Outsourcing Facilities Face Rising Drug Compounding Risks

By **Greg Levine, Joshua Oyster and Rebecca Williams** (September 18, 2019)

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In recent years, the drug compounding industry has expanded significantly, with an estimated U.S. market size of $8.9 billion in 2019 and annualized market size growth of 2.3% over the last five years.[1]

Part of this expansion can be attributed to the Drug Quality and Security Act, which Congress enacted in 2013 following a fungal meningitis outbreak caused by contaminated drugs compounded by the New England Compounding Center. The DQSA addressed certain ambiguities in existing law by creating a new category of compounder — an outsourcing facility — permitted to engage in non-patient-specific compounding if certain statutory conditions are met.

While the U.S. Food and Drug Administration to date has largely focused on the safety and quality of compounded drugs, questions about how to interpret key provisions of the DQSA have increasingly become a priority. In particular, the FDA, compounders, the pharmaceutical industry and legal practitioners have struggled with unanswered questions about when a compounded drug may be prepared from a bulk drug substance as opposed to a finished drug product and when a compounded drug is considered an inappropriate copy of an FDA-approved, commercially available product.

Recent lawsuits have tested both the FDA's authority to regulate compounding by outsourcing facilities and drug manufacturers' ability to use private litigation to address alleged regulatory noncompliance by compounders. This article provides an overview of the current state of the regulatory framework and the recent case law, and describes the implications for both drug compounders and pharmaceutical manufacturers.

FDA Framework for Outsourcing Facilities

Section 503B of the Federal Food, Drug and Cosmetic Act, enacted as part of the DQSA, provides an optional regulatory scheme for sterile drug compounders that choose to register with the FDA as outsourcing facilities. In order to be an outsourcing facility, compounders must meet the requirements of Section 503B, which include registration with FDA, periodic reporting to FDA of the drugs the facility compounds, compliance with current good manufacturing practice (cGMP) requirements, adverse event reporting and compliance with labeling requirements specific to outsourcing facilities, among other things.

The primary benefit of being an outsourcing facility under Section 503B is that, unlike non-503B compounders, outsourcing facilities are permitted to compound and dispense drugs on a non-patient-specific basis and without a patient-specific prescription.[2] Additionally, outsourcing facilities that comply with Section 503B are exempt from the FDCA's requirement to obtain FDA approval for a new drug before compounding it,[3] to provide product labeling that contains "adequate directions for use,"[4] and to meet drug supply chain security requirements.[5]

In short, outsourcing facilities are a type of hybrid: While they must meet certain of the requirements applicable to pharmaceutical manufacturers, particularly those relating to product quality and adverse event reporting, they are exempt from others, including the costly and burdensome requirements to study and obtain FDA approval of their drug products. Not surprisingly, therefore, outsourcing facilities can generally offer drugs to purchasers at lower prices than pharmaceutical manufacturers.

While the enactment of Section 503B clearly demonstrated continued congressional support for certain compounding activities, Congress imposed key limitations to avoid undermining FDA requirements applicable to pharmaceutical manufacturers. Among other things, in Section 503B, Congress limited compounding by outsourcing facilities using "bulk drug substances."[6]

Under the statute, an outsourcing facility may only use a bulk drug substance in compounding if it appears on an FDA-published list of bulk drug substances "for which there is a clinical need" (also known as the 503B bulks list) or, alternatively, on the FDA's drug shortage list, at the time of compounding, distribution and dispensing.[7] In addition, a drug compounded by an outsourcing facility must not be "essentially a copy of one or more approved drugs."[8] This latter requirement mirrors a similar condition applicable to traditional pharmacy compounding.[9]

Development of the FDA's 503B Bulks List

In 2013, 2014 and 2015, the FDA solicited nominations from the public for the 503B bulks list[10] but did not immediately initiate the notice-and-comment process mandated by the statute for establishing the formal 503B bulks list.[11] Instead, the FDA first issued a draft guidance document in October 2015,[12] followed by a final guidance document in June 2016,[13] and then ultimately by a revised final guidance document in January 2017, each setting forth the agency's interim policy with respect to compounding from bulk drug substances under Section 503B (referred to herein as the 503B interim policy).[14]

As described in the January 2017 guidance, the 503B interim policy categorizes the bulk drug substances that have been nominated for the formal 503B bulks list into one of three categories: 503B Category 1 (substances nominated for the bulks list that are currently under evaluation), 503B Category 2 (substances nominated for the bulks list that raise significant safety risks), and 503B Category 3 (substances nominated for the bulks list without adequate support).[15]

The FDA's guidance explains that "at this time FDA does not intend to take action" against outsourcing facilities that compound drugs using bulk drug substances that appear on the 503B Category 1 list on the FDA's website.[16] In contrast, the guidance says, bulk drug substances that appear on the 503B Category 2 or Category 3 lists, or that do not appear on any list,[17] may only be used to compound drugs that appear on the FDA's drug shortage list.[18]

In other words, under the 503B interim policy, outsourcing facilities may only use bulk drug substances to compound drugs if: (1) the bulk drug substance is currently included in the 503B Category 1 list published on FDA's website,[19] or (2) the bulk drug substance is used to compound a drug included on the FDA's drug shortage list.

In March 2019, the FDA issued additional guidance explaining how the agency would evaluate bulk drug substances nominated for the 503B bulks list (the clinical need

guidance).[20] That guidance explains that for bulk drug substances that are components of FDA-approved drugs, the FDA will consider the following threshold questions in evaluating clinical need:

- Is there a basis to conclude, for each FDA-approved product that includes the nominated bulk drug substance, that (1) an attribute of the FDA-approved drug product makes it medically unsuitable to treat certain patients for a condition that the FDA has identified for evaluation, and (2) the drug product proposed to be compounded is intended to address that attribute?

- 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?[21]

If the answer to either of these questions is "no," the FDA will find that there is not a clinical need for outsourcing facilities to use that bulk drug substance.[22] If the answer to both of these questions is "yes," the inquiry is not over: the FDA will then conduct a "balancing test" of various factors, including the physical and chemical characterization of the substance, any safety issues raised by use of the substance in compounding, evidence related to effectiveness of drugs compounded with the substance, and the current and historical use of the substance in compounded drugs.[23]

Analysis of Recent Cases

Although the FDA has been taking steps towards developing the formal 503B bulks list, some drug manufacturers have grown frustrated by the pace of the agency's efforts, which they claim leaves them exposed to unfair competition by compounders. In several instances, drug manufacturers have attempted to take matters into their own hands by initiating lawsuits against outsourcing facilities alleging false advertising and unfair competition[24] or against the FDA alleging that the 503B interim policy is unlawful.[25] Below we analyze each of these cases, as well as a related lawsuit against the FDA brought by an outsourcing facility.[26]

Court Challenges Against Outsourcing Facilities

In September 2017, Allergan USA Inc., a drug manufacturer, filed two lawsuits in the same federal district court against outsourcing facilities that were allegedly compounding copies of the company's FDA-approved products (Allergan v. Imprimis Pharmaceuticals and Allergan v. Prescriber's Choice).[27]

In both cases, Allergan alleged that the outsourcing facilities engaged in false advertising in violation of Section 43(a) of the Lanham Act by claiming that, among other things, the facilities' compounding operations were lawful under the FDCA and that their compounded drugs were clinically superior to commercially available products.

Additionally, Allergan alleged that the outsourcing facilities violated California's Unfair Competition Law by unlawfully selling drugs that had not been approved by the California Department of Health Services or by the FDA, in violation of California's Sherman Law.[28]

In each case, one of the key issues the court grappled with was whether the outsourcing facilities had engaged in false advertising by claiming their compounding operations were lawful under the FDCA. In Imprimis, at the motion to dismiss stage, the court ruled that even where FDA had announced a policy of enforcement discretion (such as the 503B interim policy), a defendant could be liable for false advertising if it claimed to be in compliance with FDA requirements but engaged in conduct that violated the plain text of the FDCA.[29]

At the time, the court stated that the FDA's "lack of enforcement does not make Imprimis's actions legal."[30] Despite this initial position, the court in both Imprimis and Prescriber's Choice ultimately determined that a defendant would not be liable for false advertising based on failure to comply with statutory conditions that were not being enforced by FDA.[31]

In both cases, the court issued summary judgment rulings finding that the defendant outsourcing facilities violated the FDA's 503B interim policy by compounding drugs using bulk drug substances that did not appear on the FDA's 503B Category 1 list.[32] As a result, the court concluded that the defendants' actions violated California's Unfair Competition Law and that their statements regarding the legality of their operations constituted false advertising in violation of the Lanham Act.[33]

Following the summary judgment order in Prescriber's Choice, the parties settled the case with the defendants agreeing, among other things, to include prominent disclosures in labeling and advertising that their products are not FDA approved and to refrain from making statements representing that their operations have been approved by the FDA or that their drugs are clinically superior to commercially available drugs.[34]

Although the Prescriber's Choice case settled, the Imprimis case went to a jury trial with respect to damages for the Lanham Act claim. In May 2019, a jury awarded Allergan $48,500 in damages for lost profits.[35] Then, in a July 2019 order of permanent injunction, the court required Imprimis to comply with the 503B interim policy by enjoining Imprimis from operating an outsourcing facility that compounds drugs using bulk drug substances unless those bulk substances appear on the 503B Category 1 list (or alternatively, the 503B bulks list once established).[36]

The injunction, however, is limited in its geographic scope and only applies to drugs prepared or dispensed in, or shipped to, California.[37] The parties have filed cross-appeals, which are currently pending in the U.S. Court of Appeals for the Ninth Circuit

Challenges to the FDA's 503B Bulk Policies Relating to Vasopressin

While the Allergan cases were being litigated in California, Par Sterile Products LLC and Endo Par Innovation Company LLC filed a lawsuit against the FDA, alleging that the 503B interim policy (and FDA's corresponding failure to develop the formal 503B bulks list) was contrary to law and in violation of the Administrative Procedure Act.[38]

The complaint alleged that the 503B interim policy permits compounding of any bulk substances that have been nominated with "adequate support" without consideration of clinical need, in violation of Section 503B.[39] More specifically, the complaint asserted that the FDA has "improperly authorized bulk compounding of hundreds of drugs" under this policy, including vasopressin, an unapproved drug that Par alleged was essentially a copy of its FDA-approved drug, Vasostrict.[40]

Par requested orders enjoining and vacating the 503B interim policy and enjoining FDA from authorizing bulk drug compounding using vasopressin without compliance with the new drug approval process or Section 503B.[41]

In January 2018, the parties agreed to a stay of the litigation as the FDA continued to develop the draft clinical need guidance and the 503B bulks list.[42] The draft clinical need guidance was then issued in March 2018.[43] The stay of the litigation was lifted on Aug. 15, 2018, when Athenex Pharma Solutions, an outsourcing facility intending to compound vasopressin from bulk, intervened as a defendant in the case.[44]

On Aug. 27, 2018, Par filed a motion for a preliminary injunction to enjoin the 503B interim policy or enjoin the FDA from authorizing bulk drug compounding using vasopressin.[45] At the same time, however, the FDA published a Federal Register notice proposing to exclude vasopressin from the 503B bulks list.[46] The FDA finalized this proposal in March 2019 and removed vasopressin from the 503B Category 1 List, thereby restricting outsourcing facilities from using vasopressin as a bulk drug substance in compounding unless it appears on the FDA's drug shortage list.[47]

In response to the FDA's decision to exclude vasopressin from the 503B bulks list, Athenex immediately filed a new lawsuit against FDA, alleging that FDA improperly considered the availability of Vasostrict in determining whether there was a clinical need for vasopressin, in violation of the APA.[48] Athenex argued that in making a determination of clinical need, Section 503B requires the FDA to consider only whether a bulk drug substance is necessary for patient treatment.[49]

Additionally, Athenex claimed that even under the FDA's interpretation of clinical need, the agency's decision to exclude vasopressin from the 503B bulks list was arbitrary and capricious because the FDA-approved form of vasopressin is unsuitable for certain patients who may be allergic to chlorobutanol and is a "high-alert medication" that presents serious risks from preparation or administration error.[50] Following Athenex's complaint, Par intervened as a defendant in the case in support of the FDA's position.[51]

The parties filed cross-motions for summary judgment, and on Aug. 1, 2019, the court issued an opinion resolving all claims in favor of the defendants.[52] The court not only supported the FDA's decision to exclude vasopressin from the 503B bulks list but also approved of the FDA's method for determining whether a clinical need exists for a bulk drug substance.[53]

After analyzing the statutory provision under Chevron, the court determined that the FDA's interpretation of clinical need, which requires the agency to consider whether a compounded drug product containing a particular bulk drug substance is necessary relative to the FDA-approved products containing the same bulk substance, adheres to the statutory text and is "the only interpretation compatible with the rest of the law."[54]

The court also found that the "clinical need" restriction on compounding from bulk drug substances complements, but does not make redundant, the "essentially a copy" provision in Section 503B — both provisions "constrain the commercial activities of outsourcing facilities relative to FDA-approved drug manufacturers."[55]

Moreover, the court held that the FDA's decision to exclude vasopressin from the 503B bulks list was not arbitrary and capricious as the FDA explicitly considered the threshold clinical need questions during its review.[56]

In particular, the FDA determined that Athenex's ready-to-use preparation, while advantageous, did not mean that the FDA-approved version was medically unsuitable "such that patients need a compounded drug product" and found that Athenex had not provided any evidence to show that the compounded drug product "must be made from a bulk drug substance rather than by diluting the approved drug."[57]

On Aug. 21, 2019, Athenex filed an appeal, which is currently pending in the U.S. Court of Appeals for the District of Columbia Circuit.

Key Takeaways

While the case law relevant to Section 503B and outsourcing facilities is still developing — particularly considering that both the Imprimis and Athenex cases are currently on appeal — there are already several important takeaways for both drug compounders and traditional drug manufacturers.

Outsourcing facilities that compound from bulk drug substances in compliance with the FDA's interim enforcement policy are unlikely to face liability for false advertising or unfair competition claims premised on alleged noncompliance with Section 503B.

Although some drug manufacturers may object to the FDA's interim policies that effectively provide enforcement discretion for compounders with respect to certain statutory requirements, Prescriber's Choice and Imprimis suggest that, at least for the present, courts are likely to defer to the FDA while the agency develops the official 503B bulks list.

In Athenex, the district court upheld the FDA's interpretation of clinical need and the agency's proposed process and criteria for establishing the 503B bulks list. Relying on the Athenex decision to support its approach, the FDA can be expected to move expeditiously to exclude additional bulk drug substances from the 503B bulks list. Indeed, FDA is already doing so: On Sept. 3, 2019, the FDA proposed to exclude nine additional bulk drug substances from the 503B bulks list.[58]

It is more important than ever for outsourcing facilities to scrutinize carefully the bulk drug substances they use in compounding to ensure compliance with FDA policies. Recent FDA warning letters indicate that the FDA has been increasing enforcement efforts relating to use of bulk drug substances under Section 503B.

Since September 2018, the FDA has issued four warning letters to outsourcing facilities that cite, among other things, compounding from bulk drug substances that do not appear on the 503B bulks list or the 503B Category 1 list under the 503B interim policy.[59] The FDA's actions also suggest that the 503B bulks list that emerges from the FDA's review process is likely to be significantly shorter than the 503B Category 1 list under the 503B interim policy.

Even if a bulk drug substance is permitted for use in compounding, outsourcing facilities should carefully assess whether a drug compounded from that bulk drug substance would run afoul of the "essentially a copy" restriction in 503B.[60] The FDA to date has cited this provision in only one warning letter to an outsourcing facility,[61] but the agency's guidance on this subject suggests the possibility of increased enforcement.

Conclusion

Beyond the specific issues raised by the litigation described in this article, there remain numerous other legal issues to be resolved with respect to FDA regulation of drug

compounding. These include, among others, the FDA's continued development of cGMP requirements for outsourcing facilities,[62] the finalization of a memorandum of understanding between the FDA and the states relevant to traditional pharmacy compounding under Section 503A,[63] and the provision of compounded drugs for office use under Section 503A.[64]

In sum, scrutiny of the compounding practices of outsourcing facilities is unlikely to abate moving forward.

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[1] IBISWorld, Compounding Pharmacies in the US Market Size 2003–2024, https://www.ibisworld.com/industry-statistics/market-size/compounding-pharmacies-united-states.

[2] Compare FDCA § 503B(d)(4)(C) ("An outsourcing facility may or may not obtain prescriptions for identified individual patients."), with FDCA § 503A (imposing a condition that a drug product must be "compounded for an identified individual patient based on the receipt of a valid prescription order or a notation, approved by the prescribing practitioner, on the prescription order that a compounded product is necessary for the identified patient").

[3] FDCA § 505.

[4] FDCA § 502(f)(1).

[5] FDCA § 582.

[6] The term "bulk drug substances" has the same meaning as "active pharmaceutical ingredient." 21 C.F.R. § 207.3.

[7] FDCA §503B(a)(2)(A). A bulk drug substance used in compounding under section 503B must also be manufactured by an FDA-registered establishment, be accompanied by a valid certificate of analysis, and comply with an applicable USP-NF monograph (if one exists).

[8] FDCA §§ 503B(a)(5), 503B(d)(2); see FDA, Guidance for Industry: Compounded Drug Products That Are Essentially Copies of Approved Drug Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act (Jan. 2018), https://www.fda.gov/media/98964/download.

[9] See FDCA § 503A(b)(1)(D).

[10] See 78 Fed. Reg. 72,838 (Dec. 4, 2013); 79 Fed. Reg. 37,747 (July 2, 2014); 80 Fed. Reg. 65,770 (Oct. 27, 2015).

[11] FDCA § 503B(a)(2)(A)(i).

[12] 80 Fed. Reg. 65,768 (Oct. 27, 2015).

[13] 81 Fed. Reg. 37,500 (June 10, 2016).

[14] FDA, Revised Guidance for Industry: Interim Policy on Compounding Using Bulk Drug Substances Under Section 503B of the Federal Food, Drug, and Cosmetic Act (Jan. 2017), https://www.fda.gov/media/94402/download.

[15] Id. at 5-6.

[16] Id. at 8.

[17] A bulk drug substance must be nominated for inclusion on the 503B Bulks List to be categorized by FDA, and included on the agency's current lists. Id. at 9.

[18] Id. at 10.

[19] The list of bulk drug substances nominated for the 503B Bulks List and their current categorization is accessible at https://www.fda.gov/media/94164/download.

[20] FDA, Guidance for Industry: Evaluation of Bulk Drug Substances Nominated for Use in Compounding Under Section 503B of the Federal Food, Drug, and Cosmetic Act (Mar. 2019), https://www.fda.gov/media/121315/download. The agency first issued draft guidance in March 2018, see 83 Fed. Reg. 12,952 (Mar. 26, 2018), and issued final guidance one year later, 84 Fed. Reg. 7,390 (Mar. 4, 2019).

[21] Id. at 11.

[22] Id.

[23] Id. at 11-12.

[24] Allergan USA Inc. v. Prescriber's Choice, Inc., No. 8:17-cv-01550 (C.D. Cal. filed Sept. 7, 2017); Allergan USA, Inc. v. Imprimis Pharms., Inc., No. 8:17-cv-01551 (C.D. Cal. filed Sept. 7, 2017).

[25] Par Sterile Prods., LLC v. Hargan, No. 1:17-cv-2221 (D.D.C. filed Oct. 26, 2017).

[26] Athenex, Inc. v. Azar, No. 19-cv-00603 (D.D.C. filed Mar. 4, 2019).

[27] See Compl., Prescriber's Choice, No. 8:17-cv-01550 (C.D. Cal. Sept. 7, 2017); Compl., Imprimis, No. 8:17-cv-01551 (C.D. Cal. Sept. 7, 2017).

[28] See Compl. at 26-28, Prescriber's Choice, No. 8:17-cv-01550 (C.D. Cal. Sept. 7, 2017); Compl. at 34-36, Imprimis, No. 8:17-cv-01551 (C.D. Cal. Sept. 7, 2017). In Prescriber's Choice, Allergan also alleged violations of California's False Advertising Law and Florida's Deceptive and Unfair Trade Practices Act. Compl. at 28-31, Prescriber's Choice, No. 8:17-cv-01550 (C.D. Cal. Sept. 7, 2017).

[29] Order Denying Defendant's Motion to Dismiss at 12, Imprimis, No. 8:17-cv-01551 (C.D. Cal. Nov. 14, 2017).

[30] Id.

[31] Prescriber's Choice, 364 F. Supp. 3d 1089, 1105-06 (C.D. Cal. 2019) ("The Court will not hold Sincerus liable as a matter of law for 'sell[ing], deliver[ing], or giv[ing] away any new drug' that has not been approved by the California Department of Health Services or FDA if they have complied with the Interim Policy."); Order Granting In Part Plaintiff's Motion for Partial Summary Judgment, Granting in Part Defendant's Motion for Partial Summary Judgment, and Denying Defendant's Motion for Reconsideration [hereinafter "Imprimis Summary Judgment Order"] at 15, Imprimis, No. 8:17-cv-01551 (C.D. Cal. Mar. 27, 2019) (quoting language from Prescriber's Choice).

[32] See Prescriber's Choice, 364 F. Supp. 3d at 1107, 1112 ("Defendants violated the Sherman Law and the [Unfair Competition Law's] unlawful prong by making and selling unapproved drugs without complying with Section 503B or the FDA's Interim Policy up until July 2018"); Imprimis Summary Judgment Order at 23, 25-26, Imprimis, No. 8:17-cv-01551 (C.D. Cal. Mar. 27, 2019) (finding that Imprimis violated the Sherman Law by selling unapproved drugs with two bulk drug substances that were not on the 503B Category 1 list and made literally false statements under the Lanham Act about meeting the requirements of section 503B).

[33] See Prescriber's Choice, 364 F. Supp. 3d at 1107, 1112; Imprimis Summary Judgment Order at 16-29, Imprimis, No. 8:17-cv-01551 (C.D. Cal. Mar. 27, 2019) (quoting language from Prescriber's Choice). Additionally, while the Prescriber's Choice court determined that the alleged false statements regarding clinical superiority could not be resolved on the motion for summary judgement, see 364 F. Supp. 3d at 1112, the Imprimis court held that Imprimis's superiority claims were literally false in violation of the Lanham Act. See Imprimis Summary Judgment Order at 25-28, Imprimis, No. 8:17-cv-01551 (C.D. Cal. Mar. 27, 2019).

[34] Consent Judgment at 2-3, Prescriber's Choice, No. 8:17-cv-01550 (C.D. Cal. Jan. 31, 2019).

[35] Judgment Pursuant to the Jury's Verdict, Imprimis, No. 8:17-cv-01551 (C.D. Cal. May 28, 2019).

[36] Order Granting in Part Motion for Permanent Injunction at 22, Imprimis, No. 8:17-cv-01551 (July 11, 2019).

[37] Id.

[38] Complaint at 2, Par Sterile Prods., LLC v. Hargan, No. 17-cv-02221 (D.D.C. Oct. 26, 2017).

[39] Id. at 19-21.

[40] Id.

[41] Id. at 35.

[42] Order Granting Joint Motion for Stay of the Case, Par Sterile Prods., LLC v. Hargan, No. 17-cv-02221 (D.D.C. Jan. 25, 2018).

[43] See 83 Fed. Reg. 12,952 (Mar. 26, 2018).

[44] Motion of Athenex Pharma Solutions, LLC and Athenex Pharmaceutical Division, LLC to Intervene, Par Sterile Prods., LLC v. Hargan., No. 17-cv-02221 (D.D.C. Aug. 13, 2018).

[45] Plaintiffs' Motion for Preliminary Injunction, Par Sterile Prods., LLC v. Azar, No. 17-cv-2221 (D.D.C. Aug. 21, 2018).

[46] 83 Fed. Reg. 43,877, 43,881-82 (Aug. 28, 2018) (finding "no basis to conclude that there is a clinical need for an outsourcing facility to compound using the bulk drug substance vasopressin").

[47] 84 Fed. Reg. 7,383, 7,388 (Mar. 4, 2019) (finding "no basis to conclude that drug products must be compounded using a bulk drug substance rather than" the FDA-approved version of vasopressin).

[48] Complaint, Athenex, Inc. v. Azar, No. 19-cv-00603 (D.D.C. Mar. 4, 2019).

[49] See id. at 3.

[50] Id at 14-15.

[51] See Scheduling Order at 1, Athenex, Inc. v. Azar, No. 19-cv-00603 (D.D.C. Mar. 11, 2019) (granting unopposed motion to intervene by Par).

[52] Memorandum Opinion at 2, Athenex, Inc. v. Azar, No. 19-cv-00603 (D.D.C. Aug. 1, 2019) (holding 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" and that FDA's exclusion of vasopressin was not arbitrary and capricious).

[53] Id.

[54] Id. at 26.

[55] Id. at 23-25.

[56] Id. at 29-31.

[57] Id. at 31.

[58] See 84 Fed. Reg. 46,014 (Sept. 3, 2019).

[59] See FDA Warning Letter to Imprimis NJOF, LLC (June 7, 2019) (citing inappropriate compounding of gatifloxacin from bulk); FDA Warning Letter to Bella Pharmaceuticals, Inc. (Feb. 11, 2019) (citing inappropriate compounding of fluorescein sodium from bulk); FDA Warning Letter to Hybrid Pharma, LLC (Nov. 30, 2018) (citing inappropriate compounding of sildenafil, human chorionic gonadotropin, and testosterone cypionate from bulk); FDA Warning Letter to Auro Pharmacies, Inc. (Sept. 24, 2018) (citing inappropriate compounding of zinc chloride, selenium, and L-carnitine from bulk).

[60] See FDCA §§ 503B(a)(5), 503B(d)(2); FDA, Guidance for Industry: Compounded Drug Products That Are Essentially Copies of Approved Drug Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act, at 9 (Jan.

2018), https://www.fda.gov/media/98964/download ("If a component of the compounded drug is a bulk drug substance that is also a component of an approved drug, the compounded drug product is essentially a copy of an approved drug, and cannot be compounded under section 503B, unless there is a prescriber determination of clinical difference.").

[61] See FDA Warning Letter to INCELL Corporation, LLC (Oct. 28, 2016).

[62] FDA issued a revised draft guidance outlining cGMP policies applicable to outsourcing facilities in September 2018. FDA, Draft Guidance for Industry: Current Good Manufacturing Practice—Guidance for Human Drug Compounding Outsourcing Facilities Under Section 503B of the FD&C Act (Dec. 2018), https://www.fda.gov/media/88905/download. FDA has not yet issued proposed cGMP regulations for outsourcing facilities.

[63] See FDCA § 503A(b)(3)(B). FDA issued a revised draft memorandum of understanding for consideration in September 2018. FDA, Draft Memorandum of Understanding Addressing Certain Distributions of Compounded Drug Products Between the State of [Insert State] and the U.S. Food and Drug Administration (Sept.
2018), https://www.fda.gov/media/91085/download.

[64] Although stakeholders in the 503A compounding industry have frequently urged FDA to permit limited, non-patient-specific compounding for office use under section 503A, FDA has to date remained steadfast that a patient-specific prescription is required before a drug compounded under section 503A may be distributed. See, e.g., FDA, Guidance for Industry: Prescription Requirement Under Section 503A of the Federal Food, Drug, and Cosmetic Act, at 10 (Dec. 2016), https://www.fda.gov/media/97347/download.