UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

VANDA PHARMACEUTICALS, INC., et al., **Plaintiffs,** **v.** **FOOD AND DRUG ADMINISTRATION, et al.,** **Defendants.**	**Civil No. 19-301 (JDB)**

MEMORANDUM OPINION

In December 2018, the Food and Drug Administration placed a partial clinical hold on long-term human testing of the drug tradipitant. The hold was based on FDA's conclusion that it could not properly assess the risks of long-term tradipitant use in humans until the drug's sponsor, plaintiff Vanda Pharmaceuticals, Inc., conducted a long-term toxicity study on nonrodent animals. Vanda filed this lawsuit to challenge the clinical hold. Pending before the Court are Vanda's motion for summary judgment and FDA's cross-motion for summary judgment, as well as Vanda's motion to complete and supplement the administrative record and a motion by The Humane Society of the United States for leave to file an amicus brief.

For the reasons that follow, the Court will grant summary judgment to FDA and deny each of the other motions.

Background

A. Legal Framework

New drugs cannot be sold or distributed in interstate commerce without FDA approval. 21 U.S.C. § 355(a). To obtain FDA approval, drug sponsors must submit an application to FDA containing, among other things, data demonstrating that a new drug is safe and effective for human

use. Id. § 355(b)(1). So that drug sponsors can obtain such data, the Federal Food, Drug, and Cosmetic Act ("FD&C Act") provides for a limited investigational exception to the ban on distribution of experimental drugs in interstate commerce. Id. § 355(i). Sponsors who wish to take advantage of this exception must submit an Investigational New Drug Application ("IND") to FDA containing "information on [the] design of the investigation and adequate reports of basic information . . . necessary to assess the safety of the drug for use in clinical investigation." Id. § 355(i)(2).

By statute and regulation, FDA does not need to affirmatively approve INDs for sponsors to move ahead with investigational testing. Instead, testing may automatically begin 30 days after an IND is submitted, unless FDA places a clinical hold on testing. See id. § 355(i)(3)(A). FDA can choose to impose a full or partial clinical hold at "any time," id., for a variety of reasons, see 21 C.F.R. § 312.42(b)(iv), including if FDA concludes that an IND lacks "[a]dequate information about pharmacological and toxicological studies of the drug involving laboratory animals or in vitro," id. § 312.23(a)(8). Importantly, the "kind, duration, and scope of animal and other tests required varies with the duration and nature of the proposed clinical investigations." Id. § 312.23(a)(8). A primary purpose of this regulatory framework is to ensure that testing of a given drug does not "represent[] an unreasonable risk to the safety of the persons who are the subjects of the clinical investigation." 21 U.S.C. § 355(i)(3)(B).

B. Vanda's Tradipitant IND

Tradipitant is an experimental drug that has been studied as a possible treatment for a variety of disorders but has not yet been approved by FDA for any purpose. Remand Resp. at FDA-11109.[1] On September 2, 2016, plaintiff Vanda submitted IND 131545 to begin clinical trials

[1] Citations to "FDA-" refer to the Administrative Record, located at ECF Nos. 42 and 43.

of tradipitant as a treatment for gastroparesis, a chronic but nonfatal digestive disorder that causes those suffering from it to experience nausea, vomiting, unusual feelings of fullness, and abdominal pain. Id. Vanda initially sought to conduct a 4-week clinical trial, supporting its proposal with animal toxicity studies that were "limited to durations of 6 months in rats and 3 months in dogs." Id. at FDA-11109–10. FDA allowed Vanda's proposed 4-week human trial to proceed. Id.

Then, on April 10, 2018, Vanda amended its study proposal, proposing a 12-month extension to the 4-week trial. Id. at FDA-11110. FDA informed Vanda that the 12-month extension was not permissible because, without a 9-month nonrodent toxicity study, FDA did not have sufficient data as to the safety or effects of long-term tradipitant use in humans. Id. On May 22, 2018, Vanda submitted another amendment, this time reducing the 12-month-extension proposal to 8 weeks. Id. FDA informed Vanda that that three-month trial (4 weeks plus the 8-week extension) was acceptable but reiterated that anything over three months could not move forward without long-term nonrodent studies. Id. at FDA-11110–11.

Later in 2018, Vanda twice more proposed 12-month extensions to its tradipitant trial; FDA continued to reject the extensions because of its concerns about proceeding without long-term nonrodent studies. Id. at FDA-11111. In December 2018, FDA staff consulted with members of FDA's Medical Policy and Program Review Council ("MPPRC"), who agreed with the staff view that a 9-month nonrodent study was necessary prior to allowing 12-month human trials to ensure humans were not put at undue risk. Id. at FDA-11111–12.

At that point, on December 19, 2018, FDA issued a formal decision placing a partial clinical hold on Vanda's proposed 12-month trial. Partial Clinical Hold Decision at FDA-10184. The decision noted that 9-month nonrodent toxicity studies "are required . . . per the ICH Guidance for Industry: M3(R2) Nonclinical Safety Studies for the Conduction of Human Clinical Trials and

Marketing Authorization for Pharmaceuticals." Id. at FDA-10185. The decision then cited a scientific study as summarizing the "rationale to support the ICH requirement." Id. It also cited a specific regulation, 21 C.F.R. § 312.42(b)(2)(i), and listed the particular deficiency that Vanda needed to correct: "Insufficient information to assess risks to human subjects; because you do not have adequate nonclinical safety data to support clinical trials beyond 3 months." Partial Clinical Hold Decision at FDA-10185.

C. The Present Lawsuit

Vanda filed this action on February 5, 2019, challenging FDA's partial clinical hold decision on two grounds: first, that FDA had failed to "articulate an adequate scientific basis" for its decision; and second, that FDA had allegedly applied the "non-binding ICH guidance as a binding regulation." Compl. [ECF No. 1] at 48. Just over a week later, FDA moved for a voluntary remand so it could have an "opportunity to address certain procedural issues" noted in Vanda's complaint. Mem. in Supp. of Defs.' Mot. for a Voluntary Remand ("Mot. to Remand") [ECF No. 6-1] at 2. In particular, FDA stated that it would "re-evaluate [Vanda's] scientific arguments and provide a full written explanation of the agency's analysis and ultimate position" and "review and clarify the regulatory basis for its decision, addressing the legal import of the guidance document." Id. at 6. This Court granted the remand motion to "allow FDA to cure its mistakes." Vanda Pharm. v. Food & Drug Admin., 2019 WL 1198703, at *2 (D.D.C. Mar. 14, 2019).

After completing its reevaluation of Vanda's extension proposals, FDA issued a lengthy "Remand Response," which consists of two basic parts. First, the Response analyzes Vanda's original submissions and concludes that existing tradipitant studies in nonrodents contain sufficient troubling indications of toxicity such that—while shorter-term human studies may be safe enough to proceed—FDA needs to see if those toxicity markers increase during long-term

nonrodent studies before allowing long-term human studies. Remand Resp. at FDA-11115–20. Second, the Response sets out the scientific basis for a nine-month nonrodent study requirement as the scientific minimum for clinical investigations. Id. at FDA-11120–24.

As noted, both parties have now moved for summary judgment, Vanda has moved to supplement or complete the administrative record, and the Humane Society has requested leave to file an amicus brief. The Court heard oral argument on the motions for summary judgment on December 13, 2019.

Analysis: Motions for Summary Judgment

Vanda's motion for summary judgment argues that FDA's decision to impose a partial clinical hold lacked an articulated scientific basis and that the decision treated the ICH Guidance as binding. FDA's cross-motion argues that the Remand Response leaves no question as to the scientific basis for the hold and does not treat the ICH Guidance as binding. Before reaching the merits of these arguments, however, the Court first addresses Vanda's procedural arguments that it should not consider most, or even all, of the Remand Response.

A. Procedural Arguments Against the Remand Response

1. Post Hoc Rationalization

Vanda's first procedural argument is that virtually everything contained in the Remand Response is "impermissible post hoc rationalization." Pls.' Combined Resp./Reply Mem. Regarding Summ. J. ("Pls.' Resp.") [ECF No. 35] at 10. In Vanda's view, FDA relied exclusively on the ICH Guidance as the basis for the pre-remand partial clinical hold, and any new arguments contained in the Remand Response should be disregarded. See id.

In general, when a court "remand[s] for further explanation, it is incumbent upon the court to consider that explanation when it arrives." Menkes v. U.S. Dep't of Homeland Sec., 637 F.3d

319, 337 (D.C. Cir. 2011) (quoting Alpharma, Inc. v. Leavitt, 460 F.3d 1, 6 (D.C. Cir. 2006)). While there is a rule against post hoc rationalizations, this rule "is not a time barrier which freezes an agency's exercise of its judgment after an initial decision has been made and bars it from further articulation of its reasoning." Alpharma, 460 F.3d at 6–7 (quoting Local 814, Int'l Bhd. of Teamsters v. NLRB, 546 F.2d 989, 992 (D.C. Cir. 1976)). Instead, as this Court outlined in NAACP v. Trump, 315 F. Supp. 3d 457 (D.D.C. 2018), cert. granted, ___ U.S. ___, 139 S. Ct. 2779 (June 28, 2019) (No. 18-588):

> [T]he D.C. Circuit has clarified that this rule "does not prohibit [an agency] from submitting an amplified articulation" of the reasons for its decision following a remand. Alpharma, 460 F.3d at 6 (citations omitted). Indeed, the rule's purpose is simply to prevent courts from considering "rationales offered by anyone other than the proper decisionmakers," such as those appearing "for the first time in litigation affidavits and arguments of counsel." Id. (citation omitted). Hence, when faced with an explanation offered for the first time on remand, a court must determine whether it is an "amplified articulation" of the agency's prior reasoning (which must be considered), id. (citation omitted), or instead "a new reason for why the agency could have" taken the action (which must be disregarded), Delta Air Lines, Inc. v. Export–Import Bank of U.S., 85 F. Supp. 3d 436, 453 (D.D.C. 2015); see Muwekma Ohlone Tribe v. Salazar, 708 F.3d 209, 217 n.8 (D.C. Cir. 2013) (stating that an agency's further explanation on remand "must be more than a barren exercise of supplying reasons to support a pre-ordained result" (citation omitted)).

NAACP, 315 F. Supp. 3d at 465–66.

As a preliminary matter, Vanda attempts to argue that the "proper decisionmakers" were not responsible for the Remand Response, but the Court rejects this argument. Both the pre- and post-remand decisions to impose a clinical hold were made by the FDA officials with "responsibility for review of the IND," 21 C.F.R. § 312.42(d): members of the Office of Drug Evaluation III. See FDA-10187 (initial hold decision by the Associate Director of the Office of Drug Evaluation III's Division of Gastroenterology and Inborn Errors Products); FDA-11127 (remand response decision by the Director of the Office of Drug Evaluation III). Vanda argues that the MPPRC advised on the initial decision but not the remand decision, and that the Remand

Response is thus fatally flawed because the Office of Drug Evaluation III had no ability to "overrule" the MPPRC. However, Vanda can cite no statute or regulation for the proposition that the MPPRC must re-review decisions upon remand. Cf. Delta Air Lines, 85 F. Supp. 3d at 403–04 (noting that where "no authority . . . requires" a decisionmaker higher up in the organizational hierarchy to approve a decision, lesser officials are the "proper decisionmaker"). The most Vanda can muster is a guidance document mentioned by Vanda's counsel at oral argument, the Manual of Policies and Procedures for the Center for Drug Evaluation and Research Medical Policy Council, https://www.fda.gov/media/85725/download. The Manual describes FDA's internal policies and procedures and notes that the MPPRC has authority to "[e]stablish medical policy." Id. at 7. But the Manual is not ultimately helpful to Vanda, because nothing in the procedures requires FDA to go back to MPPRC upon remand (particularly where, as here, the ultimate decision remained the same after reexamination).

Moreover, any argument that the Remand Response was issued without the full authority of FDA is refuted by the fact that the Response frames its conclusions as coming from, and having the authority of, the agency itself, with language like "FDA has determined." Remand Resp. at FDA-11127; cf. Alpharma, 460 F.3d at 7 (concluding that FDA official's letter "represents the considered views of the agency itself" because it stated that "the agency has determined," and thus "an examination of [the letter's] contents is perfectly appropriate"). The Court therefore concludes that the Remand Response was issued by the "proper decisionmaker" within the meaning of D.C. Circuit precedent.

Next, Vanda argues that the Remand Response introduces new reasons for why the clinical hold was imposed, rather than amplified articulations of FDA's original reasoning. The Court disagrees. Vanda challenges two aspects of the Remand Response as being "new reasons." First,

Vanda says that the Remand Response's extended discussion of tradipitant-specific concerns has no foundation in the pre-remand record. Statement of P.&A. in Supp. of Pls.' Mot. for Summ. J. ("Pls.' MSJ") [ECF No. 23-1] at 29–31. But while the pre-remand clinical hold letter doesn't explain FDA's tradipitant-specific concerns with as much clarity as it might have, the letter does discuss the fact that the MPPRC reviewed and agreed with the determination by FDA staff that a nine-month nonrodent study was required for tradipitant testing to continue. Partial Clinical Hold Decision at FDA-10185. Materials relating to the MPPRC's review, in turn, make clear that tradipitant-specific concerns were a basis for the MPPRC's conclusion that a partial clinical hold was appropriate. Most notably, the MPPRC report discusses adverse toxicity findings in Vanda's 3-month tradipitant dog studies, FDA-10871, as do the Powerpoint slides from the MPPRC meeting, FDA-10893–95. Given that the MPPRC meetings took place in December 2018, well before Vanda filed this lawsuit in February 2019, FDA's tradipitant-specific concerns certainly were not raised for the first time in this litigation, despite Vanda's assertions to the contrary, see Pls.' MSJ at 30–31. And while FDA expanded upon its pre-remand tradipitant-specific concerns in the Remand Response, citing new studies and comparing tradipitant to the similar drug casopitant, see Remand Resp. at FDA-11115–20, that sort of amplification is precisely what is permitted upon remand under the NAACP framework. Cf. Univ. of Colo. Health at Mem'l Hosp. v. Burwell, 164 F. Supp. 3d 56, 65 (D.D.C. 2016) (deeming it acceptable for agency to "clarify the administrative record" after a decision by "illuminat[ing] a connection . . . which the administrative record left somewhat implicit"). It is also precisely what FDA said it would do in its voluntary-remand motion. Mot. to Remand at 6 ("On remand, FDA will re-evaluate [Vanda's] scientific arguments and provide a full written explanation of the agency's analysis and ultimate position.").

The second "new reason" that Vanda identifies in the Remand Response turns out not to be new either. Vanda argues that the Remand Response's scientific defense of a 9-month nonrodent study requirement cannot be traced to any pre-remand materials. Pls.' MSJ at 31–32. But Vanda "overstate[s] the novelty of the [Remand Response's] arguments." NAACP, 315 F. Supp. 3d at 466. The pre-remand clinical hold letter itself supported the "rationale" for the requirement with a citation to a study that "noted that later toxicologic findings have been observed in the absence of earlier toxicologic findings." Partial Clinical Hold Decision at FDA-10184. This reasoning (that longer studies reveal toxicities that shorter studies may not) tracks the Remand Response's expanded scientific defense of 9-month studies. Other parts of the pre-remand record also mirror the arguments articulated more fully in the Remand Response; for example, the MPPRC report discusses "analyses by FDA, other drug regulatory authorities and regulated industry" that show that 9-month studies can reveal toxicity risks to humans that may not appear in shorter-duration studies. FDA-10871–72; see Mayo v. Jarvis, 177 F. Supp. 3d 91, 143–44 (D.D.C. 2016) (considering entire record when evaluating claim of post hoc rationalization). This justification too, then, is a permissible "amplified articulation" rather than a "new reason."[2]

2. "Skewing" of the Evidence/Failure to Consider Vanda's Additional Evidence

Vanda's next procedural argument against the Remand Response is that FDA selectively opened the record upon remand, adding new studies that support its position but failing to add

[2] At oral argument, FDA's counsel argued that the Court should construe the Remand Response not as a more detailed explication of FDA's reasons for the original decision, but instead as an entirely new decision. The effect of such a reading of the Remand Response would be to render the post hoc framework detailed above inapplicable, because the "explanations offered in [the response] would be contemporaneous and, consequently, not post hoc." NAACP, 315 F. Supp. 3d at 467 n.7. The Court's remand order did not expressly require either approach, instead ordering a remand so FDA could "cure its mistakes." Vanda Pharm., 2019 WL 1198703, at *2; cf. Ethyl Corp. v. Browner, 989 F.2d 522, 524 (D.C. Cir. 1993) (making explicit that upon remand agency was to "consider the new evidence and make a new decision"). Nor does the language of the Remand Response make plain which approach FDA adopted. See, e.g., Remand Resp. at FDA-11106 (stating that FDA "has carefully re-evaluated the evidence"). As a result, the Court adopts the alternative holding that the Remand Response constitutes a new decision and accordingly rejects Vanda's arguments that the reasoning contained in the Response is post hoc.

studies referenced in Vanda's complaint or in a letter mailed by the Humane Society to FDA. Pls.' MSJ at 32–33. Vanda argues that because it "ignor[es] evidence contradicting its position," the Remand Response is arbitrary and capricious. Id. at 32.

Vanda is correct that an agency cannot simply "ignore evidence that undercuts its judgment." Genuine Parts Co. v. EPA, 890 F.3d 304, 312 (D.C. Cir. 2018). But the universe of evidence that an agency is required to consider extends only to "the full record that was before the agency at the time the decision was made." Blue Ocean Inst. v. Gutierrez, 503 F. Supp. 2d 366, 369 (D.D.C. 2007). To succeed on its claim, then, Vanda must show that FDA "failed adequately to address relevant evidence before it." El Rio Santa Cruz Neighborhood Health Ctr., Inc. v. U.S. Dep't of Health and Human Servs., 396 F.3d 1265, 1278 (D.C. Cir. 2005) (emphasis added).

Vanda has not made such a showing. The purpose of FDA's remand motion was to "afford FDA an opportunity to address certain procedural issues . . . , including the allegations about the agency's response to scientific arguments submitted by Vanda." Mot. to Remand at 2. Specifically, FDA stated that the record "may not adequately reflect FDA's analysis of and response to Vanda's scientific submissions about the necessity of an additional animal toxicology study." Id. at 6. FDA further stated that upon remand, it would "re-evaluate those scientific arguments." Id. In the opinion granting the remand, this Court stated that the remand would "allow FDA to cure its mistakes" that were "related to the completeness and accuracy of the agency's explanation for the clinical hold." Vanda Pharm., 2019 WL 1198703, at *2. Neither the remand request nor the Court's opinion granting the request said anything about FDA being required to consider additional evidence in support of Vanda's position beyond that contained in Vanda's original submission. Indeed, Vanda's submission was legally required to be able to stand on its own merits and to contain "sufficient information . . . to assess the risks to subjects of the

proposed studies," 21 C.F.R. § 312.42(b)(iv), and if it did not contain sufficient information, FDA was legally permitted to place a clinical hold on proposed testing, id. Moreover, there is no question that the studies contained in Vanda's original submission were in the record "before the agency," see FDA-8647–9130, or that upon remand, FDA considered those studies, see FDA-11111 & n.18. FDA, therefore, did consider "evidence contradicting its position," Genuine Parts Co., 890 F.3d at 312, it just didn't find the evidence persuasive.

Ultimately, Vanda's argument boils down to a complaint that it is unfair for FDA, upon remand, to have cited new scientific studies in support of its position while failing to consider Vanda's new evidence. But even beyond the limited mandate of the remand here, no provision in the APA requires FDA to give Vanda an "opportunity to offer contrary evidence" on remand, see Pension Benefit Guar. Corp. v. LTV Corp., 496 U.S. 633, 653 (1990), and the Supreme Court has rejected this sort of "fundamental fairness" argument, which would impose additional procedures upon FDA not found in the APA or the FD&C Act, id. at 655; see also Butte Cty. v. Chaudhuri, 887 F.3d 501, 505 (D.C. Cir 2018) ("[C]ourts generally cannot compel agencies to do more than the statute demands . . . ."). Indeed, the relevant statute allows FDA to impose a clinical hold "[a]t any time," so long as it specifies a basis for the hold, even without hearing any contrary argument from the drug sponsor, let alone from a third party like the Humane Society. See 21 U.S.C. § 355(i)(3)(A); Dist. No. 1, Pac. Coast Dist., Marine Engineers Beneficial Ass'n v. Mar. Admin., 215 F.3d 37, 43 (D.C. Cir. 2000) (concluding that where no "governing statute or a regulation . . . required the agency to afford interested parties an opportunity to submit comments," it is up to an "agency's discretion" whether to accept or consider such comments).

Moreover, Vanda could have introduced its desired evidence into the administrative record through an available administrative pathway—it simply chose not to. Under 21 U.S.C. § 355, after

the Remand Response was issued, Vanda could have submitted a "written request" containing "sufficient information to support the removal" of a clinical hold, which would have resulted in a decision from FDA "within 30 days." 21 U.S.C. § 355(i)(3)(C); see also 21 C.F.R. § 312.42(e)–(f) (laying out procedures for hold removal request or appeal of an FDA hold decision). Neither the studies contained in Vanda's complaint, nor those in the Humane Society's letter, were ever provided to FDA under the prescribed administrative means. In support of its decision not to avail itself of this pathway, Vanda argues that, given FDA's responses up to that point, doing so would have been "redundant and pointless." Pls.' Resp. at 19. The Court thinks it self-evident that using an administrative pathway to achieve the relief that Vanda now seeks—the introduction of certain evidence into the administrative record and FDA's consideration of that evidence—would not have been pointless.[3]

In sum, the Court rejects Vanda's arguments that FDA skewed the administrative record on remand because (1) the remand motion did not require FDA to consider additional evidence from Vanda; (2) no legal authority required FDA to consider additional evidence from Vanda or the Humane Society; and (3) Vanda deliberately declined to take advantage of the administrative means available for introducing its desired evidence into the record.

B. Vanda's Claims

Having concluded that the Court should consider the Remand Response, the Court now addresses Vanda's two main claims.

1. The ICH Guidance

[3] Another available administrative pathway was the dispute resolution appeal procedure in 21 C.F.R. § 312.48. Vanda claims that "it attempted to use [the Formal Dispute Resolution] procedure but was rebuffed by FDA." Pls.' Resp. at 19. But the attempt Vanda is referring to occurred before the clinical hold was imposed. Remand Resp. at FDA-11111. The appeal/formal dispute resolution procedure is available only after a clinical hold has been imposed. See 21 C.F.R. § 312.42(f). Vanda did not attempt to use that procedure once it became available. Like the statutory "written request" procedure under 21 U.S.C. § 355(i)(3)(C), the dispute resolution procedure would have allowed Vanda to submit to FDA a request to resolve "scientific or medical disputes." See 21 C.F.R. § 312.48.

The first of Vanda's claims against the partial clinical hold is that FDA applied the ICH Guidance as a binding legislative rule, in violation of the APA's requirement that legislative rules must go through notice-and-comment rulemaking. Pls.' MSJ at 17. The Court concludes that, whatever the merits of such an argument may have been pre-remand, the Remand Response makes clear that the ICH Guidance is a policy statement exempt from the notice-and-comment process, and that FDA did not rely upon it as a binding rule in imposing the clinical hold.

The ICH Guidance is based upon an analysis conducted by an international panel of scientists in the 1990s (and later updated in the 2000s). Remand Resp. at FDA-11121–22. The panel "found that a 9-month toxicity study in nonrodents is the minimum duration to sufficiently characterize toxicity associated with long-term exposure to a drug." Id. In 2010, FDA published the ICH Guidance in the Federal Register, see 2010 Notice, 75 Fed. Reg. 3471 (Jan. 21, 2020), in accordance with 21 C.F.R. § 312.23(a)(8), which notes that "[g]uidance documents are available from FDA that describe ways in which [informational requirements for investigational studies] may be met." The Federal Register notice states that the

> guidance represents the agency's current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

75 Fed. Reg. at 3472.

The APA generally requires agencies issuing rules to do so through the notice-and-comment process. See 5 U.S.C. § 553(b). And FDA does not dispute that the ICH Guidance qualifies as a "rule" under the APA. See 5 U.S.C. § 551(4) (defining "rule" very broadly); Defs.' Combined Mem. in Supp. of their Cross-Mot. for Summ. J. & in Opp'n to Pls.' Mot. for Summ. J. ("Defs.' MSJ") [ECF No. 33-1] at 40. Instead, FDA argues that the ICH Guidance falls within the

APA's "general statement of policy" exception, for which the notice-and-comment requirements do not apply. Defs.' MSJ at 40.

The question put to the Court, then, is whether the ICH Guidance is a legislative rule, which requires notice and comment, or a general statement of policy, which does not. The D.C. Circuit has articulated the distinction between the two as follows: "[a]n agency action that purports to impose legally binding obligations or prohibitions on regulated parties—and that would be the basis for an enforcement action for violations of those obligations or requirements—is a legislative rule." Nat'l Mining Ass'n v. McCarthy, 758 F.3d 243, 251 (D.C. Cir. 2014). On the other hand, "[a]n agency action that merely explains how the agency will enforce a statute or regulation—in other words, how it will exercise its broad enforcement discretion or permitting discretion under some extant statute or rule—is a general statement of policy." Id. at 252.

The line between these two concepts is blurry, but several factors guide this Court's analysis. The "most important factor concerns the actual legal effect (or lack thereof) of the agency action in question on regulated entities." Id. Here, this factor favors FDA. Though some of FDA's comments pre-remand suggested that the ICH Guidance imposed a "requirement" on Vanda, even the initial clinical hold letter did not rely on the ICH Guidance as the legal source of authority—instead, it cited the controlling regulation as the basis for the hold. See Partial Clinical Hold Decision at FDA-10184. And the Remand Response independently justifies the 9-month nonrodent study requirement by reanalyzing the relevant scientific studies, mentioning the ICH Guidance only when discussing how scientific thinking in this area developed. See Remand Resp. at FDA-11120–24. In other words, the Remand Response imposed the clinical hold without relying on the ICH Guidance, making clear that the actual legal authority here is the regulation, not the Guidance. Cf. Nat'l Mining, 758 F.3d at 253 ("When an agency applies [a general

statement of] policy in a particular situation, it must be prepared to support the policy just as if the policy statement had never been issued." (quoting Pac. Gas & Elec. Co. v. Fed. Power Comm'n, 506 F.2d 33, 38 (D.C. Cir. 1974))). It is permissible for a general policy statement to forecast an agency's position, as the Guidance does here, so long as the policy statement has no actual legal effect. See id. at 252.

Other factors identified as important by the D.C. Circuit for distinguishing between legislative rules and general policy statements include "(1) the agency's own characterization of the action; (2) whether the action was published in the Federal Register or the Code of Federal Regulations; and (3) whether the action has binding effects on private parties or on the agency." Clarian Health West, LLC v. Hargan, 878 F.3d 346, 357 (D.C. Cir. 2017) (cleaned up). These factors admittedly "overlap" with the "legal effect" factor already analyzed above. Id. But they all, too, favor FDA. First, FDA characterizes the ICH Guidance as nonbinding. See 75 Fed. Reg. at 3471 (noting that the ICH Guidance "does not operate to bind" anyone); FDA-10910 (stating that ICH Guidance "contains nonbinding recommendations"). Second, the ICH Guidance was published in the Federal Register, not the Code of Federal Regulations. See 75 Fed. Reg. at 3471. And third, the ICH Guidance does not have actual binding effect, as made clear by the Remand Response's imposition of the clinical hold without relying on the Guidance.

Moreover, the hallmark of a binding rule is that "[i]t commands, it requires, it orders, it dictates." Nat'l Mining, 758 F.3d at 252–53 (quoting Appalachian Power Co. v. EPA, 208 F.3d 1015, 1023 (D.C. Cir. 2000)). Here, the text of the Guidance is "devoid of relevant commands." Nat'l Mining, 758 F.3d at 253. Instead, the Guidance couches all its statements with "recommendation" language. See, e.g., FDA-10917 (stating that the Guidance provides "Recommended Minimum Duration of Repeated-Dose Toxicity Studies to Support Clinical

Trials" (emphasis added)). Like the words "may" or "should," this "recommendation" language "suggests that the provisions . . . are meant to be precatory, not mandatory." Ass'n of Flight Attendants-CWA, AFL-CIO v. Huerta, 785 F.3d 710, 718 (D.C. Cir. 2015) (internal quotation marks omitted).

Nor does the Court agree with Vanda's related argument that the Remand Response itself is a legislative rule that "substantive[ly] amend[s]" an intentionally vague regulation by reading into it a specific numeric value (9 months). Pls.' Resp. at 8; see 21 C.F.R. § 312.23(a)(8) (stating that a clinical hold may be imposed if an IND lacks "[a]dequate information about pharmacological and toxicological studies of the drug involving laboratory animals or in vitro"). Such an argument would be applicable only if the ICH Guidance were an interpretive rule—which both sides agree it is not. See Defs.' MSJ at 45; Pls.' Resp. at 8. Rather than interpreting the regulation, FDA determined that in this case, the "adequate information" required was a 9-month nonrodent survey. This determination does not apply to future cases—it is limited to this particular IND and Vanda's specific request to be allowed to conduct a 12-month study of tradipitant in humans. See Remand Resp. at FDA-11124 ("[T]he data obtained through a 9-month toxicity study in nonrodents is scientifically necessary for an adequate assessment of the safety of a long-term clinical study of tradipitant in humans."). As the Supreme Court has said, "[t]he APA does not require that all the specific applications of a rule evolve by further, more precise rules rather than by adjudication." Shalala v. Guernsey Mem'l Hosp., 514 U.S. 87, 96 (1995). It was therefore permissible for FDA to flesh out what "adequate information" means in this case by an informal adjudication rather than by regulation.[4]

[4] During oral argument, Vanda's counsel suggested that the discussion of the scientific literature supporting a 9-month nonrodent study located at pp. 15–16 of the Remand Response, wherein FDA stated its conclusion that "such studies are the accepted scientific minimum to assess risks to human subjects in long-term clinical investigations," mandates a reading that the Response applies more broadly to cases other than this one. In effect,

For these reasons, the Court concludes (1) that the ICH Guidance is a general policy statement, not a binding legislative rule; (2) that FDA did not apply it as a binding rule in this case; and (3) that the Remand Response itself was not a binding legislative rule. Hence, notice and comment was not required.

2. Substantive Claims Against the Clinical Hold Decision

Finally, Vanda raises several arguments against the substance of FDA's scientific analysis: (1) that FDA ignored or misinterpreted studies that undercut its conclusion; (2) that FDA failed to explain why toxicity findings in nonrodent studies would be predictive of human toxicities; and (3) that the tradipitant-specific analysis in the Remand Response is litigation-driven, standardless, and ignores an intra-agency dispute over the proper interpretation of a study. The Court will first describe the general legal framework for reviewing agency scientific judgments and then take each of Vanda's arguments in turn.

In reviewing a challenge to agency action on summary judgment, the role of a district court is limited to determining "whether or not as a matter of law the evidence in the administrative record permitted the agency to make the decision it did." Ardmore Consulting Grp., Inc. v. Contreras-Sweet, 118 F. Supp. 3d 388, 393 (D.D.C. 2015) (citation omitted). "This standard of review is 'narrow,' and a court applying it 'is not to substitute its judgment for that of the agency.'"

counsel argued that any agency adjudication that analyzes scientific studies and makes a judgment call about what those studies mean or require constitutes a legislative rule, and so must first go through notice-and-comment rulemaking. The Court declines to adopt such a principle, which would make it difficult, if not impossible, for agencies to conduct adjudications. Here, FDA interpreted scientific studies, made a judgment about what those studies mean, and applied that judgment to Vanda's 12-month study proposal. Even if the agency may make a similar judgment call as to those scientific studies in similarly situated cases, the decision itself—the decision to reject Vanda's proposal—is specific to this case and does not constitute a legislative rule. The cases Vanda cites in support of its position are inapposite, as neither case took place in the context of an individual adjudication. See Safari Club Int'l v. Zinke, 878 F.3d 316, 320–21 (D.C. Cir. 2017) (rejecting agency findings, made without notice-and-comment rulemaking, that certain animal trophies could not be imported, because the agency findings did not occur in the context of "adjudicating a particular set of disputed facts" (internal quotation marks omitted)); Hudson v. Fed. Aviation Admin., 192 F.3d 1031, 1033–36 (D.C. Cir. 1999) (concluding that agency policy statement issued without notice-and-comment was proper).

Id. (quoting Motor Vehicle Mfrs. Ass'n of the U.S., Inc. v. State Farm Mut. Auto. Ins. Co., 463 U.S. 29, 43 (1983)). Courts must ensure that the agency "examine[d] the relevant [evidence]" and "articulate[d] a satisfactory explanation for its action[,] including a rational connection between the facts found and the choice made." State Farm, 463 U.S. at 43 (internal quotation marks omitted). But this explanation "need not be a model of analytic precision to survive a challenge." Coburn v. McHugh, 679 F.3d 924, 934 (D.C. Cir. 2012) (internal quotation marks omitted). Indeed, courts "must uphold a decision of less than ideal clarity if the agency's path may reasonably be discerned." Am. Radio Relay League, Inc. v. FCC, 524 F.3d 227, 248 (D.C. Cir. 2008) (emphasis added) (internal quotation marks omitted). And when reviewing an agency's scientific determinations, made "within [the agency's] area of special expertise, at the frontiers of science[,] . . . a reviewing court must generally be at its most deferential." Baltimore Gas & Elec. Co. v. Nat. Res. Def. Council, Inc., 462 U.S. 87, 103 (1983) (emphasis added); Int'l Fabricare Inst. v. EPA, 972 F.2d 384, 389 (D.C. Cir. 1992) ("In an area characterized by scientific and technological uncertainty, . . . this court must proceed with particular caution, avoiding all temptation to direct the agency in a choice between rational alternatives." (cleaned up)).

a. Vanda's claim that FDA ignored or misinterpreted studies

Vanda's first substantive claim is that FDA's analysis in the Remand Response "simply ignore[s] the Parkinson et al. study," Pls.' Resp. at 20, and misinterprets the Broadhead et al. paper, id. at 20–21.

The argument that FDA ignored the Parkinson study is difficult to understand. The Remand Response cites the Parkinson study as an example of an early study (conducted in 1992) that "provided the impetus for the international regulatory agencies to conduct a larger analysis based on a more thorough database." Remand Resp. at FDA-11122 n.52. The Response then goes

on to discuss more recent studies that, in FDA's view, adequately justify the need for 9-month nonrodent studies—in particular, a 2006–09 study that "affirmed that 6-month toxicity studies were insufficient to assess the long-term safety of drugs," and a 2015 study that "demonstrated the need for chronic toxicity studies in nonrodents . . . in the safety and risk assessment of drug products intended for long-term use in humans." Id. at FDA-11122–23. FDA clearly did not "ignore" the Parkinson study—Vanda may disagree with FDA's interpretation of the study, but where all a plaintiff does is "claim[] its own method is better, but provide[] no evidence that [the agency's] approach is unreasonable," that plaintiff's challenge cannot succeed. Petal Gas Storage, LLC v. FERC, 496 F.3d 695, 703 (D.C. Cir. 2007) (second emphasis added).

Similarly, Vanda contends that FDA has misinterpreted the Broadhead paper. This paper, in essence, looked at a set of rodent and nonrodent studies of varying durations for the purpose of, as relevant here, seeing whether toxicities (1) appeared in longer-duration studies that did not appear in shorter-duration studies, and (2) were different in rodents and nonrodents. See FDA-10701. The Remand Response referenced Broadhead for the proposition that "nonrodents frequently reveal toxicity that is not seen in rodents." Remand Resp. at FDA-11114. Vanda complains that FDA ignored other findings of the Broadhead paper, see Pls.' Resp. at 20, but upon further examination, it seems that Vanda's briefing misstates one of the Broadhead paper's conclusions[5] and ignores the paper's finding that longer-term dog studies did, in 62.5% of cases, reveal toxicity findings not present in rodent studies, FDA-10701–02. In any event, this Court's role is not to "second-guess the particular way the agency chooses to weigh the conflicting

[5] Vanda's opening brief stated that one of the Broadhead paper's "main conclusions was that there [is] not sufficient convincing evidence in the published literature to support or refute regulatory requirements for the routine use of the dog." Pls.' MSJ at 36 (internal quotation marks omitted). In fact, as Vanda later acknowledged in its response and reply brief, that was not the conclusion of the Broadhead paper, but instead was a statement from a different, earlier study. See Pls.' Resp. at 20 n.9. Vanda does not claim that the earlier study was part of the record before FDA.

evidence or resolve the dispute." United Steelworkers of Am. v. Marshall, 647 F.2d 1189, 1263 (D.C. Cir. 1980). Vanda has not shown that FDA's interpretation of the study is "unreasonable," and so its argument fails. See Petal Gas Storage, 496 F.3d at 703.

b. Vanda's claim that FDA failed to show that animal toxicities are predictive of human toxicities

Vanda's second substantive claim is that FDA did not conduct an "analysis of the predictive power of dog studies" before imposing the clinical hold. Pls.' Resp. at 22. In Vanda's view, therefore, because FDA has failed to show that dog studies can predict anything about what would happen in human studies, it has likewise failed to show a rational connection between the facts (that there are adverse toxicity findings in short-term dog tradipitant studies) and FDA's conclusion (that long-term nonrodent studies must be conducted to determine whether long-term human trials should be allowed to proceed). Id.

Vanda's argument is unpersuasive for the basic reason that the statutory and regulatory scheme here explicitly contemplates that the results of animal studies are predictive of the results of human trials. See, e.g., 21 U.S.C. § 355(i)(1)(A) (authorizing FDA to promulgate regulations for the "protection of the public health" that require drug sponsors to submit "preclinical tests (including tests on animals) . . . adequate to justify the proposed clinical [human] testing"); see also id. § 355(i)(2)(B) (requiring drug sponsors to submit "primary data tabulations from animal or human studies" (emphasis added)); 21 C.F.R. § 312.23(a)(8) (requiring drug sponsors to submit "[a]dequate information" about studies "involving laboratory animals" which allow the sponsor to conclude "that it is reasonably safe to conduct" human trials). Indeed, the entire point of conducting animal studies—which the legal framework mandates—is that the results of those studies have some relevance to humans. That is, the framework assumes that if a drug is shown not to be toxic in animals, it is at least reasonably likely to be safe to conduct human trials.

In the Remand Response, FDA acknowledged this linkage between animals and humans with the statement that "findings in animal toxicity studies are generally applicable to humans." Remand Resp. at FDA-11113. That is the rational connection that Vanda deems missing from the Remand Response. And indeed, FDA is not free, legally speaking, to simply allow drug sponsors to proceed with human trials without adequate animal studies. While Vanda is correct that FDA does not explicitly support this statement with studies, the support is implicit in the legal framework and in common sense. If Vanda has a quarrel with animal studies and their predictive power for humans in general, its fire would be more appropriately aimed at the controlling statute and regulations, not at FDA's actions in this case.

To the extent that Vanda's point is that FDA already has long-term rodent studies, and has no need for long-term nonrodent studies as well, the Remand Response clearly states its rationale for requiring studies in a second species: there was a need for a second, nonrodent species, because existing studies showed "dissimilar results in . . . two rat strains," and "inconsistent toxicities between strains of one species can be corroborated as relevant to humans if observed in a second species." Remand Resp. at FDA-11118. Moreover, the Remand Response points out that Vanda itself, in its submissions to FDA in another IND, acknowledged "that the pharmacokinetic profile of tradipitant in dogs is consistent with pharmacokinetic data in humans," further supporting the need for nonrodent (here, dogs) studies to supplement existing rodent studies. Id.

Without additional nine-month nonrodent studies, FDA would either have to attempt to extrapolate long-term toxicity risks from short-term nonrodent studies or, alternatively, allow Vanda to move forward with human studies and see what effects tradipitant has in the long term. According to the Remand Response, after a lengthy analysis of the studies supporting and opposing the 9-month nonrodent requirement, FDA has concluded that neither of those approaches would

ensure the safety of humans subjected to long-term use of tradipitant. Given that the Court is "at the apex of [its] deference," Petal Gas Storage, 496 F.3d at 702, when dealing with agency judgments "at the frontiers of science," Baltimore Gas & Elec., 462 U.S. at 103, the Court concludes that the legal framework and Remand Response here adequately supply a "rational connection" between the facts and FDA's conclusion.

c. Vanda's claims about the tradipitant-specific reasoning

Vanda also takes issue with three aspects of the Remand Response's tradipitant-specific reasoning, arguing that it (1) is litigation-driven, (2) is standardless, and (3) ignores a dispute among FDA staff as to the proper interpretation of a tradipitant study. See Pls.' Resp. at 24–28.

With respect to whether the tradipitant-specific concerns are litigation-driven, this argument is dead in the water: the administrative record makes clear that FDA had noticed and was concerned about the adverse toxicity findings in the 3-month nonrodent studies well before this lawsuit was filed in February 2019. See FDA-10871 (December 2018 memorandum discussing adverse toxicity findings); FDA-10884–85 (same); FDA-10893 (December 2018 meeting slides noting adverse toxicity findings); Remand Resp. at FDA-11117 n.32 (listing dates in 2016 that FDA had reviewed 3-month tradipitant studies and noted adverse toxicity findings).

As to whether FDA's hold decision was standardless: the regulation at issue here uses capacious language like "[a]dequate information." 21 C.F.R. § 312.23(a)(8). As Justice Kavanaugh recently noted in his concurrence in Kisor v. Wilkie, 139 S. Ct. 2400 (2019), when statutes or regulations "employ broad and open-ended terms like 'reasonable,' 'appropriate,' 'feasible,' or 'practicable,'" the terms "afford agencies broad policy discretion," id. at 2448–49 (Kavanaugh, J., concurring). Courts are "generally unwilling to review line-drawing performed by [an agency] unless a petitioner can demonstrate that lines drawn . . . are patently unreasonable,

having no relationship to the underlying regulatory problem." ExxonMobil Gas Mktg. Co. v. FERC, 297 F.3d 1071, 1085 (D.C. Cir. 2002) (internal quotation marks omitted). Here, the underlying regulatory problem is preventing unreasonably risky trials of experimental drugs on human subjects, and FDA supported its decision to require 9-month nonrodent trials in this case with reference to specific adverse findings in 3-month nonrodent trials and in trials of similar drugs. The hold decision was clearly within the "zone of reasonableness," WorldCom, Inc. v. FCC, 238 F.3d 449, 462 (D.C. Cir. 2001), even if Vanda disputes whether FDA's "numbers are precisely right," id.

And as to the internal dispute among FDA staff with respect to the proper interpretation of a tradipitant study, as FDA points out, "disagreement among agency staff during the decisionmaking process does not fatally undermine the agency's final determination, nor does it alone justify according the agency's final decision less deference than usual." Cumberland Pharm. Inc. v. FDA, 981 F. Supp. 2d 38, 52 (D.D.C. 2013); see also San Luis Obispo Mothers for Peace v. U.S. Nuclear Regulatory Comm'n, 789 F.2d 26, 33 (D.C. Cir. 1986) (en banc) ("The position of an agency's staff, taken before the agency itself decided the point, does not invalidate the agency's subsequent application and interpretation of its own regulation."). Here, though Vanda is right that an FDA official in 2005 said that "no significant adverse effects . . . were observed" in the study at issue, that official also said that the study "cannot be considered to have adequately characterized the toxic potential" of tradipitant. Ex. 2, Defs.' Reply Mem. in Support of Their Cross-Mot. for Summ. J. [ECF No. 45-2], at 6–7. And in any event, no final agency decision resulted from the 2005 memorandum. In this case, on the other hand, FDA as an agency adopted the position that the study did show adverse effects. The fact that there had been a contrary

interpretation of the study by one official years earlier "does not fatally undermine" the partial clinical hold here. Cumberland Pharm., 981 F. Supp. at 52.

* * *

In sum, then, the Court is unpersuaded by Vanda's procedural and substantive arguments against the Remand Response. Accordingly, Vanda's motion for summary judgment will be denied and FDA's cross-motion will be granted.

Analysis: Motion to Complete/Supplement the Administrative Record

Next, Vanda has moved to complete or supplement the administrative record. Many of the arguments in this motion mirror the arguments made in Vanda's motion for summary judgment, which the Court has already addressed and will not discuss again here. See supra at 11–12 (whether Vanda's post-remand submissions should have been considered when not submitted through proper administrative channels); id. at 10–11 (whether Vanda should have been allowed to rebut, pre-imposition of a hold, FDA's evidence); id. at 9–12 (whether FDA "skewed" the record); id. at 10–11 (the scope of the Court's remand order). As to the remaining arguments:

1. Vanda argues that the Court should require FDA to complete the record by including the 2005 memorandum of an FDA official evaluating a study about tradipitant. Vanda alleges that the memo was "directly or indirectly considered" by FDA. Statement of P.&A. in Supp. of Pls.' Mot. to Complete and Suppl. the Admin. R. ("Mot. to Complete") [ECF No. 25-1] at 2, 4; see Oceana, Inc. v. Ross, 290 F. Supp. 3d 73, 77 (D.D.C. 2018) ("The administrative record consists of all documents and materials that the agency directly or indirectly considered, no more and no less." (internal quotation marks omitted)).

Vanda supports its statement that the 2005 memo (which was not cited in the Remand Response) was "considered" by FDA in imposing the partial clinical hold by pointing to a more

recent memorandum (which was cited in the Remand Response). In the more recent memo, a different FDA official analyzed the same study as was at issue in the 2005 memo, at one point citing the 2005 memo to note that the author of that memo had "agreed with the sponsor that no significant adverse effects were noted in this study." FDA-10839. Because the 2005 memo was cited in a memorandum that was cited by the Remand Response, Vanda argues that the 2005 memo was indirectly considered by FDA.

But "the mere mention of a document in . . . the record does not always mean, ipso facto, that the agency considered the document." Oceana, Inc., 290 F. Supp. 3d at 79. Indeed, "[a]n agency's decision to rely on a document to support a factual assertion is different from its mere mention of a document's existence," because merely mentioning a document "may be insufficient, on its own, to show consideration," while using that same document to support a factual assertion would be sufficient, id. at 80. Here, Vanda has put forward no "concrete evidence" or "reasonable, non-speculative grounds" that the 2005 memo was actually considered by FDA in deciding to impose the partial clinical hold, and completion of the record with the memo is thus inappropriate. Charleston Area Med. Ctr. v. Burwell, 216 F. Supp. 3d 18, 23 (D.D.C. 2016) (internal quotation marks omitted); see also Forest Cty. Potawatomi Cmty. v. United States, 270 F. Supp. 3d 174, 182 (D.D.C. 2017) (denying record completion for documents cited within other record documents where there was "simply no evidence that the [defendants] actually considered those referenced documents").[6]

[6] Similarly, Vanda has submitted no evidence that its "Breakthrough Therapy" designation paperwork, see Mot. to Complete at 7, was considered by the decisionmakers responsible for the partial clinical hold. See Fort Sill Apache Tribe v. Nat'l Indian Gaming Comm'n, 345 F. Supp. 3d 1, 10 (D.D.C. 2018) ("The issue does not turn on whether specific documents were in the direct, physical possession of agency decisionmakers, but whether they were directly or indirectly considered by those decisionmakers.").

2. Vanda argues that FDA is required to include in the record the studies cited in the Humane Society letter because Janet Woodcock, the Director of the Center for Drug Evaluation and Research, sent a form response to the letter reading "Thank you for writing. We will take your comments into account and evaluate the studies you reference." Mot. to Complete, Ex. M. Setting aside the fact that Ms. Woodcock later sent the Humane Society another letter reading "[d]ue to pending legal matters, FDA won't be able to comment on your request," Ex. 1, Defs.' MSJ, Ms. Woodcock was not the person responsible for evaluating and making a clinical hold decision on Vanda's IND—that was Julie Beitz, the Director of the Office of Drug Evaluation III. See Remand Resp. at FDA-11127. And the letter was not submitted through the designated administrative channels, nor is FDA required to take account of any interested party commentary on an agency decision. See 21 U.S.C. § 355(i)(3)(A).[7]

3. Aside from its completion arguments, Vanda also argues that the Court should order that some items be added to the record as a supplement, because they are "background information . . . needed to determine whether the agency considered all the relevant factors." Mot. to Complete at 10 (quoting Oceana, Inc., 290 F. Supp. 3d at 77–78). However, supplementation "is generally not permitted." Agility Pub. Warehousing Co. v. U.S. Dep't of Defense, 246 F. Supp. 3d 34, 51 (D.D.C. 2017) (citing Cmty. For Creative Non-Violence v. Lujan, 908 F.2d 992, 998 (D.C. Cir. 1990)). To be permitted to supplement the record, Vanda "must first establish that the agency acted in bad faith or otherwise behaved improperly, or that the record is so bare that it prevents effective judicial review." Id. (citation omitted). This exception is "appropriate only in

[7] The Court also rejects Vanda's argument that the letter must be included in the record pursuant to the "Citizen Petitions" portion of FDA regulations. See Mot. to Complete at 9 n.3. Neither the letter, nor Vanda's IND, complied with the mandatory formatting or submission requirements contained in that regulation. See 21 C.F.R. § 10.30(b)–(c).

the context of 'gross procedural deficiencies.'" Id. (quoting CTS Corp. v. EPA, 759 F.3d 52, 64 (D.C. Cir. 2014)).

Vanda cannot meet this "high bar." Id. The Court has all the information it needs to determine "whether the agency considered all the relevant factors." Oceana, Inc., 290 F. Supp. 3d at 78. The relevant factor here was the adequacy of the information submitted in the IND to ensure that human subjects would not face unreasonable risks. See 21 C.F.R. § 312.23(a)(8). Here, the record already contains many studies, both for and against Vanda's position. The record is therefore not so bare as to prevent effective judicial review. Nor can Vanda show that FDA acted improperly or in bad faith in creating the record.

The Court also declines to supplement the record with declarations from the individual plaintiffs. These declarations would be useful, as Vanda points out, only if FDA challenges the plaintiffs' standing. Mot. to Complete at 11. But, as FDA acknowledges, any such challenge would be doomed, because Vanda clearly has standing, making it "immaterial that other plaintiffs might be unable to demonstrate their own standing." J.D. v. Azar, 925 F.3d 1291, 1323 (D.C. Cir. 2019).

Accordingly, the Court will deny Vanda's motion to complete or supplement the administrative record.

Analysis: Motion to File Amicus Brief

Finally, the Humane Society has moved to file an amicus brief. FDA opposes the motion. It is "solely within the discretion of the Court to determine the fact, extent, and manner of participation by the amicus." United States v. Microsoft Corp., 2002 WL 319366, at *2 (D.D.C. Feb. 28, 2002). "Courts in this district have granted leave where a movant sought to provide information regarding a significant, unclear legal issue, and denied leave where a movant sought

to present arguments and insights that were not relevant to the stage of the litigation." Hopi Tribe v. Trump, 2019 WL 2494161, at *3 (D.D.C. March 20, 2019) (citations omitted); cf. WildEarth Guardians v. Zinke, 368 F. Supp. 3d 41, 59 (D.D.C. 2019) (denying motion to file amicus brief where it did "not have unique information or perspective that can help the court"). The Court concludes that the arguments in the Humane Society's brief are either impermissible or duplicative of the arguments in Vanda's motion for summary judgment.

The brief first argues that "dog models are generally poor predictors of human responses," citing a number of extra-record studies as support. Amicus Curiae Br. of the Humane Society of the United States in Supp. of Pls. ("Humane Society Br.") [ECF No. 27-1] at 4. Even excusing the citations to extra-record studies, this argument is just a variant of an argument made by Vanda. See Pls.' MSJ at 39–40 (disputing FDA's analysis of whether the "predictive value" of 9-month nonrodent studies "is enough to justify" the studies).

The brief's second and third arguments are that "non-animal alternatives can determine human safety risks," Humane Society Br. at 6, and that dog studies are nonpredictive of human results where the dogs are inbred, id. at 8. As support for the second argument, the brief cites extra-record studies to show that computer models or in silico modeling may be able to predict human responses to drugs more effectively than dog studies. Id. at 6–8. As support for the third argument, the brief cites extra-record studies to show that many dogs used for studies are inbred and thus may be less predictive of human toxicities. Id. at 8–11. But none of these studies are in the administrative record. And there is no allegation that they were "before" FDA when it was making its decision. Thus, these arguments cannot help the Court evaluate whether FDA's partial clinical hold decision, based on the record before the agency, was arbitrary and capricious.

The brief's fourth and final argument is that FDA's explanation for the partial clinical hold is insufficient. Id. at 11. This section of the brief quite plainly makes the same arguments that Vanda made in its motion for summary judgment. For instance, the brief disputes FDA's interpretation of Broadhead and the existing studies of tradipitant, just as Vanda did. See Pls.' MSJ at 35–36, 43–45.

Accordingly, the Court will deny the Humane Society's motion for leave to file an amicus brief.

Conclusion

For the foregoing reasons, the Court will (1) grant FDA's cross-motion for summary judgment; (2) deny Vanda's motion for summary judgment; (3) deny Vanda's motion to complete or supplement the administrative record; and (4) deny the Humane Society's motion for leave to file an amicus brief. A separate order has been issued on this date.

/s/
JOHN D. BATES
United States District Judge

Dated: January 31, 2020