IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

AMNEAL PHARMACEUTICALS LLC
400 Crossing Boulevard
Bridgewater, NJ 08807

Plaintiff,

v.

FOOD AND DRUG ADMINISTRATION
10903 New Hampshire Avenue
Silver Spring, MD 02993,

STEPHEN OSTROFF, M.D.
in his official capacity as
Acting Commissioner of Food and Drugs
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 02993,

and

NORRIS COCHRAN
in his official capacity as
Acting Secretary of Health and Human Services
200 Independence Avenue, S.W.
Washington, DC 20201,

Defendants.

Civil Action No. 17-180

COMPLAINT FOR DECLARATORY AND INJUNCTIVE RELIEF

Plaintiff Amneal Pharmaceuticals LLC ("Amneal") alleges as follows:

INTRODUCTION

1. Amneal was the first generic manufacturer to submit an Abbreviated New Drug Application ("ANDA") to the Food and Drug Administration ("FDA" or "the Agency") containing a Paragraph IV certification for Forest Laboratories, Inc.'s Namenda XR® (memantine hydrochloride extended-release capsules). As a result, Amneal is entitled to 180-day exclusivity under the federal Food, Drug, and Cosmetic Act ("FDCA").

2. This action challenges FDA's finding that Amneal forfeited 180-day exclusivity for failing to obtain tentative approval of its ANDA within thirty months of filing despite the fact that Amneal's ANDA experienced extensive months-long delay resulting from changes in or reviews of the approval requirements for the application. The FDCA excuses a failure to obtain approval where it was "caused by a change in or a review of the requirements for approval of the application." 21 U.S.C. § 355(j)(5)(D)(i)(IV). Any causal connection will do, and under FDA and court precedent, "but for" causation is not required.

3. Nevertheless, FDA, under the guise of applying its precedent setting forth a favorable presumption of causation, instead applied an irrebuttable adverse presumption of no causation. The Agency then used that conclusion to deprive Amneal of the causation analysis that the FDCA mandates. FDA also improperly concluded that changes in or reviews of approval requirements required statutory changes or changes to FDA policy, and then used secret FDA policy that is contrary to FDA's own public guidance as a further basis to deny relief.

4. Under a proper review of the record, evaluation of causation, and application of the FDCA's requirements, Amneal is entitled to, and has not forfeited, 180-day exclusivity. FDA's forfeiture finding – and the Agency's approvals of third-party ANDAs for Namenda XR® that rely on it – are arbitrary, capricious, and contrary to law, and must be vacated.

PARTIES

5. Plaintiff Amneal Pharmaceuticals LLC is incorporated in Delaware and maintains a principal place of business in Bridgewater, New Jersey. Amneal is the seventh largest generic pharmaceutical manufacturer in the United States and works to bring high quality, affordable medicines to patients worldwide.

6. Defendant Food and Drug Administration is an agency of the United States government within the Department of Health and Human Services, with its headquarters and principal place of business at 10903 New Hampshire Avenue, Silver Spring, Maryland. The Secretary of Health and Human Services has delegated to FDA the authority to administer the relevant provisions of the FDCA.

7. Defendant Stephen Ostroff, M.D., is Acting Commissioner of Food and Drugs and is FDA's senior official. He is sued in his official capacity. Dr. Ostroff maintains an office at 10903 New Hampshire Avenue, Silver Spring, Maryland.

8. Defendant Norris Cochran is Acting Secretary of Health and Human Services and the official charged by law with administering the FDCA. He is sued in his official capacity. Acting Secretary Cochran maintains an office at 200 Independence Avenue, S.W., Washington, D.C.

JURISDICTION AND VENUE

9. This action arises under the FDCA, 21 U.S.C. § 301 *et seq*., and the Administrative Procedure Act, 5 U.S.C. § 500 *et seq*. This Court has jurisdiction pursuant to 28 U.S.C. §§ 1331, 1361, and 2201-2202.

10. There exists an actual and justiciable controversy between Amneal and the defendants requiring resolution by this Court.

11. Venue is proper pursuant to 28 U.S.C. § 1391(e).

STATUTORY AND REGULATORY BACKGROUND

12. The Drug Price Competition and Patent Term Restoration Act of 1984 (the "Hatch-Waxman Amendments" to the FDCA), as amended by the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. L. No. 108-173 ("MMA"), created an abbreviated approval pathway to encourage generic competition to approved drugs. Prior to the enactment of the Hatch-Waxman Amendments, generic market entry often was stifled by overly-burdensome regulations requiring submission of a full-blown New Drug Application ("NDA") even for generic drugs. This hampered access to generic medicines that typically are sold at lower, more competitive prices. The Hatch-Waxman Amendments codified the Abbreviated New Drug Application ("ANDA") pathway for expedited approval of generic versions of a drug previously approved under an NDA that are the same as and, among other things, contain the same active ingredient(s) and are shown to be bioequivalent to the previously approved drug.

13. Upon approval of an NDA for a new drug, FDA lists the approved drug as a reference listed drug ("RLD") in the "Approved Drug Products with Therapeutic Equivalence Evaluations," commonly referred to as the "Orange Book." Patents identified by the NDA holder that claim the RLD or a method of using the RLD are also listed by FDA in the Orange Book ("listed patent").

14. Congress required each ANDA applicant to include one of four patent certifications for each listed patent. One of these, relevant here, is the "Paragraph IV" certification that the listed patent is invalid, unenforceable, or will not be infringed by the proposed generic drug. An ANDA applicant making a Paragraph IV certification is required to provide notice to the holder of the challenged patent, which can and often does provoke a patent infringement lawsuit.

15. Because an unexpired listed patent generally blocks generic competition, sometimes unjustifiably, Congress included provisions to encourage and reward generic manufacturers who

challenge listed patents and assume the risk and expense of litigation. The FDCA provides the "first applicant" that "submitted an [ANDA] containing [a Paragraph IV] certification" with a 180-day exclusivity period against generic competitors during which FDA cannot approve competing ANDAs for the same RLD. 21 U.S.C. § 355(j)(5)(B)(iv)(I).

16. However, a first applicant can "forfeit" (or lose) 180-day exclusivity if certain events occur or fail to occur. *Id.* at § 355(j)(5)(D)(ii). Relevant here, a first applicant can forfeit its 180-day 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." 21 U.S.C. § 355(j)(5)(D)(i)(IV) (emphases added).

17. FDA's decisions and court precedent have made clear "but for causation is not required" under the statute in order to meet the causation exception to forfeiture of 180-day exclusivity for failure to obtain tentative approval within 30 months. *Mylan Labs. Ltd. v. FDA*, 910 F. Supp. 2d 299, 311 n.7 (D.D.C. 2012).

18. FDA has confirmed this as recently as January 13, 2017, in a draft guidance titled "Guidance for Industry – 180-Day Exclusivity: Questions and Answers" ("January 2017 Draft Guidance"), *available at* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatory Information/Guidances/UCM536725.pdf. The January 2017 Draft Guidance collects FDA's current interpretation of the law, and states that "FDA has determined that 'but-for' causation is not required to qualify for [the causation] exception." January 2017 Draft Guidance at 22. As long as "one of the causes of failure to obtain tentative or final 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 application will not forfeit eligibility for exclusivity notwithstanding

that there may have been other causes for failure to obtain tentative approval…." *Id.* *Accord* *Mylan*, 910 F. Supp. 2d at 302 (same).

19. FDA has explained that "this interpretation of the statute best effectuates the policy underlying the exception. It does not penalize applicants for FDA's reviews of, or changes in, approval requirements imposed on applicants after their ANDAs are filed that are a cause of the failure to obtain final approval or tentative approval within 30 months. This interpretation also continues to incentivize ANDA applicants to challenge patents by preserving in many instances the opportunity to obtain 180-day exclusivity." January 2017 Draft Guidance at 22.

20. As a consequence, as one court has explained:

> [A]n 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.

Mylan, 910 F. Supp. 2d at 302.

21. Thus, the causation analysis under the FDCA is flexible and fact-intensive. FDA should not impose forfeiture if, as a factual matter, there is ***any*** causal connection between the failure to obtain tentative approval and a change in or review of approval requirements for the application.

FACTS

A. The Eight-Month Delay in FDA's Receipt and Commencement of Substantive Review of Amneal's ANDA

22. On June 10, 2013, Amneal submitted ANDA No. 205825 seeking approval to market a generic version of Namenda XR® capsules in all four approved strengths, 7 mg, 14 mg, 21 mg, and 28 mg. Amneal's ANDA also included Paragraph IV certifications to the unexpired Orange-Book-listed patents for the RLD, Namenda XR®. Amneal's ANDA was the first-

submitted ANDA that included at least one Paragraph IV certification to at least one of the listed patents for Namenda XR®, thus entitling Amneal to 180-day exclusivity.

23. On November 5, 2013, nearly five months after the application was submitted, FDA sent a letter to Amneal that it was refusing to receive the ANDA because Amneal allegedly "failed to produce accelerated stability data which encompasses at least 84 days in the accelerated stability chamber for the 30 count and the 500 counts for all strengths." (By comparison, this five-month period was well after the 60 days FDA gives itself under its own regulations to complete its initial review of a full-blown NDA (*see* 21 CFR § 314.101(a)(1)).)

24. On November 6, 2013, the day before it received the letter, Amneal received a call from FDA that FDA was going to refuse to receive the application and that Amneal would receive a letter to that effect. The Agency stated that Amneal had not provided stability data encompassing 84 days. On the call, Amneal expressed surprise because it believed that it had provided the requisite 84 days of data. Amneal stated that it would immediately investigate and immediately correct any issue or misunderstanding. Amneal asked the Agency to give the company time do so before issuing the refusal to receive.

25. Amneal received FDA's letter on November 7, 2013. The morning of the very next day, Amneal told FDA that Amneal had, in fact, already produced and provided the Agency with all of the requisite data. The ANDA, FDA was told, simply contained a typographical error in a summary table of the data that incorrectly listed the stability testing initiation date as November 27, 2012, instead of November 21, 2012, when the testing had actually been started. The data within the application, however, were complete.

26. At FDA's request, Amneal emailed FDA four days later, on November 11, 2013, to confirm that Amneal initiated stability testing on November 21, 2012. In addition, even though

the requisite data were in the ANDA as originally filed on June 10, Amneal also provided, as requested by FDA, documentation (including original laboratory reports).

27. Following this, Amneal repeatedly contacted FDA for updates on the status of the review, including on November 18 and again on December 4, 2013. On December 4, at FDA's request, Amneal resubmitted the information previously provided on November 11.

28. Finally, two months later, FDA decided to rescind its refusal to receive the application. On February 18, 2014, FDA informed Amneal that "the Office of Generic Drugs has decided to rescind [FDA's] 'Refuse to Receive' letter dated November 5, 2013" and deemed Amneal's ANDA "ACCEPTABLE FOR FILING" as of the June 10, 2013 date of submission. As a consequence, FDA formally received Amneal's ANDA. It was only then, more than eight months after Amneal's original and complete ANDA submission, that FDA finally began substantive review of the application.

B. FDA's Demand for Full-Scale Commercial Batch Data Results in an Additional 14-Month Delay

29. FDA's consistent and longstanding guidance to ANDA applicants has been to submit ANDAs with pilot-size batches and corresponding production data as part of the ANDA's Chemistry, Manufacturing, and Controls ("CMC") information. Even as late as June 2014, FDA's guidance stated: "[T]he applicant should submit data from three pilot scale batches **or** should submit data from two pilot scale batches and one small scale batch. This applies to all dosage forms." *See* U.S. Food & Drug Admin., Guidance for Industry: ANDAs: Stability Testing of Drug Substances and Products: Questions and Answers at 3, 8 (May 2014) (emphasis original) ("Two of the three batches should be of at least 10 percent of the proposed [commercial] production batch or 100,000 finished dosage units, whichever is greater (i.e., pilot scale batches). The third batch can be smaller…"), *available at* http://www.fda.gov/downloads/

drugs//guidances/ ucm366082.pdf; U.S. Food & Drug Admin., Guidance for Industry: ANDAs: Stability Testing of Drug Substances and Products at 2 (June 2013) (same), *available at* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM320590.pdf; U.S. Food & Drug Admin., Guidance for Industry: Q1A(R2) Stability Testing of New Drug Substances and Products at 8 (November 2003) ("Two of the three batches should be at least pilot scale batches, and the third one can be smaller if justified."), *available at* http://www.fda.gov/downloads/drugs//guidances/ucm073369.pdf. *See also* U.S. Food & Drug Admin., Manual of Policies and Procedures 5225.1, Guidance on the Packaging of Test Batches at 5 (September 2012) ("The minimum amount to be packaged is 100,000 units.").

30. Prior to the ANDA at issue in this case, Amneal – across a portfolio of nearly 100 approved ANDAs – had never previously been required to produce a commercial-scale lot as a condition of approval.

31. Consistent with FDA practice and the Agency's guidance to industry, Amneal's ANDA submission included data from pilot-size batches of well over 100,000 units. Amneal's proposed commercial-scale batch, as described in the ANDA submission, would use the same equipment, same process, and same materials as the submitted pilot-scale batches, but was about six and a half times larger.

32. However, on September 10, 2014, the Agency issued a complete response letter informing Amneal that FDA "cannot approve this ANDA in its present form." While most of the deficiencies were minor, FDA's letter also raised a series of questions regarding the composition of Amneal's product. To address these questions, FDA's letter informed Amneal that the company would have to provide certain information. Most importantly, the letter informed Amneal that FDA had determined the application "requires the review of the resulting

data from the manufacture of a commercial size lot [i.e., batch] before application approval. In this regard, please submit all the required CMC information for the production of a 7 mg and 28 mg Memantine HCl lot of the size intended for commercial distribution."

33. Amneal immediately and diligently began work on a submission responsive to this new requirement for commercial-scale information that FDA demanded be provided "before application approval." But that process necessarily was time-consuming. To comply with this new approval requirement, Amneal had to order, and its suppliers had to produce, hundreds of kilograms of the bulk active pharmaceutical ingredient ("API") (along with the required excipients and other components), and Amneal had to process that API for use in two distinct commercial-size lots of the finished product. This process alone took several months to complete, which occurred in late January and early February 2015. The process of producing an intermediate, and producing and packaging two commercial-size lots of finished product took longer still: until mid-April 2015. Completing the CMC analysis for FDA's newly-required commercial-size lots took yet another month.

34. On May 12, 2015, roughly eight months after FDA first informed Amneal that the company's application would require the production and analysis of complete commercial-size lots as a condition of approval, Amneal submitted an amendment to its ANDA with full CMC data and analysis from the scaled-up lots. Amneal's submission also answered each of the related questions that prompted FDA to require the manufacture and analysis of commercial-size lots.

35. On August 25, 2015, FDA sent Amneal a series of follow-on questions that again focused on Amneal's proposed composition of its product based on the characteristics of the

reference listed drug and acknowledged the extended production times for the commercial-size lots Amneal had produced in response to the Agency's requests.

36. Amneal responded on September 15, 2015 by (among other things) providing further information regarding the RLD and explaining that the production of commercial-size lots involved a multistage process that included extensive sampling and analysis.

37. On October 14, 2015, during the extensive delay caused by FDA's request that Amneal provide data from a scale up to commercial-size batches, FDA issued an Import Alert against Amneal's proposed API manufacturer, Megafine Pharma (P) Limited ("Megafine"), subjecting Megafine's products to detention without physical examination. FDA's alert effectively necessitated a change in API supplier by Amneal.

38. On October 22, 2015, FDA issued an information request in which the Agency asked Amneal to "scale down the proposed commercial batch size."

39. On November 9, 2015, fourteen months after FDA's original demand for commercial-scale information, Amneal responded and agreed to FDA's request that Amneal scale down to pilot-size batches. It stated:

> As per the Agency's recommendation, Amneal will scale down the proposed commercial batch size from [the previously proposed commercial scale batch size number of] capsules to [the pilot batch size number of] capsules (same as ANDA submission batch size) for all strengths of Memantine Hydrochloride Extended Release Capsules (i.e. 7 mg, 14 mg, 21 mg and 28 mg).

40. In amendments dated November 9 and November 16, 2015, Amneal proposed a new API supplier to replace Megafine.

41. In its December 7, 2015 complete response letter, FDA wrote that it "acknowledge[s] that [Amneal] will not scale up and batch sizes will remain as per the exhibit lot size." The remaining deficiencies in the letter related to Amneal's need to replace its API manufacturer.

42. FDA completed chemistry review on September 19, 2016. Amneal's ANDA was granted final approval on October 12, 2016.

C. FDA's 180-Day Exclusivity Forfeiture Ruling

43. On December 2, 2015, counsel for Amneal wrote FDA seeking confirmation that Amneal would not forfeit 180-day exclusivity because FDA's request for data for commercial-scale lots constituted a change in or review of approval requirements that caused the failure to obtain tentative approval within 30 months of filing of the ANDA.

44. FDA responded by letter decision (the "Letter Decision") on September 28, 2016 finding that Amneal's 180-day exclusivity had been forfeited because, the Agency stated, Amneal had not received tentative approval within 30 months of submission of the ANDA. FDA stated that the Agency's request that Amneal scale up, manufacture, and conduct analysis on commercial size batches before approval was not "a cause of Amneal's failure to obtain tentative or final approval by December 10, 2015." Letter Decision at 9.

45. FDA's October 12, 2016 letter granting final approval to Amneal's ANDA reiterated this conclusion.

1. <u>FDA failed to apply the causation analysis mandated by the FDCA</u>

46. FDA's conclusion regarding causation, however, was based entirely on an overly-simplistic, rigid analysis that simply examines whether the excusing condition is present on the FDA's forfeiture date. This analysis, focused on a single dispositive factor, is contrary to the FDCA and is arbitrary and capricious.

47. The Agency began by properly recognizing that the inquiry mandated by the FDCA is whether the "failure to obtain a tentative approval or approval at the 30-month date is **caused by** [a particular] change in or review of approval requirements." Letter Decision at 2 (emphasis

original). It also correctly noted that under the Agency's precedent, "'but for' causation is not required." *Id.*

48. The Agency then recognized that it has made available a favorable presumption to ANDA filers, stating that "FDA generally will ***presume*** that the failure to obtain tentative approval or approval was caused by a change in or review of approval requirements if, at the 30-month date, the evidence demonstrates that the sponsor was actively addressing the change in or review of approval requirements (or FDA was considering such efforts), and these activities precluded tentative approval (or approval) at that time. [If the evidence does not so demonstrate,] FDA generally does ***not presume*** that the failure was caused by a change or review of approval requirements." *Id.* at 2 (emphases added).

49. Given that FDA's precedent establishes a ***presumption*** of causation, if conditions for the favorable presumption are not satisfied, the result should not be an adverse finding against the applicant. Rather, the result should be a factual analysis of the record to evaluate the existence of causation in fact in the absence of the favorable presumption, as the statute requires.

50. FDA did not do that here. FDA observed that, as of FDA's calculated forfeiture date, Amneal had (just one month earlier) agreed to FDA's request that Amneal scale down its manufacturing to the pilot-size batch. FDA noted that "[t]he Agency's request that Amneal manufacture and submit information on commercial size lots for the 7 mg and 28 mg strengths was thus resolved before the forfeiture date of December 10, 2015. Therefore, it could not preclude tentative approval at that time." Letter Decision at 15. As a consequence, the Agency found no causation.

51. In effect, the Agency converted its favorable presumption of causation into an irrebuttable adverse presumption of no causation. FDA's causation analysis was simple, rigid,

and involved only one fact: Had the change in or review of approval requirements been resolved by the forfeiture date? Because it had been, FDA apparently reasoned, the change in batch size could never have any causal connection to the failure to obtain approval. On the basis of a single fact, FDA treated the 14-month-long delay caused by its demand for commercial-scale data as irrelevant.

52. FDA's distillation of the statutorily-mandated causation analysis to a single, dispositive fact is incompatible with the flexible, fact-based causation test set forth in the FDCA.

53. FDA's simplistic analysis here is contrary even to the Agency's own guidance, which recognizes that determining causation where its favorable presumption does not apply requires consideration of multiple facts. FDA's January 2017 Draft Guidance confirms that the analysis involves a favorable "presumption," not the conclusive, irrebuttable test the Agency instead applied in Amneal's case. Moreover, the January 2017 Draft Guidance states that when the favorable presumption of causation does not apply, FDA will evaluate causation on its facts and, for example, "take into account how close the change in or review of the requirement for approval occurred to the 30-month date as well as the amount of effort needed to respond to the change. Further, if the applicant's response is submitted after the 30-month date, FDA will consider, among other factors, how close the response is submitted to the 30-month date." January 2017 Draft Guidance at 23.

54. FDCA's simplistic, rigid analysis in this case not only cannot be squared with the Agency's own guidance, but it also frustrates the statute's purpose and invites absurd results. FDA's test arbitrarily punishes applicants who face early changes in or reviews of approval requirements but provides relief to similarly-situated applicants that happen to face those changes closer to the forfeiture date.

55. In short, all that the Agency concluded in its Letter Decision was that a favorable presumption of causation was unavailable to Amneal. That analysis is insufficient under the FDCA to warrant forfeiture of Amneal's 180-day exclusivity.

2. FDA failed to provide a reasoned explanation as to why a 14-month delay had no causal effect on the timing of tentative approval

56. Because FDA failed to apply the causation test required by the FDCA, FDA did not analyze or address the factual record before it to determine the existence of causation in fact, as the statute requires. It failed to examine the relevant facts and failed to articulate a satisfactory explanation for its decision, including a rational connection between the facts found and the choice made.

57. Because of its simplistic causation analysis, FDA failed to address, consider, and explain the effect of numerous facts plainly relevant to causation. These included the length of the delay resulting from the change in or review of approval requirements, how close its resolution was to the forfeiture date, how disruptive it was to the review of the application, how it may or may not have affected the timing of approval, or how the change in or review of approval requirements interacted with other delays in the application, such as the delay in receipt of the application, to prevent timely tentative approval.

58. Indeed, FDA did not even address or analyze facts the Agency itself has identified as relevant in its own recent draft guidance. It did not address "how close the change in or review of the requirement for approval occurred to the 30-month date." *Cf.* January 2017 Draft Guidance at 22-23. In this case, issues related to FDA's scale-up demand were still being addressed until just a month before the 30-month date. Nor did the Agency address "the amount of effort needed to respond to the change," *c.f. id.*, which, in this case, was considerable.

59. All of these facts, and more, are relevant and necessary for the Agency to address and explain in order for a causation determination to be the product of reasoned decision making. FDA ignored them all. FDA provided no explanation as to how a 14-month-long delay could have no causal connection whatsoever to the failure to obtain tentative approval within 30 months.

60. The 14-month delay resulting from FDA's request for information from commercial-scale batches constituted almost half of the 30-month forfeiture period. Moreover, FDA's demand for information based on commercial-size batches occurred in the first year of FDA's substantive review of the application after the delay in its receipt. Compliance with this change then became a substantial focus of both Amneal and FDA's efforts for the next 14 months. Given the delay in receipt of the application, this 14-month period was two-thirds of the time that the application was even undergoing substantive review by FDA during the forfeiture period. The issue was only resolved on November 9, 2015, a mere month before FDA's December 10, 2015 forfeiture date. Under these circumstances, the 14-month delay plainly had a causal connection to Amneal's failure to obtain tentative approval within the 30-month period. Under the FDCA, which does not require "but for" causation, this should have prevented forfeiture of Amneal's 180-day exclusivity.

3. FDA relied on a secret policy to find that its request for commercial-scale batch information was not a change in or review of approval requirements

61. The Agency also concluded, in the alternative, that "the request to scale up and complete a commercial-size batch before approval was [not] a change in or review of the requirements for approval" imposed after the ANDA was filed. Letter Decision at 15.

62. FDA based this conclusion on its contention that neither the "statutory requirement" governing the assessment of chemistry, manufacturing, or controls nor FDA's "specific requirements for certain complex products" had changed. Letter Decision at 15.

63. FDA asserted that there was no change in the approval requirements because its demand for commercial-scale information was pursuant to an FDA policy requiring commercial-scale information for "certain" products on an application-specific basis. The Letter Decision, however, identified no specific instance, available to Amneal or to the public, in which FDA has articulated such a policy. In fact, the Letter Decision expressly states that FDA is unable to disclose when it has applied this policy due to confidentiality obligations under FDA's disclosure regulations. Letter Decision at 15 and note 43.

64. FDA also admitted that this policy is not evident from the public record available to applicants prior to filing an ANDA. In its Letter Decision, FDA conceded that "FDA's general policies on manufacturing test batches do not describe [the circumstances under which FDA might require more than pilot scale batch data], nor is it surprising that Amneal believes it has not been previously asked to provide a commercial-scale batch to support approval." Letter Decision at 16.

65. FDA's focus on "statutory" changes, or changes to its overall policy is inconsistent with the plain language of the FDCA. The FDCA does not refer to changes in the statutory standards, or to FDA's policies or guidance. Rather, the statute clearly states that forfeiture is excused if the failure to obtain tentative approval 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) (emphases added). FDA's requirement that Amneal show a change to the statute or general FDA policy sets the bar far higher than the statute

permits. Post-filing changes in or reviews of the approval requirements for a specific application are sufficient.

66. FDA's demand for commercial-scale data was a change in or review of the review of requirements for approval of ***Amneal's application*** after the date on which ***the application*** was filed. As discussed, FDA's public guidance permits the submission of pilot-scale data in support of all ANDA applications. The application complied with FDA's guidance at the time of its submission. It was only after the application was filed that FDA changed the rules of the game set forth under its public guidance and stated that further evidence would be required.

67. FDA concedes that its secret requirement for commercial-scale data is applied on a case-specific basis, and occurs only after an application is filed. FDA's Letter Decision admits that "the determination as to whether manufacture of a commercial-scale batch is necessary is application specific, and is made during the substantive review of the ANDA by the chemistry reviewers." Letter Decision at 15.

68. Contrary to the policy of the FDCA as articulated by FDA itself – *see* January 2017 Draft Guidance at 22-23 – FDA is using forfeiture to "penalize" Amneal for review or changes of approval requirements imposed by the Agency after filing that Amneal could not have anticipated prior to filing. FDA's penalizing of Amneal is particularly arbitrary given the Agency's shifting-sands approach to whether pilot-scale or commercial-scale data are sufficient. From the perspective of the public, FDA's application of its secret policy was a change in the approval requirements set forth in FDA's public policy. A secret, undisclosed reversal or change by the Agency to its guidance that is not ascertainable by prospective ANDA applicants from the public record cannot qualify as a change that the public and industry should be expected to rely upon when preparing applications for approval.

4. FDA failed to consider the effect of the months-long delay in receipt of the ANDA

69. FDA concluded that Amneal's ANDA was "filed" for purposes of the tentative approval forfeiture statute on June 10, 2013 when it was submitted to FDA.

70. Thus, all of FDA's activity regarding whether to receive the application, including the Agency's requests for information confirming the typographical error and the associated review were "imposed after the date on which the application is filed." *See* 21 U.S.C. § 355(j)(5)(D)(i)(IV).

71. The Agency's receipt of an ANDA is by necessity a condition for approval, as it is a condition for any review at all. Thus, FDA's activity regarding whether to receive the application in light of the typographical error was also a change in or review of the requirements for approval.

72. Amneal addressed the issues raised by FDA in reviewing whether to receive the ANDA immediately and explained that all the requisite data had been provided from the start despite a simple and obvious typo. Amneal then repeatedly followed up with the Agency regarding the receipt status of its ANDA. Nevertheless, even after the five-months FDA took to initially decide whether to refuse receipt of the application, FDA then inexplicably took months to review whether it would rescind its refusal to receive the application and acknowledge that its refusal to receive the application had been improper.

73. Yet, FDA's forfeiture analysis did not address, and indeed entirely overlooked, the effect of the months-long delay caused by the Agency's refusal to receive the application and subsequent rescindment of that refusal. FDA's failure to address the causal impact of this substantial delay, either alone or in combination with the delay caused by FDA's scale-up demand, was contrary to law and was arbitrary and capricious.

D. FDA's Unlawful Approval of Third-Party ANDAs

74. The same day FDA sent its forfeiture decision to Amneal, FDA granted final approval to the following three third-party ANDA applications for generic versions of Namenda XR® at all four strengths:

- ANDA 206028, sponsored by Lupin Limited ("Lupin").
- ANDA 206032, sponsored by Mylan Pharmaceuticals Inc. ("Mylan").
- ANDA 205905, sponsored by Sun Pharma Global FZE ("Sun").

75. On November 22, 2016, FDA granted final approval to a fourth ANDA for a generic version of Namenda XR® at all four strengths: ANDA 206135, sponsored by Apotex Inc.

76. Absent forfeiture, Amneal qualifies for 180-day exclusivity. Therefore, FDA's final approval of these ANDAs was unlawful, as is any other final approval that FDA has granted or may grant for generic memantine hydrochloride extended-release capsules, 7 mg, 14 mg, 21 mg, or 28 mg strengths, prior to the expiration of Amneal's 180-day exclusivity.

COUNT I
(VIOLATION OF THE FDCA AND THE ADMINISTRATIVE PROCEDURE ACT, 5 U.S.C. § 706)

77. The above paragraphs are incorporated by reference.

78. FDA's finding that Amneal forfeited 180-day exclusivity constitutes final agency action.

79. FDA's final approvals of Lupin, Mylan, Sun, and Apotex's ANDAs constitute final agency action. FDA's final approval of any other ANDAs for generic memantine hydrochloride extended-release capsules, 7 mg, 14 mg, 21 mg, or 28 mg strengths, also constitutes final agency action.

80. FDA's decision forfeiting Amneal's 180-day exclusivity violates the plain language of the FDCA. FDA's decision is in excess of its statutory authority, arbitrary, capricious, an

abuse of discretion, and otherwise not in accordance with law, in violation of 5 U.S.C. § 706. The decision must be vacated and set aside for at least the following reasons:

a. FDA's application of an irrebuttable adverse presumption of no causation if the change in or review of the approval requirements is resolved as of the forfeiture date is contrary to the causation analysis required by the FDCA and is arbitrary and capricious;

b. FDA's decision is not the product of reasoned decision making because it failed to provide an explanation for rejecting any causal connection between the 14-month delay resulting from FDA's demand for commercial-scale batch information and Amneal's ability to obtain timely tentative approval;

c. FDA's conclusion that its demand for commercial-scale batch information was not a change in or review of approval requirements because FDA had not changed a secret, undisclosed policy is contrary to the FDCA and is arbitrary and capricious;

d. FDA failed to consider the impact, either alone or in the aggregate, of the months-long delay in deciding whether to receive Amneal's ANDA. The delay in receipt was itself the product of a change in or review of approval requirements and should have been considered by FDA as a potential cause for the failure to timely obtain tentative approval. FDA should also have considered the delay in receipt in an analysis of the causal effect of FDA's demand for commercial-scale information.

81. Amneal is entitled to 180-day exclusivity under the FDCA, and has not forfeited that exclusivity under 21 U.S.C. § 355(j)(5)(D)(i)(IV), properly applied.

82. FDA's approvals of Lupin, Mylan, Sun, and Apotex's ANDAs are barred by Amneal's 180-day exclusivity, and thus were unlawful and contrary to law, and must be set aside.

83. Any other final approvals that FDA has granted or may grant for generic memantine hydrochloride extended-release capsules, 7 mg, 14 mg, 21 mg, or 28 mg strengths, prior to the expiration of Amneal's 180-day exclusivity are also unlawful and must be set aside.

RELIEF REQUESTED

WHEREFORE, Amneal requests that this Court:

1. Enter judgment for Amneal on all counts of this Complaint;

2. Vacate FDA's finding of forfeiture as contrary to law, an abuse of discretion, and arbitrary and capricious;

3. Declare that Amneal has not forfeited 180-day exclusivity under 21 U.S.C. § 355(j)(5)(D)(i)(IV);

4. Enter an order vacating or setting aside FDA's final approval of Lupin, Mylan, Sun, and Apotex's ANDAs, and any other ANDA approval FDA has granted for generic memantine hydrochloride extended-release capsules, 7 mg, 14 mg, 21 mg, or 28 mg strengths, in contravention of Amneal's 180-day exclusivity;

5. Preliminarily and permanently enjoin FDA from granting final approval to any ANDA, other than Amneal's ANDA, for generic memantine hydrochloride extended-release capsules, 7 mg, 14 mg, 21 mg, or 28 mg strengths, until the expiration of Amneal's 180-day exclusivity.

6. Postpone the effective date of FDA's final approval of any ANDA, other than Amneal's ANDA, for generic memantine hydrochloride extended-release capsules, 7 mg, 14 mg, 21 mg, or 28 mg strengths, pending judicial review pursuant to 5 U.S.C. § 705.

7. Provide such other and further relief as the Court deems just and proper.

DATED: January 27, 2017

AMNEAL PHARMACEUTICALS LLC,
By its attorneys,

/s/ Areta Kupchyk

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