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OFA
OUTSOURCING FACILITIES ASSOCIATION

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Dockets Management Staff (HFA–305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA-2016-D-0271 for "Hospital and Health System Compounding Under Section 503A 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 under current good manufacturing practices ("CGMPs"). OFA has been actively following U.S. Food and Drug Administration's (the "FDA") implementation of the Compounding Quality Act[1] ("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OFA respectfully submits this comment in response to FDA's revised draft guidance on Hospital and Health System Compounding Under Section 503A of the Federal Food, Drug, and Cosmetic Act.[2]

II. FDA Must Revise the 24-Hour Window

Under the Revised Guidance, the FDA generally does not intend to take action with respect to the prescription requirement in section 503A of the FD&C Act if a hospital or health system pharmacy that is not an outsourcing facility compounds and distributes a compounded drug product without first receiving a valid prescription order (including a chart order) for an identified individual patient if:

- The compounded drug products are used or discarded within 24 hours of transfer out of the pharmacy, i.e. the 24-Hour Window

This 24-Hour Window does not adequately mitigate safety risks as it is intended. The FDA supports the 24-Hour Window with:

[1] Drug Quality and Security Act, Pub. L. No. 113-54, 127 Stat. 587 (codified at 21 U.S.C. § 353b)
[2] Hospital and Health System Compounding Under Section 503A of the Federal Food, Drug, and Cosmetic Act; Revised Draft Guidance for Industry (Oct 7, 2021) [hereinafter Revised Guidance].

> Such a limit mitigates concerns about the amount and scope of distribution of the compounded drug product. FDA selected 24 hours as the window within which compounded drug products be used or discarded because the Agency has heard from stakeholders that non-patient-specific drugs are needed for emergency uses. FDA anticipates that non-patient-specific compounded drugs that are kept on hand for longer periods can and should be obtained from outsourcing facilities because outsourcing facilities can compound and distribute drugs without receiving patient specific prescriptions and, because they are subject to CGMPs, conduct appropriate stability tests and have more robust sterility assurance practices.[3]

The FDA must revise the term "transfer out of the pharmacy" to "compounded". If the FDA wants to permit compounding for emergency uses and encourage non-patient-specific compounded drugs kept on hand for longer periods to be obtained from outsourcing facilities, the FDA must use the verbiage "compounded" in lieu of "transfer out." If the 24-hour clock started from the time the drug was compounded, this would require the drug to be used or discarded within 24 hours. As currently drafted, the Revised Guidance would allow for a drug to be compounded and stored in the pharmacy prior to being transferred out. This allowance for a storage period in the pharmacy does not encourage compounding for emergency uses only nor does it encourage non-patient-specific compounded drugs kept on hand for longer periods to be obtained from outsourcing facilities. Replacing "transfer out" with "compounded" also resolves confusion over whether automated dispensing cabinets or storage rooms are considered part of the "pharmacy."

A revision that would permit compounding for emergency uses and encourage non-patient-specific compounded drugs kept on hand for longer periods to be obtained from outsourcing facilities would read as follows:

- The compounded drug products are used or discarded within 24 hours of **compounding**

III. FDA Must Hold Hospital Pharmacies and Outsourcing Facilities to the Same Essentially a Copy Standard

The conditions under which the FDA does not intend to take action against a hospital or health system pharmacy that is not an outsourcing facility for compounding a drug product that is essentially a copy of a commercially available drug product are too broad compared to the conditions used to evaluate whether a drug product is essentially a copy when compounded by an outsourcing facility.[4] If the FDA intends to encourage hospitals and hospital pharmacies to obtain

[3] Compounded Drug Products That Are Essentially Copies of Approved Drug Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act Guidance for Industry, Guidance for Industry (January 2018), fn 23.
[4] OFA does not endorse the current guidance on *Compounded Drug Products That Are Essentially Copies of Approved Drug Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act. See* OFA Comment on Citizen Petition from Nexus Pharmaceuticals Inc., FDA-2021-P-0358. Although OFA does not endorse the current guidance, OFA does believe that hospitals and outsourcing facilities should be held to the same standard.

compounded drug products from outsourcing facilities, the essentially a copy standard should be the same for both hospital pharmacies and outsourcing facilities. Outsourcing facilities are stepping into the shoes of the hospital pharmacy or hospitals are stepping into the shoes of an outsourcing facility. The end result is a compounded drug product. The standard by which that compounded drug product is evaluated should be the same. Under the Revised Guidance, the essentially a copy hurdle is more lenient than what is considered an essentially a copy for outsourcing facilities.[5] Hospital pharmacies are held to the essentially a copy standard for 503A pharmacies but a different, more stringent standard exists for 503B outsourcing facilities.

If outsourcing facilities are performing a service for hospitals under more robust quality standards but hospitals could otherwise perform the same compounding under a lesser quality standard, the essential copy standard should be the same so that there is an incentive for hospitals to obtain compounded drug product from outsourcing facilities.

IV. FDA Must Define "Common Ownership" and "Joint Management"

The Revised Guidance provides:

> In this guidance, *hospital pharmacy* refers to a pharmacy that is connected to a hospital through common ownership or joint management, and *health system pharmacy* refers to a pharmacy that is connected to a health system by common ownership or joint management. A pharmacy may be both a hospital pharmacy and a health system pharmacy.[6]

Left undefined, common ownership or joint management opens up loopholes for hospitals to continue compounding and obtaining compounded product from pharmacies not registered with the FDA or operating under CGMP standards. For example, when undefined, common ownership could include a hospital owning one share of stock of a holding company owning a pharmacy. Although an extreme example, this shows the need to define these terms for purposes of the guidance. Alternatively, a hospital could enter into a joint management agreement with several other hospitals, a group purchasing organization, and a pharmacy—this type of arrangement would allow one pharmacy to provide compounded medication to multiple hospitals. As noted in the Revised Guidance, it is preferred for hospitals to obtain compounded drugs from outsourcing facilities. The FDA must define "common ownership" and "joint management" to close these loopholes.

V. FDA Must Protect the Public Health by Ensuring the Safety of Compounded Drug Products

Several Commenters erroneously characterize the New England Compounding Center as a 503B outsourcing facility. This characterization is objectively false. 503B outsourcing facilities did not exist at the time of the New England Compounding Center tragedy. Instead, the New England Compounding Center was operating under the same compounding standards that hospital and

[5] Compounded Drug Products That Are Essentially Copies of Approved Drug Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act Guidance for Industry, Guidance for Industry (January 2018).
[6] Revised Guidance, fn 12.

health system pharmacies adhere to—Section 503A. Congress created Section 503B of the FD&C Act in response to the New England Compounding Center tragedy. Congress created a safer compounding environment in 503B outsourcing facilities as Congress's intent was articulated by Representative Frank Pallone (D-NJ) during the House Debate:

> The bill will permit compounders who wish to practice outside the scope of traditional pharmacy to register as outsourcing facilities but those who choose to remain traditional pharmacies will continue to be regulated as they are under current law. ***This gives doctors and hospitals the ability to purchase compounded drugs for their patients made in a facility that is subject to stringent FDA quality standards and oversight*** (emphasis added).[7]

The FDA must revise the draft guidance to improve the safety of compounded drug products. Other commenters raise concerns about the cost of compounded drug products produced by outsourcing facilities. This concern is misplaced and does not consider the substantial hidden costs incurred when a hospital pharmacy compounds a drug. Researchers note that "[f]or some hospitals, implementing best practices guidelines such as United States Pharmacopeia (USP) <797> standards can be time-consuming and costly, as addressed in the 2019 public comments for the recent revision of the USP <797>."[8] These costs are the cost for a hospital pharmacy to comply with the lesser quality standard of USP <797> instead of the more robust standard that outsourcing facilities comply with—CGMP. If a hospital pharmacy were to compound at the same standard as an outsourcing facility, hospital cost of compliance would increase, and additionally, the hospital pharmacy would need to pay the cost of registering with the FDA as an outsourcing facility.[9] When analyzing costs, hospitals must factor in recurring costs such as pharmacist and pharmacy technician salaries and insurance required to maintain adequate staff levels to compound drug products. Obtaining compounded medication from outsourcing facilities decreases all of these aforementioned costs for a hospital and increases safety.

Other commenters raise concerns over outsourcing facilities with unresolved 483 observations. OFA acknowledges these concerns and urges the FDA to commit to a close-out target of 90 days for 503B outsourcing facility inspections. However, we would also point out that many 503A pharmacies, including those affiliated or used by hospitals, have open 483s as well.

VI. Conclusion

The FDA must further revise the Hospital and Health System Compounding Under Section 503A of the Federal Food, Drug, and Cosmetic Act, Guidance for Industry to only allow compounding

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[7] Floor Debate on H.R. 3204 (Sept. 28. 2013) (statement of Rep. Pallone) at 14:40, the Honorable Frank Pallone, YOUTUBE, https://www.youtube.com/watch?v=suLWdacjcY0.

[8] Gianturco SL, Yoon S, Yuen MV, Mattingly AN. Outsourcing facilities and their place in the U.S. drug supply chain. *J Am Pharm Assoc (2003)*. 2021;61(1):e99-e102. doi:10.1016/j.japh.2020.07.021.

[9] For Fiscal Year 2022, the outsourcing facility establishment registration fee is $ 18,999 and the re-inspection fee is $17,472.

outside of a CGMP environment when necessary.

Respectfully submitted,

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Lee H. Rosebush, Chairman OFA

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