UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

FERRING PHARMS. INC.,	)	
Plaintiffs,	)	
v.	)	Civil Action No. 15-802 (RC)
SYLVIA BURWELL, Secretary of Health and Human Services, *et al*.,	)	
Defendants.	)	

DEFENDANTS' REPLY IN FURTHER SUPPORT OF ITS CROSS-MOTION FOR SUMMARY JUDGMENT

In its latest filing, *see* Memo. in Opp'n to D.s' Cross-Mot. for Summ. J. and Reply in Supp. of Pl.'s Mot. for Summ. J. ("Ferring Reply"), Ferring once again fails to demonstrate that FDA's prior interpretation of the 5-year new chemical entity ("NCE") exclusivity provision of the Federal Food, Drug, and Cosmetic Act ("FDCA") is arbitrary, capricious, or otherwise contrary to law, or that FDA's decision to apply its new interpretation prospectively was improper. As explained in FDA's opening brief, *see* Memo. in Supp. of D.s' Cross-Mot. for Summ. J. and Opp'n to Pl.'s Mot. for Summ. J. ("FDA Br.") at 5, FDA previously interpreted the 5-year NCE provision such that the word "drug" in the eligibility clause meant drug product, while "drug" in the bar clause meant drug substance. *See* 21 U.S.C. §§ 355(c)(3)(E)(ii), (j)(5)(F)(ii).[1] This interpretation was, and remains, a reasonable interpretation of an ambiguous term. FDA modified its interpretation based on emerging science, not because the agency thought its prior interpretation lacked linguistic merit.

[1] Parallel 5-year NCE exclusivity provisions apply to ANDAs and 505(b)(2) applications.

I. This is a *Chevron* Step Two Case

Ferring spends four pages purportedly arguing that "FDA's [prior] interpretation fails under *Chevron* step one," Ferring Reply at 3-6, yet strikingly absent from this section of Ferring's brief is an explanation or description of the clear and unambiguous meaning of "drug." Congress expressly defined the word "drug" in the FDCA as both a finished drug product and as the articles and components of a finished drug product (a drug substance). 21 U.S.C. § 321(g)(1)(B)-(C). Ferring does not point to anything in the text or the legislative history of the 5-year NCE exclusivity provision that embodies the express intent of Congress that "drug" in the eligibility clause of that provision mean "drug substance." Instead, Ferring focuses on its numerous disagreements with FDA's interpretation, implicitly suggesting that this case would be appropriately decided under *Chevron* step two's test of the reasonableness of the agency's interpretation.

Ferring turns logic on its head by claiming that FDA cannot interpret "drug" in the eligibility clause to mean drug product because FDA had already interpreted the word "drug" in the bar clause (i.e., the second occurrence of the term) to mean drug substance. *See* Ferring Reply at 3, 4. Ferring contends that FDA had no choice but to interpret "drug" in the bar clause to mean drug substance due to "clear Congressional intent," Ferring Reply at 4, and that FDA was therefore required to interpret "drug" in the eligibility clause in the same way. However, in issuing its interpretation of the bar clause, FDA expressly stated that the statutory language was ambiguous, in that it could support either reading of the word "drug." FDA found that it was reasonable to read "drug" in the bar clause as "drug substance" in order to preserve the incentive to innovate and improve upon initially-approved products, in accordance with the statute's purpose. Ferring conveniently ignores that FDA also relied on congressional intent in support of

interpreting "drug" in the eligibility clause to mean drug product. *See, e.g.*, FDA Br. at 5, 10-11. And rather than respond to FDA's point that the agency could have interpreted both instances to mean drug product because "drug" does not unambiguously mean drug substance,[2] Ferring simply sidesteps the issue, noting only that "FDA did not do so." Ferring Reply at 4. That is not in question; the question for Ferring is how this Court can conclude that the term "drug" is unambiguous when both parties agree that "drug" can have more than one meaning.

FDA does not dispute that courts may look at a word in context in order to decide whether *Chevron* step one or two applies. *See* Ferring Reply at 5-6. Here, however, the statutory context does not answer the question of whether "drug" means drug product or drug substance. Because the plain language, statutory context, and legislative history do not reveal the unambiguously expressed intent of Congress regarding the meaning of the word "drug" in this context, this case is a *Chevron* step two case.

The cases on which Ferring relies regarding the supposed congressional intent behind use of "a" and "the" before the word "drug" in the 5-year NCE provision, s*ee* Ferring Reply at 3-4, are unavailing. For example, in *Work v. United States*, 262 U.S. 200, 208 (1923), the Supreme Court found that use of the definite article "the" rather than "an" indicated that a new appraisement was not contemplated but rather the provision at issue referred to the same appraisement. *See also U.S. v. Wilcox*, 487 F.3d 1163, 1176 (8th Cir. 2007); *Nat'l Foods, Inc. v. Rubin*, 936 F.2d 656, 660 (2d Cir. 1991). In contrast to the cases Ferring cites, here FDA is not arguing that "a drug" and "the drug" from the 5-year NCE exclusivity provision refer to separate products, but rather that one refers to the entire finished drug product while the other refers only

[2] Note that Prepopik would not have been eligible for 5-year NCE exclusivity under that reading of the statutory provision either.

to the drug substance contained in that drug product.

Ferring dismisses the argument that the statutory text supports reading "drug" in the eligibility clause to mean "drug product" because applications are submitted for drug products rather than drug substances. Ferring claims that Congress intended FDA to approve active ingredients as well as finished drug products, *see* Ferring Reply at 6.[3] However, Ferring does not provide a single example of FDA approving an active ingredient rather than a finished drug product. Further, Ferring does not respond to FDA's point that the language in the eligibility clause refers not to what drug has been approved, but what drug is the subject of the application. Drug products, rather than drug substances are the subject of new drug applications. *See* FDA Br. at 18-19; *see also Pfizer, Inc. v. FDA*, 753 F. Supp. 171, 176 (D. Md. 1990) (Holding that where the FDCA modifies the word 'drug' by attaching the phrase 'for which the applicant submitted the application,' FDA correctly interpreted 'drug' to mean 'drug product,' because drug products, not components of drug products, are the subject of new drug applications.) The statutory text therefore supports the interpretation of "drug" in the eligibility clause to mean "drug product."

II. FDA's Prior Interpretation Does Not Violate an FDA Regulation

In order to unpack Ferring's argument that FDA's now-superseded interpretation violates one of the agency's own regulations, *see* Ferring Reply at 7, 10-11, the language of the statute and regulations bear repeating. The 5-year NCE exclusivity provision states:

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[3] The statutory provision cited by Ferring to support its claim, 21 U.S.C. § 355(j)(5)(F)(ii), discusses "a drug, no active ingredient … of which has been approved in any other [drug application]," which is commonly understood to refer to an active ingredient that is approved as a component of a finished drug product pursuant to an application submitted under 21 U.S.C. § 355, not that an active ingredient alone is approved pursuant to a drug application.

> If an application submitted under subsection (b) for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b), is approved after September 24, 1984, 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 five years from the date of the approval of the application under subsection (b) . . .

21 U.S.C. §§ 355(c)(3)(E)(ii), (j)(5)(F)(ii). Under FDA's prior interpretation, the first time "drug" appears in the provision, it means drug product, while the second time "drug" appears in the provision, it means drug substance. *See, e.g.*, FDA Br. at 5-6.

FDA's implementing regulation, 21 C.F.R. § 314.108(b)(2), provides:

> If a drug product that contains a new chemical entity was approved … in an application submitted under section 505(b) of the act, no person may submit a 505(b)(2) application or [ANDA] for a drug product that contains the same active moiety as in the new chemical entity for a period of 5 years …

Thus, under the regulation, if a drug product contains a new chemical entity, then FDA is precluded from accepting any ANDA or 505(b)(2) application for a drug product that contains the same "active moiety as in the new chemical entity" until the 5-year NCE exclusivity period has expired. *Id.* A "new chemical entity" is "a drug that contains no active moiety that has been approved by FDA in any other application submitted under section 505(b) of the act." 21 C.F.R. § 314.108(a).

To support its claim that FDA's prior interpretation renders its own regulation nonsensical, Ferring substitutes "drug product" for "drug" in the definition of "new chemical entity" and inserts the resulting definition into 21 C.F.R. § 314.108(b)(2) as follows:

> If a drug product that contains a *drug product that contains no active moiety that has been approved by FDA in any other application submitted under section 505(b) of the act* was approved … in an application submitted under section 505(b) of the act, no person may

> submit a 505(b)(2) application or [ANDA] for a drug product that contains the same active moiety as in the new chemical entity for a period of 5 years …

Ferring Reply at 10. FDA acknowledges that this reading is cumbersome.[4] But the interpretive question in this case concerns the *statutory* language and the statute allows for either reading. To that end, the parties agree that substituting either "drug product" or "drug substance" for either occurrence of "drug" in the *statute* results in a reading that makes linguistic sense (though of course the parties dispute which meaning should be given to which occurrence of "drug").

But whether as a "drug substance" or "drug product," interpreting the term "drug" in the definition of new chemical entity is a vehicle for explaining the basis on which FDA makes 5-year NCE determinations. In other words, interpreting "new chemical entity" as a "drug product" under FDA's prior interpretation meant that FDA made 5-year NCE determinations for the drug product as a whole, while interpreting "new chemical entity" as a "drug substance" under FDA's current interpretation means that FDA makes 5-year NCE determinations for each drug substance in a drug product. Ferring's attempts to muddy the waters by combining definitions into a confusing morass of words does not alter the fact that FDA's prior interpretation of the ambiguous term "drug" was a reasonable reading of the ambiguous statutory text, as is FDA's current interpretation.[5]

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[4] Of course, Ferring's preferred reading of the statute fares equally poorly if subjected to the same treatment Ferring employs on FDA's regulation, by replacing the term "drug" in the eligibility clause of the statute with the *definition* of "drug substance" (i.e. "active ingredient"). In such event, the statutory provision would read: "[i]f an application submitted under subsection (b) for a [active ingredient], no active ingredient (including any ester or salt of the active ingredient) of which…," which renders the statute as jumbled as Ferring claims FDA's interpretation renders the regulation. *See* 21 U.S.C. §§ 355(c)(3)(E)(ii) and 21 C.F.R. § 314.3(b).

[5] Ferring claims that because FDA has not amended 21 C.F.R. § 314.108(b)(2), that regulation must support the agency's new interpretation. *See* Ferring Reply at 10. Ferring is wrong. Just

Ferring's assertion, based on the textual argument above, that FDA has held not two, but three different policies and acted generally inconsistently with regard to NCE exclusivity and fixed-combination drugs, is equally misguided and contrary to the facts. As FDA explained in its opening brief, *see* FDA Br. at 19-20, before changing its interpretation (at Ferring's urging), FDA had consistently interpreted "drug" in the eligibility clause to mean drug product and in the bar clause to mean drug substance. Ferring's claim that FDA has "flip-flopped" positions multiple times is not accurate. Ferring cannot point to a single example wherein FDA, prior to announcing its change in policy, evaluated a fixed-combination drug's eligibility for NCE exclusivity by considering whether the "drug substance" had been previously approved, rather than the "drug product." It is only after careful consideration and public input that FDA, in light of recent scientific advancements, is altering that interpretation. *See Perez v. Mortgage Bankers Ass'n*, 135 S. Ct. 1199, 1206 (2015) (agency need not use notice-and-comment procedures to change an interpretation). This is not a case, like *INS v. Cardoza-Fonseca*, 480 U.S. 421, 446 n.30 (1987), where the agency's "long pattern of erratic treatment of [the] issue," led the court to show the agency's interpretation less deference. Unsurprisingly, Ferring cites to no authority for its contention that an administrative agency's interpretation is owed no deference if that interpretation, after notice and explanation, changes.[6] *See* Ferring Reply at 8.

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like the language of the statute, the term "drug" in the regulation can have more than one meaning. FDA has changed its *interpretation* of the regulation; the language of the regulation requires no change.

[6] It is well established that an agency may revise its interpretation of a statute, and such a new interpretation will still be entitled to deference, even if it constitutes a "sharp break with prior interpretations," so long as the agency justifies its change with "reasoned analysis." *Rust v. Sullivan*, 500 U.S. 173, 186-87 (1991)(*citing Chevron, U.S.A., Inc. v. Natural Res. Def. Council, Inc.*, 467 U.S. 837, 862 (1984).

Five-year NCE exclusivity was intended to provide an incentive for pharmaceutical innovation, and, as FDA previously explained, combining a new active moiety with a previously approved active moiety does not necessarily represent an innovative change. *See* FDA Br. at 16. Ferring offers no support for its bare assertion that a new active moiety combined with a previously-approved active moiety requires "just as much research." *See* Ferring Reply at 9, 11. Moreover, as FDA also explained, reading "drug" to mean drug product in the bar clause would not have preserved the incentive to improve upon the approved product during the exclusivity period. *See* FDA Br. at 17.

Finally, FDA's prior interpretation meant that when the 3-year and 5-year exclusivity provisions were read in conjunction, a single drug product could be eligible for either one or the other, but not both. *See* FDA Br. at 16. Ferring's hypothetical purporting to show that "drug products often received both types of exclusivity" under FDA's old interpretation, Ferring Reply at 11, instead merely illustrates that two different drug products, one containing a single ingredient drug substance and a later-approved fixed-combination containing that drug substance and another drug substance, could be independently eligible for 5- and 3-year exclusivity.

The 5-year NCE exclusivity that might attach to the single ingredient drug substance that contains no previously approved active moiety would also attach, under FDA's umbrella policy, to any product containing that same drug substance submitted to FDA for approval during the 5-year exclusivity period. But the drug product that initially received 5-year NCE would not also be eligible for 3-year exclusivity because 3-year exclusivity is available only for "a drug product that contains an active moiety that *has been previously approved*." 21 U.S.C. § 355(j)(5)(F)(iii) (emphasis added). In addition, the 3-year exclusivity that might be awarded to the later-

approved fixed-combination would be limited to the specific studies conducted to show that the fixed-combination is safe and effective. *Id.*

III. FDA did not Arbitrarily Treat Prepopik Differently Than Other Fixed-Combination Products

Ferring gains no traction with its claim that FDA treated Prepopik differently from other, similarly-situated fixed-combination products by granting those products 5-year NCE exclusivity and denying Prepopik the same, and that such behavior is arbitrary and capricious. Ferring Reply at 12-14. The factual differences between Prepopik and the allegedly "similarly-situated" products that Ferring brushes aside are the lynchpin to the differing exclusivity outcomes, given that FDA applied the same interpretation of the relevant statutory provision and regulations to all of the products. Contrary to Ferring's suggestion, *see id.* at 13-14, FDA did not, and does not, have a policy that new chemical entities first approved as a component of a single-ingredient product will receive 5-year NCE exclusivity while new chemical entities first approved in a fixed-combination product will not.

This "pattern" of different decisions regarding 5-year NCE exclusivity that Ferring trumpets was merely a by-product of FDA's consistent application of its established interpretation to the facts of each individual product. In other words, the differing exclusivity outcomes were an unintended consequence of FDA's prior interpretation. Indeed, this was one of the reasons FDA changed its interpretation. Far from providing no explanation for the

different exclusivity decisions, FDA's reasons for its prior interpretation have been outlined exhaustively in the filings to date in this Court.[7]

CONCLUSION

For the foregoing reasons, as well as those in the government's prior filings, judgment should be entered in favor of the government.

Respectfully submitted,

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[7] Similarly, FDA previously addressed Ferring's remaining arguments about retroactive application of FDA's new interpretation, *see* Ferring Reply at 15-17, and will not repeat that discussion here. *See* FDA Br. at 24-25.