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OUTSOURCING FACILITIES ASSOCIATION

Lee H. Rosebush
Chairman | OFA
Partner | BakerHostetler
1050 Connecticut Avenue, NW
Suite 1100
Washington, D.C. 20036-5403

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Division of Dockets Management (HFA-305)
U.S. Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

RE: Docket No. FDA–2018–N–3240 for ‘‘List of Bulk Drug Substances for Which There is a Clinical Need Under Section 503B of the Federal Food, Drug, and Cosmetic Act.’’

I About the Outsourcing Facilities Association (“OFA”)

The Outsourcing Facilities Association ("OFA") is the trade association representing FDA-registered outsourcing facilities ("503Bs") operating pursuant to Section 503B of the Federal Food, Drug, and Cosmetic Act ("FD&C Act"). OFA's members provide compounding services to patients, healthcare providers, and healthcare facilities, and strive to ensure the specific needs of both providers and patients are met with safe and effective compounded and/or repackaged medications. OFA has been actively following the U.S. Food and Drug Administration's (the "FDA") implementation of the Compounding Quality Act ("CQA") and has brought together members of industry to advocate for a safe, reasonable, and practical rollout of the CQA.

OFA respectfully submits this comment in response to the FDA’s Federal Register notice titled *List of Bulk Drug Substances for Which There is a Clinical Need Under Section 503B of the Federal Food, Drug, and Cosmetic Act* (“Bulk Notice”).[1] In the Bulk Notice, the FDA identifies two bulk drug substances that the FDA has considered and proposes to include on the 503B Bulks List to compound three categories of compounded drug products.[2] The Bulk Notice also identifies three bulk drug substances that the FDA has considered and proposes not to include on the 503B Bulks List.[3]

OFA is again submitting this comment to urge the FDA to publicly define “clinical need” and reconsider its approach to issue Federal Register Notices which create a “no clinical need” list.

II FDA should define “Clinical Need”

[1] List of Bulk Drug Substances for Which There is a Clinical Need Under Section 503B of the Federal Food, Drug, and Cosmetic Act, 87 Fed. Reg. 71,642 (Nov. 23, 2022) [hereinafter Bulk Notice].
[2] FDA proposes to include on the 503B Bulks List to compound three categories of compounded drug products: arginine hydrochloride (HCl) for oral use, lysine HCl for oral use, and lysine HCl for intravenous use in combination with FDA-approved, single-ingredient arginine HCl for intravenous use.
[3] FDA proposes **not** to include on the 503B Bulks List: etomidate, furosemide, and rocuronium bromide.

The FDA's "I know it when I see it" approach to "clinical need" is ill-advised. The FDA has yet to define "clinical need" but instead uses a two-part evaluation criteria announced in guidance. Whether a "clinical need" exists should be determined by a prescribing practitioner, not the FDA.

III FDA's proposal is contrary to the intent of Section 503B

As the OFA has expressed previously, the FDA's proposal to limit the finished dosage forms that may be compounded from bulk drug substance is contrary to Congress' intent.[4] Only allowing the compounding of certain dosage forms when compounding from bulk drug substance is not what Congress intended. If Congress did intend this limitation, Congress would have directed the FDA to make a list of finished drug products that 503Bs may compound from bulk drug substances. Congress did not. Congress instead directed the FDA to make a list of bulk drug substances that 503Bs may use in compounding. The FDA continues to misinterpret its Congressional directive regarding the 503B Bulks List.

Again, the DQSA directs the FDA to create a "clinical need list," also referred to as the "503B Bulks List." The 503B Bulks List is simply a list of bulk drug substances that may be used by 503Bs to compound drug products. The 503B Bulks List is, not a list of finished products that may or may not be compounded using bulk drug substance—that protection is supplied by the "essentially a copy" provision[5], which ensures that 503Bs are not compounding copies of FDA-approved drugs.

Worse yet, the FDA is creating a "no clinical need list" in its proposals to not include bulk drug substances on the 503B Bulks List. Instead of creating the 503B Bulks List as instructed by Congress, the FDA is conversely proposing to NOT include substances on the list. This method is a waste of resources and creates burdens to patient access if a clinical need arises in the future. For example, if there is currently no clinical need, the FDA should remain silent and allow additional nominations. The FDA states that:

> After FDA publishes a Federal Register notice making a final determination regarding whether a bulk drug substance will be placed on the 503B Bulks List, FDA will no longer consider comments submitted to the docket regarding that bulk drug substance, but interested parties may submit a citizen petition to FDA requesting specific action or relief (see 21 CFR 10.30).[6]

Section 503B provides:

> (A)(i) the bulk drug substance appears on a list
> established by the Secretary identifying bulk drug substances
> for which there is a clinical need, by--
> ``(I) publishing a notice in the Federal Register
> proposing bulk drug substances **to be included on the list**,
> including the rationale for such proposal;
> ``(II) providing a period of not less than 60 calendar
> days for comment on the notice; and

[4] *See* Judge Rotenberg Educ. Ctr., Inc. v. U.S. Food & Drug Admin., 3 F.4th 390 (D.C. Cir. 2021). ("When Congress has spoken in a statute, we assume that it says what it means and that the statute means what it says.")
[5] *See* section 503B(a)(5) of the Federal Food, Drug, and Cosmetic Act (codified at 21 U.S.C. § 353b(a)(5)).
[6] Bulk Notice at 71,645.

``(III) publishing a notice in the Federal Register designating bulk drug substances **for inclusion on the list**;

Remarkably, Section 503B does not say the FDA is to propose bulk drug substances to NOT be included on the list. Again, the FDA's proposal is contrary to Congress' intent and the FDA lacks authority to determine that there is no clinical need for a bulk drug substance.

IV FDA is Regulating the Practice of Medicine

The FDA does not have the authority to regulate the practice of medicine. Based on the legislative history[7] of the FD&C Act, courts,[8] as well as Congress are completely clear that the FDA cannot regulate the practice of medicine.

Despite this, the FDA is clearly attempting to regulate the practice of medicine here. The FDA's proposal to not include these bulk drug substances on the 503B Bulks List and limit those it does include to certain routes of administration is an act of regulating the practice of medicine. Numerous medical practitioners have expressed their desire to use compounded drugs from bulk under the current Good Manufacturing Practices ("CGMP") standards required of 503Bs. This is a stricter, more robust standard than 503A pharmacies are held to. In fact, CGMP standards are the same standards that drug manufacturers are subject to. By the FDA pushing an overly restrictive policy for 503B bulk drug compounding, the FDA is forcing medical providers to obtain compounded drug products from bulk drug substances that a compounder, subject to a lower regulatory standard, produced—in turn subjecting patients to riskier compounded drugs. Limitations on compounding from bulk drug substances directly put patients at risk of harm or even death. This policy, unfortunately to the detriment of public health, will be ripe for another NECC incident.

Second, depriving those who have the authority to practice medicine of the opportunity to practice medicine as they deem best is in fact regulating the practice of medicine. If the FDA regulates the practice of medicine in this manner, the FDA will force medical doctors to prescribe compounded medication that is prepared under the less robust quality standards of Section 503A of the FD&C Act because Section 503A allows compounding from bulk when the bulk drug substance is a component of an FDA-approved product. Per established precedent, the FDA does not regulate the practice of medicine and it should not be allowed or encouraged to do so here. For these reasons, the FDA must not finalize its proposal for the 503B Bulks List.

V Conclusion

For the foregoing reasons, the FDA should immediately include all nominated substances on the 503B Bulks List to be compounded in an unrestricted manner. The FDA should enforce the "essentially a copy" provision of Section 503B to protect the integrity of the drug approval process.

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[7] *See* U. S. Government Printing Office. Legislative History of the Federal Food, Drug & Cosmetic Act and Its Amendments (1934) (the definition of the term drug included "for purposes of this Act and not regulate the practice of medicine…"). S. 2800, 73rd Cong., 2d Sess.,§ 2(b)(1934).

[8] *See Chaney v. Heckler*, 718 F.2d 1174 (D.C. Cir. 1984), *rev'd*, 470 U.S. 821 (1985).

Respectfully submitted,

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Lee H. Rosebush

Chairman, OFA