoc. v. SEC*, 482 F.3d 481, 487 (D.C. Cir. 2007), in order "to determine whether Congress has 'unambiguously foreclosed the agency's statutory interpretation.'" *Vill. of Barrington, Ill. v. Surface Transp. Bd.*, 636 F.3d 650, 659 (D.C. Cir. 2011) (quoting *Catawba Cty., N.C. v. EPA*, 571 F.3d 20, 35 (D.C. Cir. 2009)).

The Court starts, as it must, with the text of the statute. *See Sebelius v. Cloer*, 569 U.S. 369, 376 (2013). Section 355(j)(5)(D)(ii) provides that "[t]he 180-day exclusivity period . . . shall be forfeited by a first applicant if a forfeiture event occurs with respect to that first applicant." 21 U.S.C. § 355(j)(5)(D)(ii). The statute then specifies a series of "forfeiture events," only one of which is relevant in this case. That "forfeiture event" occurs if:

> The first applicant 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. § 355(j)(5)(D)(i)(IV) (emphasis added). For present purposes, then, the question is whether this statutory text speaks directly to the question whether the FDA's request for data from a commercial-scale batch constituted "a change in . . . the requirements for approval of" Amneal's ANDA. Amneal contends that its interpretation is compelled, thus foreclosing the FDA's competing interpretation. *See Vill. of Barrington*, 636 F.3d at 659. The Court disagrees.

Although the relevant statutory terms are not defined, they are not technical or uncommon terms. A "requirement" is "a condition which must be complied with," XIII Oxford English Dictionary 682 (2d ed. 1989), and a "change" is the "substitution of one thing for another," III Oxford English Dictionary at 15. Understanding the meaning of those words, however, does little to resolve the parties' dispute. As noted above, all agree that not every request for additional information—even if the FDA will not approve the ANDA without that information—constitutes a "change" in the governing "requirements." What makes this case different, in Amneal's view, is that the FDA required *one type of data* as a condition of receipt of its ANDA—data from pilot-scale batches—and, then, required *a different type of data* as a condition of approval of the ANDA—data from a commercial-scale batch. "In other words," according to Amneal, "at the time of the ANDA's submission [the] FDA [did] not require submission of commercial-scale data and only [made] that determination later in the review process. That's a change by any definition." Dkt. 25 at 40.

In support of its contention that this "change" falls within the plain terms of the statute, Amneal argues that the statute "is not limited to broader . . . changes" in the statute or in FDA policy, but also includes "changes *applied to particular applications*." *Id.* at 43 (emphasis added). The central question under Amneal's view of the law, accordingly, is whether the applicant faced a different set of hurdles before and "after the date on which [its] application was

filed." 21 U.S.C. § 355(j)(5)(D)(i)(IV). Evidence of the statutory focus on the hurdles faced by the applicant in the context of the FDA's review of its *particular* ANDA is found, according to Amneal, in the statute's references to the requirements for approval "of the application" that are imposed after "the application" is filed. Dkt. 25 at 43–44. If the FDA were right, Amneal adds, and the focus was instead on changes in generally applicable rules and policies, the words "of the application" would be rendered meaningless, thus violating the canon against surplusage. *Id.* at 44.

The Court, of course, agrees that statutes should be construed, where possible, to avoid surplusage. *See Indep. Ins. Agents of Am., Inc. v. Hawke*, 211 F.3d 638, 644–45 (D.C. Cir. 2000). It is unpersuaded, however, that the FDA's reading of the statute runs afoul of that canon. Under the canon against surplusage, the Court must ask whether, on the FDA's reading the statute, the phrase "of the application" could be dropped from that statute with no consequence. It cannot. To the contrary, under both the FDA's and Amneal's proposed constructions of the statute, those words perform the same, essential function: they are the *object* of the phrase "the requirements for approval," and, without them, the reader would be left to ask, "approval of what?" The phrase "of the application," in short, is needed to complete the sentence.

Amneal's construction of the statute, in contrast, either reads the phrase "approval of" out of the statute or, at a minimum, gives that phrase a strained meaning. Amneal presumes that the requirements for the FDA to receive an ANDA mirror the requirements for approval. But the FDA has explained—and Amneal has not identified any evidence to the contrary—that the two requirements, even if closely related, are distinct. AR 1055 n.44. Amneal's textual argument, however, conflates the two, and, in doing so, it sidesteps the critical question whether the data from the pilot-scale batches that it submitted with its ANDA was ever sufficient (before or after

the ANDA was filed) to support *approval* of the application. Understood in this light, nothing in the statutory text supports Amneal's reading, much less unambiguously forecloses the FDA's approach. *See Vill. of Barrington*, 636 F.3d at 659.

Nor is the Court convinced that the distinction that Amneal draws between "what" the applicant must demonstrate and "how" it must do so has any bearing on the meaning of the statute. The FDA, for its part, does not dispute that either type of change may constitute a "change in . . . the requirements for approval of" the ANDA. As noted above, however, the question is not whether the requirements for receipt of the ANDA were different from the requirements for approval of the ANDA; the question is whether the FDA changed the applicable "requirements for approval" after the ANDA was filed. Whether cast as a change in *what* Amneal was required to demonstrate or *how* it was required to do so, Amneal cannot prevail in the absence of evidence that the FDA changed the requirements for approval of Amneal's ANDA.

Amneal also argues that its construction of the statute is necessary to achieve the statutory goal of "granting exclusivity to an applicant whose delay was caused by change in the review requirements 'of the application.'" Dkt. 25 at 44–45. According to Amneal, "[i]f the FDA is correct, and a substantial change in expectations like a post-filing demand for commercial-scale data is not a change sufficient to trigger the statute, then the aims of the statute will be thwarted." *Id.* at 45. "An ANDA sponsor hoping to ensure 180-day exclusivity," Amneal further asserts, would have significant reason under the FDA's reading of the statute to wait to submit its ANDA "until it has fully scaled up to commercial production and obtains all of the requisite commercial-scale data." *Id.* And that, according to Amneal, would then delay generic entry into the market, contrary to the aims of the Hatch-Waxman Act. *Id.*

This argument might more appropriately be raised under *Chevron* step two, but it is, in any event, unconvincing. Amneal is correct that Congress enacted the Hatch-Waxman Act to promote generic competition, *Teva Pharm.*, 595 F.3d at 1304, and that Congress included the 180-day exclusivity period to "reward . . . generic[] [manufacturers] 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. But by including the 30-month forfeiture rule in the statute, Congress conditioned that "reward" on prompt ANDA approval 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." *Hi-Tech Pharmacal Co.*, 587 F. Supp. 2d at 4 (quoting 149 Cong. Rec. S15746 (daily ed. Nov. 24, 2003) (statement of Sen. Schumer)); *see also Mylan Labs.*, 910 F. Supp. 2d at 311.

Even assuming that Amneal is right that its reading would provide additional incentives for generic manufacturers promptly to file ANDAs challenging the patents of the listed drugs—and that proposition is far from certain—it would do so by encouraging applicants to file as soon as they can satisfy the threshold requirements for receipt of the ANDA under 21 C.F.R. § 314.101, regardless of whether they are able to satisfy the requirements for approval. That, then, would risk creating the type of bottleneck that Congress enacted the 30-month rule to prevent. And, at the same time, it would engender increased uncertainty—and, perhaps, litigation—about whether each new request for information in the FDA review process is sufficiently "different in kind" from the information required as a condition of receipt of the ANDA that the request constitutes "a change in . . . the requirements for approval." The statutory scheme, in short, reflects a balance between creating an incentive for a generic manufacturer to be the first to challenge the branded manufacturer's patents and preventing bottlenecks that could delay

additional generic competition. Amneal's argument, however, focuses on one side of this balance, to the exclusion of the other.

The Court, accordingly, concludes that nothing in the text, structure or purposes of the statute forecloses the FDA's construction of the statute and that, indeed, the FDA's construction better coheres with the terms of the statute than the reading that Amneal posits.

2. Chevron *Step Two and Arbitrary and Capricious Review*

Amneal's claim also fails under *Chevron*'s second step and the APA's arbitrary and capricious standard. "At *Chevron* step two," the Court "defer[s] to the agency's permissible interpretation, but only if the agency has offered a reasoned explanation for why it chose that interpretation." *Vill. of Barrington*, 636 F.3d at 660. Like the *Chevron* step two analysis, moreover, the APA's "arbitrary and capricious" inquiry asks "whether an agency's actions under a statute are unreasonable." *Am. Fed'n of Gov't Emps., AFL-CIO, Local 46 v. Nicholson*, 475 F.3d 341, 355 (D.C. Cir. 2007) (internal quotation marks omitted); *see also, e.g.*, *Agape Church, Inc. v. FCC*, 738 F.3d 397, 410 (D.C. Cir. 2013) ("The analysis . . . under *Chevron* [s]tep [t]wo and arbitrary and capricious review is often the same, because under *Chevron* step two, the court asks whether an agency interpretation is arbitrary or capricious in substance." (internal quotation marks and brackets omitted)). The arbitrary and capricious standard goes a step further, however, and requires consideration, more generally, of whether the agency action is "supported by 'reasoned decisionmaking.'" *Tripoli Rocketry*, 437 F.3d at 77 (citations omitted). The "result must be logical and rational," *id.*, as well as "adequately explained" and "coheren[t]," *Fox*, 684 F.3d at 75 (citations and internal quotation marks omitted). The Court must evaluate the agency's decision, moreover, solely "on the basis articulated by the agency itself." *State Farm*, 463 U.S. at 50. Although lack of "clarity" alone is not a sufficient basis to strike down an

agency decision, *Bowman Transp., Inc. v. Arkansas-Best Freight Sys., Inc.*, 419 U.S. 281, 285–86 (1974), neither counsel nor the Court may amend or supply the agency's rationale, *see Riffin v. Surface Transp. Bd.*, 592 F.3d 195, 198 (D.C. Cir. 2010).

Amneal contends that the FDA's decision fails *Chevron* step two and the arbitrary and capricious standard on two grounds: First, it argues that the decision was premised, at least in part, on "secret, nonpublic policies." Dkt. 25 at 45. Second, it contends that the decision "is inexplicably inconsistent with FDA's prior precedent." *Id.* The Court is not convinced by either argument.

a. Nonpublic Policy

Amneal first argues that the FDA relied on a "secret" or "nonpublic policy" in its forfeiture decision. FDA's forfeiture decision asserts that "[s]ince at least 2010, the [a]gency has requested that applicants with certain complex drug products and/or a complex manufacturing process manufacture commercial scale batches to support approval of the ANDA by demonstrating that the applicant will be able to successfully scale-up its manufacturing process upon approval." AR 1055. The decision acknowledges, however, that this precedent was not publicly available because the "FDA is limited in disclosing information concerning other applications under [its] disclosure regulations." *Id.* at 1055 n.43 (citing 21 C.F.R. § 314.430). The decision continues:

> Amneal . . . represents that, across a portfolio of 95 approved ANDAs, Amneal has never previously been asked to produce a commercial-scale lot as a condition of approval. As described above, FDA's practice has been to ask for pre-approval production of commercial-scale batches in very specific circumstances: when a drug is complex or has a complex manufacturing process, and the evidence suggests that the applicant does not have a good understanding of the product and manufacturing process and lacks appropriate in-process controls. Thus, it is not surprising that FDA's general policies on manufacturing test batches do not describe these specific circumstances, nor it is surprising that Amneal believes it has not been previously asked to provide a commercial-scale test batch to support

> approval. Amneal's unfamiliarity with the case-specific requirement does not mean it reflects a "change in or review of the requirements for approval" under section 505(j)(5)(D)(i)(IV) of the [FDCA].

AR 1056. Relying on the fact that the FDA's prior requests for commercial-scale data were not publicly available, Amneal argues that it was the victim of "unfair surprise," Dkt. 25 at 46–47 (quoting *Christopher v. SmithKline Beecham Corp.*, 567 U.S. 142, 156 (2012)). That is, according to Amneal, it was "arbitrary and capricious for the [a]gency to . . . find a forfeiture of exclusivity where [Amneal's] failure to obtain approval was caused by application of a secret policy that could not have been anticipated, and which was disclosed after the application had already been filed." *Id.* at 47. This contention suffers from three flaws.

First, Amneal overstates the premise of its argument; the FDA did not adopt a "secret policy" that it merely revealed after Amneal filed its ANDA. To the contrary, the forfeiture decision makes clear that the FDA's prior requests for data from commercial-scale batches were "application specific" requests "made during the substantive review of the ANDA by the chemistry reviewers," based on the applicant's failure to "demonstrate a good understanding of its product and manufacturing process" and failure to "have appropriate in-process controls." AR 1055. Thus, rather than constituting a "secret policy," the FDA's prior requests merely represented case-by-case evaluations of whether data from a commercial-scale batch was needed to address a case-specific deficiency.

Second, as previously noted, pre-existing FDA guidance put ANDA applicants on notice that it was "critical that all testing be conducted on samples that represent the entire batch and *mimic the product which will be marketed post-approval.*" Guidance: Test Batches at 1 (emphasis added); AR 44. Amneal, accordingly, had "fair warning," *Christopher*, 567 U.S. at 156, that the FDA's chemical reviewers would conclude that the production data that Amneal

submitted with its application—involving the mixing of [redacted] of IR beads with [redacted] of ER beads—was insufficient to demonstrate that the process that Amneal proposed to use for commercial purposes—involving the mixing of two lots of IR beads with six lots of ER beads—would assure the "identity, strength, quality, and purity" of the product, 21 U.S.C. § 355(j)(4)(A);.

Amneal does not dispute that its initial submission was deficient, but contends that the cure that the FDA demanded (data from a commercial-scale batch) came as a surprise. Dkt. 69 at 16 (Tr. 16:13–19). It argues, for example, that instead of requiring data from a commercial-scale batch, the FDA might have asked that Amneal submit "a pilot batch that better mimic[ked]" the product that Amneal proposed to market. *Id.* at 28 (Tr. 28:10). That issue was not raised before the FDA and therefore is not properly before the Court. *See Nuclear Energy Inst., Inc. v. EPA*, 373 F.3d 1251, 1297 (D.C. Cir. 2004) (per curiam). And, even if the Court could reach the issue, it would owe substantial deference to the scientific judgment of the FDA regarding what type of testing is necessary to "mimic the product which will be marketed post-approval" and whether less onerous or time-consuming approaches were available. *See Marsh v. Or. Nat. Res. Council*, 490 U.S. 360, 377 (1989) ("Because analysis of the relevant documents requires a high level of technical expertise, we must defer to the informed discretion of the responsible agencies." (internal quotation marks and citation omitted)); *Serono Labs.*, 158 F.3d at 1320 (explaining that when "[t]he FDA's determination" rests on its "evaluations of scientific data within its area of expertise, [it] is entitled to a high level of deference from th[e] court" (internal citations and quotation marks omitted)).

Third, Amneal is not challenging the FDA's request for data from a commercial-scale batch, but rather the agency's forfeiture decision. The relevant question, accordingly, is not

whether Amneal was surprised by the FDA's request for the data, but whether the agency's forfeiture decision was arbitrary and capricious. That question must be considered in light of the statutory standard—whether there was "a change in . . . the requirements for approval of" Amneal's ANDA—and, for the reasons discussed above, the Court concludes that the FDA reasonably concluded that there was not. In short, Amneal was required to demonstrate that its manufacturing processes and controls were adequate to assure the "identity, strength, quality, and purity" of its product, 21 U.S.C. § 355(j)(4)(A), and it was required to produce testing on samples that would "mimic the product which [would] be marketed post-approval," Guidance: Test Batches at 1; AR 44. The fact that the FDA noted a deficiency and requested data that it concluded—in its expert judgment—was needed to meet that standard did not cross the Rubicon of the arbitrary and capricious standard. Amneal's argument to the contrary stands on its statutory argument—that the exception focuses on "application-specific requirements," Dkt. 25 at 44—and fails for the same reason its statutory argument fails.

b. Inconsistency

Amneal also argues that the FDA's interpretation is inconsistent with the agency's past decisions. In support of this contention, Amneal points to (1) a 2010 FDA letter decision excusing a failure by Nycomed U.S., Inc. to obtain approval within 30 months, *id.* at 47–48; (2) a similar decision in the case of Synthon Pharmaceuticals, Inc., *id.* at 48 n.14; (3) another similar decision in the case of Sandoz, Inc., *id.*; and, finally, (4) FDA guidance explaining that "changes in a [listed] drug's labeling or formulation that require . . . an applicant to conduct additional testing" may constitute a change in the requirements for approval, *id.* at 47.[4] Amneal fails to

[4] Amneal also points to the FDA's decision concluding the Teva Pharmaceuticals was excused for failing to obtain approval for its Irbesartan Tablets USP ANDA within 30 months, Dkt. 25 at

identify any evidence, however, that the FDA applied a standard in any of those cases that differs from the standard the FDA proffers here: the exception to the 30-month requirement applies to changes in how all similarly-situated ANDA applicants must demonstrate that their ANDAs warrant approval, and it does not apply to requests for additional information prompted by deficiencies specific to the particular ANDAs. Dkt. 33 at 24.

Nycomed, for example, sought to market a 5% Imiquimod Cream and failed to obtain approval within 30 months. The FDA nonetheless concluded that Nycomed qualified for the 180-day market exclusivity because the delay "was caused by the agency's ongoing review of the requirements for approval of Imiquimod Cream, 5%." Letter from FDA to Nycomed, U.S., Inc. at 2 (Feb. 25, 2010).[5] As the FDA has explained, that review involved "the study designs recommended to establish bioequivalence with" the listed drug. Dkt. 33 at 25 (citing Draft Guidance on Imiquimod Cream, 5% (Feb. 2010)).[6] As a result, unlike the present case, "the change in or review of the requirement[] for approval" was not prompted by a deficiency noted in Nycomed's application, and it applied to all similarly-situated applicants.

The Synthon decision cited by Amneal is distinguishable on similar grounds. As previously discussed, an ANDA applicant is required to demonstrate that its proposed label is the

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48, but the FDA's decision letter merely asserts that the agency "changed the approval requirements for Teva's proposed product" and that, "[a]s a result, Teva was required to perform additional testing and [to] include an additional drug substance specification prior to approval," Letter from FDA to Teva Pharmaceuticals USA at 2 n.1 (March 30, 2012), http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2012/077159s000ltr.pdf. Nothing contained in this brief discussion of the issue, or in any other materials identified by Amneal, explains how the Teva case supports Amneal's claim.

[5] Available at https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2010/078548s000ltr.pdf.

[6] Available at https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM201988.pdf.

same as the proposed label for the listed drug. *See* 21 U.S.C. § 355(j)(2)(A)(v); 21 C.F.R. §§ 314.94(a)(8)(iii), 314.127(a)(7). Thus, if the label for the listed drug is amended, ANDA applicants must submit new proposed labels for their products. Such a change delayed the approval of Synthon's ANDA, and, consistent with the FDA's reading of the statute, the agency concluded that Synthon had not forfeited its eligibility to the 180 days of exclusivity:

> The agency has determined that there was a change in the requirements for approval of this ANDA. Specifically, the labeling of the [listed drug] changed after submission of the ANDA. The agency has also determined that this change was the cause of your not obtaining tentative approval of the ANDA within 30 months after the date on which it was filed.

Letter from FDA to Synthon Pharmaceuticals Inc. at 2 n.1 (March 30, 2012).[7]

The same is true for the Sandoz decision. Like the labeling requirement, changes to the formulation of the listed drug requires ANDA applicants either to seek approval for their generic version based on the new formulation or to seek a determination that the old formulation was not withdrawn for safety reasons. *See* Guidance for Industry (Draft) – 180-Day Exclusivity: Questions and Answers 23 (Jan. 2017)[8] [hereinafter Draft Guidance: 180-Day Exclusivity]. In the Sandoz decision, the FDA explained that "[w]hen a change in formulation for a listed drug referenced requires an ANDA applicant to respond[,] . . . we will consider this a 'change in or review of the requirements for approval' within the meaning of [the FDCA]." Letter from FDA

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[7] Available at http://www.accessdata.fda.gov/drugsatfda_docs/appletter/2010/090229s000ltr.pdf.

[8] Available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM536725.pdf.

to Sandoz at 9 (Sept. 20, 2011).[9] Thus, this example also fails to reveal any inconsistency in administrative practice.

Finally, the FDA guidance that Amneal references is to the same effect. As with the preceding examples, that guidance merely affirms that changes in the listed drug's labeling or formulation require all ANDA applicants seeking to market a generic version of the listed drug to follow suit. *See* Draft Guidance: 180-Day Exclusivity at 23. For the reasons explained above, that rule is also consistent with the FDA's reading of the exception, and nothing it did with respect to Amneal's ANDA or request for exclusivity is at odds with the guidance.

Accordingly, the FDA's conclusion that its request for commercial-scale data did not constitute a "change in . . . requirements for approval" such that Amneal was exempt from the 30-month forfeiture date was both reasoned and consistent with agency precedent.

B. Receipt of Amneal's ANDA

Amneal's other theory of relief requires only brief discussion. Amneal argues that the FDA's "consideration of whether to receive Amneal's application notwithstanding a typographical error" also constituted a "change in or review of the requirements for approval" of its ANDA. Dkt. 25 at 41. "It is a hard and fast rule of administrative law, rooted in simple fairness, that issued not raised before an agency are waived and will not be considered by a court on review." *Nuclear Energy Inst.*, 373 F.3d at 1297. Accordingly, because Amneal did not raise this issue before the FDA, *see* AR 638–66, it may not do so now.

Moreover, even had Amneal preserved the issue, it would not advance Amneal's cause.

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[9] Available at https://www.regulations.gov/contentStreamer?documentId=FDA-2010-P-0632-0017&attachmentNumber=1.

There is no dispute that established FDA guidance counseled Amneal that ANDAs must contain 84 days of accelerated stability data, nor is there any doubt that Amneal's ANDA contained a typographical error that led the FDA reviewers to conclude that the ANDA lacked the required data. AR 63. That typographical error delayed the FDA's acceptance of the ANDA. But, the error was Amneal's, and it was not the product of any "change in or review of the requirements for approval of" the ANDA. Indeed, the only possible basis for arguing otherwise returns to Amneal's contention that the exception to the 30-month rule applies in every case in which the ANDA sponsor faces an unanticipated hurdle after delivering its application to the FDA. As explained above, that is not the law.

C. Remaining Issues

Having concluded that Amneal has failed to identify a relevant change in the requirements for approval of its ANDA, the Court need not reach Amneal's further argument that the FDA misconstrued the phrase "caused by" and impermissibly imposed a rigid, single-factor causation test. Dkt. 25 at 23–38. The Court recognizes that the FDA's causation test is difficult to square with the statutory text, but Amneal can prevail here only by demonstrating that the FDA misconstrued or misapplied both the "requirement" prong and the "caused by" prong of the proviso. Because Amneal has not cleared the first hurdle, the second hurdle is beside the point.

Finally, having concluded that Amneal's case fails on the merits and that the FDA is entitled to summary judgment, the Court need not decide whether Amneal is entitled to a preliminary injunction or temporary restraining order. "The purpose of a preliminary injunction is merely to preserve the relative positions of the parties until a trial on the merits can be held." *Univ. of Tex. v. Camenisch*, 451 U.S. 390, 395 (1981). It follows that, "[i]n the absence of a

pending claim for relief, there is no basis for the Court to issue an order designed to maintain the status quo while the merits of the dispute are resolved." *Justice v. Koskinen*, 109 F. Supp. 3d 142, 151 (D.D.C. 2015). Amneal's motion for a preliminary injunction or, in the alternative, for a temporary restraining order is, accordingly, now moot.

CONCLUSION

For the reasons set forth above, the Court will deny Amneal's motion for summary judgment, Dkt. 25, grant the FDA's and Lupin's cross-motions for summary judgment, Dkt. 30; Dkt. 34, and deny Amneal's motion for a preliminary injunction or, in the alternative, a temporary restraining order, Dkt. 62, as moot.

A separate order will issue.

/s/ Randolph D. Moss
RANDOLPH D. MOSS
United States District Judge

Date: January 23, 2018