

November 4, 2024

BY ELECTRONIC MAIL

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

Re: Docket No. FDA-2024-N-3762: Agency Information Collection Activities; Proposed Collection; Comment Request; Obtaining Information To Understand Challenges and Opportunities Encountered by Compounding Outsourcing Facilities

To Whom It May Concern:

The Pharmaceutical Research and Manufacturers of America (“PhRMA”) is pleased to submit these comments in response to the Food and Drug Administration (“FDA” or “the Agency”) notice of proposed information collection on the challenges and opportunities pertaining to human prescription drug compounding by outsourcing facilities.¹ PhRMA represents the country’s leading innovative biopharmaceutical research companies, which are laser focused on developing innovative medicines that transform lives and create a healthier world. Together, we are fighting for solutions to ensure patients can access and afford medicines that prevent, treat and cure disease. Over the last decade, PhRMA member companies have invested more than \$800 billion in the search for new treatments and cures, and they support nearly five million jobs in the United States.

PhRMA appreciates FDA’s interest in conducting research to address quality and safety problems identified during inspections of outsourcing facilities and to prevent harm associated with compounded drugs. As FDA itself recognizes, compounded drugs are subject to a lower regulatory standard than FDA-approved drugs, which meet FDA’s gold standard of safety and effectiveness.² Unlike manufacturers of FDA-approved drugs, outsourcing facilities produce and distribute compounded drugs without obtaining premarket approval, without premarket inspections, without adequate instructions for use in labeling, without drug supply chain security assurances, and without rigorous pharmacovigilance and adverse event reporting systems.³ As a result, compounded drugs pose a higher risk to patients than FDA-approved drugs.

The risks posed by drugs compounded by outsourcing facilities are growing as outsourcing facilities significantly increase their compounding and distribution activities. Outsourcing

¹ 89 Fed. Reg. 72410 (Sept. 5, 2024).

² FDA, Compounding when Drugs are on FDA’s Drug Shortages List, <https://www.fda.gov/drugs/human-drug-compounding/compounding-when-drugs-are-fdas-drug-shortages-list> (accessed Oct. 31, 2024).

³ See FDA, FD&C Act Provisions that Apply to Human Drug Compounding, <https://www.fda.gov/drugs/human-drug-compounding/fdc-act-provisions-apply-human-drug-compounding> (accessed Oct. 31, 2024).

facilities are expanding their reach beyond the historical model of supplying compounded drugs to hospitals and other providers for office stock.⁴ They are entering into new and unanticipated commercial arrangements with telehealth companies to engage in aggressive nationwide advertising.⁵ To meet the extensive market that they and their partners are generating, outsourcing facilities must compound more drugs faster than ever, making mistakes and adverse events associated with compounded drugs all the more concerning.⁶ Congress never intended outsourcing facilities to operate as conventional drug manufacturers compounding drugs without regard to individual patient need.⁷ At this critical juncture where outsourcing facilities are enlarging their scope, pace, and volume, FDA must stop outsourcing facilities from behaving like conventional drug manufacturers and do more to protect patients from the risks associated with their compounded products.

PhRMA urges FDA to prioritize patient safety by assessing and addressing compounding quality and safety issues, including by revising the proposed survey of outsourcing facilities. PhRMA's comments on the proposed survey address two of the topics on which the Agency has invited comment: (1) whether the proposed collection of information is necessary for the proper performance of FDA's functions, including whether the information will have practical utility; and (2) ways to enhance the quality, utility, and clarity of the information to be collected.

First, PhRMA believes the proposed questions are unlikely to advance the Agency's public health mission or the safety and quality objectives of the Compounding Quality Center of Excellence⁸ and are unlikely to have practical utility. Several questions focus on financial considerations and economic consequences outside of FDA's public health mission and the Compounding Quality Center of Excellence's remit: Questions 1 ("What financial and operational considerations inform outsourcing facility operational and business model decisions?"); 2 ("What factors impact developing a sustainable outsourcing facility business?"); 3 ("What financial and operational considerations inform outsourcing facility product decisions?"); and 8 ("What are the economic consequences of CGMP noncompliance and product failures for outsourcing facilities?"). These questions aim to solicit information about operational considerations that are not necessary for FDA's oversight of outsourcing facilities and are unrelated to FDA's public health mission and the quality and safety of compounded drugs.

⁴ Gabriela Barkho, *Weight loss drugs like Ozempic are giving DTC telemedicine platforms a boost*, MODERNRETAIL (Mar. 25, 2024), <https://www.modernretail.co/operations/weight-loss-drugs-like-ozempic-are-giving-dtc-telemedicine-platforms-a-boost/>.

⁵ *Id.*

⁶ See FDA, *FDA's Concerns with Unapproved GLP-1 Drugs Used for Weight Loss*, <https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/fdas-concerns-unapproved-glp-1-drugs-used-weight-loss> (accessed Oct. 31, 2024).

⁷ FDA, *Prohibition on Wholesaling Under Section 503B of the Federal Food, Drug, and Cosmetic Act: Draft Guidance*, at 3 (June 2023), <https://www.fda.gov/media/169838/download>.

⁸ FDA, *Compounding Quality Center of Excellence*, <https://www.fda.gov/drugs/human-drug-compounding/compounding-quality-center-excellence> (accessed Oct. 31, 2024) (supporting "[o]utsourcing facilities' efforts to improve the quality of drugs they produce through training, research and engagement activities with FDA and other supporting stakeholders" and "[c]ustomers of outsourcing facilities and patients who receive necessary compounded drugs to help ensure access to quality drugs in care settings with a focus on patient safety").

Second, PhRMA believes that the Agency should enhance its information collection request by centering regulatory, quality, and safety considerations related to the Agency’s oversight of outsourcing facilities. This will help ensure that the collection of information is aligned with the Agency’s public health mission and the Compounding Quality Center of Excellence’s purpose. PhRMA appreciates that FDA poses two questions—4 (“Do outsourcing facilities understand the Federal laws and policies that apply to them? What, if any, knowledge gaps do we need to address?”) and 6 (“How do outsourcing facilities implement quality practices at their facilities?”)—that inquire about compliance with FDA’s compounding framework. However, PhRMA recommends FDA probe deeper amid rampant compounding and serious and rising patient safety concerns associated with compounded drugs. The Agency should pose more probative questions to obtain information on how outsourcing facilities comply with regulatory and quality frameworks designed to prevent them from transforming into conventional manufacturers and to avoid distribution of unsafe, ineffective, and poor quality compounded drugs.

Specifically, in its survey, the Agency should ask outsourcing facilities to explain *how* they intend to comply with federal laws and policies that apply to them.⁹ PhRMA proposes the following questions for consideration:

- “What are outsourcing facilities’ written and implemented procedures for the surveillance, receipt, evaluation, and reporting of postmarketing adverse drug experiences to FDA?”¹⁰
- “How do outsourcing facilities secure compliance with the prohibitions on wholesaling and resale when they enter into commercial arrangements with other entities?”¹¹
- “Do outsourcing facilities label compounded drugs as ‘Not for Resale’ and ‘Office Use Only’ when they are selling or transferring compounded drugs outside of clinical settings?”¹²
- “How do outsourcing facilities ensure that compounded drugs are not resold or used in violation of the ‘Not for Resale’ and ‘Office Use Only’ labeling requirements?”
- “How are outsourcing facilities establishing the validity of the certificates of analyses accompanying bulk drug substances that will be used in compounding?”¹³
- “When outsourcing facilities are compounding versions of FDA-approved drugs that appear on FDA’s drug shortage list, are they ensuring that those compounded drugs are identical or nearly identical to the FDA-approved drugs currently in shortage?”¹⁴
- “How do outsourcing facilities make certain that the prescribing practitioner is arriving at their own determination that a change between a compounded drug and the comparable approved drug produces a clinical difference for an individual patient?”¹⁵

⁹ FDA also should conduct a comprehensive legal assessment of its own compounding policies to ensure that it is properly interpreting and applying the Federal Food, Drug, and Cosmetic Act to drugs compounded by outsourcing facilities, including with respect to adverse event reporting, wholesaling, bulk drug substances, copies, and advertising and promotion.

¹⁰ Federal Food, Drug, and Cosmetic Act § 503B(b)(5).

¹¹ *Id.* §§ 503B(a)(8), 301(ccc)(1).

¹² *Id.* § 503B(a)(10)(A)(IX).

¹³ *Id.* § 503B(a)(2)(D).

¹⁴ *Id.* §§ 503B(a)(5), 503B(d)(2)(A).

¹⁵ *Id.* §§ 503B(a)(5), 503B(d)(2)(B).

- “What measures are outsourcing facilities taking to ensure that they and their partners do not engage in false and misleading advertising and promotion of compounded drugs?”¹⁶

In addition, FDA can enhance the utility of the voluntary survey by supplementing it with more inspections of outsourcing facilities, especially of new outsourcing facilities that engage in compounding without any premarket FDA inspection. Doing so would be consistent with FDA’s public health mission and better focus FDA resources for compounding quality and safety.

FDA’s stated rationale for conducting this survey and “in depth research” (to implement programs to address “quality and safety problems” identified during inspections of outsourcing facilities) requires stronger, more probative questions. We urge FDA to focus on gathering information about whether outsourcing facilities are adhering to the guardrails that are intended to prevent them from operating like conventional manufacturers and to prevent patients from receiving unsafe, ineffective, and poor quality compounded drugs.

Respectfully submitted,

/s/

Kelly Falconer Goldberg
Vice President
Law/Senior Counsel for Biopharmaceutical Regulation

¹⁶ *Id.* §§ 502(a), 502(bb); FDA, Compounding and the FDA: Questions and Answers, <https://www.fda.gov/drugs/human-drug-compounding/compounding-and-fda-questions-and-answers> (accessed Oct. 31, 2024).