UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

ATHENEX INC., et al.,	)	
	)	
Plaintiffs,	)	
	)	
v.	)	**Case No. 19-cv-00603 (APM)**
	)	
ALEX M. AZAR II, et al.	)	
	)	
Defendants.	)	
	)	

MEMORANDUM OPINION

I. INTRODUCTION

In 2013, Congress added Section 503B to the Food, Drug, and Cosmetic Act, creating a new category of drug manufacturer known as an "outsourcing facility." Such facilities are permitted to sell large quantities of compounded drugs directly to hospitals and health care professionals without receiving premarket approval from the Food and Drug Administration ("FDA"), so long as the facility satisfies certain statutory requirements. One such requirement concerns when an outsourcing facility can use a "bulk drug substance"—that is, a drug's active ingredient—to compound a drug product. In such cases, FDA must declare there to be a "clinical need" for the "bulk drug substance" as a precondition to compounding with such substance.

Plaintiffs presently operate an outsourcing facility that produces a drug product using the bulk drug substance vasopressin. On March 4, 2019, FDA announced that vasopressin is not a "bulk drug substance for which there is a clinical need" because already available on the market is an FDA-approved drug that could be used to meet the very patient needs that Plaintiffs claim make it necessary to bulk compound using vasopressin. FDA's decision, if valid, forecloses Plaintiffs from selling their product.

Plaintiffs filed this action challenging FDA's refusal to place vasopressin on the Section 503B "clinical need" list. They contend that FDA's inquiry improperly took the availability of a branded drug product into account when assessing "clinical need." Instead, Plaintiffs argue, the "clinical need" inquiry should be confined to simply asking whether there is a therapeutic use for the bulk drug substance, and vasopressin easily meets that standard. Alternatively, Plaintiffs maintain that, even under FDA's reading of "clinical need," vasopressin qualifies.

The court finds that FDA's method of determining whether there is a "clinical need" for a bulk drug substance gives effect to the unambiguously expressed intent of Congress. The court also concludes that FDA's exclusion of vasopressin from the "clinical need" list was not arbitrary and capricious. Accordingly, the court grants Defendants' Cross-Motions for Summary Judgment and denies Plaintiffs' Motion for Summary Judgment.

II. BACKGROUND

A. Factual Background

1. Compounding

In the pharmaceutical drug industry, the term "compounding" refers to the act of "combining, admixing, mixing, diluting, pooling, reconstituting, or otherwise altering of a drug or bulk drug substance to create a drug." 21 U.S.C. § 353b(d)(1). The compounding of drugs performs "an important role for patients for whom an FDA-approved drug is not appropriate." Administrative Record, ECF No. 35 [hereinafter R.], at 89. Take the case of a person who is allergic to a particular ingredient in an FDA-approved drug. Through compounding, an approved drug can be reconstituted to eliminate the allergen while still delivering the drug's therapeutic benefit. *Id.* Another example is that certain patient populations may have difficulty ingesting a

drug in its approved pill form. Such a drug can be compounded to liquid form for easier consumption.

Historically, local pharmacists have been responsible for compounding drugs, typically in small quantities to fill the needs of individual patients with valid prescriptions. That practice still exists today. FDA has not in the past, nor does it now, require local pharmacists to obtain regulatory approval before creating and selling a compounded drug product. *See generally* 21 U.S.C. § 353a (Section 503A of the Food, Drug, and Cosmetic Act).

Over time, however, a new kind of drug manufacturer emerged, one that compounded drugs in bulk quantities and marketed such drugs directly to hospitals and physicians. Even though they manufactured on a larger scale, these bulk compounders, like local pharmacists, were not required to subject their compounded drug products to "premarket review for safety, effectiveness, and quality" by FDA before bringing them to market. R. at 89.

2. Drug Quality and Security Act

The era of lightly regulated bulk compounding ended following a tragic event. In 2012, the New England Compounding Center ("NECC") in Framingham, Massachusetts, produced contaminated injections that caused a meningitis outbreak, killing more than 60 people and infecting hundreds more. *See id.* Within fourteen months of the NECC outbreak, Congress passed the Drug Quality and Security Act ("DQSA"), which added Section 503B to the Food, Drug, and Cosmetic Act ("FDCA"). Section 503B created a new category of drug maker called an "outsourcing facility." *See* 21 U.S.C. § 353b. An outsourcing facility may compound drug products in large quantities without obtaining a prescription for "an identified individual patient[ ]." *Compare* 21 U.S.C. § 353b(d)(4)(C) *with* 21 U.S.C. § 353a. Such facilities are

permitted to sell bulk compounded drug products to health care practitioners and hospitals as "office stock," for providers to have available and to use on an as-needed basis. *See* R. at 52.

Section 503B also enhanced FDA's authority to regulate outsourcing facilities. An outsourcing facility remains exempt from the FDCA's premarket approval requirements and certain labeling and supply-chain requirements, but only if it satisfies eleven statutory criteria. *See* 21 U.S.C. § 353b(a) (exempting compounded drugs from 21 U.S.C. §§ 352(f)(1), 355, and 360eee-1). A non-exhaustive list of these criteria include: (1) the manufactured drug is compounded at a facility that is subject to specified FDA licensing, reporting, fees, and inspection requirements, *id.* §§ 353b(a)(1), (a)(9), (a)(11), 353b(b); (2) the ingredients used in the compounding process meet national standards, *id.* § 353b(a)(3); (3) FDA has not deemed the drug to be unsafe, nor difficult to compound, *id.* §§ 353b(a)(4), (a)(6); (4) "the drug is not essentially a copy of one or more approved drugs," *id.* § 353b(a)(5); (5) the drug is labeled in accordance with statutory requirements, *id.* § 353b(a)(10); and (6) the drug will not be sold or transferred by an entity other than the outsourcing facility, *id.* § 353b(a)(8).

In addition to the foregoing requirements, Section 503B authorizes two ways in which to bulk compound a drug. The first is known as "sterile-to-sterile compounding." Under this approach, an outsourcing facility starts with an FDA-approved drug, disassembles it, and alters it into a finished drug product for sale. The second method is known as "bulk compounding." That process starts with a "bulk drug substance," instead of an FDA-approved drug. A "bulk drug substance" is an ingredient that furnishes pharmacological activity and is incorporated into a finished drug product to achieve the intended purpose of compounding, such as removal of an

allergen.[1] The FDA requires that a drug must be "compounded in an outsourcing facility that does not compound using bulk drug substances . . . , unless the bulk drug substance appears on a list established by the Secretary identifying bulk drug substances for which there is a clinical need . . .," *id.* § 353b(a)(2)(A)(i), or "the drug compounded from such bulk drug substance appears on the drug shortage list," *id.* at (A)(ii). Thus, an outsourcing facility's legal authority to compound using a bulk drug substance depends in the first instance on a listing determination by FDA.

3. FDA's Decision Not to List Vasopressin

Plaintiffs Athenex Inc. and its affiliated entities operate an outsourcing facility that compounds with a bulk drug substance called vasopressin. Vasopressin "increase[s] blood pressure in adults with vasodilatory shock . . . who remain hypotensive despite fluids and catecholamines." R. at 27. As a result of the DQSA, Plaintiffs cannot continue to manufacture their bulk drug product using vasopressin, unless FDA places it on the "clinical need" list. The "drug shortage" list is not at issue in this case.

Plaintiffs began the process to get vasopressin listed years ago. In 2013 and 2014, FDA issued a notice seeking nominations of bulk drug substances to place on the "clinical need" list, and FDA provided "more detailed information on what it needs to evaluate a nomination." *See* R. at 1, 4. In 2015, FDA again clarified the requirements for a nomination. *See id.* at 9–13. Fifteen months later, in January 2017, FDA issued an "interim regulatory policy" for the "clinical need" list. *See id.* at 34–45. The interim guidance placed each of the nominated substances into one of three categories: Category 1 substances signified those under evaluation; Category 2 included

[1] A bulk drug substance is defined as "any substance that is intended for incorporation into a finished drug product and is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body." 21 C.F.R. § 207.1 (synonymous with "active pharmaceutical ingredient"). A finished drug product means "a finished dosage form (e.g., tablet, capsule, or solution) that contains at least one [bulk drug substance], generally, but not necessarily, in association with other ingredients in finished package form suitable for distribution to pharmacies, hospitals, or other sellers or dispensers of the drug products to patients or consumers." *Id.*

substances that raise significant safety risks; and Category 3 identified substances without adequate support for listing. *See id.* at 40–41. FDA classified vasopressin as a Category 1 substance. *See id.* at 45. For Category 1 substances, like vasopressin, FDA stated that it "d[id] not intend to take action against an outsourcing facility for compounding a drug using a bulk drug substance" during the interim review period. *See id.* at 43. Therefore, Plaintiffs continued to manufacture their bulk drug product while vasopressin remained under review for "clinical need" listing.

As of early 2018, FDA had yet to explain how it would determine whether a bulk drug substance would qualify for the "clinical need" list. That changed in March 2018, when the agency issued a draft guidance document titled, "Evaluation of Bulk Drug Substances Nominated for Use in Compounding Under Section 503B of the Federal Food, Drug, and Cosmetic Act." *See id.* at 46–67. The draft guidance stated that, if the bulk drug substance is a component of an FDA-approved drug product, the agency will consider two threshold questions. FDA framed the first question as follows:

> Is there a basis to conclude, for each FDA-approved product that includes the nominated bulk drug substance, that (i) an attribute of the FDA-approved drug product makes it medically unsuitable to treat certain patients for a condition that FDA has identified for evaluation, and (ii) the drug product proposed to be compounded is intended to address that attribute?

Id. at 60. FDA explained the reason for asking this first question is that, "[u]nless an attribute of the FDA-approved drug is medically unsuitable for certain patients, and a drug product compounded using a bulk drug substance that is a component of the approved drug is intended to address that attribute, there is no clinical need to compound using that bulk drug substance." *Id.* As to the second threshold inquiry, FDA would ask:

> Is there a basis to conclude that the drug product proposed to be compounded must be produced from a bulk drug substance rather than from an FDA-approved drug product?

Id. at 60. If the answer to either threshold question is "no," FDA stated, it would not list the bulk drug substance. *See id.* If the agency determines the answer is "yes" to both questions—or if the bulk drug substance is *not* a component of an FDA-approved drug product—the agency would make a second inquiry. At this step, FDA would consider various additional factors, including the "physical and chemical characterization of the substance; any safety issues raised by the use of the substance in compounding; the available evidence of effectiveness or lack of effectiveness of a drug product compounded with the substance, if any such evidence exists; and current and historical use of the substance in compounded drug products." *Id.* As to this second-step inquiry, FDA said that it would "conduct a balancing test . . . under which [it] would consider each factor in the context of others and to balance them, on a substance-by-substance basis, to determine whether the substance is appropriate for inclusion" on the "clinical need" list. *Id.*

In August 2018, FDA announced its intention not to include vasopressin on the "clinical need" list. *See id.* at 109. The agency followed the two-step inquiry described in the draft guidance. FDA decided that vasopressin did not make it past the first step. *See id.* FDA explained that the nomination of vasopressin "[did] not identify an attribute of Vasostrict," the FDA-approved drug containing vasopressin, "that makes [Vasostrict] medically unsuitable for patients." *Id.* Thus, there was no "clinical need" to bulk compound with vasopressin. FDA also specifically rejected the need for vasopressin at a higher concentration than the approved product. *Id.*

Plaintiffs submitted a comment challenging FDA's intent to exclude vasopressin. Plaintiffs argued that FDA had misinterpreted Section 503B and that, properly understood, the statute simply requires the agency to answer whether there is a "clinical need" for the bulk drug substance itself,

without reference to the availability and suitability of an FDA-approved product. *Id.* at 273–78. Thus, under Plaintiffs' reading, vasopressin meets the standard of "clinical need" simply because it has a demonstrated therapeutic value. *Id.* Alternatively, Plaintiffs maintained that, even under FDA's interpretation of Section 503B, vasopressin qualified for listing. Specifically, Plaintiffs asserted that Vasostrict was medically unsuitable to treat certain patients because: (1) Vasostrict contains chlorobutanol, an allergen for some patients, and (2) it is not available in ready-to-use form but must be diluted before use. *See id.* at 256. Plaintiffs' product, they insisted, filled these therapeutic gaps.

Rejecting both arguments, FDA issued a final notice on March 4, 2019, stating that it would not place vasopressin on the "clinical need" list. *See id.* at 1600–05. As to Plaintiffs' statutory interpretation argument, FDA adhered to its understanding that "Congress intended for the Agency" as part of the "clinical need" assessment "to evaluate the need for outsourcing facilities to use the bulk drug substances to compound drug products." *Id.* at 69. With respect to Plaintiffs' alternative position, FDA found lacking the asserted needs for bulk-produced vasopressin. FDA observed that there is available a chlorobutanol-free formulation of Vasostrict, and Plaintiffs "fail[ed] to explain why that formulation would be medically unsuitable for patients who have an allergy to chlorobutanol." *See id.* at 1604. The agency also rejected the need for a ready-to-use product, concluding that Plaintiffs "d[id] not show that [Vasostrict], when not manufactured in the ready-to-use form, is medically unsuitable for certain patients." *Id.* at 1605. Furthermore, even if Vasostrict were medically unsuitable, the agency found that Plaintiffs did not "establish that drug products in the relevant concentrations, including ready-to-use products, cannot be prepared from [Vasostrict]"—and instead must be prepared using vasopressin. *Id.* Other commenters had noted that a different outsourcing facility, owned by PharMEDium, compounds a ready-to-use drug with

Vasostrict as its starting material. *Id.* at 198. Consequently, FDA declined to find a "clinical need" for bulk-compounded vasopressin under Section 503B.

B. Procedural Background

On March 4, 2019, the very same day that FDA announced its final decision not to list vasopressin, Plaintiffs filed suit under the Administrative Procedure Act ("APA") and moved for a temporary restraining order and preliminary injunction. *See* Compl. ECF No. 1 [hereinafter Compl.]; *see also* Pls.' Mot. for Temporary Restraining Order and Preliminary Injunction, ECF No. 2. FDA agreed to stay any enforcement action with respect to Plaintiffs' continued bulk compounding of vasopressin until the court issued a decision on the merits. *See* Joint Mot. to Enter Scheduling Order, ECF No. 19. The court therefore denied the motion and entered a scheduling order for summary judgment briefing. *See* Order, ECF No. 20; *see also* Order, ECF No. 22. The court also permitted Par Sterile Products, LLC and Endo Par Innovation Company, LLC, the owners of Vasostrict, to intervene as defendants. *See* Order, ECF No. 20.

Plaintiffs filed their Motion for Summary Judgment on March 18, 2019, *see generally* Pls.' Mot., ECF No. 23 [hereinafter Pls.' Mot.], and the Federal Defendants[2] and Defendants Par Sterile Products and Endo Par Innovation Company filed their motions on March 29, 2019, *see* FDA Def.'s Mot., ECF No. 25 [hereinafter FDA Mot.]; *see also* Par Defs.' Mot., ECF No. 27. The court held oral argument on the motions on April 30, 2019.

III. LEGAL STANDARD

In cases that involve review of final agency action under the APA, the district court "sits as an appellate tribunal" and "the entire case on review is a question of law." *Am. Biosci., Inc. v.*

[2] The Federal Defendants are Alex M. Azar, II, in his official capacity as Secretary of Health and Human Services; the U.S. Department of Health and Human Services; Scott Gottlieb, in his official capacity as Commissioner of FDA; and FDA.

Thompson, 269 F.3d 1077, 1083 (D.C. Cir. 2001) (internal quotations omitted). The court's review is limited to the administrative record, and "its role 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." *Philip Morris USA Inc. v. FDA*, 202 F. Supp. 3d 31, 45 (D.D.C. 2016) (cleaned up).

When reviewing an agency's interpretation of a statute, the court employs the two-step inquiry set out in *Chevron U.S.A., Inc. v. Natural Resources Defense Council*, 467 U.S. 837 (1984). *See City of Arlington v. FCC*, 569 U.S. 290, 296–97 (2013). At step one, the court must determine whether "Congress has directly spoken to the precise question at issue," and if Congress has, the court "must give effect to the unambiguously expressed intent of Congress." *Chevron*, 467 U.S. at 842–43. The court must "employ the traditional tools of statutory construction to interpret the statute and to resolve any ambiguities." *Dist. of Columbia v. Dep't of Labor*, 819 F.3d 444, 449 (D.C. Cir. 2016). It must analyze "the language itself, the specific context in which that language is used, and the broader context of the statute as a whole." *Robinson v. Shell Oil Co.*, 519 U.S. 337, 341 (1997). Furthermore, for a plaintiff to prevail under *Chevron* step one, it "must do more than offer a reasonable or, even the best, interpretation; it must show the statute *unambiguously* forecloses the [agency's] interpretation." *Village of Barrington v. Surface Transp. Bd.,* 636 F.3d 650, 661 (D.C. Cir. 2011) (emphasis in original).

If Congress has not spoken directly to the issue—because "the statute is silent or ambiguous"—the court, at *Chevron* step two, must side with the agency if its answer "is based on a permissible construction of the statute." *Chevron*, 467 U.S. at 843. An agency receives deference at *Chevron* step two if it has "offered a reasoned explanation for why it chose [its] interpretation." *Village of Barrington*, 636 F.3d at 660.

IV. DISCUSSION

A. *Chevron* Step One

1. The Provision's Plain Meaning

The court starts with the "language itself." *Robinson*, 519 U.S. at 341. The disputed portion of Section 503B requires "the drug [to be] compounded in an outsourcing facility that does not compound using bulk drug substances . . . unless the bulk drug substance appears on a list established by the Secretary identifying bulk drug substances for which there is a clinical need . . . ." 21 U.S.C. § 353b(a)(i). Plaintiffs interpret the phrase "bulk drug substances for which there is a clinical need" to require FDA to focus exclusively on the bulk drug substance without looking to "which branded drugs exist at the time." *See* Pls.' Mot., Pls.' Mem., ECF No. 23-1 [hereinafter Pls.' Mem.], at 18. Plaintiffs reason that because "clinical need" modifies "bulk drug substance," FDA must ask only whether there is a clinical need for vasopressin, i.e., whether vasopressin is needed for patient treatment, and nothing more. *See id.* at 15–17. By that standard, Plaintiffs maintain, vasopressin easily qualifies, as evidenced by the fact that it is an active ingredient in an FDA-approved drug. *See id.* at 18; *see also* Compl. ¶ 54. Defendants, on the other hand, understand the provision to require FDA to consider whether a finished bulk drug product containing vasopressin is necessary *relative* to FDA-approved products containing vasopressin. *See* FDA Mot., FDA Mem., ECF No. 25-1 [hereinafter FDA Mem.], at 17–18.

The term "clinical need" does not lend itself to a straightforward reading. It is not defined in the FDCA. Nor does it appear anywhere else in the United States Code. Turning to the dictionary for guidance, "clinical" means "relating to the observation and treatment of actual patients rather than theoretical or laboratory studies," OXFORD DICTIONARY,[3] and "need" means

[3] https://en.oxforddictionaries.com/definition/clinical (last visited July 31, 2019).

"circumstances in which something is necessary; necessity," OXFORD DICTIONARY.[4] Thus, Congress required FDA to determine whether a bulk drug substance is "necessary" for the "treatment of actual patients." That question, however, begs another one: "Necessary" relative to what? Whether something is "necessary" cannot be determined in a vacuum. The presence or absence of "need" must be measured against some point of reference. Is vasopressin "necessary" as a bulk drug substance in the sense that physicians "need" it to treat patients? The answer is "yes." Vasopressin has therapeutic value for patients and therefore it is "needed" for treatment. On the other hand, is vasopressin "necessary" as a component of a bulk drug product such that, without it, physicians would be unable to treat patients? The answer is "no." The FDA-approved drug Vasostrict can serve the same clinical purpose as Plaintiffs' product. Thus, whether there is a "clinical need" for a particular bulk drug substance depends on how one frames the question.

To address this ambiguity, the court looks to the statutory purpose of the term "clinical need." *United States v. Cordova*, 806 F.3d 1085, 1099 (D.C. Cir. 2015). Congress plainly thought that there are some bulk drug substances for which there is a "clinical need" and others for which there is not. Otherwise, why else would Congress direct FDA to answer the question? Congress therefore meant for the "clinical need" inquiry to perform a sorting function. FDA's understanding of "clinical need" carries out this purpose; Plaintiffs' does not. This becomes clear when a bulk drug substance is thought of as an active pharmaceutical ingredient. *See* 21 C.F.R. § 207.1 (defining "bulk drug substance" the same as "active pharmaceutical ingredient"). An "active pharmaceutical ingredient" is "any substance that is intended for incorporation into a finished drug product and is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of

[4] https://en.oxforddictionaries.com/definition/need (last visited July 31, 2019).

the body." *Id.* Under Plaintiffs' reading, there always will be a "clinical need" for any compoundable active pharmaceutical ingredient because, by definition, such an ingredient is one that "furnishes pharmacological activity" or effects "diagnosis, cure, mitigation, treatment, or prevention of disease." In other words, it delivers some therapeutic benefit. So, for example, Plaintiffs say, there is a "clinical need" for vasopressin because it is used to treat life-threatening and emergency conditions, such as vasodilatory shock, diabetes insipidus, and gastrointestinal bleeding. *See* Compl ¶¶ 3, 54. By the same logic, there is a "clinical need" for ibuprofen, because it is used to reduce fever and treat pain or inflammation. But reading "clinical need" in this way does not create a category of active pharmaceutical ingredients for which there is *not* a "clinical need." Only when the question considers the actual way in which the active pharmaceutical ingredient supplies a therapeutic benefit—by its administration as a finished drug product—does the inquiry produce the kind of categorization that Congress surely envisioned.

Plaintiffs balk at this analysis, arguing that the agency's framing of "clinical need" improperly replaces "bulk drug substance," as that term appears in Section 503B(a)(2)(A), with the term "compounded drug product." *See* Pls.' Reply Mem. Supporting Pls.' Mot. and Opp'n to Defs.' Cross-Mots., ECF No. 30 [hereinafter Pls.' Reply], at 9–11. More concretely, Plaintiffs argue that FDA's approach improperly focuses on vasopressin as incorporated into a drug product, and not strictly as a bulk drug substance. This construction, Plaintiffs argue, is not faithful to Section 503B's plain text. *Id.*

To be sure, FDA's approach to "clinical need" involves considering the bulk drug substance as a finished product, and the term "finished product" does not appear in Section 503B(a)(2)(A). The court, however, must read a statute to give its words the effect that Congress intended. *See United States v. Braxtonbrown-Smith*, 278 F.3d 1348, 1352 (D.C. Cir. 2002) (stating

that the court "must avoid an interpretation that undermines congressional purpose considered as a whole when alternative interpretations consistent with the legislative purpose are available") (citing *United States v. Am. Trucking Ass'ns*, 310 U.S. 534, 543 (1940) ("[E]ven when the plain meaning did not produce absurd results but merely an unreasonable one 'plainly at variance with the policy of the legislation as a whole' this Court has followed that purpose, rather than the literal words.") (citation omitted)). Here, as discussed, Plaintiffs' reading would produce the unreasonable result that there is a "clinical need" for *every* bulk drug substance because, by definition, a bulk drug substance is one "intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body." 21 C.F.R. § 207.1. Plaintiffs' interpretation thus draws no actual distinction among bulk drug substances—there is a "clinical need" for all. Only when "clinical need" is assessed against the availability and suitability of an approved drug does the term perform the classifying function that Congress intended. Defendants' reading therefore faithfully adheres to Section 503B's text, while Plaintiffs' does not.

2. The Provision in Context

Viewing the term "clinical need" in its statutory context lends further support to Defendants' reading of Section 503B, and further frustrates Plaintiffs' interpretation. *See King v. Burwell*, 576 U.S. __, __, 135 S. Ct. 2480, 2489 (2015) (stating "oftentimes the meaning—or ambiguity—of certain words or phrases may only become evident when placed in context") (citing *FDA v. Brown & Williamson Tobacco Corp.*, 529 U.S. 120, 132 (2000)) (internal quotations omitted).

a. Bulk compounding as an exception within an exception

Critical to the court's interpretation of "clinical need" is how the subsection containing that provision, 503B(a)(2)(A)(i), lines up with other parts of Section 503B. The very first sentence of Section 503B exempts outsourcing facilities from the FDCA's new-drug approval process, certain labeling requirements, and certain supply chain requirements. *See* 21 U.S.C. § 353b(a) (exempting compounded drugs from 21 U.S.C. §§ 352(f)(1), 355, and 360eee-1). Products made by outsourcing facilities are thus an exception to the FDCA's usual requirements for new drug products. Next, Section 503B(a)(2) requires outsourcing facilities to compound "in an outsourcing facility that *does not* compound using bulk drug substances," generally, subject only to enumerated exceptions. 21 U.S.C. § 353b(a)(2) (emphasis added). Section 503B(a)(2)(A)(i)–(ii) specifies the exceptions, authorizing compounding with a bulk drug substance—but only if FDA lists the bulk drug substance on the "clinical need" list, or the drug compounded from the bulk drug substance appears on FDA's "drug shortage" list.

As the above recitation shows, Congress viewed compounding with a bulk drug substance as an exception within an exception. Section 503B's initial exception exempts from the FDCA's new-drug requirements compounded drug products that start with an FDA-approved product. The exception to this exception is compounding with a bulk drug substance. *See* 21 U.S.C. § 353b(a)(2)(A)(i)–(ii) ("The drug is compounded in an outsourcing facility that does not compound using bulk drug substances . . . *unless* . . .) (emphasis added). Outsourcing facilities may resort to compounding with a bulk drug substance only if: FDA determines that there is a "clinical need" for the bulk drug substance, or FDA places the compounded drug product on its "drug shortage" list. As the terms "need" and "shortage" imply, Congress meant for FDA to approve compounding with a bulk drug substance not as a matter of course. *See Gustafson v.*

Alloyd Co., Inc., 513 U.S. 561, 575 (1995) (stating the principle of construction that a "word is known by the company it keeps"). FDA's approach to assessing "clinical need" is consistent with this design.

Under Plaintiffs' interpretation, however, "clinical need" loses its character as an exception within an exception. According to Plaintiffs, a "clinical need" exists for a bulk drug substance if it has some therapeutic value. *See* Pls.' Mem. at 18. But, if that were so, then the term "clinical need" would not connote a modest "list" but an extensive catalog of active ingredients. According to Plaintiffs, that catalog would include every active ingredient contained in an FDA-approved drug *plus* active ingredients that are "not components of FDA-approved drugs . . . if their clinical need is shown some other way[.]" *Id.*[5] FDA could keep only "unproven, fringe ingredients" off the list. *Id.* Such a reading, however, swallows Congress's general directive that an outsourcing facility "*not* compound using bulk drug substances . . . ." 21 U.S.C. § 353b(a)(2) (emphasis added). And it would mean that Congress authorized large-scale compounding with a wide array of bulk drug products through the "clinical need" list. If Congress had intended to sanction such an expansive practice, the court would have expected it to say so more clearly. *See Whitman v. Am. Trucking Ass'ns*, 531 U.S. 457, 468 (2001) ("Congress, we have held, does not alter the fundamental details of a regulatory scheme in vague terms or ancillary provisions—it does not, one might say, hide elephants in mouseholes.").

[5] Plaintiffs never identify how many different bulk drug substances would appear on the "clinical need" list, if the court were to accept their reading. When FDA invited nominations for the "clinical need" list, commenters submitted 2,000 bulk drug substances for consideration. *See* R. at 38. Defendants referred the court to the "Orange Book," a 1,500-page document listing every approved drug product under Section 505 of the Food, Drug, and Cosmetic Act. *See* U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, APPROVED DRUG PRODUCTS (2019), https://www.fda.gov/media/71474/download (last visited July 31, 2019). Whatever number of active ingredients the Orange Book recognizes, the total surely exceeds the number that Congress had in mind.

Plaintiffs also point to the three additional criteria adjoined with the "clinical need" list: that the bulk drug substance must comply with a monograph,[6] if applicable; it must be manufactured at a properly registered establishment; and it must be accompanied by a valid certificate of analysis. Plaintiffs argue that the "clinical need" list, like the three additional criteria adjoining it, should focus exclusively on the bulk drug substance. *See* Pls.' Mem. at 20 (citing 21 U.S.C. § 353b(a)(2)(B)-(D)). This argument carries little weight because, like the other statutory criteria, the agency's interpretation places the bulk drug substance at the center of its "clinical need" analysis by determining whether the bulk drug substance will fill a gap in a clinical setting. That the agency takes the qualities of approved products into account to make that assessment does not result in a conflict between FDA's interpretation of "clinical need" and the other three criteria contained in Section 503B(a)(2)(B)–(D).

b. FDA's involvement in making the "clinical need" list

Another feature of Section 503B that supports Defendants' interpretation is how Congress directed FDA to go about creating the "clinical need" list. FDA must: (1) "publish[ ] a notice in the Federal Register proposing bulk drug substances to be included on the list, including the rationale for such proposal"; (2) "provide[ ] a period of not less than 60 calendar days for comment on the notice"; and (3) "publish[ ] a notice in the Federal Register designating bulk drug substances for inclusion on the list." 21 U.S.C. § 353b(a)(2)(A)(i)(I)–(III). These procedural prerequisites

[6] A "drug monograph" is a "publication that specifies for a drug (or class of related drugs) the kinds and amounts of ingredients it may contain, the conditions and limitations for which it may be offered, directions for use, warnings, and other information that its labeling must contain. The monograph may contain important information concerning interactions with other drugs." https://medical-dictionary.thefreedictionary.com/drug+monograph (last visited July 31, 2019).

make clear that Congress intended for FDA to apply its expertise in determining whether a bulk drug substance fills a "clinical need." Defendants' reading is consistent with Congress's intent.

Plaintiffs' construction of Section 503B, on the other hand, would make the agency's expertise largely irrelevant to the listing process. As Plaintiffs would have it, FDA must classify any active ingredient in any approved drug as a bulk drug substance for which there is a "clinical need." *See* Pls.' Mem. at 18. If that is what Congress intended, then why would it have instructed FDA to announce its "rationale" for each proposed listing and subject the proposed listing to public scrutiny? Such notice and comment would be a meaningless exercise for the active pharmaceutical ingredients found in FDA-approved drugs. Congress clearly wanted FDA to play a substantive role in the listing process. Only Defendants' approach allows FDA to perform that function.

Plaintiffs acknowledge that, under their reading, the "clinical need" listing of most bulk drug substances would not require FDA's expertise. *See* Hr'g Tr., ECF No. 36 [hereinafter Hr'g Tr.], at 26–27 (arguing that FDA will do "some work that's difficult and . . . some work that's easy"); *see also* Pls.' Reply at 27. Nevertheless, Plaintiffs contend that "[t]he fact that some cases are easy because the rationale is immediately apparent, and some are not does not make it pointless to use notice and comment for the whole enterprise, when that procedure can accommodate both without disrupting patient care." Pls.' Reply at 27. But that reading seems implausible. Congress could not have meant for FDA to proceed through notice and comment when listing *all* bulk drug substances, when that time-consuming and resource-intensive process would serve a meaningful purpose only for the rare, "difficult" case of a bulk drug substance that is not found in an FDA-approved drug product. *Id.* The court must assume that Congress did not impose a burdensome procedural requirement simply for the sake of imposing it. *Cf. Franchise Tax Bd. of Cal. v. U.S. Postal Service*, 467 U.S. 512, 524 (1984) (stating that there is "no reason to believe that Congress

intended to impose a meaningless procedural requirement . . ."); *Prof'l Air Traffic Controllers Org. v. Fed. Labor Relations Auth.,* 685 F.2d 547, 563–64 (D.C. Cir. 1982) ("Congress did not intend to erect meaningless procedural barriers to effective agency action.").

Moreover, a related provision suggests that if Congress really wanted all active ingredients found in FDA-approved products to automatically appear on the "clinical need" list, it passed up a straightforward way to express that intent. Section 503B's neighboring provision, Section 503A, permits traditional compounders, like licensed pharmacists, to compound "for an identified individual patient." 21 U.S.C. § 353a(a). For that practice, Congress required traditional compounders to use a "bulk drug substance" that "compl[ies] with the standards of an applicable" monograph; if such monograph does not exist, then the compounder may use "drug substances that are components of drugs approved by the Secretary"; and, if no monograph exists and the drug substance is not a component of an FDA-approved product, then the drug substance must "appear on a list developed by the Secretary through regulations issued by the Secretary . . . ." *Id.* § 353a(b)(1)(A)(i)(I)–(III). Section 503A thus spells out three different categories of bulk drug substances that can be compounded for an individual patient, only one of which requires FDA pre-approval.

As this provision demonstrates, Congress knows how to permit compounding with drug substances found in safe and effective FDA-approved products, and it also knows how to define substances that must "appear on a list developed by the Secretary." Section 503B reflects the latter approach but not the former. Congress did not include in Section 503B, as it did in Section 503A, an allowance for outsourcing facilities to compound using bulk drug substances that either comply with the standards of an applicable monograph or "are components of drugs approved by the Secretary." Instead, Congress mandated an FDA listing before use of a bulk drug substance for

mass compounding. This fundamental difference between Sections 503A and 503B supports Defendants' interpretation of "clinical need" as requiring more than a mere showing of a bulk drug substance's therapeutic value.

Plaintiffs dismiss the significance of the different text in Section 503A. They argue that the general absence of a pre-production notice-and-comment process in Section 503A (except in Section 503A(b)(1)(A)(i)(III)) makes sense because it would be nonsensical to require a local pharmacist to await a rulemaking process by FDA before compounding a drug. By contrast, Plaintiffs insist, in the context of Section 503B "there is no reason not to use the default notice and comment procedure for all bulk drug substances in the context of 503B." Pls.' Reply at 27.

This argument is unpersuasive for two reasons. First, it misses the point of the textual difference between the two provisions. If Congress wanted outsourcing facilities to manufacture using bulk drug substances already recognized in a drug product approved for safety and efficacy, it had an easy way to do so—it could have simply used the same text found in Section 503A in Section 503B. Instead, it created a new "clinical need" standard. The court must presume that this textual difference reflects a purposeful choice by Congress not to equate "clinical need" with Section 503A's standards. Second, Plaintiffs' argument does not explain why Congress would insist on a time-consuming notice-and-comment process for bulk drug substances found in drug products whose safety and efficacy are established. As discussed, no good purpose is served by requiring FDA to certify hundreds, if not thousands, of bulk drug substances already contained in approved drugs. Congress presumably would not require an agency to commit its resources to a perfunctory rulemaking process. The textual differences between Sections 503A and 503B therefore support Defendants' reading of "clinical need."

c. Plaintiffs' interpretation renders the "drug shortage list" superfluous

Yet another contextual feature of Section 503B bolsters Defendants' interpretation: the "drug shortage list." Congress allowed outsourcing facilities to compound with a bulk drug substance, without undergoing notice and comment, if the drug compounded from the bulk drug substance appears on the "drug shortage list in effect under section 356e of this title at the time of compounding, distribution, and dispensing." *See* 21 U.S.C. § 353b(a)(2)(A)(ii). The drug shortage list predates the DQSA, and its requirements are codified in 21 U.S.C. § 356e. That provision directs the Secretary to maintain a list of drugs that are in short supply in the United States for various listed reasons, including regulatory delay, shortage of an active or inactive ingredient, delay in shipping of the drug, or demand increase for the drug. *See id.* § 356e. The list must include the name of the drug in shortage, its manufacturer, the reason for the shortage, and the estimated duration of the shortage. *Id.* § 356e(b).

Plaintiffs' interpretation of "clinical need," if accepted, would violate a basic rule of statutory construction: "[E]very word and every provision is to be given effect and that none should needlessly be given an interpretation that causes it to duplicate another provision or to have no consequence." *Nielsen v. Preap*, 586 U.S. ___, ___, 139 S. Ct. 954, 969 (2019) (cleaned up and citation omitted). Recall, under Plaintiffs' understanding of "clinical need," FDA would be required to list every bulk drug substance found in an FDA-approved drug. That list would be long. If the "clinical need" list were to contain hundreds of active ingredients, then the drug shortage list would have little or "no consequence." *Id.* Not because there would be no drug shortages. But because any active ingredient contained in a drug placed on the shortage list already is likely to appear on the "clinical need" list because of its therapeutic value. Stated differently, FDA rarely, if ever, would need to authorize compounding based on a drug shortage, because the

active ingredient contained in such a scarce drug already will be on the "clinical need" list and greenlighted for use. Thus, the statutory allowance for using a bulk drug substance based on drug shortage would serve little or no function under Plaintiffs' interpretation.

Plaintiffs respond that, under their reading of "clinical need," the drug shortage list still would have utility. For instance, there could be future drug product innovations where the component bulk drug substance is not yet placed on the clinical need list due to the required notice-and-comment period, but there is an immediate need for the drug itself due to shortage. *See* Hr'g Tr. at 30–33. Is this scenario possible? Maybe. But it is doubtful that Congress intended for the drug-shortage listing to cover only outlier scenarios, such as when a drug manufacturer comes to market with a new FDA-approved product but does not produce enough of it to meet demand during the time period the product's active ingredient is under review for placement on the "clinical need" list. When Congress passed the DQSA, it understood the importance of the drug shortage list. Congress could not have not intended for the "clinical need" list to fully eclipse the drug shortage list, leaving the latter as a mere "backstop" to the former. *See id.* at 33.

d. The "essentially a copy" provision

To support their interpretation, Plaintiffs point to a provision that limits outsourcing facilities to producing a "[compounded] drug [that] is not essentially a copy of one or more approved drugs." *See* 21 U.S.C. § 353b(a)(5). The statute defines "essentially a copy of an approved drug" to mean:

> (A) a drug that is identical or nearly identical to an approved drug, or a marketed drug not subject to section 353(b) of this title and not subject to approval in an application submitted under section 355 of this title, unless, in the case of an approved drug, the drug appears on the drug shortage list in effect under section 356e of this title at the time of compounding, distribution, and dispensing; or

> (B) a drug, a component of which is a bulk drug substance that is a component of an approved drug or a marketed drug that is not subject to section 353(b) of this title and not subject to approval in an application submitted under section 355 of this title, unless there is a change that produces for an individual patient a clinical difference, as determined by the prescribing practitioner, between the compounded drug and the comparable approved drug.

21 U.S.C. § 353b(d)(2). As a result of the "essentially a copy" provision, unless the drug product appears on the shortage list, outsourcing facilities can compound using a bulk drug substance that is a component of an approved drug only if the bulk-compounded drug supplies to "an individual patient a clinical difference" from the approved drug. *Id.* Congress left it to medical practitioners to make the "clinical difference" determination. *Id.*

Plaintiffs argue that FDA's "clinical need" interpretation makes redundant the "essentially a copy" provision. They contend that the "essentially a copy" definition ensures that outsourcing facilities will not compound drug products that rival FDA-approved drugs, so the clinical need provision cannot fulfill the same purpose. *See* Pls.' Mem. at 22–26. By drawing a comparison to approved drugs during the "clinical need" inquiry, Plaintiffs maintain, FDA "disturbs the balance Congress struck when it made the policy decision of how best to account for the competing interest in encouraging the use of the drug approval process." *See id.* at 23. Defendants, on the other hand, assert that the "essentially a copy" provision is consistent with its "clinical need" interpretation. Their reading, they say, ensures that health practitioners will only use the compounded drug for patients who need the compounded drug to fill therapeutic gaps left by an FDA-approved drug. *See* Hr'g Tr. at 64.

Plaintiffs are correct that the "essentially a copy" provision works to protect the new drug approval process and, by extension, provides a market advantage to FDA-approved drugs over those produced by outsourcing facilities. *Compare* R. at 108 (FDA justifying "clinical need"

interpretation to protect drug approval process) *with* FOOD AND DRUG ADMINISTRATION, COMPOUNDED DRUG PRODUCTS THAT ARE ESSENTIALLY COPIES OF APPROVED DRUG PRODUCTS UNDER 503B OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT: GUIDANCE FOR INDUSTRY 4 (January 2018), https://www.fda.gov/media/98964/download (last visited July 31, 2019) [hereinafter Essential Copy Guidance] (FDA stating that the essentially a copy provision "protects the integrity and effectiveness of the new drug . . . approval process[]"). But the fact that FDA's method of determining "clinical need" furthers that same purpose is not fatal to the agency's interpretation. "In some cases, redundancy may reflect the broad purpose of a congressional statute." *Nat'l Ass'n of Clean Water Agencies v. EPA*, 734 F.3d 1115, 1126 (D.C. Cir. 2013). Here, multiple provisions within Section 503B reflect Congress's intent that bulk compounded drugs be used primarily to fill gaps left by FDA-approved drugs. Perhaps the clearest such expression is the general rule, discussed above, that outsourcing facilities "not compound using bulk drug substances . . . ." 21 U.S.C. § 353b(a)(2). That rule creates a clear market advantage for approved drugs. Congress also required outsourcing facilities to sell their drug products directly to hospitals and physicians for use as "office stock," and expressly prohibited them from using wholesalers to make sales. *Id.* § 353b(a)(8). Wholesalers are critical to the drug supply chain and cutting off that path of distribution limits an outsourcing facility's ability to sell its product. In short, like the "essentially a copy" provision, these other conditions constrain the commercial activities of outsourcing facilities relative to FDA-approved drug manufacturers. That FDA's understanding of "clinical need" has a similar market effect therefore does not conflict with Congress's overall design.

Moreover, FDA's method of determining "clinical need" easily co-exists with the "essentially a copy" provision. As a general rule, the "essentially a copy" provision prohibits

outsourcing facilities from producing a compounded drug "a component of which is a bulk drug substance that is a component of an approved drug." *Id.* § 353b(d)(2)(B). In other words, a compounded drug cannot be made with a bulk drug substance if such substance already is contained in an approved product. The exception to that general rule is if the compounded drug entails a change from the approved product "that produces for an individual patient a clinical difference, as determined by the prescribing practitioner . . . ." *Id.* FDA's "clinical need" determination mirrors, but does not duplicate, the "essentially a copy" provision. It asks whether the bulk drug product fills a gap of medical unsuitability left by an approved drug and, if so, whether that gap cannot be filled by compounding with the approved drug. Thus, both the "essentially a copy" provision and FDA's "clinical need" inquiry are directed at identifying whether the compounded product is one that fills a therapeutic purpose unmet by the approved drug. The two provisions therefore complement each other in furthering the statutory purpose.

Plaintiffs complain that reading Section 503B in this way is impermissible because, through its pre-market "clinical need" inquiry, FDA is in effect making the "clinical difference" determination that the statute leaves to treatment providers. The agency is thus impermissibly regulating the practice of medicine, say Plaintiffs. *See* Pls.' Mem. at 27. Not so. Take the case of vasopressin. FDA's decision not to recognize a "clinical need" for vasopressin does not interfere with a physician's decision whether to treat a patient with the approved product, Vasostrict, or a compounded version of Vasostrict that meets a patient's individual need. FDA's vasopressin decision only regulates the type of drug that reaches the marketplace. Such a decision rests well within FDA's regulatory authority under the FDCA, and it does not intrude on the

practice of medicine.[7] *See United States v. Evers*, 643 F.2d 1043, 1048 (5th Cir. 1981) ("[W]hile the [FDCA] was not intended to regulate the practice of medicine, it was obviously intended to control the availability of drugs for prescribing by physicians.").

* * *

"A provision that may seem ambiguous in isolation is often clarified by the remainder of the statutory scheme . . . because only one of the permissible meanings produces a substantive effect that is compatible with the rest of the law." *United Sav. Ass'n of Tex v. Timbers of Inwood Forest Assocs., Ltd.*, 484 U.S. 365, 371 (1988). Here, the broader structure of Section 503B, as well as its relationship to Section 503A, compel the court to conclude that FDA's interpretation of "clinical need" is the only interpretation "compatible with the rest of the law."

e. Legislative History

In addition to a statute's text and structure, legislative history is a relevant consideration at *Chevron* step one. *See Sierra Club v. EPA*, 551 F.3d 1019, 1027 (D.C. Cir. 2008) ("Although *Chevron* step one analysis begins with the statute's text, the court must . . . exhaust the traditional tools of statutory construction, including examining the statute's legislative history . . . .") (internal quotation marks omitted). The legislative history for the DQSA is sparse. Neither chamber produced a committee report. Yet, no one disputes that the event that motivated Congress to enact the DQSA was the deadly meningitis outbreak caused by the contaminated injections produced by the New England Compounding Center ("NECC"). *See The Fungal Meningitis Outbreak: Could it have been Prevented? Before the Subcomm. on Oversight and Investigations of the H. Comm. on Energy and Commerce*, 112th Cong. 181 (2012) [hereinafter House Hearing] (Chairman Stearns

[7] Relatedly, Plaintiffs argue that the agency's determination of "medical unsuitab[ility]" is an unlawful regulation of medicine. *See* Pls.' Reply at 33. But the inquiry focuses on whether the approved drug is unsuitable for a patient population; it does not make a clinical determination about a specific patient.

stating, "we convene this hearing . . . to examine the recent outbreak . . . linked to contaminated products made by [NECC] . . . the first question we all ask is, Could this have been prevented? . . . the answer appears to be yes"); *see also* Hr'g Tr. at 42; *see also* Compl. ¶ 17. NECC, and other compounders like it, had grown beyond the traditional notion of a local pharmacist compounding individual prescriptions. *See* House Hearing (Margaret Hamburg, former FDA Commissioner, stating "the industry has evolved well beyond the neighborhood pharmacist"). By amending the FDCA, Congress wished to strengthen federal regulatory authority over bulk compounders that produced drugs on a large scale that were not subject to the FDA's new-drug efficacy and safety standards.

FDA's method of determining "clinical need" better comports with the DQSA's primary objective of protecting public safety. Plaintiffs' interpretation, if accepted, would substantially constrain FDA's judgment and expertise with respect to the "clinical need" list, and concomitantly would enable outsourcing facilities to compound using a wide array of bulk drug substances to create drug products that are not subject to any premarket efficacy or safety review. FDA's view, by contrast, grants the agency a more prominent role before a bulk compounded drug hits the market, and favors compounding with an FDA-approved product that has undergone rigorous premarket efficacy and safety review. FDA's approach better achieves the public health and safety objective that Congress had in mind when it passed the DQSA. *Cf. Thompson v. W. States Med. Ctr.*, 535 U.S. 357, 369 (2002) ("Preserving the effectiveness and integrity of the FDCA's new drug approval process is clearly an important governmental interest, and the Government has every reason to want as many drugs as possible to be subject to that approval process. The Government also has an important interest, however, in permitting the continuation of the practice of

compounding so that patients with particular needs may obtain medications suited to those needs.").

For their part, Plaintiffs rely on a comment by Senator Lamar Alexander that the DQSA was not intended to "limit access to quality compounded drugs for providers and patients or alter the practice of medicine." Pls.' Mem. at 19 (citing 159 Cong. Rec. S8072 (daily ed. Nov. 18, 2013)). That general statement does not, however, carry the weight Plaintiffs attribute to it. In fact, right before making this statement, Senator Alexander said that "I want to make clear that all involved on this legislation have no intent of limiting patient or provider access to quality compounded drugs *that fill a clinical need*." 159 Cong. Rec. S8072 (emphasis added). The Senator's statement leads the court right back to where it began—when is there a "clinical need" for a drug compounded from a bulk drug substance?

* * *

For the foregoing reasons, the court finds that Defendants prevail at *Chevron* step one. FDA's method of determining "clinical need" for a bulk drug substance by referring to the approved product is supported by the text, structure, and purposes of Section 503B.

B. *Chevron* Step Two

In the interest of completeness, the court proceeds to *Chevron* step two. Defendants also would prevail at *Chevron* step two, if the statute were to remain ambiguous after employing the traditional tools of statutory construction. For the reasons already discussed, FDA's interpretation of "clinical need" is "based on a permissible construction of the statute." *Chevron*, 467 U.S. at 843.

Further, as required to receive *Chevron* deference, the agency "offered a reasoned explanation for why it chose [its] interpretation." *Village of Barrington*, 636 F.3d at 660. In its

final notice excluding vasopressin, FDA explained that it formulated its methodology to avoid "unnecessarily expos[ing] patients to the risks associated with drug products that do not meet the standards applicable to FDA-approved drug products for safety, effectiveness, quality, and labeling and would undermine the drug approval process." R. at 108. FDA also explained that it sought to determine whether compounding must occur with a bulk drug substance, as opposed to the FDA-approved product, because the statute requires the FDA to "determine that there is a clinical need for outsourcing facilities to compound a drug product using the bulk drug substance." *Id.* (emphasis in original omitted). These explanations suffice to show that the agency had reasonable grounds for its construction of "clinical need."

Plaintiffs offer no new arguments at *Chevron* step two that they did not raise at *Chevron* step one. *See* Pls.' Mem. at 28–29. Those arguments did not persuade the court at the first step, and they fare no better at the second step.

C. FDA's Decision to Exclude Vasopressin from the "Clinical Need" List was Not Arbitrary and Capricious

Alternatively, Plaintiffs challenge FDA's decision to exclude vasopressin from the "clinical need" list as arbitrary and capricious, even under the agency's approach to assessing "clinical need." *See* Pls.' Mem. at 30–37. Under the "narrow" arbitrary and capricious standard of review, the court may not "substitute its judgment for that of the agency," but must instead determine whether the agency "examine[d] the relevant data and articulate[d] a satisfactory explanation for its action including a rational connection between the facts found and the choice made." *Motor Vehicle Mfrs. Ass'n of U.S., Inc. v. State Farm Mut. Auto. Ins. Co.*, 463 U.S. 29, 43 (1983) (internal quotation marks and citation omitted). An agency action is "arbitrary and capricious" and will be set aside if the agency "has relied on factors which Congress has not intended it to consider, entirely failed to consider an important aspect of the problem, offered an

explanation for its decision that runs counter to the evidence before the agency, or is so implausible that it could not be ascribed to a difference in view or the product of agency expertise." *Id.*

Plaintiffs contend that their vasopressin drug product meets a "clinical need" even under FDA's interpretation for two reasons. First, Plaintiffs argue that Vasostrict is medically unsuitable for certain patients because it contains the allergen chlorobutanol, thereby giving rise to a "clinical need." *See* Pls.' Mem. at 35–37. But in denying listing, FDA identified a chlorobutanol-free version of Vasostrict. R. 1604. It noted that vasopressin's sponsor had "fail[ed] to explain why that formulation would be medically unsuitable for patients who have an allergy to chlorobutanol." *Id.* Plaintiffs do not appear to dispute this agency finding, as they do not contest it in their reply brief. *See generally* Pls.' Reply. FDA's explanation satisfies the arbitrary and capricious standard.

Second, Plaintiffs assert that their product is available in a ready-to-use, intravenous version, which offers safety benefits for patients relative to Vasostrict. To support this contention, Plaintiffs point out that vasopressin has been designated a "high alert" drug that presents a serious risk of patient harm from preparation or administration error. *See* Pls.' Mem. at 30–35; *see also* R. at 464. Their ready-to-use version, Plaintiffs claim, is safer than Vasostrict, which requires dilution before intravenous delivery. As Plaintiffs put it, their drug product "giv[es] emergency rooms an option other than [Vasostrict's] 16-step process . . . resembling compounding on the fly." *See* Pls.' Mem. at 31.

FDA considered Plaintiffs "ready-to-use" claim but rejected it.[8] First, the agency found that commenters did not "identify a basis to conclude that there is an attribute of [Vasostrict] that

[8] Plaintiffs incorrectly assert that FDA did not consider the "high alert" designation of vasopressin. Pls.' Mem. at 31, 33. FDA may not have used the words "high alert," but it certainly recognized and addressed Plaintiffs' argument that its ready-to-use product fills a "clinical need." *See* R. at 1598–99 ("[T]he comments contended that [ready-to-use] products compounded from bulk drug substances can reduce the risk of medication errors or contamination, decrease access times, and increase efficiencies in healthcare facility operations. They state these advantages are particularly important for drugs in emergency settings.").

makes [it] unsuitable such that patients need a compounded drug product." R. at 1599. As the agency put it, manufacturing a drug that is ready-to-use to "improve[] efficiency" or to "address the *possibility* that the approved drug might be mishandled by a medical professional" is not addressing clinical need. *Id.* at 1605 (emphasis added). Instead, the ready-to-use capability just provides an "advantage[], relative to the approved drug product[]." *Id.* at 1599. Even though Plaintiffs may have demonstrated that ready-to-use is advantageous, that does not mean that Vasostrict—because it is not ready-to-use—is medically unsuitable. The FDA's view on this issue is not "so implausible that it could not be ascribed to a difference in view or the product of agency expertise." *State Farm*, 463 U.S. at 43.

Second, and as importantly, the agency found that the commenters did not show that the proposed drug product "must be made from a bulk drug substance rather than by diluting the approved drug." R. at 1599. Another drug supplier, PharMEDium Services, operates an outsourcing facility that compounds Vasostrict into a ready-to-use formulation. *See id.* at 1599; *see also id.* at 198. Plaintiffs have not asserted that their ready-to-use bulk compounded product meets a clinical need that PharMEDium's sterile-to-sterile compounded product does not. *See* Pls.' Mem; *see also* Pls.' Reply (not mentioning PharMEDium's product). FDA's rejection of a "clinical need" for vasopressin therefore was not arbitrary and capricious.

V. CONCLUSION

For the reasons set forth above, the court denies Plaintiffs' Motion for Summary Judgment, ECF No. 23, and grants Defendants' Cross-Motions for Summary Judgment, ECF Nos. 25 and 27. A final order accompanies this Memorandum Opinion.

Dated: August 1, 2019

Amit P. Mehta
United States District Court Judge