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

SANDOZ INC.,

*Plaintiff*,

v.

XAVIER BECERRA, Secretary, United States Department of Health and Human Services,[1] *et al.*,

*Defendants.*

No. 21-cv-600 (DLF)

**MEMORANDUM OPINION**

Sandoz Inc. challenges a decision of the Food and Drug Administration (FDA) that granted four years of market exclusivity to the sponsor of a new drug, Aubagio. *See* Compl. ¶ 1, Dkt. 1. Sandoz argues that the sponsor was not entitled to exclusivity because the FDA had previously approved the use of Aubagio's active ingredient in another drug, Arava. *See id.* ¶¶ 66–85. Before the Court is Sandoz's Motion for Summary Judgment, Dkt. 14, and the government's Cross-Motion for Summary Judgment, Dkt. 20. For the reasons that follow, the Court will grant the government's motion and deny Sandoz's motion.

## I. BACKGROUND

### A. Legal Background

The Food, Drug, and Cosmetic Act (FDCA) prohibits introducing "any new drug" into interstate commerce without prior approval by the FDA. 21 U.S.C. § 355(a). Pharmaceutical

[1] When this complaint was filed, Norris Cochran IV was the Acting Secretary of Health and Human Services. When Xavier Becerra became Secretary, he was substituted pursuant to Fed. R. Civ. P. 25(d).

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companies may obtain that approval in two ways. First, a company may submit a new drug application (NDA) under § 505 of the FDCA. 21 U.S.C. § 355(b). The FDA may then approve that application only if the company demonstrates that its drug is safe and effective for its proposed use—a process that often requires clinical trials. *See id.* § 355(d); *see also id.* § 355(b)(1)(A), (d) (specifying other requirements for NDAs). Alternatively, after the FDA has approved a new drug and certain rights of that drug's sponsor have expired, *see, e.g.*, *id.* § 355(j)(5)(B)(ii), a second company may apply to market a generic version of the drug by submitting an abbreviated new drug application (ANDA), *id.* § 355(j). The FDA may approve an ANDA upon finding that a generic drug is equivalent to the original, listed drug in several respects—a process that rarely requires clinical trials. *See id*. § 355(j)(4); *Ipsen Biopharm., Inc. v. Becerra*, 2021 WL 4399531, at *1 (D.D.C. Sept. 24, 2021).

When a company obtains approval to market a new drug, the FDCA may also grant it a period of market exclusivity. *See, e.g.*, 21 U.S.C. § 355(j)(5)(F)(ii). These periods are "designed to compensate manufacturers for research and development costs as well as the risk of litigation from patent holders." *Teva Pharms., USA, Inc. v. Leavitt*, 548 F.3d 103, 104 (D.C. Cir. 2008). Although the FDCA contains multiple provisions that confer exclusivity, *see Amarin Pharms. Ireland Ltd. v. FDA*, 106 F. Supp. 3d 196, 199 (D.D.C. 2015), only two are relevant here.[2]

First, the FDCA grants at least four years of exclusivity to companies that successfully submit an NDA for any new drug, "no active ingredient . . . of which has been approved in any

[2] Because Sandoz challenges the grant of exclusivity to Aubagio, the Court considers the text of the FDCA that was operative as of that drug's approval, September 12, 2021. *See* A.R. 1456.

other [NDA]."[3] 21 U.S.C. § 355(j)(5)(F)(ii) (2012). This benefit, which is commonly called new chemical entity (NCE) exclusivity, prevents other companies from submitting ANDAs that "refer[] to" the approved drug for at least four years. *Id.* For this purpose, the term "active ingredient" refers to "any component 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 body." 21 C.F.R. § 314.3(b). The FDA determines a drug's active ingredients by looking to its chemical structure before it enters the human body, as opposed to after its metabolization. *See* A.R. 1580–82; *see also Actavis Elizabeth LLC v. FDA*, 625 F.3d 760, 764–66 (D.C. Cir. 2010) (approving this approach).

Separately, the FDCA grants 180 days of exclusivity to the "first applicant" that successfully submits an ANDA that contains a Paragraph IV "certification." 21 U.S.C. § 355(j)(5)(B)(iv). By way of background, each application to market a generic drug must submit a certification regarding any patents that claim the associated listed drug. *See id.* § 355(j)(2)(A)(vii). This certification may provide that a patent "has expired," *id.* § 355(j)(2)(A)(vii)(II), that it "will expire," *id.* § 355(j)(2)(A)(vii)(III), or—under Paragraph IV—that it "is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted," *id.* § 355(j)(2)(A)(vii)(IV). Submitting a Paragraph IV certification "comes with a risk" because it constitutes a technical act of patent infringement and may spark "costly litigation." *Teva Pharms. USA, Inc. v. Sebelius*, 595 F.3d 1303, 1305 (D.C. Cir. 2010) (citing 35 U.S.C. § 271(e)(2)). It is for that reason that the FDCA confers a limited period of exclusivity to certain "first applicant[s]." 21 U.S.C. § 355(j)(5)(B)(iv). The benefit of exclusivity

[3] The current version of § 355(j)(5)(F)(ii) replaces the term "active ingredient" with "active moiety." *See* Act to Amend the Federal Food, Drug, and Cosmetic Act, Pub. L. No. 117-9, 135 Stat. 256, 256 (Apr. 2, 2021).

seeks to offset the cost of litigation, thereby "expediting the availability of generic equivalents." *Teva*, 595 F.3d at 1305.

As relevant here, the FDCA allows multiple companies to share "first applicant" status. *See* 21 U.S.C. § 355(j)(5)(B)(iv)(II)(bb). A company can obtain the status by being the first to submit a "substantially complete" ANDA that includes a Paragraph IV certification. *Id.* Other companies may also obtain the same status by filing "substantially complete" Paragraph IV ANDAs "on the [same] day" as the initial application. *Id.* When multiple companies share "first applicant" status, their periods of exclusivity overlap. *See id.* § 355(j)(5)(B)(iv)(I). And when any first applicant benefits from exclusivity, no other company may market a generic version of the same listed drug. *See id.* Accordingly, any generic manufacturer that intends to submit a Paragraph IV ANDA has an incentive to submit that application on the first possible date—*i.e.*, four years from the approval of the initial, listed drug. *See id.* § 355(j)(5)(B)(iv).

**B. Factual Background**

This case arises from the approval of two drugs—Arava and Aubagio—that contain the same ingredient—teriflunomide.

The FDA approved Arava in 1998 for the treatment of "adults with active rheumatoid arthritis." A.R. 19, 360. That approval identified Arava's sole active ingredient as leflunomide, *see* A.R. 265, 325–326—a chemical that is closely related to teriflunomide. When leflunomide enters the human body, it "is metabolized . . . to teriflunomide which is responsible for essentially all of [the former]'s in vivo activity." A.R. 1455. Leflunomide also tends to degrade into teriflunomide over time, even before it enters the human body. *See* A.R. 1445, 1459. For that reason, the FDA noted that Arava contains trace amounts of teriflunomide. *See* A.R. 1459.

Specifically, the agency designated those amounts as impurities in Arava and provided that they could be no more than 0.3% of the drug. *See* A.R. 1459.

The FDA approved the second relevant drug, Aubagio, on September 12, 2012, to treat "patients with relapsing forms of multiple sclerosis." A.R. 402, 1456. That approval noted that teriflunomide was the sole active ingredient in Aubagio. *See* A.R. 418–19, 1456–57. It also determined that the FDA had not previously approved another drug with the same active ingredient. *See* A.R. 1171, 1457. For that reason, the FDA granted Aubagio at least four years of NCE exclusivity pursuant to § 355(j)(5)(B)(iv). *See* A.R. 1457. In doing so, the FDA took the position that no generic manufacturer could submit a Paragraph IV ANDA that referenced Aubagio until September 12, 2016. *See* 21 U.S.C. § 355(j)(5)(B)(iv).

On August 31, 2016, Sandoz wrote to the FDA for the purpose of challenging Aubagio's exclusivity. *See* A.R. 1393. Sandoz argued that the exclusivity was unwarranted because teriflunomide was "physically present as a bioavailable and physiologically/pharmacologically active component of" Arava. A.R. 1401. It also argued that the sponsor of both Arava and Aubagio—Sanofi-Aventis US LLC (Sanofi)[4]—was aware of the ingredient's presence in Arava and viewed it as beneficial. *See* A.R. 1396–97. On that issue, Sandoz pointed to several patent applications and patent infringement suits in which Sanofi claimed positive interactions between leflunomide and teriflunomide. *See* A.R. 1396–99; *see, e.g.*, U.S. Patent No. 7,071,222, at [1] (filed Mar. 7, 1997) (issued July 4, 2006) (noting that a "combination preparation" of leflunomide and teriflunomide "exhibits surprisingly advantageous immunosuppressive effects"). Finally, Sandoz insisted that its position did not rest on the fact that "teriflunomide is the active metabolite

[4] Sandoz represents that the original sponsor for Arava was Hoechst Marion Roussel, Inc.—a predecessor in interest to Sanofi. *See* Pl.'s Mem. in Supp. of Mot. for Summ. J. at 10, Dkt. 16.

of leflunomide." A.R. 1401. In this respect, Sandoz declined to challenge the FDA's general approach for identifying active ingredients, which looks to drugs' structure prior to their metabolization. *See Actavis Elizabeth*, 625 F.3d at 764–66.

Sandoz subsequently filed two Paragraph IV ANDAs to market generic teriflunomide. *See* A.R. 1403–10. Sandoz filed its first application on September 7, 2016—five days before Aubagio's exclusivity was set to expire. *See* A.R. 1403. That application referenced Sandoz's challenge letter and asked the FDA, if it accepted the challenge, to "deem [the application] received" on the date of its submission. *Id.* Sandoz then filed a second and nearly identical application on September 12—the first day after Aubagio's scheduled exclusivity. *See* A.R. 1407. The FDA acknowledged the receipt of both applications and advised that it would "take action on only one" of them. A.R. 1416. It also advised that, if Sandoz prevailed in its exclusivity challenge, Sandoz could choose which application would proceed. *Id.*

This arrangement positioned Sandoz to benefit from its exclusivity challenge. The FDA received twenty-one ANDAs on September 12, 2016, that sought to market generic versions of teriflunomide. *See* FDA, *Paragraph IV Patent Certifications*, at 73, https://www.fda.gov/media/133240/download (last visited July 21, 2022). Sandoz appears to be the only company, however, that filed a substantially complete ANDA before that date. *See* Pl.'s Mem. in Supp. of Mot. for Summ. J. at 16, Dkt. 16 (undisputed). For that reason, if Sandoz prevailed in its challenge, it would be the only "first applicant" for that generic and thus receive 180 days of market exclusivity. *See* 21 U.S.C. § 355(j)(5)(B)(iv). In contrast, if its challenge did not prevail, Sandoz would be one of twenty-one "first applicants" for the generic and would need to share its exclusivity with those other companies. *Id.*

The FDA rejected Sandoz's exclusivity challenge on July 27, 2018. *See* A.R. 1436–49. The agency explained that it did not consider teriflunomide to be an active ingredient in Arava at the time that it reviewed that drug's NDA. *See* A.R. 1445. Instead, it viewed teriflunomide as an impurity, which was neither "added intentionally" to nor required to be present in the drug. A.R. 1445–46. The agency further reasoned that leflunomide was the "sole active ingredient in Arava" because it was "the sole component of [that drug] intended to furnish pharmacological activity . . . in the treatment of adults with active rheumatoid arthritis." A.R. 1447. Moreover, the agency reasoned that, "[i]f Arava contained more than one active ingredient, then additional showings would need to have been made by Sanofi to support [the drug's] safety and effectiveness." A.R. 1447. Finally, the agency reasoned that its treatment of Arava was consistent with its past practice and that Sandoz's contrary approach would raise administrative difficulties, such as "exponentially increas[ing] the number of substances that would need to be considered for purposes of the 5-year exclusivity analysis." A.R. 1447–48. The FDA thus denied Sandoz's first ANDA, *see* A.R. 1465, which put Sandoz on track to share its period of exclusivity.

Sandoz filed an administrative appeal with the FDA on October 10, 2018. *See* A.R. 1473–80. In that appeal, Sandoz argued that teriflunomide was an active ingredient in Arava because Sanofi "knew that the teriflunomide present in Arava was physiologically active," regardless of whether the FDA considered that activity. A.R. 1477. Sandoz further argued that the FDA had "inherent authority to correct past mistakes" regarding its classification of active ingredients and had "done so in the past." A.R. 1477 n.2. Finally, as a rebuttal to the argument that its position would raise administrative difficulties, Sandoz argued that its case presented unique circumstances—namely, that Sanofi knew about the presence and effect of teriflunomide at the time of Arava's approval. *See* A.R. 1478.

The FDA denied Sandoz's administrative appeal on February 12, 2021, relying on substantially the same reasoning as its previous decision. *See* A.R. 1481–84. The agency also accepted Sandoz's second ANDA, such that Sandoz became eligible for "180 days of shared generic exclusivity." A.R. 1485–86. Under the FDCA, that period of exclusivity is set to begin on "the date of the first commercial marketing of [generic teriflunomide] . . . by any first applicant." 21 U.S.C. § 355(j)(5)(B)(iv)(I). The parties report that this marketing will not occur until March 2023 at the earliest. *See* Joint Status Report of June 29, 2022, Dkt. 39.

In this action, Sandoz challenges the rejection of its first ANDA under the Administrative Procedure Act, 5 U.S.C. § 551 *et seq.* Compl. ¶¶ 1, 66–92. Sandoz first argues that the rejection was inconsistent with 21 U.S.C. § 355(j)(5)(F)(ii). Under its reading of that statute, Aubagio is ineligible for NCE exclusivity simply because the "FDA approved Arava knowing it contained teriflunomide," regardless of whether it approved teriflunomide "as an active ingredient." Pl.'s Mem. at 2 (emphasis omitted). In the alterative, Sandoz argues that teriflunomide *is* an active ingredient in Arava. *See id.* at 32–39. And finally, Sandoz argues that awarding NCE exclusivity to Aubagio was arbitrary and capricious insofar as it was inconsistent with a past agency decision. *See id.* at 39–43. For those reasons, Sandoz asks this Court to set aside both the rejection of its first ANDA and the preceding grant of NCE exclusivity to Aubagio. *See* Compl. at 40; *see also* 5 U.S.C. § 706(2).

## II. LEGAL STANDARD

A court will grant summary judgment if the moving party "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); *see also Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 247–48 (1986). A "material" fact is one with potential to change the substantive outcome of the litigation. *See Liberty Lobby*,

477 U.S. at 248; *Holcomb v. Powell*, 433 F.3d 889, 895 (D.C. Cir. 2006). And a dispute is "genuine" if a reasonable jury could determine that the evidence warrants a verdict for the nonmoving party. *See Liberty Lobby*, 477 U.S. at 248; *Holcomb*, 433 F.3d at 895.

In cases arising under the Administrative Procedure Act, summary judgment "serves as the mechanism for deciding, as a matter of law, whether the agency action is supported by the administrative record and otherwise consistent with the APA standard of review." *Sierra Club v. Mainella*, 459 F. Supp. 2d 76, 90 (D.D.C. 2006). The Court will thus "hold unlawful and set aside" agency action that is "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law," 5 U.S.C. § 706(2)(A), "in excess of statutory jurisdiction, authority, or limitations, or short of statutory right," *id*. § 706(2)(C), or "unsupported by substantial evidence," *id.* § 706(2)(E).

## III. ANALYSIS

### A. Sandoz has Article III standing

Before reaching the merits of this case, the Court must determine whether Sandoz has Article III standing. *See Steel Co. v. Citizens for a Better Env't*, 523 U.S. 83, 93–95 (1998). To establish standing, Sandoz must demonstrate that it has suffered an "injury in fact" that is "concrete and particularized" and "actual or imminent, not conjectural or hypothetical." *Lujan v. Defenders of Wildlife*, 504 U.S. 555, 560–61 (1992) (internal quotation marks omitted). It must also establish that there is "a causal connection between the injury and the conduct complained of" and that it is "likely, as opposed to merely speculative, that the injury will be redressed by a favorable decision." *Id.* (internal quotation marks omitted). Each of these elements "must be supported in the same way as any other matter on which the plaintiff bears the burden of proof." *Id.* at 561.

Sandoz has adequately established Article III standing. The D.C. Circuit has previously held that the denial of market exclusivity is an injury in fact because it exposes plaintiffs to

"allegedly unlawful competition." *Teva*, 595 F.3d at 1312. Sandoz falls within that holding because it is slated to receive shared market exclusivity instead of sole market exclusivity, which will expose it to a similar competitive harm. *See supra* section I.B. Sandoz has also shown that the FDA caused its injury. And finally, Sandoz has shown that its injury is redressable through setting aside the FDA's denial of its first ANDA, *see* 5 U.S.C. § 706(2)—a result that would make Sandoz the only "first applicant" for generic teriflunomide, 21 U.S.C. § 355(j)(5)(B)(iv)(II), and grant it sole exclusivity for 180 days following that drug's "first commercial marketing," *id.* § 355(j)(5)(B)(iv)(I). For those reasons, and because the Court otherwise has subject-matter jurisdiction under 28 U.S.C. § 1331, the Court will reach the merits of the parties' dispute.

### B. NCE Exclusivity Turns on Whether the Active Ingredient of the New Drug Was Approved as an Active Ingredient in a Prior Drug

To determine whether Aubagio is entitled to NCE exclusivity, the Court must determine the standard for assigning NCE exclusivity in general. That standard is set forth in 21 U.S.C. § 355(j)(5)(F)(ii), which provides:

> If an application submitted under subsection (b) of this section for a drug, no active ingredient . . . of which has been approved in any other application under subsection (b) of this section, is approved . . . , no application may be submitted under this subsection which refers to the drug for which the subsection (b) application was submitted before the expiration of [at least four years].

21 U.S.C. § 355(j)(5)(F)(ii). The phrase "subsection (b)" refers to 21 U.S.C. § 355(b), which governs the process for submitting and evaluating NDAs. *See id.* § 355(b). Accordingly, § 355(j)(5)(F)(ii) confers exclusivity upon the approval of an NDA "for a drug, no active ingredient of which has been approved in any other" NDA. *Id.* § 355(j)(5)(F)(ii).

The parties offer competing interpretations of this provision, and especially of its adjectival phrase, "no active ingredient . . . of which has been approved." *Id.* The FDA argues that the

language confers exclusivity when the "active ingredient[s]" of a new drug have not previously "been approved" *as active ingredients* in a prior drug. *See* Gov't's Mem. in Supp. of Summ. J. at 12, Dkt. 22. Under that view, Aubagio would be entitled to exclusivity unless the FDA both considered teriflunomide to be an active ingredient in Arava and approved it as such. In contrast, Sandoz argues that § 355(j)(5)(F)(ii) confers exclusivity when the "active ingredient" of a new drug has not previously "been approved" *in any capacity*, including as an impurity in a prior drug. *See* Pl.'s Mem. at 22. Under that view, the fact that the FDA considered teriflunomide at all in the course of approving Arava would prevent Aubagio from receiving exclusivity. For the reasons that follow, the Court agrees with the FDA's interpretation of § 355(j)(5)(F)(ii).

To begin, the plain text of § 355(j)(5)(F)(ii) favors the FDA's position. On its face, that provision refers both to one new NDA, which resulted in the approval of a new drug, and to all previously approved NDAs. *See* 21 U.S.C. § 355(j)(5)(F)(ii). The provision then asks whether any "active ingredient" of the new drug was "approved" in the NDA for any prior drug. *Id.* It is true that this language does not elaborate on what that approval entails. But because the provision expressly refers to the approval *of* active ingredients, its most natural reading considers their approval *as* active ingredients. *See Hibbs v. Winn*, 542 U.S. 88, 101 (2004) (counseling "that statutory language must be read in context [since] a phrase gathers meaning from the words around it").

Sandoz's contrary reading of the text strains the ordinary meaning of "approved." To approve something means "to accept [it] as satisfactory," Merriam Webster's Collegiate Dictionary (10th ed. 1997), or "to give [it] formal sanction," Black's Law Dictionary (11th ed. 2019). Here, Sandoz submits that § 355(j)(5)(F)(ii) contemplates not only the approval of drugs and their active ingredients, but also the approval of what the FDA defines as those drugs'

impurities. *See* Pl.'s Mem. at 21, 26. But the FDA defines an impurity as a drug component that is "added [un]intentionally . . . as a result" of the drug's "manufacturing [or] storage." A.R. 1459. The FDA also notes that it does not require drugs to contain a "minimum level" of any impurity and may instead limit the amount of impurities that drugs may contain. *See id.*; *see also* 21 U.S.C. § 355(d) (requiring the FDA to assess whether the process for manufacturing, processing, and packing a drug is adequate to "preserve its . . . purity"). That regulatory approach is not naturally described as deeming impurities to be satisfactory, let alone giving them formal sanction. So although the FDA plainly considers impurities in approving drugs, an ordinary English speaker would not say that it approves those impurities themselves.

By way of example, consider the subset of drugs that contain carcinogenic impurities. Although the FDA may approve those drugs on the ground that they contain only trace amounts of their impurities, no ordinary person would say that the agency thereby "approved" the impurities themselves. 21 U.S.C. § 355(j)(5)(F)(ii). Instead, that person would say that the agency approved the drugs *despite* their impurities—or instead that the agency simply tolerates those impurities. This example weighs against reading § 355(j)(5)(F)(ii)'s "approved" language to cover any impurity, as the provision lacks a textual basis for distinguishing harmful impurities from harmless ones. Indeed, Sandoz concedes that the provision has "no textual basis for distinguishing" impurities from inactive ingredients. Pl.'s Reply at 13, Dkt. 27. The best reading of § 355(j)(5)(F)(ii) thus refers only to approval of active ingredients as active ingredients.

That conclusion is consistent with the use of the verb "approve" throughout § 505 of the FDCA. *See Henson v. Santander Consumer USA*, 137 S. Ct. 1718, 1722–23 (2017) (applying the presumption that "identical words used in different parts of the same statute carry the same meaning" (internal quotation marks omitted)). The full text of that section refers to the approval

of "application[s]," 21 U.S.C. § 355(a); "supplement[s]" to applications, *id.* § 355(j)(5)(F)(iv); "drug[s]," *id.* § 355(b)(4)(A); "method[s] of using" drugs, *id.* § 355(b)(1)(viii)(II); and the "labeling" for drugs, *id.* § 355(j)(10)(A)(i). It also refers to the approval of "active ingredient[s]." *Id.* § 355(j)(5)(F)(ii). But the statute never refers the approval of other drug components, as distinct from the approval of new drugs themselves, *see id.* § 355(d) (asking whether a "drug is safe for use" and requiring an assessment of "its identity, strength, quality, and purity"). And because the FDCA never describes the individualized review of those drug components, this Court will not read that review to be implied within § 355(j)(5)(F)(ii).

This Court's conclusion is also consistent with the role of active ingredients elsewhere in the Hatch-Waxman Act, which has been codified in 21 U.S.C. § 355(j). *See* Hatch-Waxman Act, Pub. L. No. 98-417, 98 Stat 1585 (Sept. 24, 1984). That Act governs not only the standard for NCE exclusivity for new drugs, *see* 21 U.S.C. § 355(j)(5)(F)(ii), but also the submission and approval of ANDAs, *see id.* § 355(j)(2), (4). And as relevant here, the Act allows approving an ANDA only if the proposed generic contains the same active ingredients as a listed drug. *See id.* § 355(j)(2)(A)(ii); *see also id.* § 355(j)(2)(A)(ii)(III) (noting one exception). That point goes to the overall "design" of the Hatch-Waxman Act, *Wolf Run Min. Co. v. FMSHRC*, 659 F.3d 1197, 1200 (D.C. Cir. 2011): Because the Act uses the overlap of active ingredients to determine ANDA eligibility, there are good reasons to think that the Hatch-Waxman Congress intended that same variable to foreclose NCE exclusivity. For one, there is a logical symmetry between granting exclusivity to certain new drugs and authorizing generic versions of certain established drugs. And because Congress concluded that an overlap of active ingredients was relevant to identifying the latter, it presumably deemed the same metric to be relevant in identifying the former. Another consideration is the efficient use of agency resources. Because the overlap of active ingredients is

relevant to assessing ANDAs, *see* 21 U.S.C. § 355(j)(2)(A)(ii), the Hatch-Waxman Congress presumably expected the FDA to track those ingredients over time. The Congress would have accordingly assumed that the FDA could also that same information to assess NCE exclusivity. In contrast, Sandoz does not identify any other provision of the FDCA that would require the FDA to track "impurities controlled in approved NDAs," Gov't's Mem. at 22, and the agency does not track them at present, *see id.* (undisputed). The design of the Hatch-Waxman Act thus supports the agency's broader argument that Sandoz's position would create a substantial administrative burden. *See* Gov't's Mem. at 22.

Finally, the Court need not resolve the parties' dispute regarding the exact purpose of § 355(j)(5)(F)(ii). Both parties agree that Congress enacted the provision to promote the creation of certain novel drugs. *See* Pl.'s Mem. at 27–28; Gov't's Mem. at 16–19. From there, the FDA argues that Congress wanted to promote the creation of drugs that are the first to use a given substance as an active ingredient, *see* Gov't's Mem. at 17–19, whereas Sandoz argues that Congress wanted to promote drugs that are the first to use a new substance that qualifies an active ingredient, *see* Pl.'s Mem. at 27–28; Pl.'s Reply at 7. But neither party has provided a compelling reason to prefer its theory on this discrete issue. Indeed, there are good reasons why Congress might want to promote either of the above subsets of drugs, and Sandoz's reliance on legislative history sheds no light on the question.[5] Regardless, it is appropriate to "begin and end with the plain" and unambiguous text of the FDCA, *United States v. Novo A/S*, 5 F.4th 47, 54 (D.C. Cir. 2021). *See Eagle Pharms., Inc. v. Azar*, 952 F.3d 323, 340 (D.C. Cir. 2020). And that text makes

[5] As a general matter, "legislative history is not the law." *Azar v. Allina Health Servs.*, 139 S. Ct. 1804, 1814 (2019) (citation omitted). And here, Sandoz gains nothing from the proposition that § 355(j)(5)(F)(ii) promotes the development of "new chemical entities," Pl.'s Mem. at 27 (quoting 130 Cong. Rec. 24,425 (Sept. 6, 1984) (statement of Rep. Waxman)), as this entire case concerns what that provision recognizes to be "new."

clear that NCE exclusivity turns on whether the active ingredient of the new drug was previously approved *as an active ingredient*.

Sandoz's remaining arguments do not persuade.

First, both of Sandoz's cases are inapposite. *See* Pl.'s Mem. at 24 (citing *Baker Norton Pharms., Inc. v. FDA*, 132 F. Supp. 2d 30 (D.D.C. 2001), and *Pharmanex v. Shalala*, 221 F.3d 1151 (10th Cir. 2000)). *Baker Norton* states that the NDA process "consider[s] the safety of all parts of any new drug," but it does so only to contrast the scope of § 505 of the FDCA from that of the Orphan Drug Act. 132 F. Supp. 2d at 35. The case did not address whether the FDA individually approves each ingredient and impurity in its approved drugs. *See id.* Moreover, although *Pharmanex* rejects as "too simple" the suggestion that "ingredients are in no sense 'approved' in the new drug approval process," its only proffered nuance is that the "approval of active ingredients is integral to the overall new drug approval process." 221 F.3d at 1156 (citing 21 CFR § 314.50(d)(1)). The case thus says nothing about whether the FDA can be said to "approve[]" drug components other than active ingredients. 21 U.S.C. § 355(j)(5)(F)(ii).

Second, Sandoz gets no milage out of § 355(j)(5)(F)(iii). *See* Pl.'s Mem. at 25–26; Pl.'s Reply at 7–9. That provision confers three years of exclusivity, even when a drug's active ingredient already "has been approved" in a prior NDA, if the application "contains reports of new clinical investigations . . . [that were] essential to the approval of the application and conducted or sponsored by the applicant." 21 U.S.C. § 355(j)(5)(F)(iii). The provision thus confers a shorter term of exclusivity for producing new and valuable clinical investigations, rather than for relying on new active ingredients (however defined). *See id.* In this respect, the provision does not support either party's interpretation of § 355(j)(5)(F)(ii), as both enable some set of drugs to obtain exclusivity under § 355(j)(5)(F)(iii). And contrary to Sandoz's objection, the FDA's interpretation

"is defining the line between three- and five-year exclusivity, not eviscerating it." *Actavis Elizabeth*, 625 F.3d at 765.

Finally, this Court's interpretation of § 355(j)(5)(F)(ii) will not give any company a "windfall," Pl.'s Mem. at 27. Sandoz laments that the FDA's reading of § 355(j)(5)(F)(ii) would "extend exclusivity to those who simply adapt existing chemicals in new ways," even if those chemicals had long been in use as inactive ingredients. Pl.'s Reply at 8. But Congress could have reasonably intended that outcome, on the thought that adapting existing chemicals to be active ingredients is a significant, scientific contribution. *See* A.R. 1443 (noting that teriflunomide was "not an approved drug product anywhere in the world" at the time of Aubagio's approval). And as discussed above, Sandoz has failed to show that Congress shared its particular account of the statute's purpose, which closely resembles the FDA's alternative. *See supra*.

For those reasons, the Court holds that NCE exclusivity turns on whether the active ingredient of the new drug was approved as an active ingredient in any prior drug. Accordingly, Aubagio is entitled to that exclusivity unless the FDA previously approved teriflunomide as an active ingredient.

### C. Teriflunomide Was Not Previously Approved as an Active Ingredient

The FDA did not previously approve teriflunomide as an active ingredient. As discussed above, the agency approved Arava on the understanding that leflunomide was its only active ingredient. *See* A.R. 265 (listing Arava's ingredients); A.R. 326 (describing Arava's mechanism of action); A.R. 1454–56 (discussing Arava's approval). Moreover, in approving Arava, the agency assessed teriflunomide only as an impurity. *See* A.R. 264 (noting that Arava contains the impurity "A77 1726"); A.R. 271 (discussing the accumulation of "A77 1726" in the drug product); A.R. 1455 n.28 (noting that "A77 1726" refers to teriflunomide). Finally, Sandoz has not identified

any other drug, prior to Aubagio, in which the FDA approved teriflunomide as an active ingredient. For those reasons, the FDA properly concluded that "no active ingredient of [Aubagio] ha[d] been approved in any other" NDA. 21 U.S.C. § 355(j)(5)(F)(ii).

In addition, Sandoz has failed to show that teriflunomide is an active ingredient in Arava. *See* Pl.'s Mem. at 32–39; Pl.'s Reply at 16–24. The FDA defines "active ingredient" to mean "any [drug] component 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 body." 21 C.F.R. § 314.3(b). Under that definition, which Sandoz does not challenge in this case, a drug component qualifies as an active ingredient only if it is "intended" to play a pharmacological role. *Id.* And here, Sandoz has failed to show that Sanofi intended teriflunomide to play a pharmacological role in Arava. Sandoz invokes patent materials that claim a positive interaction between leflunomide and teriflunomide in general terms. *See* Pl.'s Mem. at 33–34. But it is undisputed that the teriflunomide is present *in Arava* only due to the degradation of leflunomide. *See* A.R. 1459–60. Sanofi does not add teriflunomide to Arava deliberately. *See id.* Nor did Sanofi tout teriflunomide's purported pharmacological benefits in applying for Arava's approval. And although Sandoz argues that the presence of teriflunomide in a Arava results from Sanofi's chosen method of manufacturing, there is no indication that Sanofi adopted that method with the "inten[t]" for degraded teriflunomide to "furnish pharmacological activity"—as 21 C.F.R. § 314.3(b) requires.

The combination of two patents that Sanofi submitted before the approval of Aubagio—Canadian Patent Application No. 2,201,040 and United States Patent No. 7,071,222—does not suggest the necessary intent. *See* Pl.'s Mem. at 33–34; Pl.'s Reply at 23–24. Sandoz reads the Canadian patent to show that Sanofi "knew some portion of a leflunomide drug product would

inevitably degrade into teriflunomide during manufacturing and storage," and the United States patent to show that Sanofi "regarded the supplementation of leflunomide with small amounts of teriflunomide as therapeutically beneficial." Pl.'s Reply at 23–24. It accordingly argues that the "patents together demonstrate Sanofi's intent" to harness degraded teriflunomide for a beneficial effect. *Id.* at 24 (emphasis omitted). But the Canadian application concerned a technique for slowing the degradation of leflunomide during its storage, on the ground that such degradation "make[s] difficult an accurately dosed, constant, controlled administration of [that substance]." A.R. 389–90. And the United States patent concerned the benefits of deliberately adding fixed amounts of teriflunomide to fixed amounts of leflunomide, as opposed to the benefits of allowing leflunomide to degrade into teriflunomide over time. *See* A.R. 398, 400. The combination of those patents does not suggest that Sanofi intended the degradation of leflunomide in Arava to have a beneficial effect. *See* 21 C.F.R. § 314.3(b). To the contrary, the Canadian application suggests that Sanofi may have intended to slow that degradation altogether.[6]

Finally, the fact that the leflunomide in Arava metabolizes to teriflunomide *in vivo* is inapposite. *See* Pl.'s Mem. at 26. The FDA has elected to determine drugs' active ingredients by looking to their chemical structure *ex vivo*. *See* A.R. 1580–82. The D.C. Circuit has previously approved that approach. *See Actavis Elizabeth*, 625 F.3d at 764–66. And Sandoz declined to challenge the approach in its administrative proceedings. *See* A.R. 1401 (declining to argue that "NCE exclusivity for Aubagio should be rescinded merely because teriflunomide is the active

[6] Sandoz also invokes two efforts by Sanofi to enforce foreign patents: one before a New Zealand court in 2009 and the other before a German court in 2011. *See* Pl.'s Mem. at 34. But it is hard to see how patent litigation in those years could bear on Sandoz's intent either during the development of Arava in the 1990s, 21 C.F.R. § 314.3(b), or when the drug was "approved" in 1998, 21 U.S.C. § 355(j)(5)(F)(ii).

metabolite of leflunomide"). Any challenge to the approach thus falls outside the scope of this case.

For those reasons, the Court holds, first, that the FDA did not approve teriflunomide as an active ingredient in Arava and, second, that teriflunomide is not an active ingredient in that drug.[7] Aubagio thus was entitled to NCE exclusivity. *See* 21 U.S.C. § 355(j)(5)(F)(ii).

**D. The FDA's Decision Was Neither Arbitrary Nor Capricious**

The remainder of this case is straightforward. Because Aubagio was entitled to NCE exclusivity, no company could "submit[]" an ANDA that "refer[red] to" it within four years of its approval. *Id.* The FDA approved Aubagio on September 12, 2021. A.R. 1456. Sandoz filed its first ANDA for teriflunomide, however, on September 7, 2016—five days before Aubagio's exclusivity expired. *See* A.R. 1403. The FDCA thus required the FDA to reject Sandoz's first ANDA as untimely. *See* 21 U.S.C. § 355(j)(5)(F)(ii). And as such, the agency's decision was not "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A); *see* Compl. ¶¶ 66–92.

The Court need not resolve Sandoz's remaining argument regarding the separate drug, Zegerid. *See* Pl.'s Mem. at 39–43; Pl.'s Reply at 24–26. It is true that the FDA must "treat similar cases in a similar manner unless it can provide a legitimate reason for failing to do so." *Kreis v. Secretary of the Air Force*, 406 F.3d 684, 687 (D.C. Cir. 2005) (citation omitted). But on Sandoz's

[7] Because the Court concludes that teriflunomide is not an active ingredient in Arava, the Court need not decide whether § 355(j)(5)(F)(ii) requires the FDA to reconsider that question over twenty years after Arava's approval. *See* 21 U.S.C. § 355(j)(5)(F)(ii) (using the present perfect tense to ask whether an active ingredient "has been approved" in a prior NDA). In addition, the Court need not decide whether the patent materials in this case suffice to show that degraded teriflunomide has "pharmacological activity" in Arava, 21 C.F.R. § 314.3(b). *Compare* Gov't's Mem. at 26–27 (arguing that the FDA "has not been presented with scientific evidence" of that activity), *with* Pl.'s Reply at 23 (arguing that the agency "cannot ignore scientific disclosures just because they appear in patents rather than journals").

own account, Zegerid is only similar to Arava if the latter contains two active ingredients, *see* Pl.'s Mem. at 40–41, which it does not. For that reason, the Court does not "consider it necessary to go into the details of" the Zegerid decision. *Actavis Elizabeth*, 625 F.3d at 766.

**CONCLUSION**

For the above reasons, this Court will deny Sandoz's Motion for Summary Judgment, Dkt. 14, and grant the government's Cross Motion for Summary Judgment, Dkt. 20. A separate order consistent with this decision accompanies this memorandum opinion.

DABNEY L. FRIEDRICH
United States District Judge

July 22, 2022