UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

VELOXIS PHARMACEUTICALS, INC.,	)	
Plaintiff,	)	
v.	)	Civil Action No. 14-2126 (RBW)
UNITED STATES FOOD AND DRUG ADMINISTRATION, et al.,	)	
Defendants.	)	

MEMORANDUM OPINION

The plaintiff, Veloxis Pharmaceuticals, Inc., filed this civil suit against the defendants—the United States Food and Drug Administration ("FDA"); Margaret Hamburg, the Commissioner of the FDA; the United States Department of Health and Human Services ("DHHS"); and Sylvia Burwell, the Secretary of the DHHS—seeking declaratory and injunctive relief to redress the FDA's decision to delay complete and final approval of Envarsus XR, which is the plaintiff's anti-rejection medication for kidney transplant recipients. Complaint for Declaratory and Injunctive Relief ("Compl.") ¶ 1. Without such approval from the FDA, the plaintiff cannot market Envarsus XR until July 2016. Id. ¶ 7. The plaintiff alleges that the FDA's decision violates the Administrative Procedure Act ("APA"), 5 U.S.C. § 706(2) (2012). Id. ¶¶ 114-28. The plaintiff initially filed a motion for a preliminary injunction, but the parties subsequently agreed to "advance the trial on the merits and consolidate it with the hearing [on the plaintiff's motion for a preliminary injunction]." Fed. R. Civ. P. 65(a)(2); see also January 15, 2015 Order at 1 & n.1. The parties then filed cross-motions for summary judgment, which

are now ripe for resolution.[1] Plaintiff's Motion for Summary Judgment ("Pl.'s Summ. J. Mot."); Defendants' Motion to Dismiss, or in the Alternative, Motion for Summary Judgment ("Defs.' Summ. J. Mot."). After careful consideration of the parties' submissions,[2] the Court concludes for the reasons below that it must deny the plaintiff's summary judgment motion and grant the defendants' summary judgment motion.

I. BACKGROUND

A. Statutory Background

1. The Hatch-Waxman Amendments

The Food, Drug, and Cosmetic Act ("FDCA") governs the pharmaceutical drug approval process for both new and generic drugs. See 21 U.S.C. § 355(a) (2012) ("No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to . . . this section is effective with respect to such drug."). The FDCA was later amended by the Drug Price Competition and Patent Term Restoration Act of 1984 ("Hatch-Waxman Amendments"), Pub. L. No. 98-417, 98 Stat. 1585. "The significance of the Hatch-Waxman Amendments to [the FDCA] cannot be understated." Allergan, Inc. v. Crawford, 398 F. Supp. 2d 13, 17 (D.D.C. 2005). "Prior to 1984, all [sponsors] seeking to

[1] The parties' summary judgment motions spawned additional motions for the Court's consideration: the Plaintiff's Motion for Leave to File Surreply and Statement of Points and Authorities in Support Thereof ("Pl.'s Surreply Mot.") and the Plaintiff's Motion to Supplement the Administrative Record and Statement of Points and Authorities in Support Thereof ("Pl.'s Supplement Mot.").

[2] In addition to the filings already mentioned, the Court considered the following submissions in rendering its decision: (1) the Joint Appendix of the Administrative Record ("A.R."); (2) the Plaintiff's Memorandum of Points and Authorities in Support of [the] Plaintiff's Motion for Summary Judgment ("Pl.'s Summ. J. Mem."); (3) the Defendants' Memorandum of Points and Authorities in Support of Their Motion to Dismiss, or in the Alternative, for Summary Judgment and in Opposition to [the] Plaintiff's Summary Judgment Motion ("Defs.' Summ. J. Mem."); (4) the Plaintiff's Reply Memorandum in Support of Its Motion for Summary Judgment and in Opposition to [the] Defendants' Motion to Dismiss, or in the Alternative, for Summary Judgment ("Pl.'s Reply"); (5) the Defendants' Reply in Support of [the] Defendants' Motion to Dismiss, or in the Alternative, for Summary Judgment ("Defs.' Reply"); (6) the Defendants' Memorandum in Opposition to [the] Plaintiff's Motion to Supplement the Administrative Record ("Defs.' Opp'n to Pl.'s Supplement Mot."); and (7) the Defendants' Opposition to [the] Plaintiff's Motion for Leave to File a Surreply ("Defs.' Opp'n to Pl.'s Surreply Mot.").

market pioneer drugs . . . had to file [a new drug application] containing, inter alia, extensive scientific data demonstrating the safety and effectiveness of the drug. As a result, few generic . . . drugs were approved by FDA." Id. The Hatch-Waxman Amendments sought to strike a "balance [between] two competing interests in the pharmaceutical industry: (1) inducing pioneering research and development of new drugs and (2) enabling competitors to bring low-cost, generic copies of those drugs to market." Takeda Pharms., U.S.A., Inc. v. Burwell, _ F. Supp. 3d _, _, 2015 WL 252806, at *1 (D.D.C. 2015) (internal quotation marks omitted). "[The] Hatch-Waxman Amendments created an abbreviated approval process for generic . . . drugs, while retaining incentives for [sponsors of] pioneer drugs, such as marketing exclusivity . . . ." Allergan, 398 F. Supp. 2d at 17 (citations omitted); see also AstraZeneca Pharms. LP v. FDA, 850 F. Supp. 2d 230, 234 (D.D.C. 2012) ("Through the Hatch-Waxman Amendments, even while creating new incentives for the development of generic drugs, Congress sought to encourage innovation. To this end, pioneer drug companies are entitled to certain periods of marketing exclusivity . . . .").

The length of a pioneer drug's marketing exclusivity varies. See Allergan, 398 F. Supp. 2d at 17 ("Because Congress still wanted to provide incentives for new drug development, alongside the [Abbreviated New Drug Application] process that eased the marketing of generic drugs, [the] Hatch-Waxman [Amendments] entitle[d] [a New Drug Application] applicant to a period of market exclusivity ([three] or [five] years, depending on the degree of innovation reflected in the NDA)."). For example, certain provisions in the Hatch-Waxman Amendments provide three years of marketing exclusivity ("three-year exclusivity"). See 21 U.S.C. § 355(c)(3)(E)(iii), (j)(5)(F)(iii)-(iv) (providing three-year exclusivities).

Under the Hatch-Waxman Amendments, sponsors seeking to market new or generic drugs can obtain FDA approval for their drug products through one of three pathways: (1) a full New Drug Application ("NDA"), see 21 U.S.C. § 355(b)(1)[3]; (2) an Abbreviated New Drug Application ("ANDA"), see 21 U.S.C. § 355(j); or (3) an intermediate process referred to as a Section 505(b)(2) NDA, see 21 U.S.C. § 355(b)(2). As recently explained by another member of this Court:

> The full NDA process requires the [sponsor] to submit detailed safety and efficacy data for the drug, including, among other things, "full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use" (i.e., clinical trials); all components of the drug; the methods used for the drug's manufacture, processing, and packing; [and] examples for proposed labeling for the drug . . . . This path is used by [sponsors] for "new branded drugs," which are sometimes called "pioneer" or "innovator" drugs.
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> A [sponsor] may also choose to file an . . . ANDA . . . . The ANDA process facilitates efficient approval of generic versions of pioneer drug products that have already been determined to be safe and effective. Rather than requiring generic [sponsors] to conduct expensive and time consuming clinical trials, the ANDA process allows the [sponsors] to rely on the clinical trials already performed in connection with the approval of the previously approved drug, provided that the generic [sponsor] can show that its drug has the same relevant characteristics (including, inter alia, the same labeling, active ingredient, route of administration, dosage form, strength, and bioequivalency). In other words, an ANDA does not attempt to demonstrate safety or effectiveness; instead, the [sponsor]'s only goal is to establish that the generic product is equivalent to another drug that is already known to be safe and effective. Thus, this path is used by [sponsors] "for the introduction of generic versions of previously approved branded drugs."
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> The Section 505(b)(2) NDA is a sort of hybrid of the other two pathways. Like the full NDA, a 505(b)(2) NDA must directly demonstrate that the proposed drug product is safe and effective; however, like the ANDA, a 505(b)(2) [sponsor] can rely on clinical studies that were previously submitted to [the] FDA in support of another drug and that were not conducted or licensed by the 505(b)(2) [sponsor]. The drug for which the borrowed studies were conducted is referred to as the

[3] This is also known as a 505(b)(1) NDA, as Section 505 of the FDCA is codified in Section 355 of Title 21 of the United States Code.

> "Reference Listed Drug" (RLD), and the RLD-related clinical studies that a Section 505(b)(2) [sponsor] relies upon may be proffered to satisfy the [sponsor]'s entire burden of proving safety and effectiveness, or they may only support some of the necessary findings; in the latter case, the [sponsor] can supplement with studies of its own. This means that a Section 505(b)(2) NDA may include the [sponsor]'s own research supporting the basic safety and efficacy of the drug in addition to the research studies related to the RLD, or it may rely entirely on the RLD, but, in any event, the Section 505(b)(2) [sponsor] must present information that bears upon the safety and effectiveness of its drug product in light of the difference between the pioneer drug product and the [sponsor]'s modification of that drug product. The 505(b)(2) NDA pathway is often used when the new drug differs only slightly from the pioneer drug, and this pathway is often favored by [sponsors] seeking to market drugs that are neither "entirely new" nor "simply a generic version of a branded drug."

Takeda Pharms., _ F. Supp. 3d at _, 2015 WL 252806, at *4 (alteration, citations, footnote, and internal quotation marks omitted).

2. The Food and Drug Administration Modernization Act of 1997

The Food and Drug Administration Modernization Act of 1997 ("FDAMA"), Pub. L. No. 105-115, 111 Stat. 2296, further amended the FDCA. ViroPharma, Inc. v. Hamburg, 898 F. Supp. 2d 1, 6 (D.D.C. 2012). Leading up to the passage of the FDMA,

> "antibiotic" drugs were approved under Section 507 of the [FDCA] and non-antibiotic drugs were approved under Section 505. This difference had a long history, dating back to the development of penicillin, the first drug to have the capacity to kill microbes, i.e., be "anti-biotic." . . .
>
> Two key consequences arose from these different treatments. [Sponsors] for generic versions of antibiotic drugs were only requested to show conformance with statutorily-mandated, published standards of identity, strength, quality, and purity for the antibiotic substance, as reflected in antibiotic "monographs" published by [the] FDA. [Sponsors] did not have to submit the safety and efficacy data that was required for pioneer and generic non-antibiotic drugs. Therefore, generic antibiotics were developed and marketed fairly readily. However, antibiotic drugs did not receive the . . . marketing exclusivity benefits available to pioneer and non-antibiotic drugs after enactment of the [Hatch-Waxman Amendments] . . . .
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> In 1997, with the enactment of the FDAMA, Congress extended Hatch-Waxman to antibiotics by repealing Section 507 of the [FDCA] and requiring that all applications for antibiotic drugs be submitted under Section 505 . . . . However, .

> . . [in] eliminat[ing] the separate approval pathway for antibiotics, [Congress only] made antibiotics approved after the statute's effective date, but not [o]ld [a]ntibiotics,[4] eligible for exclusivity . . . .
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> Congress closed this gap when it enacted the QI Program Supplemental Funding Act of 2008, Pub. L. No. 110-379, 122 Stat. 4075 (the "QI Act") . . . [, which provided marketing exclusivity benefits to old antibiotics].

Id. at 6-8 (alteration and citations omitted); see also 21 U.S.C. § 355(v)(1)(A)-(B) (three-year exclusivity to old antibiotics, so long as Section 505(b) NDA submitted after October 8, 2008).

B. Factual Background

1. Kidney Transplant Patients

When a kidney is transplanted from a donor to a recipient, the immune system of the recipient will try to reject the kidney. A.R. at FDA 00006. At the time the kidney is transplanted, the recipient is generally referred to as a "de novo patient." Id.

To prevent rejection, the de novo patient must take "drugs that suppress the immune system . . . at the time the [kidney] is transplanted . . . ." Id. An immunosuppressive drug regimen usually contains a combination of three or four drugs. Id. at FDA 00007. The recipient must be on the regimen from the time the kidney is transplanted, and continue to be on it as long as the kidney is "viable." Id. at FDA 00006. The "intensive level of immunosuppression administered" to a de novo patient, which lasts "until early after the [transplant] surgery," is called "induction." Id. at FDA 00006-7. After the transplant surgery, "the [recipient]'s regimen of . . . immunosuppressants is carefully and frequently monitored . . . and may be adjusted to minimize the development of adverse reactions while keeping the [recipient]'s immune system from rejecting the kidney." Id. at FDA 00007. "The goal is to customize the regimen to find the

[4] "Old antibiotics" were antibiotics that "were [the] subject of pre-[FDAMA] applications." Allergan, 398 F. Supp. 2d at 18.

optimum balance between the efficacy and the toxicity of the immunosuppressive regimen." Id. Once the de novo patient achieves the optimum balance, the recipient is referred to as a "maintenance patient." Id. Thereafter, one of the three to four immunosuppressive drugs the patient had been receiving can be discontinued and replaced with another drug. Id. at FDA 00008. This replacement process is called "conversion." Id.

2. Tacrolimus

i. Prograf

Tacrolimus is an immunosuppressant approved for use in preventing organ rejection. Id. at FDA 00009. Astellas Pharma US, Inc. ("Astellas") submitted, and the FDA approved, a Section 505(b)(1) NDA for a tacrolimus formulation in 1994, under the trade name Prograf ("Prograf NDA"). Id. Prograf is a twice-daily, immediate release capsule that is used for the "prophylaxis of organ rejection in patients receiving," among other organ transplants, "kidney . . . transplants." Id.

Tacrolimus is also considered an antibiotic drug by statute. See id. (citing 21 U.S.C. § 321(jj)). And because it was the subject of a NDA before the FDAMA was enacted in 1997, it is considered an "old antibiotic." Id. at FDA 00010; see also Allergan, 398 F. Supp. 2d at 18 (explaining old antibiotics).

ii. Astagraf XL

In 2005, Astellas submitted a Section 505(b)(1) NDA for a different tacrolimus formulation under the trade name Astagraf XL ("Astagraf XL NDA"). A.R. at FDA 00010. For this formulation, it sought approval for a once-daily, extended release capsule for the "prophylaxis of organ rejection following," again among other organ transplantations, a "kidney transplantation." Id. at FDA 00010. In 2009, Astellas withdrew the Astagraf XL NDA after the

FDA identified some deficiencies in the NDA. See id. at FDA 00011-12; id. at FDA 00874. Astellas submitted a new Astagraf XL NDA in 2012, id. at FDA 00015, and the FDA fully approved the latest iteration of the Astagraf XL NDA in 2013, id. Essential to the FDA's approval of Astagraf XL were two clinical trials Astellas conducted: Study 158 and Study 12-03. Id. at FDA 00016. Study 158 had previously been conducted in conjunction with the Prograf NDA. Id. at FDA 00011. These two clinical studies demonstrated that Astragraf XL—the once-daily, extended release tacrolimus formulation—could be used for the "prophylaxis of organ rejection in patients receiving de novo kidney transplants," and thus was approved for such use.[5] Id. at FDA 00015-16. And because these two clinical studies were essential to the FDA's approval of the Astagraf XL NDA, the FDA determined that Astagraf XL was eligible for and entitled to receive three-year exclusivity for these conditions of approval. Id. at FDA 00016; see also 21 U.S.C. § 355(c)(3)(E)(iii). This exclusivity is scheduled to expire in July 2016. A.R. at FDA 00016.

3. Envarsus XR

The plaintiff submitted a Section 505(b)(2) NDA for a tacrolimus formulation, under the trade name Envarsus XR in December 2013 ("Envarsus XR NDA"). Id. at FDA 00016. Envarsus XR is a once daily, extended-release tablet, used for the "prophylaxis of organ rejection in both de novo and conversion kidney transplant patients." Id. at FDA 00018. The Envarsus XR NDA relies on its own independent clinical studies, as well as clinical studies relied upon for the approval of the Prograf NDA. Id. at FDA 00016. The FDA tentatively approved Envarsus XR in October 2014. Id. at FDA 00018. That same month, however, the FDA determined that

[5] The FDA did not approve Astagraf XL for the prophylaxis of organ rejection for use in conversion patients. A.R. at FDA 00016.

Astagraf XL's three-year exclusivity prevented the FDA from fully approving Envarsus XR in all respects. Id. at FDA 00019. Specifically,

> [the] FDA concluded that the [three-year] exclusivity for Astagraf XL cover[ed] [the Envarsus XR extended release] dosage form and its once-daily dosing regimen [for de novo patients], both of which were changes from the previously approved tacrolimus drug, Prograf, and were supported by new clinical investigations essential to the approval of Astagraf XL. Because Envarsus XR is also an [extended release] dosage form of tacrolimus with a once-daily dosing regimen [for de novo patients], [the] FDA determined . . . that Envarsus XR shares Astagraf XL's exclusivity-protected conditions of approval.

Id. Because the FDA withheld final approval of Envarsus XR for the prophylaxis of organ rejection in de novo kidney transplant patients, the plaintiff cannot market Envarsus XR for this use. See id.

C. Procedural Background

In November 2014, the plaintiff met with the FDA and expressed its belief that the FDA had erred for several reasons in delaying complete and final approval of Envarsus XR on the basis of Astagraf XL's three-year exclusivity. Id. at FDA 00019-20; see also id. at FDA 01588-90, 1592-1622, 1623-25, 1626-43. Thereafter, in December 2014, the plaintiff provided additional arguments to the FDA as to why its delay of complete and final approval was erroroneous. Id. at FDA 01739-42. Upon review of the plaintiff's submissions to the FDA, the FDA proposed a compromise: "it could [fully] approve Envarsus XR before expiry of Astagraf XL's [three-year] exclusivity [in] July . . . 2016, but only with an indication that would cover 'conversion' from tacrolimus immediate-release to Envarsus XR in kidney transplant patients . . . ." Id. at FDA 01748. The FDA, therefore, declined to approve Envarsus XR for use in de novo kidney transplant patients, concluding that such approval would be inconsistent with Astagraf XL's three-year exclusivity. See id. at FDA 01748-49. The plaintiff rejected this proposal, see id. at FDA 01751-52, continuing to insist that the FDA had no basis to delay complete and final

approval of Envarsus XR, see id. at FDA 01759-61. The FDA ultimately decided in January 2015, that it would not approve Envarsus XR for use in de novo kidney transplant patients until the expiry of Astagraf XL's three-year exclusivity. See id. at FDA 00005-57. The plaintiff now seeks judicial review of this agency action.

II. STANDARD OF REVIEW

In cases involving review of final administrative actions, the summary judgment standard of review set forth in Federal Rule of Civil Procedure 56 does not apply.[6] See, e.g., ViroPharma, Inc. v. Hamburg, 916 F. Supp. 2d 76, 79 (D.D.C. 2013). Instead, "[the] FDA's administrative decisions are subject to review under the [APA], which requires the reviewing court to set aside an agency action that is 'arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law.'" ISTA Pharms., Inc. v. FDA, 898 F. Supp. 2d 227, 230 (D.D.C. 2012) (quoting 5 U.S.C. § 706). Thus, "[s]ummary judgment is the proper mechanism for deciding, as a matter of law, whether an agency action is supported by the administrative record and consistent with the APA standard of review." Loma Linda Univ. Med. Ctr. v. Sebelius, 684 F. Supp. 2d 42, 52 (D.D.C. 2010) (citing Stuttering Found. of Am. v. Springer, 498 F. Supp. 2d 203, 207 (D.D.C. 2007)), aff'd, 408 Fed. App'x 383 (D.C. Cir. 2010); see also Richards v. INS, 554 F.2d 1173, 1177 & n.28 (D.C. Cir. 1977).

"The scope of review under the 'arbitrary and capricious' standard is narrow and a court is not to substitute its judgment for that of the agency." Motor Vehicle Mfrs. Ass'n of U.S., Inc.

[6] The FDA moves for dismissal under Federal Rule of Civil Procedure 12(b)(6), or, in the alternative, for summary judgment under Federal Rule of Civil Procedure 56. Defs.' Summ. J. Mot. at 1. Because claims under the APA present only questions of law, the claims may be considered on their merits pursuant to either a motion to dismiss under Rule 12(b)(6) or a motion for summary judgment under Rule 56. Marshall Cnty. Health Care Auth. v. Shalala, 988 F.2d 1221, 1226 (D.C. Cir. 1993). While "there is no real distinction in this context between the question presented on a 12(b)(6) motion and a motion for summary judgment," id.,"[i]t is probably better practice for a district court to always convert to summary judgment," id. at 1226 n.5. The Court will adhere to this suggestion.

v. State Farm Mut. Auto. Ins. Co., 463 U.S. 29, 43 (1983). The agency must show that it "examine[d] the relevant data and articulate[d] a satisfactory explanation for its action including a rational connection between the facts found and the choice made." Id. (internal quotation marks omitted). "Under the APA, it is the role of the agency to resolve factual issues to arrive at a decision that is supported by the administrative record, whereas the function of the district court is to determine whether or not as a matter of law the evidence in the administrative record permitted the agency to make the decision it did." Hi-Tech Pharmacal Co. v. FDA, 587 F. Supp. 2d 13, 18 (D.D.C. 2008) (internal quotation marks and citation omitted). "[T]here is a presumption in favor of the validity of the administrative action." Teva Pharms., Indus., Ltd. v. FDA, 355 F. Supp. 2d 111, 116 (D.D.C. 2004) (Walton, J.) (alteration and internal quotation marks omitted), aff'd sub nom., Teva Pharms. Indus. Ltd. v. Crawford, 410 F.3d 51 (D.C. Cir. 2005). Courts "will uphold a decision of less than ideal clarity if the agency's path may reasonably be discerned." Pub. Citizen, Inc. v. FAA, 988 F.2d 186, 197 (D.C. Cir. 1993) (internal quotation marks omitted). Courts cannot "substitute its judgment for that of the agency," Motor Vehicle Mfrs. Ass'n, 463 U.S. at 43, especially where the agency's scientific expertise informed its judgment, see Balt. Gas & Elec. Co. v. Natural Res. Def. Council, Inc., 462 U.S. 87, 103 (1983) (holding that "[w]hen examining . . . [a] scientific determination . . . a reviewing court must generally be at its most deferential"). In sum, "when a party seeks review of agency action under the APA, the district . . . [court] sits as an appellate tribunal," and "[t]he 'entire case' on review is a question of law." Am. Bioscience, Inc. v. Thompson, 269 F.3d 1077, 1083 (D.C. Cir. 2001) (footnote and citations omitted).

III. ANALYSIS

All of the plaintiff's arguments are premised on the allegation that the FDA incorrectly interpreted and applied various portions of the FDCA, as amended. See, e.g., Compl. ¶¶ 7-9. The Court must review the FDA's interpretations of the FDCA under the two-step framework outlined in Chevron, U.S.A., Inc. v. Natural Res. Def. Council, Inc., 467 U.S. 837 (1984). This is

> a staged analysis that requires the [C]ourt to consider, first, "whether Congress has 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." If there is no clear answer, however, the [C]ourt must proceed to the second step, which involves giving deference to FDA's interpretation of the statute so long as FDA's reading of the statute is "based on a permissible construction."

Takeda, _ F. Supp. 3d at _, 2015 WL 252806 at *22 (quoting Chevron, 467 U.S. at 842-43); see also Pharm. Research & Mfrs. of Am. v. Thompson, 251 F.3d 219, 224 (D.C. Cir. 2001) (explaining that under the first step of Chevron, the Court must exhaust the "traditional tools of statutory construction," such as analyses of the "text, structure, purpose, and legislative history" of the statute"). "Chevron deference is frequently given to the FDA's interpretation of the FDCA, as well as its own regulations." Teva Pharms., Indus., 355 F. Supp. 2d at 116 (internal quotation marks omitted).

A. The QI Program Supplemental Funding Act

The plaintiff contends that the FDA should not have granted three-year exclusivity to Astagraf XL because the Astagraf XL NDA was submitted and pending before October 2008, and the QI Act conferred three-year exclusivity on an old antibiotic only if the NDA was submitted after October 2008. See Pl.'s Summ. J. Mem. at 40-43. Although the FDA concedes that the Astagraf XL NDA was submitted and pending before October 2008, it nevertheless

maintains that Astagraf XL was properly awarded three-year exclusivity because the Astagraf XL NDA was withdrawn in 2009, and then a new Astagraf XL NDA was submitted in 2012. See Defs.' Summ. J. Mem. at 22-23; see also A.R. at FDA 00031-33.

Under the FDCA, as amended by the QI Act, the Court agrees with the parties that the language is clear that an old antibiotic can be afforded three-year exclusivity to the extent that it was the subject of a new NDA that was submitted after October 8, 2008. 21 U.S.C. § 355(v)(1)(A)-(B); see also Pl.'s Summ. J. Mem. at 41; Defs.' Summ. J. Mem. at 23. Here, although an Astagraf XL NDA was pending before October 2008, it was eventually withdrawn in 2009 and a new Astagraf XL NDA was submitted in 2012, which contained clinical information absent from the previous Astagraf XL NDA. See A.R. at FDA 00010-16 (describing composition of Astagraf XL NDA "050811," submitted before October 2008, and Astagraf XL NDA "206406," submitted after October 2008 (emphasis added)); id. at FDA 00902-03; see also Defs.' Summ. J. Mem. at 23-24 (citing A.R. at FDA 00032, 888-906). Under these circumstances, Astagraf XL is eligible for the FDCA's three-year exclusivity.

To the extent that Congress did not address the precise conflict presented here, i.e., the FDCA is silent as to the withdrawal and "resubmission" of an old antibiotic NDA that was pending on or before October 2008,[7] the FDA's interpretation of the statute to allow three-year exclusivity for an old antibiotic that is the subject of a withdrawn and resubmitted NDA is reasonable. The FDA granted three-year exclusivity for Astagraf XL because its NDA demonstrated "a significant new use for an [o]ld antibiotic . . . ." A.R. at FDA 00033; see also Pl.'s Reply at 14 (the plaintiff concedes that Astagraf XL is a new antibiotic drug in that it is a

[7] The Court notes that "the fact that a statute can be applied in situations not expressly anticipated by Congress does not demonstrate ambiguity. It demonstrates breadth." PGA Tour, Inc. v. Martin, 532 U.S. 661, 689 (2001) (internal quotation marks omitted).

once-daily, extended release capsule—as opposed to a twice-daily, immediate release capsule like Prograf—for use in "de novo kidney transplant patients treated without induction"). The FDA's decision to afford the benefit of three-year marketing exclusivity to Astagraf XL is consistent with congressional intent in passing the QI Act—to "balance the need to encourage development of new antibiotic drugs to combat the growing number of disease-resistant bacterial infections and the desire to ensure access to previously approved antibiotics through approval of generic versions of such antibiotics." ViroPharma, 898 F. Supp. 2d at 20 (internal quotation marks omitted); see also id. (QI Act was "an important step forward to help spur research on new antibiotics" (internal quotation marks omitted)). "While [the plaintiff] may argue with that interpretation on policy grounds and present alternative readings of the provision's purpose and legislative history, such [arguments] fail in the face of the agency's carefully considered decision." Id. (internal quotation marks omitted). This is especially so where the limitation advanced by the plaintiff would discourage, rather than "encourage[,] [the] development of new antibiotic drugs," id., as a sponsor of a 505(b) NDA would abandon and forever lose the costs associated with its research and development efforts where its drug products were the subjects of a previously-submitted and withdrawn NDA.[8] In short, the FDA made a "reasonable policy

[8] The plaintiff contends that its limiting interpretation of the statute is necessary to "prevent [sponsors] from abusing the process to extend the life of old" antibiotics and curtail their "anti-competitive behavior." Pl.'s Summ. J. Mem. at 41-42. The Court rejects the plaintiff's reasoning for several reasons. First, the plaintiff's limitation would elevate form over substance in a manner contrary to Congress's intent to spur development of new antibiotics. ViroPharma, 898 F. Supp. 2d at 20. Second, the FDA's interpretation will not result in the consequences alleged by the plaintiff because there is a safeguard in place. In order for the pioneers of an old antibiotic to receive three-year exclusivity for the old antibiotic, they must research and develop a significant new use for the old antibiotic, which imposes a "higher hurdle for exclusivity . . . than there is for another kind of product seeking [three]-year exclusivity." Id. at 13 (internal quotation marks omitted). This hurdle ensures that old antibiotics are not excessively rewarded for insignificant uses.

The plaintiff further argues that "[i]f Astellas had addressed the deficiencies [in its original NDA] without withdrawing and submitting a purportedly 'new' NDA, there is no question that it would not be entitled to exclusivity under the QI Act." Pl.'s Reply at 24. That could be true, but that does not mean the FDA's interpretation here is unreasonable. Cf. ViroPharma, 898 F. Supp. 2d at 21 ("interpretive line drawing lies at the (continued . . .)

choice" in permitting Astagraf XL to receive the benefit of the three-year marketing exclusivity, id. at 21 (internal quotation marks omitted), and the Court will not "substitute its judgment for that of the agency," Motor Vehicle Mfrs. Ass'n, 463 U.S. at 43.

B. 21 U.S.C. § 355(c)(3)(E)(iii)

Once an old antibiotic, such as tacrolimus, is eligible for marketing exclusivities, the FDCA entitles those antibiotics to limited marketing exclusivities. In pertinent part, the FDCA states:

> If an application submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application approved under subsection (b) of this section, is approved after September 24, 1984, and if such application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under subsection (b) of this section for the conditions of approval of such drug in the approved subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) of this section if the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

21 U.S.C. § 355(c)(3)(E)(iii). According to the plaintiff, this provision does not bar the FDA from granting final approval of Envarsus XR for the prophylaxis of organ rejection in de novo kidney transplant patients because: (1) the Envarsus XR NDA "did not rely upon any of the

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(. . . continued)
heart of Chevron deference" (internal quotation marks omitted)). "[I]t was well within the [FDA]'s authority [and discretion] to set the bounds" of the statutory limitation prohibiting three-year exclusivity to an old antibiotic NDA submitted before October 2008. Id. Consistent with the legislative intent behind the QI Act, the FDA has permissibly chosen to interpret 21 U.S.C. § 355(v)(1)(A)-(B) in a narrow manner. In other words, it is within the FDA's authority and discretion to preclude eligibility for three-year exclusivity to only those antibiotics where the NDA was completely submitted and never withdrawn prior to October 8, 2008. See Allergan, 398 F. Supp. 2d at 22 ("Policy judgments made by an agency within its area of expertise are also entitled to deference from the courts . . . ." (citing Nat'l Rifle Ass'n v. Reno, 216 F.3d 122, 132 (D.C. Cir. 2000))).

studies or data supporting approval of Astagraf XL or upon [the] FDA's prior findings that Astagraf XL is safe and effective"; (2) Envarsus XR and Astagraf XL are significantly different drugs; and (3) the plaintiff is "not seek[ing] approval of Envarsus XR for the specific use studied in Astagraf XL's sole 'new clinical investigation.'" Pl.'s Summ. J. Mem. at 2. The Court will address each of the plaintiff's arguments in turn.

1. "Relied Upon"

The parties' conflicting interpretations of the term "relied upon" in 21 U.S.C. § 355(c)(3)(E)(iii) stand in stark contrast to one another. On the one hand, the plaintiff argues that the term "relied upon" "unambiguously requires" that the three-year exclusivity of a first-in-time 505(b) drug, i.e., the drug that is the subject of a first-in-time 505(b) NDA, can block a second-in-time 505(b)(2) drug from market entry, i.e., the drug that is the subject of a second-in-time 505(b)(2) NDA, only if the second-in-time 505(b)(2) NDA has "relied upon" the first-in-time 505(b) NDA.[9] Specifically, the plaintiff contends that there must be "an overlap" between the "new clinical investigations" in both NDAs. Pl.'s Summ. J. Mem. at 18. On the other hand, the FDA argues that the contested term "does not . . . mean that reliance is required to trigger exclusivity." Defs.' Summ. J. Mem. at 33. Rather, according to the defendant, the term "is used only to distinguish [between] 505(b)(1) [NDAs] from 505(b)(2) [NDAs]," because it is included in the statutory provision "as part of the lengthier [FDCA] definition of a 505(b)(2) [NDA]." Id. In other words, "[n]owhere in this provision does . . . [it] say that a[] [second-in-time 505(b)(2) NDA] will be blocked only if the [clinical] studies it 'relied upon' were . . . included in the . . . [first-in-time 505(b) NDA]." Id.

[9] The terms "first-in-time" and "second-in-time" are necessary when alluding to the statutory provision at issue here because the provision has a temporal quality inherent to it, i.e., after the first drug has received marketing exclusivity, the marketing approval of subsequent drugs may be affected.

The term "relied upon" is not defined in the FDCA. Nevertheless, the statutory provision is clear as to how three-year exclusivity operates and can be unambiguously parsed into essentially two components: entitlement to exclusivity and scope of that exclusivity. See, e.g., Goldstein v. SEC, 451 F.3d 873, 878 (D.C. Cir. 2006) ("The lack of a statutory definition of a word does not necessarily render the meaning of a word ambiguous . . . ."). Under the plain language of this provision, entitlement to three-year exclusivity requires: (1) submission of a 505(b) NDA[10]; (2) a drug that contains an active ingredient approved after September 1984; and (3) at least one new clinical investigation, excluding bioavailability studies, that is essential to the conditions of approval for the 505(b) drug. See 21 U.S.C. § 355(c)(3)(E)(iii); Takeda Pharms., _ F. Supp. 3d at _, 2015 WL 252806, at *7 n.11 ("FDA may grant a drug sponsor a [three]-year period of exclusivity for conduc[t]ing new clinical investigations essential to the approval of an application[.]" (citing 21 U.S.C. § 355(c)(3)(E)(iii)))[11]; Allergan, Inc. v. Alcon Inc., No. 04-cv-968(GMS), 2005 WL 3336535, at *1 (D. Del. Dec. 8, 2005) ("An additional three-year period of exclusivity is awarded to an NDA holder for obtaining FDA approval for a new use or new formulation of a previously approved brand drug." (citing 21 U.S.C. § 355(c)(3)(E)(iii)-(iv))).

Once exclusivity is appropriately granted to the drug that is the subject of the first-in-time 505(b) NDA, the FDA

> may not make the approval of an application submitted under subsection (b) of this section for the conditions of approval of such drug in the approved subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) of this section if the

[10] Submission of either a 505(b)(1) NDA or a 505(b)(2) NDA.

[11] Aside from general background information about the Hatch-Waxman Amendments, Takeda Pharms. is irrelevant to the case at bar. Takeda Pharms. concerned an unrelated, FDCA provision that addresses "the scope of a Section 505(b)(2) [sponsor]'s patent certification." E.g., _ F. Supp. 3d at _, 2015 WL 252806, at * 23.

> investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

21 U.S.C. § 355(c)(3)(E)(iii) (emphasis added). In other words, the FDA may not approve a second-in-time NDA that shares "conditions of approval" with the first-in-time 505(b) drug. Id. Moreover, the FDA is prohibited only from approving a second-in-time NDA that is a 505(b)(2) NDA, as this provision does not speak to a second-in-time 505(b)(1) NDA. Compare id. § 355(b)(2) ("An application submitted under paragraph (1) for a drug for which the investigations described in clause (A) of such paragraph and relied upon by the applicant for approval of the application 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 . . . ." (emphasis added)), with id. § 355(c)(3)(E)(iii) (no approval of second-in-time application where "the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted" (emphasis added)); see also Vill. of Barrington, Ill. v. Surface Transp. Bd., 636 F.3d 650, 664 (D.C. Cir. 2011) ("The normal rule of statutory construction is that identical words used in different parts of the same act are intended to have the same meaning." (alterations and internal quotation marks omitted)). Exclusivity under 21 U.S.C. § 355(c)(3)(E)(iii) is triggered by an overlap in the conditions of approval between the first-in-time 505(b) drug and the second-in-time 505(b)(2) NDA and not an overlap between the "new clinical investigations" supporting the first-in-time 505(b) NDA and second-in-time 505(b)(2) NDA. Indeed, it would frustrate Congress's intent to incentivize new drug development through, among other means, marketing exclusivities, if a second-in-time 505(b)(2)

NDA could escape the reach of the three-year exclusivity by simply relying on a 505(b) NDA different than the first-in-time 505(b) NDA. That result would reduce the incentive of the sponsor of the first-in-time 505(b) NDA to research and develop new drugs.[12] See, e.g., Blackman v. District of Columbia, 456 F.3d 167, 176 (D.C. Cir. 2006) ("If the language has a 'plain and unambiguous meaning,' . . . [the] inquiry ends so long as the resulting 'statutory scheme is coherent and consistent.'" (quoting United States v. Barnes, 295 F.3d 1354, 1359 (D.C. Cir. 2002))).

The plaintiff goes to great lengths to avoid the plain meaning of 21 U.S.C. § 355(c)(3)(E)(iii). First, the plaintiff merely notes that the term "relied upon" is contained in the statutory provision, and then jumps inexplicably to the conclusion that a second-in-time 505(b)(2) NDA can be blocked by the three-year exclusivity only where it relies on clinical investigations from the first-in-time 505(b) NDA, see Pl.'s Summ. J. Mem. at 18-19, ignoring other words in 21 U.S.C. § 355(c)(3)(E)(iii) that shed light on how the provision operates. See 21 U.S.C. § 355(c)(3)(E)(iii) (words surrounding "relied upon" track language found in 21 U.S.C. § 355(b)(2), which define a 505(b)(2) NDA); see also Abramski v. United States, _ U.S. _, _, 134 S. Ct. 2259, 2267 (2014) ("interpret . . . relevant words not in a vacuum, but with reference to the statutory context, structure, history, and purpose" (internal quotation marks omitted)); TRW Inc. v. Andrews, 534 U.S. 19, 31 (2001) (noting that courts must construe the language of a statute so that "no clause, sentence, or word shall be superfluous, void, or insignificant" (internal quotation marks omitted)). The Court will not make that same inferential leap as the plaintiff, absent some rational bridge, which does not exist here.

[12] For this same reason, to the extent there is any hint of ambiguity, the Court would nevertheless conclude that the FDA has provided a reasonable construction of the term "relied upon" in the provision.

Second, the plaintiff insists that the "importance of reliance" is confirmed by the "FDA's implementing regulation, which provides that a [second-in-time] 505(b)(2) [NDA] will be blocked by three-year exclusivity [only] to the extent that it 'relies on the information supporting the conditions of approval of an original new drug application.'" Pl.'s Summ. J. Mem. at 18-19 (quoting 21 C.F.R. § 314.108(b)(4)(iv) (2012)). But the plaintiff has misread the regulation, which in fact supports the FDA's position. The regulation states that:

> (4) If an application:
>
> (i) Was submitted under section 505(b) of the act;
>
> (ii) Was approved after September 24, 1984;
>
> (iii) Was for a drug product that contains an active moiety that has been previously approved in another application under section 505(b) of the act; and
>
> (iv) Contained reports of new clinical investigations (other than bioavailability studies) conducted or sponsored by the applicant that were essential to approval of the application, the agency will not make effective for a period of [three] years after the date of approval of the application the approval of [1] a 505(b)(2) application or [2] an abbreviated new drug application for the conditions of approval of the original application, or [3] an abbreviated new drug application submitted pursuant to an approved petition under section 505(j)(2)(C) of the act that relies on the information supporting the conditions of approval of an original new drug application.

21 C.F.R. § 314.108(b)(4)(i)-(iv). Thus, the regulation identifies three, second-in-time drug applications, that cannot receive final FDA approval during the exclusivity period of the first-in-time 505(b) drug—one being "a 505(b)(2) [NDA] . . . for the conditions of approval of the [first-in-time 505(b) NDA]." Id. § 314.108(b)(4)(iv). The element of "reliance" is relevant only where "an [ANDA is] submitted pursuant to an approved petition under section 505(j)(2)(C) of the [FDCA] . . . ." Id.

Third, the plaintiff implores the Court to examine other provisions of the FDCA because "[h]ad Congress simply intended to describe a 505(b)(2) application [in 21 U.S.C. § 355(c)(3)(E)(iii)], . . . it could have used the same phraseology that appears in other portions of . . . [the FDCA]." Pl.'s Summ. J. Mem. at 19. The plaintiff assumes that Congress cannot use different words to express the same idea. Yet, the case authority indicates otherwise. See Simon v. FEC, 53 F.3d 356, 359 n.1 (D.C. Cir. 1995) (recognizing that while two statutory provisions may be "worded slightly differently," they can "carry the same meaning"); Stowell v. Sec'y of Health & Human Servs., 3 F.3d 539, 542 (1st Cir. 1993) ("Congress, in its wisdom, may choose to express the same idea in many different ways." (citing Estate of Cowart v. Nicklos Drilling Co., 505 U.S. 469, 478 (1992))).

Fourth, the plaintiff asserts that the FDA's decision to delay complete and final approval of Envarsus XR for the prophylaxis of organ rejection in de novo kidney transplant patients "upends the balance sought to be achieved by Congress" under the Hatch-Waxman Amendments. Pl.'s Summ. J. Mem. at 22. Specifically, the Hatch-Waxman Amendments were enacted to, among other objectives, incentivize pharmaceutical companies and reward them for researching and developing innovative drugs. See id. at 20-23. But here, according to the plaintiff, it is "reap[ing] no reward for its own innovation and investment, while Astagraf XL is inappropriately shielded from competition against an innovative product . . . ." Id. at 23. The Court is not persuaded.[13] As the Court will explain below, Envarsus XR is not innovative to the

[13] The plaintiff takes issue with the fact that "an ANDA seeking approval of a generic version of Prograf and relying on the same Prograf data [the plaintiff] cited in the Envarsus XR NDA would be approved immediately, whereas Envarsus XR is blocked from the marketplace for relying on that same data even though it conducted additional[,] independent[,] and costly studies . . . ." Pl.'s Summ. J. Mem. at 23. The plaintiff deems this an "absurd result." Id. Not so. Indeed, this is the precise result contemplated by Congress when it passed the Hatch-Waxman Amendments. See Allergan, 398 F. Supp. 2d at 17 ("Because Congress still wanted to provide incentives for new drug development, alongside the ANDA process that eased the marketing of generic drugs, [the] Hatch-Waxman [Amendments] entitle[d] an NDA [sponsor] to a period of market exclusivity ([three] or [five] years, depending on (continued . . .)

extent that it is a once-daily, extended release tacrolimus formulation for the prophylaxis of organ rejection in de novo kidney transplant patients, as these were conditions of approval for Astagraf XL. And to the extent that Envarsus XR's innovation is its once-daily, extended release formulation for use in conversion kidney transplant patients, the plaintiff has voluntarily declined to market Envarsus XR for only this use, see A.R. at FDA 01751-52 (the plaintiff refusing to accept the FDA's proposal for final approval of Envarsus XR in use in conversion kidney transplant patients), and is not in a position to complain that the FDA's interpretation of 21 U.S.C. § 355(c)(3)(E)(iii) is preventing it from enjoying the fruits of its labor. In sum,[14] the FDA has correctly interpreted 21 U.S.C. § 355(c)(3)(E)(iii) to delay approval of a second-in-time

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the degree of innovation reflected in the NDA)."). Were the FDA to permit the entry of Envarsus XR into the marketplace for prophylaxis of organ rejection in de novo kidney transplant patients before the expiry of Astagraf XL's three-year exclusivity, the FDA would in fact be eviscerating an incentive for sponsors such as Astellas to research and develop new drugs.

[14] Assuming the term "relied upon" in 21 U.S.C. § 355(c)(3)(E)(iii) is somehow ambiguous, and it became necessary to proceed to the second step of the Chevron analysis, the Court finds that the FDA has reasonably interpreted the term in the context of the statute. As already explained, the FDA's interpretation of "relied upon" is incongruous with neither the words of the statute nor the intent of Congress. Further, the FDA's interpretation is consistent with its past practices. See AstraZeneca Pharms., 872 F. Supp. 2d at 83, 86-88 (finding comparison between the FDA's challenged agency action and its past practices probative in determining whether FDA statutory interpretation was reasonable); see also Novo Nordisk A/S v. Caraco Pharm. Labs., Ltd., 649 F. Supp. 2d 661, 663 n.2, 674 (E.D. Mich. 2009) (quoting excerpt from the FDA Orange Book preface: "Such investigations must have been conducted or sponsored by the applicant and must have been essential to approval of the application. If these requirements are met, the approval of a subsequent ANDA or an application described in Section 505(b)(2) of the Act may not be made effective for the same drug or use, if for a new indication, before the expiration of three years from the date of approval of the original application. If an applicant has exclusivity for a new application or 505(b)(2) application for the drug product with indications or use, this does not preclude the approval of an ANDA or 505(b)(2) application not covered by the exclusivity."); Defs.' Summ. J. Mem. at 38 (1989 Proposed Rule stating that "when exclusivity attaches to an innovative change in an already[-]approved drug, the effective date of approval of 505(b)(2) applications for a drug with that innovative change will be delayed until the innovator's exclusivity has expired regardless of the specific listed drug product to which the 505(b)(2) application refers" (ellipses and internal quotation marks omitted)). The plaintiff cites precedent allegedly indicating otherwise, but the FDA has sufficiently analogized the precedent to this case. Compare Pl.'s Summ. J. Mem. at 25-26 (contending that the FDA has approved second-in-time NDAs in similar circumstances as the Envarsus XR NDA), with Defs.' Summ. J. Mem. at 34-37 (explaining how second-in-time NDAs cited by the plaintiff are not analogous to the Envarsus XR NDA); see also A.L. Pharma, Inc. v. Shalala, 62 F.3d 1484, 1490 (D.C. Cir. 1995) ("[C]ourts give a high level of deference to an agency's evaluations of scientific data within its area of expertise."). And even if "the FDA's interpretation[] [here] may be inconsistent with its prior interpretations," that is "immaterial" where the Court has concluded that "the FDA interpreted the statute consistent with the clear and unambiguous language used by Congress." Teva Pharms., 355 F. Supp. 2d at 119. In short, deference to the FDA's interpretation of the term "relied upon" in 21 U.S.C. § 355(c)(3)(E)(iii) is warranted.

505(b)(2) NDA where it shares conditions of approval with a first-in-time 505(b) NDA, even if the second-in-time 505(b)(2) NDA does not rely on clinical investigations from the first-in-time 505(b) NDA.

2. "Conditions of Approval"

The parties agree that the scope of Astagraf XL's marketing exclusivity is limited to the "conditions of approval" based upon the "new clinical investigations" that were conducted in support of the Astagraf XL NDA. Pl.'s Summ. J. Mem. at 29, 35; Def.'s Summ. J. Mem. at 24-25. They also agree that Envarsus XR should be excluded from the marketplace only to the extent that Astagraf XL and Envarsus XR "share 'conditions of approval.'" Pl.'s Summ. J. Mem. at 35 (citing 21 U.S.C. § 355(c)(3)(E)(iii)); see also Defs.' Summ. J. Mem. at 24-25. Where they differ is whether the FDA identified the relevant conditions of approval shared between Astagraf XL and Envarsus XR—once-daily, extended release formulation of tacrolimus—despite there being a "myriad [of] differences" between the two drugs. Pl.'s Summ. J. Reply at 19; see also Defs.' Summ. J. Mem. at 27-28; A.R. at FDA 000024-28, 36-37.

Because the parties agree that the term "conditions of approval" is undefined in the FDCA and that no FDA implementing regulation clarifies the meaning of that term, Pl.'s Summ. J. Mem. at 35; Defs.' Reply at 18, the parties essentially concede that the term is ambiguous, and the Court thus proceeds to step two of the Chevron test to assess whether the FDA's interpretation of the FDCA is reasonable and entitled to deference, which the Court concludes it is. The FDCA sets up a "logical relationship between the change in the product for which the new clinical investigations were essential to approval of the [NDA], and the scope of any resulting three-year exclusivity." AstraZeneca Pharms. LP v. FDA, 872 F. Supp. 2d 60, 80 (D.D.C. 2012) (internal quotation marks omitted), aff'd sub nom., AstraZeneca Pharms. LP v.

FDA, 713 F.3d 1134 (D.C. Cir. 2013)[15]; see also id. at 83 ("substantive relationship between new clinical studies and changes in the [NDA] . . . dictates what changes receive exclusivity"); id. at 85 ("The FDA's interpretation of the statute as only granting exclusivity for significant innovations is reasonable given the statute's careful balance between providing exclusivity rights to promote innovation and making generic alternatives available to patients."). The scope of Astagraf XL's three-year exclusivity can only be as broad as the conditions of approval that were based upon the new clinical investigations identified in the Astragraf XL NDA. See id. at 80, 83, 85.

There is no dispute that the new clinical investigations that were essential to the FDA's approval of Astagraf XL and that led to three-year exclusivity for Astagraf XL were Study 158 and Study 12-03. E.g., Pl.'s Summ. J. Mem. at 30; Defs.' Summ. J. Mem. at 30. There is also no dispute that Study 158 examined "Astagraf XL in de novo kidney transplant patients with induction" and Study 12-03 investigated "Astagraf XL in de novo kidney transplant patients without induction." Pl.'s Summ. J. Mem. at 30 (citing A.R. at FDA 00035); see also A.R. at FDA 00034-35 (FDA finding that both studies demonstrated the safety and efficacy of Astagraf XL for the prophylaxis of organ rejection in de novo kidney transplant patients). In light of the results adduced from these new clinical investigations, the FDA concluded that Astagraf XL was entitled to three-year exclusivity for those innovations that distinguished it from Prograf—a once-daily, extended release tacrolimus formulation for prophylaxis of organ rejection in de novo kidney transplant patients. See AstraZeneca Pharms., 872 F. Supp. 2d at 80, 83, 85. It

[15] The Court finds AstraZeneca Pharms. persuasive authority, as that case dealt with 21 U.S.C. § 355(j)(5)(F)(iv), an analogous provision to the one disputed by the parties here. Compare 21 U.S.C. § 355(c)(3)(E)(iii) (prohibiting final approval of second-in-time 505(b)(2) NDA for three years, where it shares "conditions of approval" with the first-in-time 505(b) NDA), with id. § 355(j)(5)(F)(iv) (prohibiting approval of second-in-time ANDA for three years, where it shares "a change approved in" supplemental 505(b) NDA); see also Pl.'s Summ. J. Mem. at 29 & n.21.

follows that because Astagraf XL and Envarsus XR share these conditions of approval, complete and final approval of the Envarsus XR NDA must be delayed until the expiry of Astagraf XL's three-year exclusivity.[16]

The plaintiff makes much of the fact that despite the similarities between Astagraf XL and Envarsus XR—that is, they are both once-daily, extended release tacrolimus formulations—there are many other "clinically meaningful" differences between Astagraf XL and Envarsus XR. Pl.'s Summ. J. Mem. at 36. But that is beside the point.[17] The effect of marketing exclusivity in 21 U.S.C. § 355(c)(3)(E)(iii) turns on whether a second-in-time 505(b)(2) NDA shares any conditions of approval with the first-in-time 505(b) drug granted exclusivity.[18] See AstraZeneca Pharms., 872 F. Supp. 2d at 80, 83, 85.

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[16] The plaintiff is troubled by the timing of the FDA's determination concerning the scope of a 505(b) drug's exclusivity. See Pl.'s Reply at 20-21 (explaining that the plaintiff did not learn that Astagraf XL's three-year exclusivity was a statutory hurdle to complete and final approval of the Envarsus XR NDA until the end of the approval process). This has no bearing on the Court's ruling. Regardless of when the FDA determines the scope of exclusivity, it can be no broader than the innovations presented to the FDA in the new clinical investigations that led to the FDA's approval of the first-in-time 505(b) NDA. And this determination must necessarily occur when a second-in-time 505(b)(2) NDA is on the verge of final approval because that is when the conditions of approval sought by the second-in-time 505(b)(2) NDA become clear; otherwise exclusivity never becomes an issue. See Defs.' Reply at 20; Serono Labs., Inc. v. Shalala, 158 F.3d 1313, 1325 (D.C. Cir. 1998) ("'The post hoc rationalization rule' is not a time barrier which freezes an agency's exercise of its judgment after an initial decision has been made and bars it from further articulation of its reasoning. It is a rule directed at reviewing courts which forbids judges to uphold agency action on the basis of rationales offered by anyone other than the proper decisionmakers."); cf. Depomed, Inc. v. U.S. Dep't of Health & Human Servs., No. 12-cv-1592(KBJ), 2014 WL 4457225, at *10 (D.D.C. Sept. 5, 2014) ("As luck would have it for the FDA, the agency has the ability and the opportunity to control the circumstances under which marketing exclusivity attaches . . . and it is also the agency that has the duty of deciding when and under what circumstances a drug will be approved for marketing."), appeal dismissed sub nom., Depomed Inc. v. U.S. Dep't of Health & Human Servs., No. 14-5271, 2014 WL 5838247 (D.C. Cir. Nov. 7, 2014). Further, although it may be true that the timing of any FDA determination of exclusivity introduces some uncertainty into the 505(b)(2) NDA approval process for second-in-time sponsors, see Pl.'s Reply at 20, that uncertainty is the product of congressional design, as 21 U.S.C. § 355(c)(3)(E)(iii) essentially creates "a race to approval," i.e., once a first-in-time 505(b) drug receives the three-year exclusivity, the sponsor of that NDA need not worry about exclusivity. This race to exclusivity spurs new drug development, consistent with Congress's intent in enacting the Hatch-Waxman Amendments. See supra (citing Allergan, 398 F. Supp. 2d at 17).

[17] And the Court will not—as it need not—weigh in on whether these differences are in fact clinically significant.

[18] Likewise, the plaintiff's attempt to demonstrate that the FDA's position with respect to Envarsus XR is inconsistent with past FDA decisions must fail, see Pl.'s Summ. J. Mem. at 25, 36-37 (citing FDA approvals of Concerta and Metadate CD, which are both once-daily, extended release drugs for the treatment of attention deficit hyperactivity disorder), because the plaintiff, unlike the FDA, has not engaged in the proper statutory analysis,

(continued . . .)

3. "New Clinical Investigations"

The plaintiff has devoted substantial effort to explain why the FDA erroneously identified Study 158 as a "new clinical investigation" pursuant to 21 U.S.C. § 355(c)(3)(E)(iii). E.g., Pl.'s Summ. J. Mem. at 30-33. This argument was neither brought to the FDA's attention prior to this lawsuit nor even alluded to in the plaintiff's complaint.

"Simple fairness to those who are engaged in the tasks of administration, and to litigants, requires as a general rule that courts should not topple over administrative decisions unless the administrative body not only has erred but has erred against objection made at the time appropriate under its practice." United States v. L.A. Tucker Truck Lines, Inc., 344 U.S. 33, 37, (1952). The District of Columbia Circuit has consistently held that courts "are bound to adhere to the '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.'" Coburn v. McHugh, 679 F.3d 924, 929 (D.C. Cir. 2012) (quoting Nuclear Energy Inst. v. EPA, 373 F.3d 1251, 1297 (D.C. Cir. 2004) (per curiam)); see also CSX Transp., Inc. v. Surface Transp. Bd., 584 F.3d 1076, 1079 (D.C. Cir. 2009) (acknowledging the "well-established doctrine of issue waiver, which permits courts to decline to hear arguments not raised before the agency where the party had notice of the issue"). This principle applies to legal, as well as factual, arguments. See Nuclear Energy Inst., 373 F.3d at 1290 ("To preserve a legal or factual argument, . . . [a] proponent [must] have given the agency a 'fair opportunity' to entertain it in the administrative forum before raising it in the judicial one." (quoting Wash. Ass'n for Television & Children v.

(. . . continued)
focusing on the conditions of approval between a first-in-time drug and a second-in-time drug, see Defs.' Reply at 11 (explaining that Concerta and Metadate CD did not share a common pharmacokinetic profile, which was the relevant condition of approval with respect to determining the scope of marketing for Concerta (citing A.R. at FDA 00050-51)).

FCC, 712 F.2d 677, 681 (D.C. Cir. 1983))). And the Circuit has clarified that the standard for waiver in administrative law cases focuses on whether the "specific argument" put forth by the plaintiff was raised before the agency. See Koretoff v. Vilsack, 707 F.3d 394, 398 (D.C. Cir. 2013). Under this standard, the Circuit "require[s] 'the argument [the plaintiff] advances here' to be raised before the agency, not merely the same general legal issue." Id. (quoting Nuclear Energy Inst., 373 F.3d at 1291).

On November 17, 2014, the FDA sent the plaintiff the "FDA Exclusivity Summary for Astagraf XL." Plaintiff's Motion for Preliminary Injunction ("Prelim. Inj. Mot."), Exhibit ("Ex.") 4 (Declaration of Jennifer L. Bragg ("Bragg. Decl")) ¶ 6; see also A.R. at FDA 01082-89. The FDA Exclusivity Summary for Astagraf XL ("Astagraf XL Summary") identified Study 158 as a "new clinical investigation" that was essential to the approval of Astagraf XL and that supported the three-year exclusivity for the drug.[19] A.R. at FDA 01086-87. After receiving the Astagraf XL Summary and having notice that the FDA relied on Study 158 for granting Astagraf XL's three-year exclusivity, the plaintiff thereafter could have challenged the fact that Study 158 was a "new clinical investigation" pursuant to 21 U.S.C. § 355(c)(3)(E)(iii) on several occasions with the FDA. See A.R. at FDA 01739-42 (providing bases to FDA for contesting Astagraf XL's exclusivity on December 2, 2014); id. at FDA 01748-50 (conferring with FDA about, among other things, Astagraf XL's exclusivity on December 5, 2014); id. at FDA 01751-58 (objecting to Astagraf XL's exclusivity on December 8, 2014); id. at FDA 01759-61 (directing FDA to relevant precedent regarding Astagraf XL's exclusivity on December 12, 2014); id. at 01768-70 (threatening court intervention to resolve exclusivity dispute on December 16, 2014).

[19] Contrary to the plaintiff's suggestion, the FDA's final decision in January 12, 2015, was not the first time it learned that Study 158 was a "new clinical investigation" supporting Astagraf XL's three-year exclusivity. See Pl.'s Reply at 14 n.8.

Perhaps most egregious is that the plaintiff omitted any mention in its thirty-two page complaint that the FDA's decision to delay final approval of Envarsus XR for the prophylaxis of organ rejection in de novo kidney transplant patients and bar its entry into the marketplace was in contravention of the APA because it used Study 158 to support Astragraf XL's three-year exclusivity. See Montanans For Multiple Use v. Barbouletos, 568 F.3d 225, 229 n.1 (D.C. Cir. 2009) ("To the extent [the] plaintiffs suggested at oral argument that the [agency] acted in an arbitrary and capricious manner . . . , [the] plaintiffs did not develop that argument in their brief, and the complaint does not include such a cause of action. We therefore do not consider it."); Morrison v. Sec'y of Def., 802 F. Supp. 2d 6, 11 n.3 (D.D.C. 2011) (claim not raised in complaint waived). Because the plaintiff did not give the FDA an opportunity to consider the merits of its arguments concerning whether Study 158 was a "new clinical investigation" pursuant to 21 U.S.C. § 355(c)(3)(E)(iii), the plaintiff has waived judicial review of the arguments related to it.[20]

C. The Plaintiff's Motion to Supplement the Administrative Record

The plaintiff seeks to supplement the administrative record with "the FDA's own Statistical Review and Evaluation from the [Prograf] supplemental New Drug Application" ("Prograf Review and Evaluation") and the "FDA's minutes of a June 17, 1997 meeting between FDA and the sponsor of Duoneb" ("Douneb Meeting Minutes").[21] Pl.'s Supplement Mot. at 1. The plaintiff contends that supplementation is necessary because these documents either are adverse to the FDA's decision to delay complete and final approval of Envarsus XR and were

[20] In light of this ruling, the Court will deny the plaintiff's motion for leave to a file a surreply, as the plaintiff only sought leave to file the surreply to inject additional arguments regarding the novelty of Study 158. See Pl.'s Surreply Mot. at 1.

[21] Hereinafter, the Court will collectively refer to these two items as the "documents."

deliberately or negligently excluded, or are necessary as background information for the Court's determination as to whether the FDA considered all relevant factors in making its decision. Id. at 4. Both positions are rejected because supplementation of the administrative record is improper in this case.

Supplementation of the administrative record is only appropriate in exceptional or "unusual" circumstances. City of Dania Beach v. FAA, 628 F.3d 581, 590 (D.C. Cir. 2010) ("[W]e do not allow parties to supplement the record 'unless they can demonstrate unusual circumstances justifying a departure from this general rule.'" (quoting Tex. Rural Legal Aid v. Legal Servs. Corp., 940 F.2d 685, 698 (D.C. Cir. 1991))); see also Cape Hatteras Access Pres. Alliance v. U.S. Dep't of Interior, 667 F. Supp. 2d 111, 112 (D.D.C. 2009) ("A court that orders an administrative agency to supplement the record of its decision is a rare bird."). This is because "[t]here is a strong presumption that the agency properly compiled the administrative record." Ivy Sports Med., LLC v. Sebelius, No. 11-cv-1006(RLW), 2012 WL 5248176, at *1 (D.D.C. Oct. 24, 2012). Thus, "[s]upplementation of the administrative record is the exception, not the rule." Id. (internal quotation marks omitted).

To rebut the strong presumption of regularity afforded to the administrative record compiled by the agency, the party seeking supplementation must "put forth concrete evidence that the documents it seeks to 'add' to the record were actually before the decisionmakers." Marcum v. Salazar, 751 F. Supp. 2d 74, 78 (D.D.C. 2010). Conclusory statements will not suffice; rather, the plaintiff "must identify reasonable, non-speculative grounds for its belief that the documents were considered by the agency and not included in the record." Id. at 78 (quoting Pac. Shores Subdivision Cal. Water Dist. v. U.S. Army Corps of Eng'rs, 448 F. Supp. 2d 1, 6 (D.D.C. 2006)) (internal quotation marks omitted). "Therefore, absent clear evidence to the

contrary, an agency is entitled to a strong presumption of regularity, that it properly designated the administrative record." Ivy Sports Med., 2012 WL 5248176, at *1 (internal quotation marks omitted).

The District of Columbia Circuit has recognized three narrow instances where supplementation of an administrative record may be appropriate: "(1) if the agency 'deliberately or negligently excluded documents that may have been adverse to its decision,' (2) if background information was needed 'to determine whether the agency considered all the relevant factors,' or (3) if the 'agency failed to explain administrative action so as to frustrate judicial review."[22] City of Dania Beach, 628 F.3d at 590 (quoting Am. Wildlands v. Kempthorne, 530 F.3d 991, 1002 (D.C. Cir. 2008)).

Here, the strong presumption of regularity has not been rebutted by the plaintiff for several reasons. First, the plaintiff relies on conclusory allegations that the FDA negligently or deliberately omitted these documents, as opposed to concrete evidence. See Pl.'s Supplemental Mot. at 5, 7. Second, the documents are not adverse to the FDA's decision to delay final approval of Envarsus XR until the expiry of Astagraf XL's three-year exclusivity. The argument that Study 158 was not a "new clinical evaluation" has been waived by the plaintiff, and thus the Prograf Review and Evaluation is irrelevant. And the Douneb Meeting Minutes are cumulative, as the FDA has already included its substance in the administrative record. Compare Pl.'s Supplemental Mot., Ex. B (June 17, 1997 Meeting Minutes ("Duoneb Meeting Minutes")) at 6 (FDA "expressed . . . opinion that . . . [the Duoneb NDA] could not be approved pending expiration of . . . exclusivity for Combivent NDA even if . . . [the Duoneb NDA] does not reference the Combivent NDA and even if [the Duoneb NDA] provides data in support of the

[22] According to the plaintiff, only the first two instances are applicable here. Pl.'s Supplement Mot. at 4. The Court will follow the plaintiff's lead and address only these circumstances.

combination product from the literature . . . ."); with A.R. at FDA 00047-48 (explaining how FDA "concluded that it likely would not be able to fully approve Duoneb's 505(b)(2) NDA . . . due to Combivent's existing exclusivity," notwithstanding that the application "did not rely on Combivent"). Finally, any background information that may be useful from these documents has already been compiled in the administrative record by the FDA, and thus supplementation for that purpose is unnecessary. See A.R. at FDA 00047-48 (discussing exclusivity position with respect to Duoneb and Combivent); id. at 01082-89 (demonstrating reliance on Study 158 in approval of Astagraf XL). Accordingly, for all of these reasons, the Court concludes that it has appropriately reviewed the FDA's decision to delay complete and final approval of Envarsus XR, using a properly designated administrative record.

IV. CONCLUSION

For the foregoing reasons, the Court concludes that the FDA's decision to delay final approval of Envarsus XR for the prophylaxis of organ rejection in de novo kidney transplant patients was neither arbitrary and capricious nor in excess of the FDA's statutory authority.[23]

SO ORDERED this 12th day of June, 2015.

REGGIE B. WALTON
United States District Judge

[23] The Court has contemporaneously issued an Order consistent with this Memorandum Opinion.