UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

AMGEN INC.,

Plaintiff,

v.

ERIC D. HARGAN, Acting Secretary, Department of Health and Human Services, *et al.*,

Defendants,

and

TEVA PHARMACEUTICALS USA, INC., *et al.*,

Intervenor-Defendants.

Civil Action No. 17-1006 (RDM)

MEMORANDUM OPINION AND ORDER

To encourage pharmaceutical companies to study the safety and effectiveness of pediatric uses of drugs approved for adults, the Federal Food, Drug, and Cosmetic Act ("FFDCA") grants six months of "pediatric exclusivity" to the sponsor of a brand-name drug if the sponsor conducts studies that "fairly respond" to a "written request" from the Food and Drug Administration ("FDA"). 21 U.S.C. § 355a(d)(4). At the urging of Plaintiff Amgen Inc., the FDA issued a written request asking that Amgen conduct pediatric studies of its drug Sensipar (cinacalcet hydrochloride), and Amgen endeavored to fulfill the request. Ultimately, however, the FDA found that Amgen had failed to complete a study on the safety of cinacalcet hydrochloride in children ages 28 days to < 6 years and concluded that Amgen's studies did not "fairly respond" to the written request. The FDA, accordingly, denied Amgen's request for pediatric exclusivity.

Subsequently, the FDA denied both Amgen's request for reconsideration and its appeal of that decision.

Amgen challenges the FDA's decision as well as the agency's underlying interpretation of the "fairly respond" requirement. The matter is now before the Court on Amgen's motion for summary judgment, Dkt. 60, and cross-motions for summary judgment filed by the FDA, Dkt. 65, and four intervenor-defendants, Dkt. 63. For the reasons that follow, the Court will **DENY** in part and **GRANT** in part Amgen's motion and will **DENY** in part and **GRANT** in part the FDA's and the intervenor-defendants' cross-motions for summary judgment.

I. BACKGROUND

A. Statutory Background

A manufacturer seeking to market a new drug in the United States must first obtain approval from the FDA. The approval process is both time-consuming and expensive. Among other things, the applicant—or "sponsor"—must submit a new drug application ("NDA") containing the extensive data and information necessary to demonstrate that the new—or "pioneer"—drug is "safe" and "effective," 21 U.S.C. § 355(b)(1), as well as a "certification" relating to each patent that claims the drug or a use of the drug, 21 U.S.C. § 355(b)(2).

The Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98–417, 98 Stat. 1585—popularly known as the Hatch-Waxman Act—created an alternative path for manufacturers of generic drugs. Instead of submitting its own clinical data on safety and efficacy, a generic manufacturer may submit an abbreviated new drug application ("ANDA") showing that the generic version of the drug contains the same active ingredient as the pioneer drug and is "bioequivalent" to that drug. 21 U.S.C. § 355(j); *see AstraZeneca Pharm. LP v. FDA*, 713 F.3d 1134, 1136 (D.C. Cir. 2013) ("ANDAs need not include new clinical studies

demonstrating . . . safety or efficacy, but must propose the same basic labeling as approved for the pioneer drug."). In creating this shortcut, Congress sought to encourage "the development of generic drugs to increase competition and lower prices." *Amarin Pharm. Ireland Ltd. v. FDA*, 106 F. Supp. 3d 196, 198 (D.D.C. 2015). But, at the same time, Congress recognized that it needed to maintain "incentives for pharmaceutical companies to invest in innovation and the creation of new drugs." *Id.* Accordingly, Congress "provided increased intellectual property rights and periods of market exclusivity for those pioneer manufacturers that invent new drugs." *Id.*; *see also* 21 U.S.C. § 355(j)(5)(F); *AstraZeneca*, 713 F.3d at 1136. After the period of marketing exclusivity ends, however, the FDA may ordinarily approve ANDAs, thus authorizing the marketing of competing, generic versions of the pioneer drug. *AstraZeneca*, 713 F.3d at 1136; *see* 21 U.S.C. § 355(j).

Although this statutory scheme proved successful in encouraging generic competition while maintaining the impetus to innovate, it failed to provide sufficient incentives for drug companies to conduct research on the effects of new drugs on children. In 1997, Congress found that the pharmaceutical industry had "studied and labeled for use in children" only a small portion of the drugs on the market, even though "children suffer from many of the same diseases as adults and are often treated with the same medicines." S. Rep. No. 107–79, at 3–4 (2001). After looking for the cause of this lack of pediatric research, Congress concluded that "there [was] little incentive for drug sponsors to perform studies for medications which they intend to market primarily for adults and [the] use [of which] in children is expected to generate little additional revenue." *Id.* at 4 (quoting S. Rep. No. 104–284 (1996)). The absence of information on pediatric drug safety and efficacy, moreover, exposed children to a number of unique risks:

> Dosing children based merely on their lower weight is often imprecise, since their bodies can metabolize medicines differently than adults. Some drugs may have

> different adverse side effects or toxicities in children than in adults, so estimating dosages for children from dosages found to be safe and effective in adults may not be appropriate. The lack of pediatric studies and labeling information may lead to unintended medical errors and place children at risk of being under-dosed or over-dosed with medication. The lack of age-appropriate formulations (e.g., liquid form) can also make it difficult to give children and infants prescribed amounts of a needed medication.

Id. at 3.

To address this problem, Congress enacted a "pediatric exclusivity" statute. *See* Food and Drug Administration Modernization Act of 1997, Pub. L. No. 105–115, § 111, 111 Stat. 2296, 2305–09; Best Pharmaceuticals for Children Act, Pub. L. No. 107–109, 115 Stat. 1408 (2002); *see also Mylan Labs., Inc. v. Thompson*, 389 F.3d 1272, 1276 (D.C. Cir. 2004). Under that law, a drug sponsor that receives "pediatric exclusivity" is entitled to an additional six months of market exclusivity. AR 1390. This protection, moreover, is sweeping; it applies to all "products containing the active moiety that has existing patent protection or exclusivity,"[1] and it applies both to patent rights and to the FDA's authority to approve ANDAs for competing products. *Id.*

Five events must occur for a sponsor to qualify for pediatric exclusivity: (1) the FDA must determine "that information relating to the use of [the] drug in the pediatric population may produce health benefits in that population;" (2) the FDA must make a "written request for pediatric studies;" (3) the applicant must agree to that request; (4) the studies must be "completed using appropriate formulations for each age group for which the study is requested within [the specified] timeframe;" and—most importantly for present purposes—(5) the reports from those studies must be "submitted [to] *and accepted*" by the FDA. 21 U.S.C. § 355a(b)(1)

[1] An "active moiety" is "the molecule or ion . . . responsible for the physiological or pharmacological action of the drug substance." 21 C.F.R. § 314.3(b); *see Amarin Pharm.*, 106 F. Supp. 3d at 199.

(emphasis added). A sponsor may ask the FDA to issue a written request by filing "a proposed pediatric study request" ("PPSR"). 21 U.S.C. § 355a(d)(3). Before issuing the written request, the FDA must consult with the sponsor, 21 U.S.C. § 355a(d)(1)(A), and submit the request for review by the Pediatric Review Committee, 21 U.S.C. § 355a(f)(1), (2). That committee includes experts in, among other fields, pediatrics, biopharmacology, chemistry, and "the appropriate expertise pertaining to the pediatric product under review." 21 U.S.C. § 355d. When issued, the written request asks the sponsor to "conduct pediatric studies" within a certain timeframe and to "propose pediatric labeling resulting from such studies." 21 U.S.C. § 355a(d)(1)(A).

The written request "serves as a yardstick against which the sponsor's eligibility for pediatric exclusivity is later measured." Dkt. 65-1 at 16. As the FDA explains, "[g]iven the breadth of the benefit available to sponsors who qualify for pediatric exclusivity, the agency generally asks for a full range of studies designed to provide meaningful information regarding use of the drug in all of the pediatric populations in which the drug is likely to be used." *Id.* at 15–16. The written request also includes "specific details regarding study design and endpoints, [the] number of patients to be studied, and study duration." *Id.* at 16.

After the sponsor completes the studies and submits its reports, the FDA is required to decide within 180 days whether to "accept or reject such reports." 21 U.S.C. § 355a(d)(4). The FDA must accept the reports if the sponsor's studies satisfy the three exclusive conditions set forth in the statute. In the words of the statute:

> The Secretary's *only* responsibility in accepting or rejecting the reports shall be to determine, within the 180-day period, whether the studies [1] fairly respond to the written request, [2] have been conducted in accordance with commonly accepted scientific principles and protocols, and [3] have been reported in accordance with the requirements of the Secretary for filing.

Id. (emphasis added). The Pediatric Review Committee may review the studies for purposes of making a recommendation on whether the FDA should accept or reject the reports, but it is not required to do so. 21 U.S.C. § 355a(f)(3).

B. Regulatory Background

This case turns on the meaning of the "fairly respond" requirement, and, it is fair to say, the FDA's approach to this statutory language has "[e]volv[ed]" over the years. Dkt. 60-1 at 13. Prior to 2001, the FDA apparently required that the sponsor satisfy each and every term of the written request. In *Merck & Co. v. FDA*, 148 F. Supp. 2d 27 (D.D.C. 2001), a drug sponsor challenged that interpretation after the FDA denied its request for pediatric exclusivity. *Id.* at 30. Judge Robertson concluded that denying pediatric exclusivity "for failure to meet a single term of a written request would not be in accordance" with the statute. *Id.* The statute, he explained, "plainly does not require compliance with every single provision of a written request, but requires only that a pediatric study 'fairly respond' to a written request." *Id.* The Court, accordingly, extended its earlier temporary restraining order, which had "stayed the effectiveness . . . of the FDA's refusal" of pediatric exclusivity. *Id.* at 31.

The FDA's most recent interpretation of the statute is set forth in a letter decision issued by the Deputy Director for Clinical Science, Center for Drug Evaluation and Research on August 2, 2017, resolving Amgen's administrative appeal. *See* AR 1632–50. Under the interpretation set forth in that letter, the "fairly respond" requirement can be satisfied in two ways. First, "[w]hen a sponsor meets the terms" of the written request, "the resulting studies" will "fairly respond" to the request because "studies that are carried out in accordance with the trial's plans and objectives, as expressed in the [written request], will generally satisfy the statutory goal of obtaining pediatric use information." AR 1637. Neither party disputes this aspect of the FDA's interpretation. The parties' disagreement, instead, centers on the second prong of the test. Under

that prong, even where "specific terms" of the written request are not met, the FDA will nonetheless "generally consider the sponsor's studies to have 'fairly responded'" to the written request if the agency, "apply[ing] its scientific expertise," determines that the underlying "objectives of the [written request] have . . . been met." *Id.* That is, the studies will be accepted if the FDA determines that the studies yielded information that is "clinically meaningful across all age groups and uses cited in the" written request. *Id.*

C. Factual Background

In March 2004, the FDA approved Amgen's drug Sensipar, or cinacalcet hydrochloride, for secondary hyperparathyroidism ("HPT") in adult patients with chronic kidney disease on dialysis, hypercalcemia in adult patients with parathyroid carcinoma, and hypercalcemia in adult patients with primary HPT who are unable to undergo parathyroidectomy. AR 1403. Several of Amgen's patents claim Sensipar, one of which expires on March 8, 2018. Dkt. 65-1 at 17.

Amgen, believing that there was "an unmet medical need for the treatment of secondary HPT" in children, submitted a Proposed Pediatric Study Request to the FDA in May 2007. AR 18, 38–42. At that time, cinacalcet's "safety [and] effectiveness in pediatric patients had not been established." Dkt. 65-1 at 17 (citing AR 14). Amgen, then, submitted a new Proposed Pediatric Study Request in December 2009, stressing that there was a need for pediatric studies because cinacalcet was "already being used off-label in a significant portion of the pediatric dialysis patient population." AR 1633–34. In May 2010, after "several years of discussions and a pre-clinical study," Dkt. 60-1 at 14, the FDA issued a written request to Amgen, *see* AR 647. As the agency explained, pediatric studies on cinacalcet were necessary because its efficacy in adults "cannot be extrapolated to the pediatric population": secondary HPT progresses differently in children, and cinacalcet poses unique risks to pediatric patients, whose "skeletal

and vascular system[s]" are still developing. AR 648. The written request, accordingly, proposed that Amgen conduct two pediatric studies on "the potential use of cinacalcet hydrochloride in the treatment of secondary hyperparathyroidism" in children "with chronic kidney disease . . . receiving dialysis." AR 647. The objective of the written request was to obtain information on cinacalcet's efficacy, safety, and tolerability in pediatric patients, including "pediatric patients ages 28 days to < 6 years." AR 647–48.

Over the next several years, the written request was amended five times to relax the study parameters, reduce the scope of the studies, or expand the ways in which the requested information could be obtained. *See* AR 730–48, 755–68, 990–1007, 1035–51, 1076–90; *see also* Dkt. 60-1 at 14–15; Dkt. 65-1 at 18–19. The final—and operative—version of the written request asked Amgen to complete four clinical studies:

> *Study 1:* A single dose [*pharmacokinetics/pharmacodynamics* ("PK/PD")] *study* in pediatric patients *ages 28 days to < 6 years* with chronic kidney disease and secondary hyperparathyroidism receiving dialysis.
>
> *Study 2:* A 30-week, randomized, double-blind, placebo-controlled, *safety and efficacy study* with a 30-week, open-label, safety extension in pediatric patients *ages 6 years to < 18 years* with chronic kidney disease and secondary hyperparathyroidism receiving dialysis. This study will include an assessment of pharmacokinetic (PK) parameters using a sparse sampling design. Study 2 has been terminated early and will be analyzed with available data.
>
> *Study 3:* A 26-week or time-until-transplantation (whichever comes first), open-label, *safety study* in pediatric patients *ages 28 days to < 6 years*. . . .
>
> *Study 4:* A 20-week, randomized, open-label, controlled study in pediatric subjects between the *ages of 6 and < 18 years*, with secondary hyperparathyroidism and chronic kidney disease who are receiving either hemodialysis or peritoneal dialysis.

AR 1080 (emphasis added). Although Study 1 and Study 3 both involved pediatric patients ages 28 days to < 6 years, they focused on different questions. Study 1 examined cinacalcet's pharmacokinetics (the drug's "movement . . . within the body" such as "absorption, distribution, [and] metabolism") and pharmacodynamics ("the characteristics of the action of" the drug). Dkt.

60-1 at 15 n.4 (internal quotation marks and citation omitted). Study 3, in contrast, focused on the drug's safety in the youngest pediatric patients. Compared to Study 2, which also examined safety but in older pediatric patients, Study 3 was "shorter, smaller[,] [and] of limited scope" with a minimum of only 15 completers. Dkt. 65-1 at 19–20; *see* AR 1063. For a variety of reasons, Amgen struggled to locate an adequate number of patients for Study 3, AR 664–66, but eventually enrolled 18, AR 1159.

In December 2012, a patient enrolled in Study 2 died. AR 840. Following standard protocol, the FDA issued a partial clinical hold, or a temporary suspension, on further testing on pediatric patients with secondary HPT. *Id.* While the hold was in effect, Amgen and the agency discussed potential next steps. *See* AR 858–64. Amgen opted to continue the studies, AR 862, and the FDA replaced Study 2 with Study 4, AR 991–92. The hold, however, affected Amgen's ability to complete Study 3. As Amgen explains, "enrolled patients were not receiving treatment, and five of the eight patients then[-]enrolled in Study 3 discontinued their participation." Dkt. 60-1 at 17. Amgen and the FDA continued to correspond regarding Amgen's efforts to complete Study 3. *See* AR 1391–95.

In late 2015, the FDA rejected Amgen's request for a sixth amendment, which would have lowered the minimum number of completers in Study 3 from fifteen patients to four patients—"the number of completers in the study available at the time." AR 1338. The agency "did not agree that [four] completers . . . would allow for an adequate characterization of safety for the intended use" and "was not willing to further amend" the written request to lower the study parameters to fit "the amount of data collected." AR 1138–39. Amgen also sought a meeting with the FDA to discuss Study 3 and the submission of Amgen's supplemental NDA. AR 1099. The FDA denied Amgen's request, asserting that it would "not have any more

discussion on" Study 3 and indicating that Amgen's request to meet regarding Amgen's supplemental NDA was premature. AR 1102. The agency eventually met with Amgen on September 21, 2016, "to discuss the overall cinacalcet pediatric development program." AR 1116.

On November 23, 2016, Amgen submitted its study reports to the FDA, requested pediatric exclusivity, and sought approval for a pediatric indication for Sensipar. AR 1152. The "only discrepancy" between Amgen's studies and the written request was "the number of completers" for Study 3. AR 1159. The written request required a minimum of 15 patients; Amgen enrolled 18. *Id.* But only 11 patients exceeded 12 weeks of treatment, and even fewer—just 4 patients—completed the full 26-week study. *Id.* Nevertheless, Amgen reported, it had collected "sufficient data" to "satisfy the primary objectives" of Study 3, which were to "evaluate the safety and tolerability" of cinacalcet in pediatric patients ages 28 days to < 6 years. AR 1160. In Amgen's opinion, its data was "sufficient . . . to support an indication" in that pediatric population. *Id.*

On May 22, 2017, the FDA denied Amgen's request for pediatric exclusivity in a letter decision. AR 1389–98. The agency explained that, in issuing the written request, it sought to "characterize the risks" of using cinacalcet to treat secondary HPT in children with chronic kidney disease on dialysis. AR 1391. But the FDA found that it could not draw "any conclusions about the safety" of the drug in a key age group—patients ages 28 days to < 6 years—because of "Amgen's failure to provide sufficient safety data." AR 1398. This conclusion was based on the "totality of safety information" Amgen provided, not merely the data generated in Study 3. *Id.* As the FDA explained, Amgen's reports "could [have] be[en] considered a fair response to the [written request] as a whole" if the company's findings in the

aggregate "provided an appropriate safety assessment in younger children." *Id.* Instead, the "lack of sufficient safety data" on pediatric patients ages 28 days to < 6 years "led to the inability to clearly establish the safety profile of the drug . . . in accordance with [the] objectives of the amended [written request]." *Id.*

D. Procedural History

Three days after the FDA issued its decision, Amgen filed this action "to compel the FDA" to accept Amgen's reports and to grant pediatric exclusivity for Sensipar. Dkt. 1 at 2 (Compl. ¶ 1). Amgen claimed that the FDA's interpretation of "fairly respond" was contrary to the pediatric exclusivity statute under the Administrative Procedure Act ("APA"), 5 U.S.C. § 701 *et seq.*, Dkt. 1 at 21–23 (Compl. ¶¶ 50–56); that its denial of pediatric exclusivity for Sensipar was arbitrary and capricious, *id.* at 29–31 (Compl. ¶¶ 76–88); and that its application of its standard violated Amgen's due process rights, *id.* at 31 (Compl. ¶¶ 89–90). On the same day, Amgen moved for a temporary restraining order or preliminary injunction, arguing that it might "lose the full benefit of its pediatric exclusivity" absent injunctive relief. Dkt. 3 at 10. The Court held a hearing on Amgen's motion on June 2, 2017. Minute Entry (June 2, 2017). After the hearing, however, the parties agreed that Amgen would seek reconsideration and administrative dispute resolution before the FDA and that the proceedings before the Court would be stayed. Dkt. 14. Based on the parties' stipulation, the Court denied Amgen's motion for preliminary relief as moot and stayed the case pending completion of the renewed administrative process. Dkt. 15.

On remand, the FDA denied both Amgen's request for reconsideration, AR 1484, as well as its appeal of that decision in the FDA's administrative dispute resolution process, AR 1632. During those proceedings, Amgen "pressed the same arguments it makes here"—that the FDA's

interpretation of "fairly respond" is foreclosed by the statute and that FDA's application of that standard to Amgen "violated foundational principles of administrative law and due process." Dkt. 60-1 at 22. In a final letter decision denying Amgen's administrative appeal, the agency set forth the interpretation of "fairly respond" described above. *See supra* Part I.B. Applying that standard, the FDA affirmed its earlier conclusions that Amgen's studies did not "fairly respond" to the written request because (1) Amgen "fail[ed] to carry out Study 3 in accordance with the [written request]" and (2) Amgen failed to provide "meaningful pediatric use information in children 28 days to < 6 years of age." AR 1648.

The dispute then returned to this Court, where the parties jointly proposed an expedited briefing schedule. Dkt. 24. Before either side moved for summary judgment, four generic drug companies—Teva Pharmaceuticals USA, Inc., Barr Laboratories, Inc., Watson Laboratories, Inc., and Amneal Pharmaceuticals LLC—moved to intervene as defendants, Dkt. 26; Dkt. 33, and the Court granted their motions, *see* Minute Order (Aug. 15, 2017); Dkt. 61. In addition, Amgen moved to complete or supplement the administrative record with several sets of documents that Amgen asserted were considered by the FDA in denying Amgen pediatric exclusivity. Dkt. 38. The Court denied Amgen's motion in part from the bench at a hearing held on September 20, 2017, and directed that the parties meet and confer regarding the remaining portion of Amgen's motion. *See* Minute Entry (Sept. 20, 2017). After the parties were unable to reach an agreement, they set forth their respective positions in a further filing, Dkt. 53, and the Court denied the remainder of Amgen's request, *see* Minute Order (Oct. 11, 2017); Dkt. 61.

Three motions are now before the Court: Amgen's motion for summary judgment, Dkt. 60, the FDA's cross-motion, Dkt. 65, and the intervenor-defendants' joint cross-motion, Dkt. 63. The Court held a hearing on those motions on January 11, 2018. *See* Minute Entry (Jan. 11,

2018). Because Amgen has represented that a "key patent[] covering Sensipar" is due to expire on March 8, 2018, Dkt. 1 at 4–5 (Compl. ¶ 9), the Court has expedited its resolution of the pending motions.

II. LEGAL STANDARD

Under Federal Rule of Civil Procedure 56, summary judgment is ordinarily available if the movant demonstrates "that there is no genuine dispute as to any material fact" and that, based on the uncontested facts, "the movant is entitled to judgment as a matter of law." Fed. R. Civ. P. 56(a). In the unique context of a case brought under the APA, however, the district court "sit[s] as an appellate tribunal," *Marshall Cty. Health Care Auth. v. Shalala*, 988 F.2d 1221, 1222–23 (D.C. Cir. 1993), to decide "as a matter of law [whether] the agency action is supported by the administrative record and is otherwise consistent with the APA standard of review," *Coal. for Common Sense in Gov't Procurement v. United States*, 821 F. Supp. 2d 275, 280 (D.D.C. 2011); *see also Citizens to Preserve Overton Park, Inc. v. Volpe*, 401 U.S. 402, 415 (1971); *Sw. Merch. Corp. v. NLRB*, 53 F.3d 1334, 1341 (D.C. Cir. 1995). In short, it is the role of the administrative agency to "resolve factual issues" and to "arrive at a decision that is supported by the administrative record," while it is the role of the district court "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).

III. ANALYSIS

Amgen argues that the FDA's decision denying it pediatric exclusivity for Sensipar is unlawful and must be set aside for three reasons. First, Amgen contends that the FDA's interpretation of "fairly respond" "violate[s] the pediatric exclusivity statute." Dkt. 60-1 at 25. Second, it argues that the FDA's denial was arbitrary and capricious because the agency treated

Amgen differently from similarly situated entities and refused to consider evidence on the challenges of enrolling participants in Study 3. *Id.* Finally, Amgen contends that the FDA's application of its "fairly respond" standard to Amgen "without any notice" contravened both "due process and APA principles." *Id.* The FDA responds that its interpretation of "fairly respond" is entitled to deference under *Chevron, U.S.A., Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837 (1984); that it correctly and fairly applied the standard in rejecting Amgen's studies; and that Amgen was fully aware of the FDA's interpretation. Dkt. 65-1 at 11–12. The Court will consider each argument in turn.

A. Statutory Claim

According to Amgen, the FDA's interpretation of "fairly respond" is incompatible with the text of the pediatric exclusivity statute. Dkt. 60-1 at 25. As explained above, that interpretation recognizes two ways in which a sponsor's studies may "fairly respond" to the written request. First, if the sponsor's studies meet the "specific terms" of the written request, the studies "fairly respond" to the written request. AR 1637. Second, even if the studies deviate from the "specific terms" of the written request, the FDA will nonetheless conclude that they "fairly respond" to the written request if they yield "clinically meaningful" information "across all age groups and uses cited in the" written request. *Id.* Because all agree that Study 3 did not meet the "specific terms" of the FDA's written request, the first prong of the test has no bearing on this case. Instead, the focus is on the second prong. It is this prong of the test that Amgen contends is both narrower than the statute mandates and "incompatible" with the "limited role" Congress accorded the FDA. Dkt. 60-1 at 26.

To determine "whether an agency's construction of its authorizing statute is permissible," the Court looks to the two-step inquiry set forth in *Chevron*. *Safari Club Int'l v. Zinke*, 878 F.3d

316, 326 (D.C. Cir. 2017). The Court must first ascertain "'whether Congress has directly spoken to the precise question at issue,'" and, in doing so, must employ "the ordinary tools of statutory construction." *City of Arlington v. FCC*, 569 U.S. 290, 296 (2013) (quoting *Chevron*, 467 U.S. at 842). If Congress has spoken directly to the question, that is "the end of the matter" because the Court—and the agency—"must give effect to the unambiguously expressed intent of Congress." *Chevron*, 467 U.S. at 842–43. But if, instead, the statute is ambiguous, the Court must "defer to the agency construction so long as it is reasonable." *Safari Club*, 878 F.3d at 326.

1. Chevron *Step Zero*

As an initial matter, Amgen disputes that the *Chevron* framework applies to the FDA's "fairly respond" interpretation. Dkt. 60-1 at 26–30. For *Chevron* to govern, the agency must have "acted pursuant to congressionally delegated authority to make law and with the intent to act with the force of law." *Safari Club*, 878 F.3d at 326 (citing *United States v. Mead Corp.*, 533 U.S. 218, 226–27, 229 (2001)); *see Menkes v. U.S. Dep't of Homeland Sec.*, 637 F.3d 319, 331 (D.C. Cir. 2011). Often referred to as *Chevron* "step zero," this threshold inquiry delimits the types of agency actions that qualify for *Chevron* deference. Amgen offers a number of arguments why the FDA's interpretation of "fairly respond" falls outside *Chevron*'s ambit, but none are persuasive.

First, Amgen argues that Congress's use of the adjective "only" to describe the FDA's "responsibility in accepting or rejecting" a sponsor's reports, 21 U.S.C. § 355a(d)(4), signals that Congress "did not intend to delegate rulemaking authority" concerning the meaning of "fairly respond" to the FDA, Dkt. 60-1 at 27. The statute, in relevant part, reads as follows: "[t]he [FDA's] *only* responsibility in accepting or rejecting the reports shall be to determine . . . whether the studies fairly respond to the written request" and fulfill the other two statutory

criteria. 21 U.S.C. § 355a(d)(4) (emphasis added). Amgen is partly correct—but only partly. It is correct that the word "only" "narrow[s] . . . the agency's discretion" by "expressly limit[ing] what the agency can and cannot do." Dkt. 60-1 at 27. But it is incorrect that this limitation has anything to do with the FDA's authority to interpret the phrase "fairly respond." Indeed, just the opposite is true. The statute accords the agency the "responsibility . . . *to determine* . . . whether the studies fairly respond to the written request." 21 U.S.C. § 355a(d)(4) (emphasis added). Without construing the meaning of "fairly respond," the FDA cannot discharge that statutory responsibility. It follows, moreover, that—to the extent "fairly respond" is ambiguous, which is the sole question presented at *Chevron* step one—Congress must have intended to confer interpretative authority on the FDA.

Second, Amgen asserts that "a court does not defer to an agency's interpretation under *Chevron*" if the matter does not "implicate[] the agency's unique technical or scientific expertise." Dkt. 60-1 at 27. This misunderstands the relevance of expertise to the *Chevron* framework. Expertise can come into play at two levels. First, Congress might opt to delegate interpretive power to an agency because, in Congress's judgment, the agency possesses valuable expertise. But, if it does so, the justification for judicial deference to an agency's interpretation is the congressional delegation itself, not the Court's assessment of the agency's expertise. As the Supreme Court explained in *City of Arlington v. FCC*, 569 U.S. 290 (2013):

> *Chevron* is rooted in a background presumption of congressional intent: namely, "that Congress, when it left ambiguity in a statute" administered by an agency, "understood that the ambiguity would be resolved, first and foremost, by the agency, and desired the agency (rather than the courts) to possess whatever degree of discretion the ambiguity allows."

Id. at 296 (quoting *Smiley v. Citibank (South Dakota), N.A.*, 517 U.S. 735, 740–41 (1996)); *see also Mead*, 533 U.S. at 229 (explaining that when "circumstances" indicate that Congress "expect[ed] the agency" to "speak with the force of law" in addressing a statutory ambiguity, "a

reviewing court has no business rejecting an agency's exercise of its generally conferred authority to resolve [that] statutory ambiguity"); *AKM LLC v. Sec'y of Labor*, 675 F.3d 752, 765 (D.C. Cir. 2012) (Brown, J., concurring) ("It is by Congress's 'delegation of authority to the agency to elucidate a specific provision of the statute' that an agency's interpretation is deserving of the court's deference." (quoting *Chevron*, 467 U.S. at 843–44)); Antonin Scalia, Judicial Deference to Administrative Interpretations of Law, 1989 Duke L.J. 511, 514 ("If it is . . . the constitutional duty of the *courts* to say what the law is, we must search for something beyond relative competence as a basis for ignoring that principle when agency action is at issue."). In short, the *Chevron* framework "is premised on the theory that a statute's ambiguity constitutes an implicit delegation from Congress to the agency to fill in the statutory gaps," *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 159 (2000), and that rationale stands regardless of whether filling the relevant gap requires a PhD. Second, courts may at times accord *heightened* deference to the scientific or technical expertise of an agency. *See A.L. Pharma, Inc. v. Shalala*, 62 F.3d 1484, 1490 (D.C. Cir. 1995); *Sanofi-Agentis U.S. LLC v. FDA*, 842 F. Supp. 2d 195, 211 (D.D.C. 2012). But that does not mean that *Chevron* is inapplicable in other cases. Amgen cites no authority for its sweeping contention that *Chevron* applies only in cases that require specialized expertise, nor is the Court aware of any. To the contrary, *Chevron* is commonly applied in cases involving no greater call for expertise than at issue here. *See, e.g.*, *City of Arlington*, 569 U.S. at 294, 301.

Amgen relies on *King v. Burwell*, 135 S. Ct. 2480 (2015), but that case is fully consistent with the delegation-based justification for *Chevron*. In *King*, *Chevron* did not apply because the "extraordinary" nature of the case, which implicated "billions of dollars" in government spending and "millions of people," suggested that Congress did not intend to delegate

interpretive authority to the agency. *Id.* at 2488–89. Although the Court noted that it was "especially unlikely" that Congress "would have delegated" the power to decide such "a question of deep 'economic and political significance' that [was] central to th[e] statutory scheme," *id.* (citation omitted), to an agency that lacked any "expertise" in crafting the relevant type of policy, this reasoning serves only to reaffirm that delegation—not expertise—is what matters. Here, in contrast to *King*, Amgen offers no plausible reason to doubt that Congress intended to delegate interpretive authority to the FDA.

Third, Amgen argues that the FDA's interpretation of "fairly respond" lacks "the traditional hallmarks of deference." Dkt. 60-1 at 28; *see Mead*, 533 U.S. at 227. According to Amgen, the FDA's pediatric exclusivity determinations have been "ad hoc," "freewheeling," and non-public. Dkt. 60-1 at 28. As a result, Amgen concludes, *Chevron* does not cover the agency's decision in this case, which was set forth in the letter decisions denying Amgen pediatric exclusivity. *Id.* The Court is, once again, unpersuaded. The D.C. Circuit has expressly held that "the FDA's interpretations of the [Federal] Food, Drug, and Cosmetic Act adopted in letter rulings" are to be "evaluate[d] . . . under the familiar two-part *Chevron* framework." *Teva Pharm. USA, Inc. v. Sebelius*, 595 F.3d 1303, 1315 (D.C. Cir. 2010); *see also Mylan Labs.*, 389 F.3d at 1279–80; *Abbott Labs. v. Young*, 920 F.2d 984, 986–89 (D.C. Cir. 1990); *Mylan Pharm., Inc. v. Sebelius*, 856 F. Supp. 2d 196, 208 (D.D.C. 2012); *Hi-Tech Pharmacal*, 587 F. Supp. 2d at 19. As the FDA explains, pediatric exclusivity decisions "are generally unpublished" because they "often contain confidential commercial . . . information." Dkt. 65-1 at 34. But their non-public nature does not deprive these determinations of "those 'relatively formal administrative procedure[s]' that 'tend[] to foster the fairness and deliberation that should underlie a pronouncement' of legal interpretation." *Fogo De Chao (Holdings) Inc. v. U.S. Dep't of*

Homeland Sec., 769 F.3d 1127, 1137 (D.C. Cir. 2014) (quoting *Mead*, 533 U.S. at 230). This case, moreover, highlights the "relative formal[ity]" of the FDA's "administrative procedure[s]," *id.*; the FDA issued three detailed letter decisions setting forth its analysis of the statute and the relevant facts, and it allowed Amgen to be heard before the agency issued its original decision, its reconsideration decision, and its appeal decision, *see* AR 1389–99; AR 1483–96; AR 1632–50.

Finally, Amgen invokes *Encino Motorcars, LLC v. Navarro*, 136 S. Ct. 2117 (2016), for the proposition that "*Chevron* deference is not warranted where the regulation is 'procedurally defective'—that is, where the agency errs by failing to follow the correct procedures in issuing the regulation." *Id.* at 2125 (quoting *Mead*, 553 U.S. at 227); *see* Dkt. 60-1 at 28–29. Amgen argues that the FDA's construction of the statute is "procedurally unsound" because it was not announced publicly and because the agency did not provide a "reasoned explanation" for its "unexplained about-face" from its pre-*Merck* interpretation. Dkt. 60-1 at 28–29. The Court is unpersuaded.

The holding in *Encino Motorcars* was premised on the concern that "longstanding policies may have 'engendered serious reliance interests that must be taken into account.'" *Encino Motorcars*, 136 S. Ct. at 2126 (quoting *FCC v. Fox Television Studios, Inc.*, 556 U.S. 502, 515 (2009)). But Amgen cannot claim such reliance interests. The "flip-flop" that Amgen apparently targets was the FDA's change in position following this Court's decision in *Merck & Co. v. FDA*, 148 F. Supp. 2d 27 (D.D.C. 2001). That change, however, *expanded* the agency's interpretation of "fairly respond." Before *Merck*, the FDA required sponsors to meet all the terms of the written requests to qualify for pediatric exclusivity, while, after *Merck*, the FDA has accepted imperfect reports of studies that nonetheless met the objectives of the written requests.

See AR 1643. It is difficult to see how the FDA's relaxation of the standard could have frustrated any serious reliance interest that Amgen may have had.

The FDA's change in position, moreover, hardly came out of the blue; it followed a judicial decision concluding that the FDA's prior reading of the "fairly respond" requirement was "[in]consistent with the statutory standard." *Merck*, 148 F. Supp. 2d at 30. And, although Amgen correctly notes that the FDA's intervening decisions were not released publicly, there is nothing surprising in the FDA's conclusion that studies "fairly respond" to a written request if they comply with its terms *or* meet its goals by providing "clinically meaningful" information across the relevant uses and age groups. Finally, Amgen's contention that the FDA's current reading of the statute constitutes "an unexplained about-face from [its] prior understanding," Dkt. 60-1 at 29, is belied by the administrative record. In addressing Amgen's arguments, the FDA explained the basis for its reading of the statute, and it explained that the test that it has now adopted is "consistent with the holding in *Merck*," which requires the agency to consider the results of a sponsor's studies "as a whole." AR 1485; *see also* AR 1636–38.

2. Chevron *Step One*

Under *Chevron* step one, the Court "must first determine whether . . . 'Congress has directly spoken to the precise question at issue.'" *Vill. of Barrington v. Surface Transp. Bd.*, 636 F.3d 650, 659 (D.C. Cir. 2011) (quoting *Chevron*, 467 U.S. at 842). This inquiry requires that the Court ask "whether Congress has 'unambiguously foreclosed the agency's statutory interpretation." *Id.* (quoting *Catawba Cty. v. EPA*, 571 F.3d 20, 35 (D.C. Cir. 2009)); *see also Animal Legal Def. Fund, Inc. v. Perdue*, 872 F.3d 602, 616 (D.C. Cir. 2017) [hereinafter *ALDF*] ("We thus must determine whether the agency's [interpretation] is unambiguously foreclosed by the statute." (citation omitted)); *Otsuka Pharm. Co. v. Price*, 869 F.3d 987, 995 (D.C. Cir. 2017)

(same). If the agency's interpretation "violate[s] Congress's precise instructions or exceed[s] the statute's clear boundaries," then "the agency's interpretation is unlawful." *Vill. of Barrington*, 636 F.3d at 660.

The Court "begin[s], of course, with the statutory text." *ALDF*, 872 F.3d at 616 (citing *Maslenjak v. United States*, 137 S. Ct. 1918, 1924 (2017)). The pediatric exclusivity provision sets forth an intricate, multi-step process for determining when a sponsor's pediatric research justifies a valuable, six-month extension of the sponsor's market exclusivities and patent rights. The FDA, tasked with effectuating this process, occupies center stage in the statutory scheme. Among other duties, the agency is charged with deciding whether to "accept or reject" the sponsor's "reports of [its] studies." 21 U.S.C. § 355a(d)(4). Fulfilling this "responsibility" requires the FDA "to determine . . . whether the studies fairly respond to the written request." *Id.* As noted, the agency has found that a sponsor's study reports constitute a "fair response" if they either meet the specific terms of the written request or meet its objectives by yielding "information [that] is clinically meaningful across all age groups and uses." AR 1637.

The statute provides important guidance by specifying that the requirement can be satisfied by something short of perfect compliance: the sponsor need only "fairly" respond to the written request. *See Merck*, 148 F. Supp. 2d at 30–31. If perfect compliance were required, the adverb "fairly" would serve no purpose, and that result "would risk running headlong into the rule against superfluity." *Lockhart v. United States*, 136 S. Ct. 958, 966 (2016). But this is where the text runs out. The statute does not define what constitutes a "fair" response, and, as the FDA argues, "fairly respond" is "an inherently ambiguous term." Dkt. 65-1 at 30. To take just one source, the Oxford English Dictionary suggests that the term "fairly" has two different

senses. Fairly, adv., Oxford English Dictionary (2018) [hereinafter OED].[2] The first "relat[es] to amount, extent, or degree," suggesting a more quantitative assessment. *Id.* Amgen's preferred definitions—"moderately," "passably," and "reasonably well"— fall within this category. Dkt. 60-1 at 31; *see also* Fairly, Merriam-Webster Dictionary (2018) ("to a full degree or extent");[3] Fairly, Collins English Dictionary (2018) ("to quite a large degree").[4] The second sense, however, draws on a more substantive conception of the term: "[i]n a fair manner, so as to be fair." OED. This sense of the word "fairly" includes definitions such as "[b]y proper or legal means; legitimately," "[i]n accordance with what is right or just[;] . . . with good reason, rightfully," and—perhaps most relevant here—"[i]n a proper or suitable manner; appropriately, fittingly." *Id.* The FDA interprets the word "fairly" in a manner that draws on both senses: "how much of a response there was" as well as "the quality of the response." Dkt. 65-1 at 31. The statute does not dictate one sense of the word "fairly" over the other, nor does it indicate which of the competing meanings within each sense (for instance, "moderately" versus "to a full degree") Congress intended. What *is* clear, however, is that the FDA's "clinically meaningful information" interpretation is not "unambiguously foreclosed" by the statutory text. There is no textual or other evidence that the statute prohibits the agency from considering the extent to which the data responds to the goals of the study.

Amgen offers a number of counterarguments, none of which compels a different conclusion. First, Amgen contends that "fairly respond" necessarily means "answer reasonably well," Dkt. 60-1 at 31, and that—when combined with the limiting term "only"—this shows that

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[2] Available at http://www.oed.com/view/Entry/67727.

[3] Available at https://www.merriam-webster.com/dictionary/fairly.

[4] Available at https://www.collinsdictionary.com/us/dictionary/english/fairly.

Congress unambiguously foreclosed the FDA from adopting a "results[-]oriented" standard, Dkt. 74 at 33 (Tr. 33:10–11, :21–23). But, for the reasons explained above, the word "only" does not modify the phrase "fairly respond;" it merely means that the FDA should not add requirements to those that Congress specified. Reading the phrase "fairly respond" to mean "answer reasonably well," moreover, does nothing to clarify the standard; "answer reasonably well" is just as ambiguous as "fairly respond." For purposes of *Chevron* step one, the question is whether Congress left a gap for the agency to fill, and substituting the phrase "answer reasonably well" for "fairly respond" neither fills the existing gap nor demonstrates that the FDA's reading of the statute is unambiguously foreclosed.

When asked at oral argument to describe how the FDA should "decide whether [a] response was reasonable," Dkt. 74 at 21 (Tr. 21:12–14), Amgen offered that the agency must assess reasonableness in light of "the volume of what . . . [was] put in front of the agency" as well as "what the sponsor did in order to achieve that data," *id.* at 24 (Tr. 24:17–19). In other words, Amgen explained, "reasonableness includes both the extent of the data [provided] and the amount of the effort [undertaken]." *Id.* at 27 (Tr. 27:10–12). Amgen concludes that, under that standard, it "did everything it could . . . to satisfy the terms of the [written] request," *id.* at 24 (Tr. 24:23–25), and it is therefore entitled to pediatric exclusivity. An effort-based interpretation of "fairly respond," however, finds no warrant in the statutory text. The question is whether the *study reports*—not the sponsor—"fairly respond" to the written request. In other words, the statute focuses on the studies themselves, not the length of time the studies took, nor the number of attempts needed to complete the studies, nor the expenses incurred in carrying out the studies. An effort-based interpretation of "fairly respond" is untenable.

Amgen offers an additional reading of the statute, which includes a textual anchor and builds on the FDA's goal-focused approach. Under this interpretation, a sponsor's studies suffice if they generate any information that results in a labeling change mandated by 21 U.S.C. § 355a(j). That provision provides:

> If . . . the [FDA] determines that a pediatric study . . . does or does not demonstrate that the drug [in question] is safe and effective, including whether such study results are inconclusive, in pediatric populations or subpopulations, the [FDA] shall order the labeling of such product to include information about the results of the study and a statement of the [FDA's] determination.

Id. According to Amgen, because the results of its studies were added to the Sensipar label pursuant to § 355a(j), the FDA was not free to second-guess *the congressional* determination that the results were meaningful. Dkt. 60-1 at 32.

Amgen's argument suffers from a number of flaws. First, § 355a(j)'s labeling requirement was enacted ten years after Congress imposed the "fairly respond" requirement, *compare* Food and Drug Administration Amendments Act, Pub. L. No. 110–85, § 502, 121 Stat. 823, 876–90 (2007) (adding 21 U.S.C. § 355a(j)), *with* Food and Drug Administration Modernization Act, Pub. L. No. 105–115, § 111, 111 Stat. 2296, 2305–09 (1997) (adding "fairly respond" requirement), and there is no evidence that Congress intended § 355a(j) to amend or clarify the meaning of its earlier enactment. Second, the FDA has explained that it has interpreted § 355a(j) to require labeling changes regardless of whether the studies yielded any clinically meaningful results; rather, according to the FDA, § 355a(j) applies mechanically to *all* such studies. Understood in this light, Amgen's argument proves too much. It would mean, among other things, that the "fairly respond" requirement is meaningless and that the FDA must grant pediatric exclusivity to a sponsor that is utterly unsuccessful in responding to a written request. At oral argument, for example, Amgen acknowledged that this argument would mean

that it would have "fairly responded" to the FDA's written request even if only "one patient" had completed Study 3. Dkt. 74 at 90 (Tr. 90:10–15).

Finally, Amgen asserts that the FDA's "clinically meaningful information" standard would undermine the incentive structure Congress envisioned when it provided for pediatric exclusivity. *See* Dkt. 60-1 at 34–36. This contention, however, bears more on the reasonableness of the FDA's interpretation than on whether the statute "unambiguously forecloses" the FDA's approach. The Court will therefore consider Amgen's purposive argument at *Chevron*'s second step.

Because the phrase "fairly respond" is ambiguous, *Chevron* teaches that Congress "has implicitly delegated the authority" to interpret this term to the FDA. *ALDF*, 872 F.3d at 617. That conclusion is particularly apt, moreover, because—as this case demonstrates—the meaning attached to that phrase implicates the type of policy-laden judgment that is better left to the politically accountable executive branch than to the unelected judiciary. *See Chevron*, 467 U.S. at 864 ("[P]olicy arguments are more properly addressed to legislators or administrators, not to judges."). Construing "fairly respond" is, in short, "precisely the type of statutory gap-filling that 'involves difficult policy choices that agencies are better equipped to make than courts.'" *ALDF*, 872 F.3d at 617 (quoting *Nat'l Cable & Telecomms. Ass'n v. Brand X Internet Servs.*, 545 U.S. 967, 980 (2005)).

3. Chevron *Step Two*

The next question is whether the FDA "has reasonably explained how the permissible interpretation it chose is 'rationally related to the goals of' the statute." *Vill. of Barrington*, 636 F.3d at 665 (quoting *AT&T Corp. v. Iowa Utils. Bd.*, 525 U.S. 366, 388 (1999)). The Court's review "at this stage is 'highly deferential.'" *Id.* (quoting *Nat'l Rifle Ass'n of Am. v. Reno*, 216

F.3d 122, 137 (D.C. Cir. 2000)). But this deference is "not absolute," *Mylan Labs. Ltd. v. FDA*, 910 F. Supp. 2d 299, 306 (D.D.C. 2012), and it must give way in the absence of "reasoned decisionmaking," *Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 52 (1983); *see also Fox v. Clinton*, 684 F.3d 67, 74–75 (D.C. Cir. 2012); *Tripoli Rocketry Ass'n v. Bureau of Alcohol, Tobacco, Firearms, & Explosives*, 437 F.3d 75, 77 (D.C. Cir. 2006).

The FDA's explication of its "clinically meaningful information" standard expressly links that standard to the underlying goal of the pediatric exclusivity statute. The agency's final decision on Sensipar describes both the purpose of the pediatric exclusivity statute and how the FDA's interpretation furthers that goal: the statute's purpose is "to encourage [sponsors to] conduct . . . clinical studies that would result in a public health benefit for pediatric patients," and, in particular, "to address the lack of meaningful information about pediatric uses of drugs, which impairs the ability of health care practitioners and pediatric patients to appropriately use such drugs." AR 1636. The FDA works to achieve this goal by drafting each written request, with input from the Pediatric Review Committee, "to maximize the potential to elicit such information." AR 1637. The FDA then assesses the study reports against the objectives of the written request. *Id.* Accordingly, even if the "specific terms of the [written request] are not met," the FDA will "apply its scientific expertise to determine [whether] the objectives of the [written request] have nevertheless been met," and, if so—"consistent with the goals of the . . . statute"—the FDA "will generally consider the sponsor's studies to have 'fairly responded' to the [written request]." *Id.* (emphasis omitted).

All three of the FDA's decisions in this matter note the significance of meaningful labeling changes as indicia of whether the sponsor's studies provided clinically meaningful information. The agency's initial decision observed, for example, that the FDA "considers

whether the submission" enables the agency "to approve pediatric labeling (including negative pediatric labeling) for all of the age groups and indications" cited in the written request. AR 1391. The FDA's reconsideration decision elaborated on this standard. *See* AR 1485. Because the FDA "draft[s] each [written request] to elicit all of the information needed for use in all relevant pediatric populations," those objectives will be served where a sponsor's studies comply perfectly with the written request or where the information "suffic[es] to enable the [FDA] to approve meaningful labeling." *Id.* Finally, the FDA's appeal decision reiterated "that the purpose of a [written request] is to elicit information that would . . . lead to the addition of pediatric use information to the drug's labeling." AR 1639; *see also* AR 1637 (noting that the "FDA drafts each [written request] to maximize the potential to elicit" clinically meaningful information, "as expressed in the drug's labeling"). Indeed, Amgen itself stressed in its PPSR that "[t]he overall objective of [its] proposed program [was] inclusion of data in the Pediatric Use section of the label." AR 24.

In other words, the goal of the pediatric exclusivity statute is to elicit "information" that "may produce health benefits" in children. 21 U.S.C. § 355a(b)(1). The agency has determined that this objective is best served by an interpretation of "fairly respond" that allows the agency to accept a sponsor's reports when (1) there is perfect compliance or (2) the studies generate "information" that "is clinically meaningful," *i.e.*, information that practitioners would find useful. AR 1637. Although this interpretation may not be the best one, it is eminently reasonable in light of the "the goals of the [statute]" and is "rationally related" to those objectives. *AT&T Corp.*, 525 U.S. at 388.

Amgen offers three counterarguments. It first contends that the FDA's "clinically meaningful information" standard goes beyond "the limited assessment Congress empowered the

agency to make." Dkt. 60-1 at 37. But, for the reasons discussed at the first step of the *Chevron* inquiry, Amgen has not offered a persuasive account of "the limited assessment" that it believes Congress contemplated. It is true that Congress limited the FDA to considering the requirements identified in the statute, but it did not limit the FDA's authority to consider whether *those* requirements were satisfied. *See supra* Part III.A.1.

Second, Amgen notes that the FDA initially had only 90 days to decide whether to accept or reject a sponsor's reports, and it argues that the original allotment of 90 days would not have afforded the FDA enough time to conduct its "clinically meaningful information" inquiry. Dkt. 60-1 at 37 (citing 21 U.S.C. § 355a(d)(3) (2003)). Given the fact that the FDA participates in the ongoing process—and, indeed, formulates the written request and any amendments to it—that contention is far from convincing. And, the fact that Congress subsequently extended the time allowed for the FDA's review, if anything, supports the conclusion that Congress did not intend for the decision whether to accept or reject a sponsor's reports to be a mechanical one.

Finally, as noted above, Amgen contends that the FDA's interpretation is at odds with congressional intent because it injects "deep uncertainty into the process" and thus "radically undermines the terms of Congress's bargain." Dkt. 60-1 at 34–35. Even assuming that Amgen is correct that "[t]he central feature of this statutory bargain is that the sponsor knows the terms of th[e] bargain before it . . . decide[s] whether to conduct the pediatric studies," Dkt. 60-1 at 34 (emphasis omitted), it is far from clear that Amgen's reading of the statute provides greater certainty or predictability than the FDA's. Under the FDA's construction of the statute, a sponsor can earn six months of additional exclusivity if its studies either (1) meet the terms of the written request or (2) yield clinically meaningful information that achieves the specified objectives of the written request. Either way, the sponsor's success can be measured against the

prescribed terms and goals of the written request. Under Amgen's proposed construction of the statute, in contrast, the FDA would be required to assess the quantity of information provided and the sponsor's effort without any specified benchmark or standard. Similarly, it is not obvious that Amgen's reading of the statute is likely to yield more information about pediatric uses of drugs. Although Amgen might be correct that sponsors may be more likely to submit PPSRs to the FDA with a more forgiving interpretation of the statute, they may also be less likely to complete their studies in the manner contemplated by the written requests. It is not, of course, the Court's role to decide whether Amgen's account of the relevant incentives is more or less compelling than the FDA's, but only to determine whether the FDA's understanding of the statutory scheme is a reasonable one. For the reasons explained above, the Court concludes that it is.

Because the term "fairly respond" is ambiguous and because the FDA's interpretation of that term is reasonable, the Court must defer to the FDA's statutory construction.

B. Arbitrary and Capricious Claim

Under the Administrative Procedure Act, the Court must "set aside" the FDA's denial of pediatric exclusivity if that decision is "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." 5 U.S.C. § 706(2)(A). In applying this standard, the Court must consider whether the FDA "relied on factors which Congress has not intended it to consider, entirely failed to consider an important aspect of the problem, [or] offered an explanation for its decision that runs counter to the evidence before the agency." *State Farm*, 463 U.S. at 43. Although the Court must assess whether the FDA "examine[d] the relevant data and articulate[d] a . . . rational connection between the facts found and the choice made," it may not "substitute its [own] judgment for that of the [FDA]." *Id.* Deference to the agency's determination, moreover, "is especially warranted where," as here, "the decision at issue 'requires a high level of technical

expertise.'" *Safari Club*, 878 F.3d at 325–26 (quoting *Marsh v. Or. Nat. Res. Council*, 490 U.S. 360, 377 (1989)).

The FDA concluded that Amgen's reports did not "fairly respond" to the written request because the data from Study 3 and the other sources did not yield "clinically meaningful" information on cinacalcet's safety—an objective of the written request—in one of the specified age groups, pediatric patients ages 28 days to < 6 years. AR 1647–48. The agency looked both to the results of Study 3 and the rest of Amgen's data before concluding that Amgen had "failed to obtain the safety data called for in the [written request]" and, thus, the "needed information" on cinacalcet's use in children. AR 1638. With respect to Study 3, the FDA explained that "[t]he choice of a minimum of 15 patients reflect[ed] a reasonable balance between study feasibility and data sufficiency." AR 1645. But the data that Amgen generated was "not sufficient to evaluate the primary endpoint of safety in the younger population" because there were "only 4 completers." *Id.* Another problem was that "almost no participants provid[ed] safety data at effective dose levels;" by the twenty-fourth week of the twenty-six-week study, data on a key metric of cinacalcet's efficacy was not available for 95% of the participants. *Id.* In addition, the FDA concluded that it could not rely on "additional safety data gathered" in other studies "to inform safety in the intended use for the youngest pediatric population." AR 1647. As the foregoing discussion demonstrates, the FDA drew on its expertise and articulated a "rational connection between the facts" and its decision to deny pediatric exclusivity for Sensipar.

Amgen offers three reasons why, in its view, the FDA's denial of pediatric exclusivity was arbitrary and capricious: (1) its studies satisfied the "fairly respond" requirement, even under the FDA's reading of the statute; (2) the FDA arbitrarily refused to consider evidence of

Amgen's efforts to enroll additional patients in Study 3; and (3) the FDA treated Amgen differently than two similarly situated entities, without offering a reasoned basis for doing so. The first two arguments fail, but the third—Amgen's claim of inconsistent treatment—warrants further consideration from the agency.

1. *Satisfaction of the FDA's Standard*

Amgen contends that it "achieved 'meaningful labeling,'" Dkt. 60-1 at 38, because, pursuant to 21 U.S.C. § 355a(j)'s labeling requirement, Sensipar's label was updated with information from Amgen's studies, Dkt. 60-1 at 38–39. For the reasons discussed above, the Court is unpersuaded that § 355a(j) is coterminous with the FDA's "clinically meaningful information" standard, *see supra* Part III.A.2; *see also* Dkt. 65-1 at 42, and more to the point for present purposes, the FDA has rejected the linkage that Amgen posits, and the FDA's reading of the relevant provisions is eminently reasonable. As the FDA has explained, § 355a(j) mandates the inclusion of all results of studies undertaken in response to a written request, regardless of whether those results are clinically meaningful. The agency's decision to require labeling changes for Sensipar pursuant to § 355a(j), accordingly, does not mean that Amgen's studies "achieved 'meaningful labeling'" for purposes of the "fairly respond" requirement.

2. *The FDA's Refusal To Consider Evidence of Amgen's Effort*

According to Amgen, the FDA "acted arbitrarily" by "refusing" to accept and consider a "'briefing document . . . describ[ing] the efforts Amgen . . . made enrolling pediatric patients'" for Study 3. Dkt. 60-1 at 50 (quoting AR 1096). Amgen further asserts that the FDA erred in claiming that Amgen "could have" achieved the minimum number of patients for Study 3 with "greater effort." AR 1646; *see* Dkt. 60-1 at 51. Although it is true, as Amgen argues, that an agency acts arbitrarily by "fail[ing] to consider an important aspect of the problem," *State Farm*, 463 U.S. at 43, that did not occur here. For the reasons already discussed, the FDA has

reasonably interpreted the "fairly respond" requirement in a manner that does not encompass a sponsor's *efforts*. Thus, information on Amgen's work on enrollment is not an "important aspect" of the "fairly respond" determination because the FDA did not deny pediatric exclusivity based on Amgen's efforts (or lack thereof).

3. *Inconsistent Treatment*

Amgen also argues that the FDA's decision should be set aside because it is inconsistent with the approach the FDA has taken in similar cases. Dkt. 60-1 at 45–50. When an agency "treat[s] similarly situated parties differently," it must provide an "adequate explanation to justify" the disparate outcomes. *Burlington N. & Santa Fe Ry. Co. v. Surface Transp. Bd.*, 403 F.3d 771, 776 (D.C. Cir. 2005); *see also Cty. of Los Angeles v. Shalala*, 192 F.3d 1005, 1022 (D.C. Cir. 1999); *Transactive Corp. v. United States*, 91 F.3d 232, 237 (D.C. Cir. 1996); *Petroleum Commc'ns, Inc. v. FCC*, 22 F.3d 1164, 1172 (D.C. Cir. 1994); *New Orleans Channel 20, Inc. v. FCC*, 830 F.2d 361, 366 (D.C. Cir. 1987). Without such a "reasoned explanation," the agency's "action is arbitrary and capricious and cannot be upheld." *Burlington N. & Santa Fe*, 403 F.3d at 777. Relying on this rule, Amgen contends that the FDA's decisions granting pediatric exclusivity for Orencia (abatacept) and Ortho Tri-Cyclen (ethinyl estradiol; norgestimate) are inconsistent with its denial for Sensipar, and that the agency has failed to "provide a legitimate reason" for treating Sensipar differently. Dkt. 60-1 at 45 (quoting *Bracco Diagnostics, Inc. v. Shalala*, 963 F. Supp. 20, 27 (D.D.C. 1997)). As explained below, the Court agrees with Amgen about one of these precedents, but not the other.

As an initial matter, the Court is unconvinced that the FDA, without explanation, applied a more onerous standard in rejecting Amgen's studies than it applied in accepting the studies submitted by Orencia's sponsor, Bristol-Myers Squibb ("BMS"). Amgen is correct that the FDA granted pediatric exclusivity for Orencia even though one of BMS's studies—involving the

intravenous use of Orencia in patients ages 6 to 17 years, AR 1727—did not meet the terms of the written request. AR 1492. As the FDA explained to Amgen in its reconsideration decision, however, it granted pediatric exclusivity because the "overall data" from the studies BMS conducted "provided a sufficient safety database to draw supportable conclusions about the drug's safety in the relevant pediatric age groups" and "was sufficient to label the product for pediatric use." *Id.* The difference between the BMS and Amgen studies, moreover, was marked: BMS submitted data from 164 of the required 180 patients, whereas Amgen submitted data from only 4 of the required 15 patients in Study 3. *Id.* In the FDA's expert opinion, BMS's studies produced "robust clinical trial data," while Amgen's studies, in contrast, "did not yield an interpretable evaluation of product safety." *Id.*

Notwithstanding these "important" differences, *id.*, Amgen contends that the FDA's Orencia decision is inconsistent with its Sensipar decision for two reasons. First, Amgen argues that the FDA considered the "overall data" from the two Orencia studies to assess whether they yielded "clinically meaningful information," but for Sensipar the FDA restricted itself to "analyzing Study 3 in isolation." Dkt. 60-1 at 50. The record, however, contradicts that characterization of the FDA's approach to Sensipar. The agency found that "[d]ata from Study 3 were not sufficient to evaluate . . . safety in the younger population," AR 1645, and that this "shortage" was "not compensated by additional safety data gathered in children < 6 years old in Study 1 (single dose study), a retrospective observational study, and a prospective cohort registry study," AR 1647. The FDA thus considered overall data in both cases.

Second, Amgen contends that the FDA rejected its study reports because they did not result in meaningful labeling changes but accepted BMS's reports even though BMS's studies did not result in a labeling change. Dkt. 60-1 at 48. The fact that the FDA did not require a

labeling change for Orencia, however, does not mean that the BMS's studies did not yield meaningful labeling information or, indeed, "information . . . sufficient to label the product for pediatric use." AR 1492. Rather, as all agree, the FDA had previously approved labeling information regarding the intravenous use of the drug in pediatric patients. *See* AR 1736, 1773–74. The FDA reasonably concluded that an additional study was nonetheless warranted, and it reasonably concluded that the results of that study and the overall data confirmed that "the product was safe for use" by patients ages 6 to 17 years. AR 1491–92. Although Amgen suggests that this confirmation must not have been "clinically meaningful" because the FDA, under its own regulations, required "substantial evidence" to approve the prior label, Dkt. 67 at 27–28, that argument asks that the Court tread on the agency's expert assessment of whether a further study was warranted in the first place.

For Ortho Tri-Cyclen, however, Amgen has a point. In its reconsideration decision for Sensipar, the FDA distinguished the agency's grant of exclusivity for Ortho Tri-Cyclen on the ground that the studies conducted by Ortho Tri-Cyclen's sponsor, Johnson & Johnson, AR 1888, met all of the terms of the written request. AR 1493; *cf.* AR 1485. As Amgen argues, however, it is—at best—unclear from the administrative record whether that premise is correct.

> The written request asked Johnson & Johnson to conduct two studies:
>
> *Study 1:* A randomized, double-blind, placebo-controlled study to examine the efficacy and safety of Ortho Tri-Cyclen® in the treatment of adolescent patients with anorexia nervosa (AN).
>
> *Study 2:* A pharmacokinetics (PK) study to assess the single-dose and steady-state or alternatively, population PK of ethinyl estradiol (EE), norgestrel (NG), and norelgestromin (NGMN) in pediatric patients with [anorexia].

AR 1871. The objective of Study 1 was to "assess the effect" of Ortho Tri-Cyclen "on bone mineral density (BMD) of the lumbar spine and hip in patients with anorexia." *Id.* The objective

of Study 2 was to "assess the single-dose and steady-state or, alternatively, population [pharmacokinetics] of [norelgestromin], [norgestrel], and [ethinyl estradiol] in pediatric patients with [anorexia]." *Id.* The written request set forth more detailed requirements for both studies. As relevant here, Study 1 specified the following design parameters: one year in duration and "approximately 120 adolescent women" ages "12 through 17 years" with anorexia as defined by the Diagnostic and Statistical Manual of Mental Disorders, fourth edition ("DSM-IV"). AR 1872. Amgen contends that many of the women enrolled in Study 1 "did not meet . . . the DSM-IV diagnostic criteria for anorexia." Dkt. 60-1 at 47 (quoting AR 1916).

In its Sensipar reconsideration decision, the FDA offers little support for its conclusion that Johnson & Johnson satisfied the terms of Study 1. The agency acknowledges that it was "unable to locate the Board's decision granting exclusivity" to Johnson & Johnson, and asserts, without explanation, that the deciding official "reviewed other relevant documents and determined that the sponsor's studies met the terms" of the written request. AR 1493. In its brief before this Court, moreover, the FDA identifies only one possible source supporting its conclusion: in a clinical review prepared after the FDA had granted Johnson & Johnson's request for pediatric exclusivity, a medical reviewer noted that he had previously "recommended that [Johnson & Johnson] receive pediatric exclusivity, since the requested study was conducted in agreement with the [w]ritten [r]request." AR 1885. This document reflects the reviewer's recommendation on exclusivity, but not the analysis or conclusions of the deciding official. And the reviewer did not explain what he meant by "conducted in agreement with the [w]ritten [r]equest." Given the deferential standard of review, however, this might ordinarily suffice to sustain the FDA's decision. *See, e.g.*, *Envtl. Def. Fund, Inc. v. Costle*, 657 F.2d 275, 283 (D.C.

Cir. 1981). But other material in the administrative record casts doubt on whether Johnson & Johnson, in fact, met the terms of the written request with respect to Study 1.

From what the Court can glean from the record, Johnson & Johnson enrolled "146 randomized and 123 treated subjects," all of whom were "female and aged 10 to 17 years at screening."[5] AR 1918. Following a May 2005 clinical review, however, the FDA found that "the majority of the 123 subjects treated . . . did *not* meet either the DSM-IV diagnostic criteria for anorexia nervosa or the DSM-IV diagnostic criteria modified by the sponsor for anorexia nervosa."[6] AR 1916; *see also* AR 1921 (noting that only 77 of the 123 patients "had the word 'anorexia' listed" in their medical histories). In particular, 76 patients "had a baseline Body Mass Index (BMI) at or above the 10th percentile for age and [therefore] should not have been enrolled into the study." AR 1948. And, at least in part because "a significant number" of treated patients "did not me[e]t the DSM-IV criteria," the FDA "reviewer consider[ed] the data . . . insufficient to address safety concerns regarding the use of Ortho Tri-Cyclen in subjects with anorexia." AR 1937.

Based on this record, Amgen argues that the FDA granted pediatric exclusivity even though the sponsor's study reports "neither met the terms of the written request nor generated meaningful labeling." Dkt. 60-1 at 45. Although the FDA addresses some of Amgen's arguments, it has not responded to Amgen's contention that the majority of the 123 patients treated in Study 1 did not meet the DSM-IV diagnostic criteria for anorexia nervosa, as required by the written request. There may be an answer to Amgen's contention. It is possible, for

[5] Two of these patients were 10 or 11, yielding a total of 121 treated subjects ages 12 through 17 years. *See* AR 1951.

[6] Of the 123 treated patients with anorexia nervosa, 61 received active treatment and 62 received placebos. AR 1907.

instance, that the FDA granted Johnson & Johnson's pediatric exclusivity based on the mistaken belief that Study 1 was conducted in full compliance with the terms of the written request, and that the failure to enroll patients meeting the DSM-IV criteria was discovered only after the fact. Or it may be that Johnson & Johnson's study did, in fact, comply with the requirement. Or the FDA may have some other basis for distinguishing, disregarding, or abandoning the Ortho Tri-Cyclen precedent. If so, however, the agency must explain that rationale and identify the relevant evidence for its conclusions in the administrative record. Because the FDA has yet to do so, the Court concludes that the agency's decision is—at least in this one respect—arbitrary and capricious and that a limited remand is necessary. *See Lilliputian Sys., Inc. v. Pipeline & Hazardous Materials Safety Admin.*, 741 F.3d 1309, 1313 (D.C. Cir. 2014) ("[A]n agency cannot treat similarly situated entities differently unless it 'support[s] th[e] disparate treatment with a reasoned explanation and substantial evidence in the record.'" (quoting *Burlington N. & Santa Fe*, 403 F.3d at 777)).

This disposition raises one final question: whether to remand the matter with or without vacatur of the FDA's denial of pediatric exclusivity. The Court must consider "two factors: the likelihood that [the] 'deficiencies' . . . can be redressed on remand, even if the agency reaches the same result, and the 'disruptive consequences' of vacatur." *Black Oak Energy, LLC v. FERC*, 725 F.3d 230, 244 (D.C. Cir. 2013) (quoting *Allied-Signal v. Nuclear Regulatory Comm'n*, 988 F.2d 146, 150–51 (D.C. Cir. 1993)). The parties, however, have not addressed the question of vacatur—nor is it obvious what practical consequences, if any, turn on the question given that the FDA denied Amgen's request for pediatric exclusivity and that setting aside that decision would not accord Amgen the ultimate relief that it seeks. Rather than decide the issue without input from the parties, the Court will order the parties to appear for a status conference

(1) to address whether the limited remand required by this decision should be with or without vacatur, and (2) to develop a schedule for the FDA promptly to address the Ortho Tri-Cyclen precedent on remand.

With respect to Amgen's arbitrary and capricious claim, the Court, accordingly, will grant summary judgment to the FDA in part and to Amgen in part, and will remand the matter to the FDA for further consideration of its Ortho Tri-Cyclen decision.

C. Notice Claims

Amgen argues that the "FDA's application of its previously unannounced" interpretation of "fairly respond" to Amgen's request for pediatric exclusivity violated the "fair notice" principle of the APA and the due process clause and constituted impermissible retroactive rulemaking. Although these contentions overlap in substantial part, the Court will address each in turn.

1. *Fair Notice*

With respect to its "fair notice" claim, Amgen asserts that it lacked "[a]dvance knowledge" of the FDA's interpretation of "fairly respond" and that it "had no way to predict at the time it agreed" to the written request that the agency would adopt such an interpretation. Dkt. 60-1 at 42. This lack of notice, Amgen continues, "had real consequences for Amgen" because the company "spent vast time and resources undertaking pediatric testing." *Id.* at 42–43. As explained below, Amgen's argument fails on both the law and the facts.

As to the law, Amgen's contention that the APA (or due process) precludes an agency from applying an interpretation of a statute or regulation that cannot be discerned in advance with "ascertainable certainty," Dkt. 60-1 at 41 (citing *Gen. Elec. Co. v. EPA*, 53 F.3d 1324, 1328–29 (D.C. Cir. 1995)), overstates the law. The "ascertainable certainty" standard "applies where . . . a party is deprived of 'property,' or where 'sanctions are drastic.'" *Darrell Andrews*

Trucking, Inc. v. Fed. Motor Carrier Safety Admin., 296 F.3d 1120, 1130 n.8 (D.C. Cir. 2002) (quoting *Gen. Elec.*, 296 F.3d at 1328–29). It precludes an agency from imposing a criminal or civil penalty or sanction on a regulated party without fair notice. *See, e.g.*, *Darrell Andrews Trucking*, 296 F.3d at 1130; *Gen. Elec.*, 53 F.3d at 1328–29. And, it precludes an agency from rejecting a filing as untimely or for failing to comply with some other filing requirement if the agency has not provided fair notice of the time limit or filing requirement. *See, e.g.*, *PMD Produce Brokerage Co. v. USDA*, 234 F.3d 48, 52–53 (D.C. Cir. 2000). But Amgen has failed to identify any precedent beyond those contexts in which the courts have applied the "ascertainable certainty" requirement to agency adjudicative actions involving questions of statutory or regulatory interpretation. It is common, moreover, for agencies to set forth their statutory interpretations in the adjudicative process. Against that backdrop, the implication of Amgen's argument—that the "ascertainable certainty" standard applies to all adjudications in which a party has a substantial stake or a reliance interest—would substantially rework the regulatory process. And it would do so for no good reason: *Chevron* and the overarching arbitrary and capricious standard already prevent agencies from engaging in the type of "Kafkaesque" endeavors that Amgen fears. *See* Dkt. 60-1 at 41.

Amgen's argument also fails on the facts. The "ascertainable certainty" rule prevents agencies from taking regulated parties by surprise. *See Gen. Elec.*, 53 F.3d at 1329–30 (citing *Rollins Envtl. Servs., Inc. v. EPA*, 937 F.2d 649, 651 (D.C. Cir. 1991); *Satellite Broad. Co. v. FCC*, 824 F.2d 1, 2 (D.C. Cir. 1987); *Gates & Fox Co. v. OSHRC*, 790 F.2d 154, 155 (D.C. Cir. 1986)). Here, however, Amgen knew that its reports would need to "fairly respond" to the written request, *see* 21 U.S.C. § 355a(d)(4), Amgen knew what the written request required, and Amgen knew what the written request sought to attain, AR 1076–89. Amgen was aware,

moreover, that the FDA had previously required that the requested studies "meet [every] single term of [the] written request." *Merck*, 148 F. Supp. 2d at 30. And, Amgen knew that one district court had held that perfect compliance was not required and that, instead, it was sufficient "if the stud[ies] as a whole [provide] a fair response to the written request." *Id.* The fact that the FDA subsequently adopted a *more* generous reading of the statute—and expanded the universe of study responses that it considered sufficient—does not constitute *unfair* surprise.

The administrative record, moreover, confirms that Amgen was not blind to the relevant requirements. Among other things, when Amgen realized that it would be unable to meet the terms of the written request, it sought to amend that request—it did not simply rest on the assumption that its best efforts or the limited results that it did obtain would suffice. AR 1091–92. In addition, when Amgen submitted its study report and requested pediatric exclusivity, AR 1152, it argued that pediatric exclusivity was warranted because

> sufficient data has been collected in the overall cinacalcet pediatric development program . . . *to satisfy the primary objectives of this study*, which were to evaluate the safety and tolerability of cinacalcet in pediatric patients ages 28 days to < 6 years and to characterize the PK profile in pediatric patients.

AR 1160 (emphasis added). Although not a perfect match, Amgen's argument for why it deserved pediatric exclusivity closely reflects the FDA's understanding that the studies must produce results sufficient to meet "the objectives of the" written request. AR 1637.

Finally, Amgen relies on the following statement from the FDA's website, which it argues is inconsistent with the FDA's interpretation: "Pediatric exclusivity is not tied to approval of labeling containing information on pediatric use based on the studies conducted." Dkt. 60-1 at 40 (quoting Dkt. 60-2 at 3 (emphasis omitted)). The website, however, goes on to explain that the FDA's decision whether to grant pediatric exclusivity is based on the agency's assessment of whether "the [sponsor's] studies were conducted in accordance with the terms of the [w]ritten

[r]equest." Dkt. 60-2 at 3. That statement is entirely consistent with the first prong of the test that the FDA now espouses: the FDA will grant pediatric exclusivity to a sponsor that "properly execute[s]" the requested studies, even if the sponsor's studies fail to "result in pediatric use information"—*i.e.*, information useful in labeling. AR 1637. The statement that Amgen identifies from the FDA website, accordingly, can be faulted—if at all—for addressing only the first prong of the current test, and not adding that a sponsor can also qualify for pediatric exclusivity if it fails to "properly execute[]" the studies but, nonetheless, achieves results that satisfy the objectives of the studies. That omission does nothing to advance Amgen's "fair notice" argument. The fact that the FDA subsequently applied a *more* generous test than the one articulated on its website could not have *unfairly* surprised Amgen. Amgen would hardly be better off if the FDA had relied solely on the test alluded to on its website.

The Court, accordingly, will grant the FDA summary judgment on Amgen's APA claim and due process claim based on a purported lack of "fair notice."

2. *Retroactivity*

Amgen's contention that the FDA's determination violated "the principles of retroactive rulemaking," Dkt. 60-1 at 43, fares no better. According to Amgen, those principles "protect regulated entities from the surprise of having newly developed standards applied to them in the course of an adjudication," *id.*, and the FDA's current reading of "fairly respond" constitutes "an abrupt departure from the previously announced rule and from the reasonably ascertainable meaning of the statute," *id.* at 44. This argument misunderstands how principles of retroactivity apply to agency adjudications.

Unlike the rules applicable to notice-and-comment rulemaking, *see Bowen v. Georgetown Univ. Hosp.*, 488 U.S. 204, 208–09 (1988), "[r]etroactivity is the norm in agency adjudications no less than in judicial adjudications," *Am. Tel. & Tel. Co. v. FCC*, 454 F.3d 329, 332 (D.C. Cir.

2006). To be sure, "'judicial hackles' are raised when 'an agency alters an established rule defining permissible conduct which has been generally recognized and relied on throughout the industry that it regulates." *Id.* (quoting *NLRB v. Majestic Weaving Co.*, 355 F.2d 854, 860 (2d. Cir. 1966) (Friendly, J.)). Beyond those limited circumstances, however, courts will set aside new interpretations of existing law adopted in agency adjudications only if retroactive application of the new interpretation "would work a 'manifest injustice.'" *Verizon Tel. Cos. v. FCC*, 269 F.3d 1098, 1109 (D.C. Cir. 2001) (citation omitted); *see also Qwest Servs. Corp. v. FCC*, 509 F.3d 531, 539 (D.C. Cir. 2007); *Am. Tel.*, 454 F.3d at 332; *Clark-Cowlitz Joint Operating Agency v. FERC*, 826 F.2d 1074, 1081 (D.C. Cir. 1987) (en banc).

In determining that Amgen's studies did not "fairly respond" to the written request, the FDA did not jettison a "generally recognized" rule that Amgen—or any other regulated entity—relied upon. Indeed, the only earlier articulation of the governing rule that Amgen has identified is the perfect compliance rule discussed—and rejected—in the *Merck* case. 148 F. Supp. 2d at 30. After *Merck* was decided, there may have been some uncertainty regarding the relevant standard, but Amgen cannot plausibly contend that the FDA altered an "established" and "generally recognized" rule when, in relevant respects, it adopted the rule suggested by the *Merck* decision. *Id.* (holding that the key question is whether "the study as a whole is a fair response to the written request"). Even more to the point, Amgen cannot plausibly contend that it relied on the FDA's earlier, more restrictive reading of the statute. If there was some other "established" and "generally recognized" prior articulation of the standard that, if applied here, would have required the FDA to accept Amgen's studies, Amgen has yet to identify it.

This leaves the question whether retroactive application of the test recognized in the FDA's decisions in this matter would result in a "manifest injustice." As the D.C. Circuit has

explained, it "has not been entirely consistent in enunciating a standard to determine when to deny retroactive effect in cases involving 'new applications of existing law, clarifications, and additions' resulting from adjudicatory actions." *Verizon*, 269 F.3d at 1109–10 (citing a five-factor balancing test adopted in *Clark-Cowlitz*, 826 F.2d at 1081–86, a three-factor test set forth in *Dist. Lodge 64 v. NLRB*, 949 F.2d 441, 447–49 (D.C. Cir. 1991), and "other cases . . . jettison[ing] the multi-pronged balancing approaches altogether"). The most recent cases from the D.C. Circuit have eschewed a formal application of a five- or three-factor test in favor of a more flexible inquiry. *See Qwest Servs.*, 509 F.3d at 539–40; *Consol. Edison Co. of N.Y. v. FERC*, 315 F.3d 316, 323–24 (D.C. Cir. 2003). Two principles, however, are clear—and dispositive here. First, "a mere lack of clarity in the law does not make it manifestly unjust to apply a subsequent clarification of that law to past conduct." *Qwest Servs.*, 509 F.3d at 540. Indeed, "[c]larifying the law and applying that clarification to past behavior are routine functions of adjudication." *Id.* Second, the manifest injustice standard is satisfied only if the affected party has "detrimentally relied on the established legal regime." *Consol. Edison*, 315 F.3d at 323 (citing *Clark-Cowlitz*, 826 F.2d at 1081; *Hatch v. FERC*, 654 F.2d 825, 835 (D.C. Cir. 1981)). It is not enough to show that the affected party might have relied on an assumption regarding the state of law; the relevant question is whether it reasonably relied "on settled law contrary to the rule established in the adjudication." *Qwest Servs.*, 509 F.3d at 540.

For the reasons discussed above, the FDA's retroactive application of its "clinically meaningful information" standard did not work a manifest injustice. Indeed, if anything, it is Amgen's proposed standard that lacks any precedential pedigree. The truth is, the FDA relied on an overly restrictive test before *Merck*; the district court in that case correctly observed that the FDA's prior test could not be squared with the statutory text; and, in this case, the FDA

articulated a standard that is consistent with the statutory text and the *Merck* decision. There is nothing unfair, much less "manifestly unjust," about the FDA's application of that standard to Amgen.

Accordingly, the Court will grant summary judgment to the FDA with respect to Amgen's retroactivity claim.

CONCLUSION

For the reasons stated above, it is hereby **ORDERED** that Amgen's motion for summary judgment, Dkt. 60, is **DENIED** in part and **GRANTED** in part; and it is further

ORDERED that the FDA's motion for summary judgment, Dkt. 65, and the intervenor-defendants' motion for summary judgment, Dkt. 63, are **DENIED** in part and **GRANTED** in part; and it is further

ORDERED that the case is remanded to the FDA for the limited purpose of addressing whether the agency's prior decision granting pediatric exclusivity for Ortho Tri-Cyclen is consistent with its decision denying pediatric exclusivity for Sensipar and, if not, whether there is a reasoned explanation for the disparate outcomes.

SO ORDERED.

/s/ Randolph D. Moss
RANDOLPH D. MOSS
United States District Judge

Date: January 26, 2018