UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

FERRING PHARMACEUTICALS, INC.,	:	
	:	
Plaintiff,	:	Civil Action No.: 15-0802 (RC)
	:	
v.	:	Re Document Nos.: 20, 22
	:	
SYLVIA M. BURWELL, *et al.*,	:	
	:	
Defendants.	:	

MEMORANDUM OPINION

GRANTING IN PART AND DENYING IN PART DEFENDANTS' MOTION FOR SUMMARY JUDGMENT AND DENYING PLAINTIFF'S MOTION FOR SUMMARY JUDGMENT

I. INTRODUCTION

Plaintiff Ferring Pharmaceuticals, Inc. ("Ferring") is the manufacturer of PREPOPIK, a fixed-dose combination drug product that contains three drug substances: sodium picosulfate, magnesium oxide, and anhydrous citric acid. When it submitted a New Drug Application ("NDA") for PREPOPIK to the U.S. Food and Drug Administration ("the FDA"), Ferring sought a five-year period of marketing exclusivity because one of the drug substances, sodium picosulfate, had never previously been approved in a NDA. The Federal Food, Drug, and Cosmetics Act ("FDCA") provides for a five-year period of marketing exclusivity when a drug application is approved "for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application." 21 U.S.C. § 355(j)(5)(F)(ii). During that five-year period, "no application may be submitted . . . which refers to the drug for which the subsection (b) application was submitted." *Id.*

The dispute in this case is whether the statutory term "drug," as used in this provision of the FDCA, can reasonably be read to refer to a "drug product" (the finished dosage form of a

drug), or must be read to refer to a "drug substance" (the active ingredient of the drug). *See* 21 C.F.R. § 314.3 (defining "drug product" and "drug substance"). Because PREPOPIK's other two active ingredients had previously been approved for market, the FDA applied its then-existing interpretation of the FDCA and determined that PREPOPIK was not entitled to a five-year period of marketing exclusivity. Ferring filed a Citizen Petition challenging the FDA's interpretation. In response, the FDA—acknowledging the policy concerns Ferring and two other pharmaceutical companies raised regarding the agency's interpretation—concluded that the FDCA could reasonably be read to refer to "drug substances," and announced that it would change its interpretation and permit five-year exclusivity for fixed-combination drug products that contained a novel drug substance, even if that drug product also contained other previously-approved drug substances. Yet, the victory was a pyrrhic one for Ferring: the FDA concluded that it would apply its interpretation only prospectively, and declined to alter its exclusivity determination for PREPOPIK.

In this Administrative Procedure Act ("APA") action, Ferring challenges the FDA's prior interpretation as contrary to the plain language of the FDCA, or an unreasonable interpretation of statutory ambiguity, under *Chevron, U.S.A., Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837 (1984). Alternatively, Ferring claims that even if the FDA's prior interpretation was permissible, the agency's refusal to apply its new interpretation retroactively is arbitrary and capricious. For the foregoing reasons, the Court concludes that the term "drug" as used in the five-year exclusivity provision is ambiguous and that the FDA's prior interpretation was a reasonable one. This conclusion preserves the agency's discretion to choose among the reasonable interpretations of an ambiguous statutory term, and accords with the Supreme Court's admonition that "'change is not invalidating, since the whole point of *Chevron* is to leave the

discretion provided by the ambiguities of a statute with the implementing agency.'" *Nat'l Cable & Telecomms. Ass'n v. Brand X Internet Servs.*, 545 U.S. 967, 981 (2005) (quoting *Smiley v. Citibank (South Dakota), N.A.*, 517 U.S. 735, 742 (1996)). Thus, the Court will grant summary judgment in part to Defendants on the *Chevron* issues. The Court concludes that supplemental briefing is necessary on the retroactivity question, however, and the Court will deny both motions for summary judgment on that ground, without prejudice. The Court will direct the parties to file renewed motions for summary judgment on the retroactivity issue that discuss the authorities identified below.

II. FACTUAL & STATUTORY BACKGROUND

A. Statutory Background

The FDCA requires that all new prescription drugs be approved by the FDA before they can be marketed. *See* 21 U.S.C. § 355(a). Generally, when a pharmaceutical manufacturer submits a NDA for approval, it must support that application with full reports of clinical studies that demonstrate that the product is safe and effective. *See id.* § 355(b). In 1984, Congress altered aspects of this process when it enacted what are popularly referred to as the Hatch-Waxman Amendments. *See* Drug Price Competition and Patent Term Restoration Act, Pub. L. No. 98-417, 98 Stat. 1585 (1984); *see also Abbott Labs. v. Young*, 920 F.2d 984, 985 (D.C. Cir. 1990). The Hatch-Waxman Amendments "created a new system for protecting both the interests of drug manufacturers who produce new drugs and the interests of generic drug manufacturers and their consumers." *Abbott Labs.*, 920 F.2d at 985. "Facing the classic question of the appropriate trade-off between greater incentives for the invention of new products and greater affordability of those products, Congress struck a balance between expediting generic drug applications and protecting the interests of the original drug manufacturers." *Id.*

As part of that balance, Congress simplified the approval process for generic versions of listed drugs. The Hatch-Waxman Amendments provided for the submission of an abbreviated new drug application ("ANDA") for the generic version of a previously approved drug. *See* 21 U.S.C. § 355(j)(1). To file an ANDA, a pharmaceutical manufacturer may rely on the FDA's finding that a previously approved drug—referred to as the "listed drug"—is safe and effective, so long as the applicant can demonstrate that the proposed generic drug is the "same as" the reference listed drug in several essential respects. *See generally id.* § 355(j)(2)(A). The Hatch-Waxman Amendments also provide for the approval of a NDA in which some or all of the investigations relied upon to show that the drug is safe and effective "were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted." *Id.* § 355(b)(2). Such applications are referred to as "505(b)(2) applications."

Despite the availability of these less onerous approval avenues, Congress also put in place incentives to promote the development of new drugs. As relevant to this case, the Hatch-Waxman Amendments established a five-year marketing exclusivity period for certain types of drugs, protecting a manufacturer from the submission of an ANDA or 505(b)(2) application and, thus, from generic competition. As amended, the FDCA provides that:

> If an application submitted under subsection (b) of this section [21 U.S.C. § 355(b)] for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, is approved after September 24, 1984, no application may be submitted under this subsection [concerning ANDAs] which refers to the drug for which the subsection (b) application was submitted before the expiration of five years from the date of the approval of the application under subsection (b) of this section . . . .

21 U.S.C. § 355(j)(5)(F)(ii); *see id.* § 355(c)(3)(E)(ii) (parallel provision providing the same five-year exclusivity period to prevent the filing of a 505(b)(2) application).

Even if a drug is not eligible for a five-year period of marketing exclusivity, the Hatch-Waxman Amendments provide for a shorter, three-year period of exclusivity for certain changes to previously approved drugs. If an applicant submits one or more new clinical studies in support of a change in the conditions of an approved drug's use, the FDCA confers a three-year period of marketing exclusivity, so long as the FDA considers those studies to have been essential to the agency's approval of the change. 21 U.S.C. § 355(j)(5)(F)(iii); *see also id.* § 355(c)(3)(E)(iii). Unlike the five-year exclusivity provision, which prohibits the FDA from even *accepting* an application during the exclusivity period, the three-year exclusivity provision only precludes the FDA from making a new ANDA or 505(b)(2) application *effective* before the end of the three-year period. *Compare id.* § 355(j)(5)(F)(ii), *with id.* § 355(j)(5)(F)(iii).

The two clauses of the five-year exclusivity provision relevant to this case are what the parties refer to as the "eligibility" and the "bar" clauses. *See* A.R. 203; Pl.'s Mem. Supp. Summ. J. at 13 ("Pl.'s Mem. Supp."), ECF No. 20-1. The "eligibility clause" describes whether a drug is eligible for five-year exclusivity. To be eligible, a drug must be "a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of [§ 355]." 21 U.S.C. § 355(j)(5)(F)(ii). If a drug meets that requirement, it will bar the types of ANDAs or 505(b)(2) applications identified in the "bar clause." Specifically, "no application may be submitted . . . which *refers to the drug for which the subsection (b) application was submitted* before the expiration of five years from the date of the approval of the application." *Id.* (emphasis added).

The meaning of the word "drug" as used in the five-year exclusivity provision (or the other exclusivity provisions, for that matter) is not defined in section 355. In the FDCA Congress has codified various definitions of that term. *See* 21 U.S.C. § 321(g)(1). "Drug" can

alternatively mean: "articles recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them"; "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals"; or "articles (other than food) intended to affect the structure or any function of the body of man or other animals." *Id.* § 321(g)(1)(A)–(C). But, "drug" can also mean any "articles intended for use *as a component* of any article specified in" those prior three definitions. *Id.* § 321(g)(1)(D) (emphasis added).

By regulation, the FDA has also defined two key terms that the parties invoke in this case: "drug product" and "drug substance." The FDA defines a "[d]rug product" as "a finished dosage form, for example, tablet, capsule, or solution, that contains a drug substance, generally, but not necessarily, in association with one or more other ingredients." 21 C.F.R. § 314.3(b). A "[d]rug substance" is defined in relevant part as "an active ingredient that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure or any function of the human body." *Id.*

Until recently, the FDA read the term "drug" in the "eligibility clause" to refer to a finished "drug product." In a 1988 guidance letter to the industry, and before regulations implementing the Hatch-Waxman Amendments were promulgated, Dr. Carl Peck, Director of the Center for Drug Evaluation and Research, advised NDA and ANDA holders and applicants that the FDA "considers *a drug product* eligible for the five-year period if it contains no active moiety that was previously approved by the agency." A.R. 324 (emphasis added). To assist the agency in making exclusivity determinations, Dr. Peck therefore encouraged applicants to inform the agency whether "any active moiety *in the drug product* for which approval is sought has ever

been approved *in another drug product* in the United States either as a single entity or as part of a combination product." *Id.* (emphases added).

The FDA codified its interpretation of the five-year exclusivity provision in 21 C.F.R. § 314.108, proposed in 1989 and finalized in 1994. *See* Abbreviated New Drug Application Regulations, 54 Fed. Reg. 28,872 (July 10, 1989) [hereinafter "Proposed Rule"]; *see also* Abbreviated New Drug Application Regulations; Patent and Exclusivity Provisions, 59 Fed. Reg. 50,338 (Oct. 3, 1994) [hereinafter "Final Rule"]. The regulation provides that:

> If a drug product that contains a new chemical entity was approved after September 24, 1984, in an application submitted under section 505(b) of the act, no person may submit a 505(b)(2) application or abbreviated new drug application under section 505(j) of the act for a drug product that contains the same active moiety as in the new chemical entity for a period of 5 years from the date of approval of the first approved new drug application . . . .

21 C.F.R. § 314.108(b)(2). The regulation further defines several of these terms. First, the FDA defined "new chemical entity" as "a drug that contains no active moiety that has been approved by FDA in any other application submitted under section 505(b) of the [A]ct." *Id.* § 314.108(a). "[A]ctive moiety," in turn, is defined as "the molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule, responsible for the physiological or pharmacological action of the drug substance." *Id.*

Consistent with Dr. Peck's guidance letter, the FDA admits that it interpreted the term "drug" in the regulation's definition of a "new chemical entity" ("a drug that contains no active moiety that has been approved . . .") to mean a "drug product." *See, e.g.*, A.R. 208. Under that interpretation, those "drug products" that contain no active moiety that had previously been approved would be eligible for five-year exclusivity. *See id.* At the time it promulgated the

regulation, however, the FDA acknowledged that the statute posed a potential problem for the exclusivity holder, and that the Act "is ambiguous as to which ANDA[s] or 505(b)(2) applications are affected by an innovator's exclusivity." Proposed Rule, 54 Fed. Reg. at 28,897. Specifically, under a narrow interpretation of the "bar clause," in which the "protection offered by exclusivity is that exclusivity covers only specific drug products . . . , an innovator's exclusivity could lose its value as soon as FDA approved a second full new drug application for a version of the drug." *Id.* That is because "an ANDA could be approved by reference to the *second approved version of the drug*"—a separate drug product—"which would not be covered by exclusivity." *Id.* (emphasis added). Thus, "[d]epending on the meaning of the phrase 'refer to' and the word 'drug,'" the FDA was concerned that the five-year exclusivity provision and the other exclusivity provisions in the Hatch-Waxman Amendments "could be interpreted to allow ANDA[s] and 505(b)(2) applicants, once FDA approved subsequent new drug applications for different versions of the same drug, to circumvent the innovator's exclusivity by 'referring to' the subsequent versions of the innovator's drug." *Id.*[1]

By contrast, FDA noted that a possible "broader interpretation" of the bar clause "is that it covers the active moieties in new chemical entities . . . rather than covering only specific drug

[1] This possibility assumes that the bar clause bars only ANDAs and section 505(b)(2) applications, and does not similarly prevent the submission of a new full NDA for a novel drug. The parties appear to share this assumption, although they do not fully explain it. In any event, the FDA preamble does note that "[t]he exclusivity provisions of the act do not provide any protection from the marketing" of a drug if that drug "is the subject of a full new drug application submitted under section 505(b)(1) of the act." Proposed Rule, 54 Fed. Reg. at 28,896; *see also Small Business Assistance: Frequently Asked Questions for New Drug Product Exclusivity*, U.S. Food & Drug Admin. (Feb. 11, 2016), http://www.fda.gov/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/ucm069962.htm (explaining that the "new drug product exclusivity provisions do not provide any protection" from "the marketing of a duplicate version of the same drug product if the duplicate version is the subject of a full new drug application submitted under 505(b)(1) of the Act").

products," which "would protect the new active moiety of a new chemical entity . . . from generic competition even after FDA had approved subsequent full new drug applications for subsequent versions of the drug." *Id.* Because the FDA did not "believe that Congress intended the exclusivity provisions to discourage innovators from making improvements in their drug products nor from authorizing the marketing of competitive products," the FDA concluded that the "broader interpretation of the scope of exclusivity should be applied." *Id.* The FDA has coined this interpretation its "umbrella policy," which it describes as providing that "5-year NCE [new chemical entity] exclusivity does not attach only to the first approved drug product that was eligible for 5-year NCE exclusivity, but also to the line of products containing the same active moiety." A.R. 206. And, although it is not quite spelled out in the proposed rule's preamble, the FDA now acknowledges that its umbrella policy resulted from the agency's interpretation of "drug" in the bar clause to mean "drug substance." *Id.* at 225.

Taken together, then, prior to 2014, the FDA interpreted the five-year exclusivity provision to provide that only *drug products* containing no previously approved drug substances were eligible for exclusivity. Once eligible, however, the FDA interpreted the bar clause to bar all ANDAs and 505(b)(2) applications referencing that drug product or any later-approved products containing the product's *drug substances*, in order to preserve the innovator's exclusivity to the greatest extent possible.

B. Factual & Procedural History

Ferring's drug product PREPOPIK is intended for use in cleansing the colon in preparation for colonoscopy in adults. Compl. ¶ 32, ECF No. 2. PREPOPIK is a fixed-dose combination drug product. *Id.* Fixed-dose combination drug products "generally include two or more drug substances (active ingredients) in a fixed ratio, synthetically combined in a single

dosage form." A.R. 200. PREPOPIK in fact contains three different active ingredients: sodium picosulfate, magnesium oxide, and anhydrous citric acid. *Id.* at 201; Compl. ¶ 32. Two of these ingredients, magnesium oxide and anhydrous citric acid, had previously been approved in a NDA. By contrast, sodium picosulfate, a stimulant laxative, had never previously been approved in any NDA. A.R. 201. Because sodium picosulfate constituted a new drug substance, Ferring sought five-year exclusivity for PREPOPIK when it submitted its NDA. *See* Pl.'s Mot. Summ. J. Ex. 3 at 2, ECF No. 20-6. Ferring alleges that it was unable to seek a NDA for sodium picosulfate as a single-ingredient drug product because picosulfate's therapeutic benefit is realized only in combination with the other active ingredients. A.R. 70 Ferring points out that the FDA did not require factorial studies—which are employed to evaluate the contribution of each of a drug product's individual substances to the drug's overall efficacy—because of "serious ethical concerns" that "each component as a stand alone would result in inadequate colon cleansing for colonoscopy." Pl.'s Mot. Summ. J. Ex. 2 at 40; A.R. 70.

The FDA approved Ferring's NDA for PREPOPIK on July 16, 2012. *See* Compl. ¶ 33; A.R. at 201. Consistent with its interpretation of the five-year exclusivity provision, however, the FDA only awarded Ferring three-year exclusivity because the drug product contained two active moieties (magnesium oxide and citric acid) that had previously been approved. *See* Pl.'s Mot. Summ. J. Ex. 3 at 3; A.R. at 201.

Ferring submitted a Citizen Petition on January 29, 2013 requesting that the FDA change its exclusivity determination. A.R. 64. In short, Ferring argued that the FDA's denial of five-year exclusivity was inconsistent with Congress's intent in passing the Hatch-Waxman Amendments, as discerned from the relevant legislative history, *id.* at 70–76, and that the interpretation also conflicted with various other FDA policies, *id.* at 76–94. Around the same

time, two other pharmaceutical companies, Gilead Sciences, Inc., and Bayer Healthcare Pharmaceuticals, Inc., whose respective fixed-combination drug products had also been denied five-year exclusivity on the ground that at least one of the active ingredients had been previously approved, filed similar Citizen Petitions challenging the FDA's prevailing interpretation. *See generally id.* at 98–140; *id.* at 144–158.

On February 21, 2014, the FDA issued a single response to all three companies' Citizen Petitions. *Id.* at 199. In that response, the FDA summarized its prior interpretation of the FDCA and its own regulation. *Id.* at 207–09. The FDA stated that although it believed its "current interpretation of the relevant statute and regulations is permissible, Petitioners have articulated an alternative interpretation of the relevant statute and regulations that would also be permissible." *Id.* at 212. As the FDA asserted, "in either the eligibility or the bar clause, FDA may reasonably interpret 'drug' narrowly to mean 'drug product' or broadly to mean 'drug substance.'" *Id.* The agency further acknowledged, however, that "recent changes in drug development, particularly in the field of fixed-combination development in the last 20 years, and the importance of fixed-combinations to key therapeutic areas—such as HIV, cardiovascular disease, tuberculosis, and cancer—warrant[ed] revising [its] current policy," particularly as "fixed-combinations containing new active moieties are becoming more prevalent in drug development." *Id.* The FDA noted that combination therapies could improve treatment response, lower risks of developing resistance to drugs, and lower the rate of adverse effects, in addition to simplifying drug regimens and improving patients' adherence to those regimens. *Id.* at 212–13. Because of these changes, the FDA conceded that its existing interpretation "may result in drug development strategies that are suboptimal from a public health perspective" because if sponsors "prefer to submit two NDAs"—one for a single-entity drug containing the

new active moiety and another for a combination product—"undue importance" may be placed on "the order in which these two NDAs are approved." *Id.* at 213–14. Additionally, "in some situations, such a strategy may not be available if a new active moiety does not clinically lend itself to approval in a single-entity drug product." *Id.* at 214.

As a result, the FDA "agree[d] that the increasing importance of fixed-combinations for certain therapeutic areas means that it would be in the interest of public health to encourage the development of fixed-combinations as a policy matter," and determined that "[o]ne way to accomplish this goal would be to adopt a new interpretation of the relevant statutory and regulatory authorities that would encourage the development of fixed-combinations that contain novel drug substances . . . irrespective of whether the fixed-combination also includes a drug substance that contains a previously approved active moiety or moieties." *Id.* at 214. To that end, the FDA issued draft guidance and proposed to seek public comment on a new interpretation which would "recognize 5-year NCE exclusivity for a drug substance that does not contain a previously approved active moiety, even where such a drug substance is approved in a fixed-combination with another drug substance that contains at least one previously approved active moiety." *Id.*

Despite altering its interpretation of the five-year exclusivity provision, the FDA declined to recognize five-year exclusivity for PREPOPIK and the other drugs sponsored by the companies that had filed the Citizen Petitions. *See id.* at 216. The agency concluded that "[e]xclusivity runs from the date of approval of a product," and noted that the agency's existing interpretation had been in effect when the drugs at issue were approved. *Id.* at 215. The agency based its decision on several factors, including that its "existing interpretation of these provisions is longstanding and has been consistently applied in many prior cases presenting similar facts,"

that the agency wished to "avoid any unnecessary disruptions to the regulated industry," and that the new interpretation "could impose a burden on the ANDA sponsors, who relied on [the agency's] existing interpretation in filing their applications." *Id.* The agency also concluded that applying its new interpretation to the companies' drugs would not further the goals of the Hatch-Waxman Amendments because the products had "already . . . been developed and approved." *Id.*

Ferring filed a Petition for Reconsideration and Petition for Stay, arguing that the FDA's new interpretation is the correct one—indeed, the only one in line with congressional intent—and that, in any event, it was arbitrary and capricious for the agency to decline to apply its new interpretation to Ferring's products. *See id.* at 1–42. The FDA denied that petition. *See id.* at 829–42.

Ferring then initiated this APA action, alleging that the FDA's action was contrary to the FDCA and the agency's own regulations, and that its decision was arbitrary and capricious, in violation of 5 U.S.C. § 706(2)(A). *See* Compl. ¶¶ 58–71. Ferring has now moved for summary judgment (ECF No. 20), and the government has cross-moved for summary judgment (ECF No. 22).

III. LEGAL STANDARD

A court may grant summary judgment when "the movant shows that there is no genuine dispute as to any material fact and the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a). When assessing a motion for summary judgment in an APA case, however, "the district judge sits as an appellate tribunal." *Am. Bioscience, Inc. v. Thompson*, 269 F.3d 1077, 1083 (D.C. Cir. 2001). In such cases the complaint "actually presents no factual allegations, but rather only arguments about the legal conclusion to be drawn about the agency

action." *Marshall Cnty. Health Care Auth. v. Shalala*, 988 F.2d 1221, 1226 (D.C. Cir. 1993). Therefore, "[t]he entire case on review is a question of law, and only a question of law." *Id.* The Court's review "is based on the agency record and limited to determining whether the agency acted arbitrarily or capriciously," *Rempfer v. Sharfstein*, 583 F.3d 860, 865 (D.C. Cir. 2009), or in violation of another standard set out in section 10(e) of the APA, *see* 5 U.S.C. § 706.

IV. ANALYSIS

Ferring challenges the FDA's action here as "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law" in several ways. 5 U.S.C. § 706(2)(A). First, Ferring contends that the FDA's prior interpretation, under which PREPOPIK was denied five-year exclusivity, contravened the plain language of the FDCA. Second, Ferring argues that, even if the language of the FDCA is ambiguous, the FDA's interpretive choice to read "drug" in the eligibility clause to mean "drug product" was an unreasonable reading of the statute or was arbitrary and capricious because it treated similarly situated parties differently. Finally, Ferring claims that, even if the FDA's prior interpretation was permissible, its decision not to apply the new interpretation retroactively was arbitrary and capricious. The Court considers each argument in turn.

A. *Chevron* Step One

First, Ferring argues that "Congress plainly intended that a drug *substance* would be entitled to five-year exclusivity if it is based on a novel active ingredient."[2] Pl.'s Mem. Supp. at

[2] The FDA briefly asserts that Ferring failed to make a plain language argument below. *See Nuclear Energy Inst., Inc. v. EPA*, 373 F.3d 1251, 1297 (D.C. Cir. 2004) ("It is a hard and fast rule of administrative law, rooted in simple fairness, that issues not raised before an agency are waived and will not be considered by a court on review."). Yet, the agency does not explicitly invoke waiver as a bar to the Court's consideration of the argument, so the Court will consider the *Chevron* Step One claim. In any event, and contrary to the FDA's contention, it

12 (emphasis in original). The interpretation of an administrative agency's guiding statute typically follows a two-step process. "First, always, is the question whether Congress has directly spoken to the precise question at issue. If the intent of Congress is clear, that is the end of the matter; for the court, as well as the agency, must give effect to the unambiguously expressed intent of Congress." *Chevron, U.S.A., Inc. v. Nat. Res. Def. Council, Inc.*, 467 U.S. 837, 842–43 (1984). However, if "Congress has not directly addressed the precise question at issue, the court does not simply impose its own construction of the statute, as would be necessary in the absence of an administrative interpretation." *Id.* at 843 (footnote omitted). In this latter situation, a court instead proceeds to step two of the *Chevron* framework: "[I]f the statute is silent or ambiguous with respect to the specific issue, the question for the court is whether the agency's answer is based on a permissible construction of the statute." *Id.* "[A] court may not substitute its own construction of a statutory provision for a reasonable interpretation by the administrator of an agency." *Id.* at 844.

The five-year exclusivity provision does not itself define the term "drug." And the FDCA, generally, is of limited assistance. The Act provides several alternative definitions of the term, which the parties agree can encompass both the terms "drug product" and "drug substance." *See* 21 U.S.C. § 321(g)(1); *see also* Pl.'s Mem. Supp. at 13–14; Defs.' Mem. Supp. Cross-Mot. Summ. J. & Opp'n Pls.' Mot. at 15 ("Defs.' Mem. Supp."), ECF No. 22. Even the Supreme Court has acknowledged that the FDCA's definition *must* include both "active ingredient" and "drug product"—lest the fourth statutory definition be rendered mere surplusage.

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does appear that the agency understood the companies' claims to encompass a plain language argument. *See, e.g.*, A.R. 831 (noting on reconsideration that in FDA's original response "we disagreed with Petitioners that the term drug *can only mean* drug substance in the 5-year NCE exclusivity eligibility context" (emphasis added)).

See United States v. Generix Drug Corp., 460 U.S. 453, 458–60 (1983) (concluding that the term drug "is plainly intended throughout the Act to include entire drug products, complete with active and inactive ingredients" and must "include more than just active ingredients . . . unless subsection (D) is to be superfluous"). Collectively, these circumstances strongly indicate that an ambiguous statutory term is at hand.

Ferring resists this conclusion by pointing out that a term that appears ambiguous in the abstract may, upon closer inspection and, after considering statutory structure and context, reveal itself to be unambiguous. *See* Pl.'s Mem. Supp. at 12–13; *see also Brown v. Gardner*, 513 U.S. 115, 118 (1994) ("Ambiguity is a creature not of definitional possibilities but of statutory context."). True enough. But here Ferring has not persuasively identified any statutory structure or context that definitively resolves whether "drug," when used in the five-year exclusivity provision, means "drug product" or "drug substance."

Ferring first contends that both uses of the term "drug" must be read the same. Ferring relies on the eligibility clause's use of the indefinite article "*a*" in the phrase "*a drug*, no active ingredient . . . of which has been approved," followed by the bar clause's subsequent use of the definite article "*the*" in the phrase "no application . . . which refers to *the drug* for which the subsection (b) application was submitted." 21 U.S.C. § 355(j)(5)(F)(ii) (emphases added); *see* Pl.'s Mem. Supp. at 14–15. In Ferring's view, Congress's use of "the" definitively indicates that "the drug" was meant to refer back to the same "a drug" mentioned earlier in the eligibility clause. Ferring cites several cases construing Congress's use of the definite article "the" in this way.[3] *See, e.g.*, *Work v. U.S. ex rel. McAlester-Edwards Coal Co.*, 262 U.S. 200, 208 (1923);

[3] Ferring's reading of *Work* is not quite accurate, and thus not as closely aligned to the five-year exclusivity provision as its memorandum makes the case appear. Although Ferring reads the Supreme Court in *Work* to have concluded that Congress's use of the word "the"

United States v. Wilcox, 487 F.3d 1163, 1176 (8th Cir. 2007) (determining that "*the* victim" referred to in the federal restitution statute referred to "the victim described at the beginning of the subsection" (emphasis in original)); *Nat'l Foods, Inc. v. Rubin*, 936 F.2d 656, 660 (2d Cir. 1991) (construing a New York statute's second use of the term "the court" as referencing "the same [court] referred to the first time"). Moreover, Ferring invokes the familiar principle of statutory construction that, absent some indication to the contrary, a statutory term should be given the same meaning when repeated in close proximity. *See, e.g.*, *Brown*, 513 U.S. at 118 ("[T]here is a presumption that a given term is used to mean the same thing throughout a statute, a presumption surely at its most vigorous when a term is repeated within a given sentence." (citation omitted)).

Even if one were to share Ferring's conclusion that the two uses of "drug" should be read to mean the same thing, however, the weak link in Ferring's chain of reasoning is that nothing in the statute indicates *which* definition of "drug" Congress intended to apply in the eligibility or bar clauses. Ferring latches onto *the agency*'s interpretation of the bar clause's use of "drug" to mean "drug substance." Pl.'s Mem. Supp. at 14. Only by doing so is Ferring able to claim that "the first 'drug'—the 'a' drug—must mean drug substance, too." *Id.* Contrary to Ferring's claim, though, the FDA's interpretation was not grounded on "clear Congressional intent," at least in the sense that the FDA had concluded that the term could only mean "drug substance." Instead, the FDA specifically concluded that the FDCA was "ambiguous as to which ANDA[s] or 505(b)(2) applications are affected by an innovator's exclusivity." Proposed Rule, 54 Fed.

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demonstrated an intent to refer to "the appraisement referenced earlier in the same sentence," Pl.'s Mem. Supp. at 14, 15, the Court in fact concluded that "*the* appraised value" of the surface lands at issue referred to the appraisement provided for in an entirely separate statute that had been passed six years previously—and not the mineral appraisement that was, by contrast, referenced in the same sentence, *see Work*, 262 U.S. at 208.

Reg. at 28,897. That the FDA believed one reading would more readily further Congress's intent does not indicate that the statute must unambiguously be read that way at *Chevron* Step One. There is nothing in *the statute*, so far as either party has identified, compelling a particular definition for "drug."[4]

Accordingly, the Court considers the term "drug" to be ambiguous at *Chevron* Step One.

B. *Chevron* Step Two

The Court therefore moves to Step Two of the *Chevron* framework, and assesses whether the FDA's interpretation in effect when PREPOPIK was approved was reasonable.

Chevron instructs that if a statute is "silent or ambiguous with respect to the specific issue, the question for the court is whether the agency's answer is based on a permissible construction of the statute." 467 U.S. at 843. Unlike the Court's assessment under Step One, the Court's review at Step Two "is 'highly deferential.'" *Village of Barrington, Ill. v. Surface Transp. Bd.*, 636 F.3d 650, 665 (D.C. Cir. 2011) (quoting *Nat'l Rifle Ass'n of Am., Inc. v. Reno*, 216 F.3d 122, 137 (D.C. Cir. 2000)). The permissibility of an agency's interpretation is assessed "in light of [the statute's] language, structure, and purpose.'" *Nat'l Treasury Empls. Union v. Fed. Labor Relations Auth.*, 754 F.3d 1031, 1042 (D.C. Cir. 2014) (quoting *Am. Fed'n of Labor v. Chao*, 409 F.3d 377, 384 (D.C. Cir. 2005)). *Chevron* Step Two "does not require the best

[4] For similar reasons, the Court rejects Ferring's argument that "drug" must mean "drug substance" because the FDA has often interpreted the phrase "a drug no active ingredient (including any ester or salt of the active ingredient) of which has been approved" when used elsewhere in the statute to refer to a "drug substance." *See* Pl.'s Mem. Supp. at 17–18. Yet again, none of these examples cast useful light on the interpretation compelled *by the statute.* Moreover, Ferring also concedes that the FDA has taken the alternative position in at least one circumstance, although that proposed guidance was never finalized. *Id.* at 17 n.8. And the most recent guidance Ferring relies upon, involving the approval of priority review vouchers for rare pediatric diseases, was promulgated *after* the FDA changed its interpretation of the bar clause in this case, making that example of limited use in attempting to cast the FDA's prior interpretation as an outlier. *Id.* at 18 (noting that the draft guidance was promulgated in November 2014).

interpretation, only a reasonable one," *Am. Forest & Paper Ass'n v. FERC*, 550 F.3d 1179, 1183 (D.C. Cir. 2008), and the court therefore "need not conclude that the agency construction was the only one it permissibly could have adopted to uphold the construction, or even the reading the court would have reached if the question initially had arisen in a judicial proceeding," *Chevron*, 467 U.S. at 843 n.11. If "the implementing agency's construction is reasonable, *Chevron* requires a federal court to accept the agency's construction of the statute, even if the agency's reading differs from what the court believes is the best statutory interpretation." *Nat'l Cable & Telecomms. Ass'n v. Brand X Internet Servs.*, 545 U.S. 967, 980 (2005).

An agency's interpretation of an ambiguous statutory term may invariably require some measure of policy-making or line drawing. And it is "entirely appropriate" for an agency "to make such policy choices—resolving the competing interests which Congress itself either inadvertently did not resolve, or intentionally left to be resolved by the agency charged with the administration of the statute in light of everyday realities." *Chevron*, 467 U.S. at 865–66. "*Chevron* demands" a court's "deference when an agency's interpretation is 'a reasonable accommodation of conflicting policies that were committed to the agency's care by the statute.'" *Van Hollen, Jr. v. FEC*, 811 F.3d 486, 494 (D.C. Cir. 2016) (quoting *Chevron*, 467 U.S. at 845). At Step Two, a court must simply ask whether the agency "has reasonably explained how the permissible interpretation it chose is 'rationally related to the goals of' the statute." *Village of Barrington, Ill.*, 636 F.3d at 665 (quoting *AT&T Corp. v. Iowa Utils. Bd.*, 525 U.S. 366, 388 (1999)). A "'reasonable' explanation of how an agency's interpretation serves the statute's objectives is the stuff of which a 'permissible' construction is made." *Northpoint Tech., Ltd. v. FCC*, 412 F.3d 145, 151 (D.C. Cir. 2005) (quoting *Chevron*, 467 U.S. at 863).

In the Court's view, and assessed with the appropriate level of deference to the FDA, the agency's prior interpretation of the term "drug" in the eligibility clause as referring to a "drug product" was reasonable. As already noted, the FDCA explicitly defines the term "drug" in a way that encompasses entire drug products. *See* 21 U.S.C. § 321(g)(1); *accord Generix Drug Corp.*, 460 U.S. at 458–60. Unless the statute unambiguously requires otherwise—and the Court has already determined that it does not—it would be odd for the Court to nevertheless conclude that the agency's choice of one statutory definition over the other was unreasonable. In addition, the eligibility clause makes reference to "an *application submitted under subsection (b)* of [§ 355] for a drug . . . ." 21 U.S.C. § 355(j)(5)(F)(ii) (emphasis added). The agency contends that because "applications are generally submitted for drug products, not drug substances, a reading of 'drug' as 'drug product' flows logically" from this language. A.R. 208. To be sure, the reference to an application may not be definitive. Ferring urges that because the subsection continues on to reference "no active ingredient . . . of which has been approved in any other application," the FDA's reading is inconsistent with the statute because active ingredients, in addition to drug products, are "approved" through NDAs. *See* Pl.'s Mem. Supp. at 16; Pl.'s Mem. in Opp'n to Defs.' Cross-Mot. for Summ. J. & Reply at 6 ("Pl.'s Reply"), ECF No. 23; *accord Amarin Pharm. Ir. Ltd. v. FDA*, 106 F. Supp. 3d 196, 214 (D.D.C. 2015) (concluding that "[i]t is not correct, however, to say that the FDA does not approve 'active ingredients' when it approves drugs or drug products"). Yet, the FDA draws what the Court considers a conceivable distinction between the article for which an application is *submitted*—a finished drug product—and what the agency *approves*, even if a drug's approval inevitably results in the approval of the active ingredients or drug substances contained within a finished drug product. *See* Defs.' Mem.

Supp. at 18; A.R. 208. This distinction is not implausible, and lends at least some measure of support to the agency's reading.[5]

In addition, the statute speaks of a drug "*no active ingredient . . . of which has been approved*," implying that the "drug" may contain several active ingredients. 21 U.S.C. § 355(j)(5)(F)(ii). But the agency's definition of a "drug substance" appears to treat a drug substance as the equivalent of a single active ingredient. 21 C.F.R. § 314.3(b) (defining "[d]rug substance" as "an active ingredient that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure or any function of the human body"). Ferring seems to share this view. Pl.'s Mem. Supp. at 6 (asserting that "[a] drug substance usually is comprised of an active ingredient intended to furnish pharmacological activity"). Thus, the Court does not consider it unreasonable for the FDA to have read "drug" to refer to an article that presumably might include more than one active ingredient. This tracks the agency's regulation implementing the various exclusivity provisions—analyzed in more detail below—which asks whether an entire "drug product" contains "a new chemical entity" or instead contains "an active moiety that has been previously approved." 21 C.F.R. § 314.108(b)(2), (b)(4)(iii).

Indeed, there appears to have been an implicit assumption persisting from the time of Dr. Peck's guidance letter, through the agency's promulgation of its regulations, and unchallenged—at least as far as the parties have identified—until Ferring's Citizen Petition, that the term "drug"

[5] The Court acknowledges that the bar clause contains similar language when it prohibits an application from being "submitted . . . which refers to the drug for which the subsection (b) application was submitted," 21 U.S.C. § 355(j)(5)(F)(ii), and that, in that context, the agency interpreted drug to mean "drug substance." As explained below, however, the FDA did so because it concluded that a broader definition was more compatible with its understanding of Congress's purpose. *See* Proposed Rule, 54 Fed. Reg. at 28,897.

in the eligibility clause meant "drug product." Although the Court acknowledges that the presumption in favor of reading a statutory term in close proximity to mean the same thing is a weighty one, once the FDA resolved the eligibility clause's ambiguity in favor of the term "drug product," it made ample sense for the agency to broadly interpret the five-year exclusivity provision "once it attaches, such that it protects not only the drug product that is the subject of the application but also subsequently approved drug products that contain the same active moiety." A.R. 209. To conclude otherwise would have meant that "an innovator's exclusivity could lose its value as soon as FDA approved a second full new drug application for a version of the drug." Proposed Rule, 54 Fed. Reg. at 28,897. The FDA "d[id] not believe that Congress intended the exclusivity provisions to discourage innovators from making improvements in their drug products nor from authorizing the marketing of competitive products." *Id.* Under these circumstances, and although the FDA appreciated that reading the bar clause to also refer to "drug products" "would have been the more natural reading," the agency reasonably "declined to adopt this reading in the context of the umbrella policy, because such a reading would not preserve the incentive to innovate and improve upon the initially approved product during the exclusivity period." A.R. 209.

To the extent Ferring hints that the need to make such an accommodation should have caused the FDA to doubt its eligibility clause interpretation—and to instead conclude that both clauses referred to *drug substances*—nothing in the record indicates that to have been a contemporaneous concern. The proposed and final rulemaking notices contain absolutely no discussion of the issue, nor do they reflect any comments urging the agency to interpret "drug" as referring to "drug substance" or raising the types of policy concerns Ferring raised in its Citizen Petition. *See* Proposed Rule, 54 Fed. Reg. at 28,896–902; *see also* Final Rule, 59 Fed.

Reg. at 50,356–60. This is unsurprising. The record in fact suggests that the submission of NDAs for fixed-combination drug products that contain new drug substances is of more recent vintage. *See* A.R. 212 (explaining that, as of February 2014, "[i]n the nearly 20 years since FDA finalized the regulations on exclusivity, the Agency has approved 19 NDAs for fixed-combinations containing at least one new active moiety," and that "[m]ore than half of these NDAs have gained approval within the last 7 years," which "suggest[s] that fixed-combinations containing new active moieties are becoming more prevalent in drug development"). It simply appears that in 1988 and 1994, in light of the science and circumstances at that time, the FDA had not anticipated the possibility that fixed-combination drug products containing a novel drug substance could be disadvantaged by the agency's interpretation. The agency has now, of course, revisited its interpretation in light of more "recent changes in drug development" and "the increasing importance of fixed-combinations for certain therapeutic areas." *Id.* at 212, 214. But that interpretive revision turns on questions of policy, left to the agency's discretion. *See Chevron*, 467 U.S. at 865–66; A.R. 214 (concluding that "it would be in the interest of public health to encourage the development of fixed-combinations as a policy matter"). Nothing indicates that the FDA's initial interpretation, selecting one statutory definition of "drug product" over the other, was unreasonable.

Ferring's various counterarguments are not persuasive. First, Ferring contends that the FDA's prior interpretation patently conflicts with the agency's own regulation. That regulation, as noted above, provides that:

> If a drug product that contains a new chemical entity was approved after September 24, 1984, in an application submitted under section 505(b) of the act, no person may submit a 505(b)(2) application or abbreviated new drug application under section 505(j) of the act for a drug product that contains the same active moiety as in the new chemical entity for a period of 5 years from the date of the approval of the first approved new drug application . . . .

21 C.F.R. § 314.108(b)(2). A "new chemical entity," in turn, is defined as "*a drug* that contains no active moiety that has been approved by FDA in any other application submitted under section 505(b) of the act." *Id.* § 314.108(a) (emphasis added). From these definitions, Ferring contends that the regulation makes clear that a drug product *contains* the "new chemical entity," requiring one to read the reference to "drug" in the "new chemical entity" definition to mean "drug substance." Pl.'s Mem. Supp. at 20–21. Were one instead to read "drug" to mean "drug product," and substitute that definition in the place of "new chemical entity," Ferring urges that the regulation would redundantly read: "If a drug product that contains a drug product that contains no active moiety . . . . ." *Id.* at 21. Courts are "hesitant to substitute an alternative reading" of a regulation "for the Secretary's unless that alternative reading is compelled by the regulation's plain language or by other indications of the Secretary's intent at the time of the regulation's promulgation." *Gardebring v. Jenkins*, 485 U.S. 415, 430 (1988). But Ferring claims this is one such instance. *See* Pl.'s Mem. Supp. at 21.

The Court disagrees. "An agency's interpretation of its own regulations is entitled to judicial deference." *Actavis Elizabeth LLC v. FDA*, 625 F.3d 760, 763 (D.C. Cir. 2010). That deference is "all the more warranted when" a regulation concerns "'a complex and highly technical regulatory program,' in which the identification and classification of relevant 'criteria necessarily require significant expertise and entail the exercise of judgment grounded in policy concerns.'" *Thomas Jefferson Univ. v. Shalala*, 512 U.S. 504, 512 (1994) (quoting *Pauley v. BethEnergy Mines, Inc.*, 501 U.S. 680, 697 (1991)). An "agency's interpretation of its own rule is given 'controlling weight unless it is plainly erroneous or inconsistent with the regulation.'" *High Plains Wireless, L.P. v. FCC*, 276 F.3d 599, 606 (D.C. Cir. 2002) (quoting *Capital Network Sys., Inc. v. FCC*, 28 F.3d 201, 205 (D.C. Cir. 1994)). The Court acknowledges that the

regulation is imprecise—and perhaps internally redundant—because it uses the general term "drug" following the more specific term "drug product." Even the FDA concedes "this reading is cumbersome." Defs.' Reply at 6, ECF No. 25. But, as Dr. Peck's guidance letter evidences, even before it first promulgated the regulation, the FDA maintained that the statute granted five-year exclusivity to new drug *products* only if they contained no previously-approved active moiety. *See* A.R. 324. It would be strange, indeed, to conclude that the FDA unintentionally hamstrung itself from achieving its stated interpretation through its somewhat confusingly worded regulation. Moreover, both the three- and five-year exclusivity provisions in the regulation are framed at the "drug product" level, and ask whether a "drug product" contains a "new chemical entity" or "an active moiety that has been previously approved." *Compare* 21 C.F.R. § 314.108(b)(2), *with id.* § 314.108(b)(4)(iii). Although the FDA now interprets "drug" in the definition of "new chemical entity" to mean "drug substance," and not "drug product," it is difficult to conclude that the regulation's text plainly *compels* that reading, given its overall emphasis on "drug products." At most, like the statute, the regulation is somewhat ambiguous, and thus falls short of providing the "plain language" necessary to compel Ferring's preferred interpretation.[6]

This conclusion similarly brushes aside Ferring's second contention: that the FDA's prior interpretation merits less deference because "the agency has offered several different inconsistent interpretations of the statute." Pl.'s Mem. Supp. at 22. In the Court's view the agency has taken only two positions. And those interpretations are not erratic, as Ferring seems to imply. While an "[u]nexplained inconsistency" might be "a reason for holding an interpretation to be an

[6] This conclusion also resolves Ferring's duplicative argument that, even beyond *Chevron* Step Two, the FDA's prior interpretation is invalid because it conflicts with the agency's regulation. *See* Pl.'s Mem. Supp. at 23.

arbitrary and capricious change from agency practice under the Administrative Procedure Act," *Brand X*, 545 U.S. at 981, "[a]n initial agency interpretation is not instantly carved in stone," *Chevron*, 467 U.S. at 853–64. An agency "must consider varying interpretations and the wisdom of its policy on a continuing basis." *Id.* Thus, "if the agency adequately explains the reasons for a reversal of policy, 'change is not invalidating, since the whole point of *Chevron* is to leave the discretion provided by the ambiguities of a statute with the implementing agency.'" *Brand X*, 545 U.S. at 981 (quoting *Smiley v. Citibank (South Dakota), N.A.*, 517 U.S. 735, 742 (1996)). Here, the agency has thoroughly explained both its prior and its new position, and thus there is no reason to avoid deferring to either.

Finally, Ferring claims that the FDA's prevailing interpretation at the time it submitted the NDA for PREPOPIK was out of step with the statute's purpose because the interpretation denied exclusivity to some fixed-dose combination products that contained a new active ingredient. In Ferring's view, it "should not matter under the statute whether the active ingredient is approved alone or in combination with other, older active ingredients" because the statute was intended to "encourage drug companies to research and develop new drug substances." Pl.'s Mem. Supp. at 23. But the legislative history phrases that purpose in the most general terms and, facing "the classic question of the appropriate trade-off between greater incentives for the invention of new products and greater affordability of those products," Congress endeavored to strike "a balance between expediting generic drug applications and protecting the interests of the original drug manufacturers." *Abbott Labs.*, 920 F.2d at 985. The ambiguous use of the word "drug" leaves some question about exactly where Congress intended to draw that line. In such circumstances, courts leave it to the relevant agency to "resolv[e] the competing interests which Congress itself either inadvertently did not resolve, or intentionally

left to be resolved by the agency charged with the administration of the statute in light of everyday realities." *Chevron*, 467 U.S. at 865–66. While the FDA now acknowledges that "recent changes" in the development and importance of fixed-combination drugs "warrant[ed] revisiting [its] current policy," A.R. 212, the Court does not view the FDA's previous interpretation as outside the boundaries of the reasonable policy choice that the ambiguous phrase "drug" committed to the agency's discretion.

This conclusion largely resolves Ferring's related claim that FDA's prior interpretation was arbitrary and capricious. The scope of a court's "arbitrary and capricious" review "is narrow" and "a court is not to substitute its judgment for that of the agency." *Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Ins. Co.*, 463 U.S. 29, 43 (1983). To satisfy the standard, an agency "must examine the relevant data and articulate a satisfactory explanation for its action including a 'rational connection between the facts found and the choice made.'" *Id.* (quoting *Burlington Truck Lines v. United States*, 371 U.S. 156, 168 (1962)). "The analysis of disputed agency action under *Chevron* Step Two 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.'" *Agape Church, Inc. v. FCC*, 738 F.3d 397, 410 (D.C. Cir. 2013) (quoting *Judulang v. Holder*, 132 S. Ct. 476, 483 n.7 (2011)); *see also Nat'l Ass'n of Broad. v. FCC*, 789 F.3d 165, 171 (D.C. Cir. 2015) ("[A] *Chevron* step-two argument and a claim that the agency has acted arbitrarily and capriciously (which petitioners also assert here) overlap.").

Ferring argues, however, that even if the FDA's prior interpretation was a reasonable reading of the statute, it arbitrarily treated similarly situated fixed-dose combination drug products differently. *See* Pl.'s Mem. Supp. at 25–27; *see also, e.g.*, *Indep. Petroleum Ass'n of Am. v. Babbitt*, 92 F.3d 1248, 1258 (D.C. Cir. 1996) (noting that, to "satisfy the arbitrary and

capricious standard" an agency "must treat similar cases in a similar manner unless it can provide a legitimate reason for failing to do so"). Ferring posits that the FDA's interpretation and umbrella policy, in combination, created circumstances in which a drug substance's eligibility for the five-year exclusivity period turned arbitrarily on the order in which NDAs were approved. Ferring contends that "if a *single*-entity drug product containing a new active ingredient is approved before a fixed-dose *combination* drug product containing the same active ingredient, both products—the single-entity and the combination—receive the benefit of the five-year NCE exclusivity," but that if "the order of the approvals had been reversed and the fixed-dose combination drug product had been approved just hours before the single-ingredient product, *none* of the products would have been awarded NCE exclusivity." Pl.'s Mem. Supp. at 25, 26 (emphases in original). Ferring cites several examples of situations in which a single-entity product was first approved and then a combination-drug product including that new single-entity product was later approved and, by operation of the umbrella policy, was therefore able to share in whatever remained of the original product's exclusivity period. *See* Pl.'s Mem. Supp. at 25–27; *see also* A.R. 907–10.

If there were, in fact, situations in which a drug was eligible for five-year exclusivity under the FDA's prevailing interpretation but failed to receive it because of the order in which it was approved, those circumstances might render the FDA's policy arbitrary and capricious. Instead, the distinction Ferring identifies flows naturally from the policy choice the FDA made when it settled on its prior interpretation. In each example Ferring identifies, a drug was first approved in a single entity drug product,[7] and then *later* approved as part of a fixed-combination

[7] Although neither Ferring nor the FDA identify an example, presumably a new drug substance would also receive exclusivity if it was included in a fixed-combination drug product

product—a straightforward application of the FDA's umbrella policy. *See* A.R. 209 (explaining that, under the umbrella policy, once exclusivity "attaches," it "protects not only the drug product that is the subject of the application but also subsequently approved drug products that contain the same active moiety"). Moreover, although in some instances the FDA approved the NDAs for the single-entity drug and later iterations on the same day, the administrative record reveals that the NDAs for each of the single-entity drug products were submitted long before the combination-drug products (in some cases only six months prior, but in others up to eighteen months prior). *See id.* at 907–10. This progression accords with the umbrella policy's effort to ensure that innovators would not be discouraged from "making improvements in their drug products." Proposed Rule, 54 Fed. Reg. at 28,897.

What distinguishes PREPOPIK is not the mere *sequence* in which its NDA was approved, but that PREPOPIK's novel active ingredient, sodium picosulfate, was not appropriate in a single-entity form. The difference is subtle, but significant. Unlike the other drug substances Ferring identifies (and unless sodium picosulfate was included in a combination product that contained only new active ingredients) the drug substance was never even *eligible* for five-year exclusivity under the FDA's prevailing policy. This distinction aligns with the agency's resolution of the statute's ambiguity by granting exclusivity only to the "most innovative drugs" and focusing on entire "drug products." A.R. 208. Indeed, everything in the record indicates that before the FDA altered its policy, it took a *consistent* position that only entire drug products that contained never-before approved active ingredients were eligible for five-year exclusivity—even if fixed-combination drug products including those novel drug

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in which *all* of the active ingredients were new—in line with the FDA's contemporaneous interpretation that all active moieties in the drug product must be novel.

products also received protection under the umbrella policy, and even if the FDA's focus on final "drug products" collaterally excluded drug substances that were inappropriate for use in a single-ingredient drug from exclusivity eligibility. As the FDA explains, the "'pattern' of different decisions regarding 5-year NCE exclusivity that Ferring trumpets was merely a by-product of FDA's consistent application of its established interpretation to the facts of each individual product." Defs.' Reply at 9.

As a result of the statute's ambiguity, the FDA was left to determine at what level of specificity to define "drug": at the "drug product" level, and in reference to *all* of the product's "drug substances," or at the "drug substance" level. Although scientific and policy considerations may have now persuaded the FDA to modify its interpretation, given the statutory ambiguity and the considerations discussed above, it was neither unreasonable nor arbitrary and capricious for the FDA to define "drug," in the "eligibility clause" as "drug product," and to thereafter ensure the greatest benefit for pharmaceutical manufacturers who are provided with exclusivity by interpreting "drug" in the "bar clause" as "drug substance." Therefore, Ferring's *Chevron* Step Two argument fails.

C. Retroactivity

That leaves Ferring's argument regarding the FDA's decision to apply its new interpretation only prospectively. Ferring frames the issue as a question of whether the FDA acted arbitrarily and capriciously. Yet, neither party cites a case considering an agency's decision to apply a new interpretation retroactively (or not) under that framework. Overall, the parties' arguments on this issue are thin on legal citations. In addition, the Court's review of the FDA's initial response to Ferring's Citizen Petition reveals that the agency cited the D.C. Circuit's decision in *Retail Wholesale & Department Store Union v. NLRB*, 466 F.2d 380 (D.C. Cir. 1972) as support for the agency's conclusion that its retroactivity decision "strikes the

appropriate balance among the congressional intent of the Hatch-Waxman Amendments and the interests of the parties who may be affected by [the FDA's] decision." A.R. 215. And that case does appear to be potentially relevant here.

The D.C. Circuit has described *Retail Union* as "provid[ing] the framework for evaluating retroactive applications of rules announced in agency adjudications." *Clark-Cowlitz Joint Operating Agency v. FERC*, 826 F.2d 1074, 1081 (D.C. Cir. 1987) (en banc); *see also Williams Nat. Gas Co. v. FERC*, 3 F.3d 1544, 1553–54 (D.C. Cir. 1993). *Retail Union* instructs a court to consider the following when determining whether retroactive application of a new interpretation is warranted, or should be avoided:

> (1) whether the particular case is one of first impression, (2) whether the new rule represents an abrupt departure from well established practice or merely attempts to fill a void in an unsettled area of law, (3) the extent to which the party against whom the new rule is applied relied on the former rule, (4) the degree of the burden which a retroactive order imposes on a party, and (5) the statutory interest in applying a new rule despite the reliance of a party on the old standard.

466 F.2d at 390. These "factors 'boil down . . . to a question of concerns grounded in notions of equity and fairness," *Cassell v. FCC*, 154 F.3d 478, 486 (D.C. Cir. 1998) (quoting *Clark-Cowlitz*, 826 F.2d at 1082 n.6), and a Court should ask whether "the inequity in applying" the new rule in the case before the agency "outweighs the interests that might be furthered if it were applied," *Retail Union*, 466 F.2d at 390; *accord McDonald v. Watt*, 653 F.2d 1035, 1044 (5th Cir. Unit A Aug. 1981) ("In general, the ill effect of retroactivity is the frustration of the expectations of those who have justifiably relied on a prior rule; the ill effect of prospectivity is the partial frustration of the statutory purpose which the agency has perceived to be advanced by the new rule." (citing *Retail Union*, 466 F.2d at 390)). Determining "[w]hich side of the balance preponderates" in a particular instance is "a question of law," which a court should resolve "with

no overriding obligation of deference to the agency decision." *Retail Union*, 466 F.2d at 390; *accord Qwest Servs. Corp. v. FCC*, 509 F.3d 531, 537 (D.C. Cir. 2007).

The Circuit has also drawn a "basic distinction . . . between (1) new applications of law, clarifications, and additions, and (2) substitution of new law for old law that was reasonably clear.'" *Williams Nat. Gas Co.*, 3 F.3d at 1554 (internal quotation mark omitted) (quoting *Aliceville Hydro Assocs. v. FERC*, 800 F.2d 1147, 1152 (D.C. Cir. 1986)). In the former circumstances, the court "start[s] with the presumption of retroactivity for adjudications," *Qwest*, 509 F.3d at 539, but under the latter circumstances the D.C. Circuit has suggested that a "new rule may justifiably be given prospective[]-only effect in order to 'protect the settled expectations of those who had relied on the preexisting rule,'" *Pub. Serv. Co. of Colo. v. FERC*, 91 F.3d 1478, 1488 (D.C. Cir. 1996) (quoting *Williams Nat. Gas Co.*, 3 F.3d at 1554). If the *Retail Union* line of authority applies in this case, this distinction may also be of import.

Despite the FDA's citation to *Retail Union*, the parties' here neither grapple with that case and its progeny nor explain, alternatively, why it is inapplicable. The parties' limited reliance on case law is also a hindrance to the Court's analysis of the retroactivity question. And because the Court has held that the FDA's prior interpretation passes muster under *Chevron*, the retroactivity issue will be dispositive of Ferring's claims. Accordingly, the Court will deny each party's motion for summary judgment on this ground, without prejudice. The parties will be directed to file renewed motions for summary judgment that more fully address the retroactivity issue, as reflected in the order accompanying this memorandum opinion.

V. CONCLUSION

For the foregoing reasons, Defendants' motion for summary judgment (ECF No. 22) is **GRANTED IN PART AND DENIED WITHOUT PREJUDICE IN PART** and Ferring's

motion for summary judgment (ECF No. 20) is **DENIED WITHOUT PREJUDICE**. An order consistent with this Memorandum Opinion is separately and contemporaneously issued.

Dated: March 15, 2016

RUDOLPH CONTRERAS
United States District Judge