

July 15, 2016

Robert M. Califf, M.D.  
Commissioner of Food and Drugs  
Division of Dockets Management (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, Room 1061  
Rockville, MD 20852

***RE: Draft Guidance for Industry – Docket No. FDA-2016-D-0271: Hospital and Health System Compounding Under the Federal Food, Drug, and Cosmetic (FD&C) Act; Docket No. FDA-2016-D-0238: Facility Definition under Section 503B of the Federal FD&C Act; and, Docket No. FDA-2016-D-0269: Prescription Requirement under Section 503A of the Federal FD&C Act.***

Dear Dr. Califf:

On behalf of our nearly 5,000 member hospitals, health systems and other health care organizations, and our 43,000 individual members, the American Hospital Association (AHA) appreciates the opportunity to comment on the Food and Drug Administration's (FDA) draft compounding guidance documents including: Hospital and Health System Compounding Under the Federal Food, Drug, and Cosmetic (FD&C) Act; Facility Definition Under Section 503B of the FD&C Act; and Prescription Requirement Under Section 503A of the FD&C Act. **The AHA appreciates the FDA's efforts to ensure that its compounding regulatory framework allows hospitals and health systems to continue to deliver safe and high-quality care to patients.** We also applaud the FDA for holding listening sessions to ensure that stakeholders, including hospitals and health systems, had the opportunity to provide in-person input to the draft guidance. **However, as discussed below, we are concerned that the one-mile radius limitation proposed by the FDA would not be workable for hospitals and health systems with centralized compounding pharmacies.** The AHA comments that follow are intended to assist the FDA in the development of a compounding regulatory framework that is supportive of and strengthens the hospital and health system care delivery model while ensuring high-quality compounding of drugs that are safe and able to be administered timely to patients within our hospitals and health systems.

Section 503A of the FD&C Act describes the conditions under which drug products compounded by state-licensed pharmacies, including hospital and health system pharmacies, are exempted from the drug manufacturing requirements, such as requirements for new drug approval, labeling



and current good manufacturing practices (CGMP). Among these conditions is the “prescription requirement” that requires that the drugs must either be compounded: (1) after the receipt of a valid prescription or order for an identified individual patient; or (2) in limited quantities *before* receipt of a valid prescription or an order for an identified individual patient (i.e. anticipatory compounding), as long as there is an established relationship and a history of the receipt of valid prescriptions between the licensed pharmacist preparing the compounded drug and the prescribing physician. While Section 503A permits a pharmacy to conduct such anticipatory compounding, the FDA believes that 503A does not generally permit compounded drug products to be *distributed* outside of the pharmacy before it receives a patient-specific prescription or order. However, recognizing that hospital and health system pharmacies must sometimes distribute non-patient-specific compounded products in anticipation of a patient who presents with an urgent need for a compounded drug, the FDA proposes an exception. Specifically, it proposes that it would not take enforcement action against a hospital or health system if:

- The drug products are distributed only to health care facilities that are owned and controlled by the same entity that owns and controls the hospital pharmacy ***and that are located within a one-mile radius of the compounding pharmacy***; (emphasis added)
- The drug products are only administered within the health care facilities to patients within the health care facilities, pursuant to a patient-specific prescription or order; and
- The drug products are compounded in accordance with all other provisions of Section 503A and other requirements of the FD&C Act.

**One-Mile Radius Criterion. While we appreciate the FDA’s intent in proposing this exception, the AHA is concerned that the one-mile radius limitation would not be workable for many hospitals and health systems that have centralized their sterile compounding activities in a single location and distribute compounded products to their other system hospitals and health care facilities located more than one mile away. We believe that this limitation would be counterproductive, reducing timely access to care and potentially having a negative impact on patient safety and quality of care.**

The compounding of sterile drug products is a fundamental part of pharmacy practice in hospitals and health care systems. As the FDA recognizes in its draft guidance, many hospitals and health systems have centralized compounding pharmacies that, in advance of a patient-specific prescription or order, prepare and distribute quantities of compounded drugs to other hospitals and health care facilities that are part of their system, many of which may be located more than one mile away. These sterile compounded drugs are then held at the system’s hospitals or its outpatient facilities until a patient presents with a need for the drug. It is important to note that even in these circumstances, drugs are only dispensed for administration to a patient upon a patient-specific prescription or, more commonly, an order written into the patient’s chart.

Centralized sterile compounding in health systems helps ensure that products can be prepared efficiently, safely, and in compliance with strict standards for quality and consistency. Hospitals

and health systems are subject to significant oversight with regard to their sterile compounding activities. While all 503A compounding falls under the purview of the States' Boards of Pharmacy, hospitals and health systems are also subject to additional quality and safety standards. These include the United States Pharmacopeial Convention (USP) standards, such as USP Chapter 797 for sterile compounding and USP Chapter 800 for hazardous drug preparation. In addition, hospitals and health systems must comply with The Joint Commission (TJC) standards, the Centers for Medicare & Medicaid Services (CMS) conditions of participation for hospitals, and other state and local regulation. After the tragic 2012 New England Compounding Center meningitis outbreak, many hospitals and health systems in-sourced and consolidated their sterile compounding activities into a single facility, in order to assure patient quality and safety. These centralized compounding pharmacies use state-of-the-art technologies and are staffed with highly-trained, certified and competent individuals. This allows the preparation of sterile compounds that have the benefit of economy of scale, better patient access, improved quality assurance and the reduction in the potential for errors that may otherwise occur if different staff prepare these compounded drugs at multiple locations or if physicians or nurses were to compound drugs at the patient bedside.

Centralized sterile compounding is also intended to ensure that patients can receive appropriate and high-quality treatment in a timely manner. For example, sterile compounded drugs are commonly distributed this way for urgent uses in surgeries and in emergency departments. Also, drugs that are not otherwise commercially available in the right dosages or forms or cannot be ordered timely from commercial manufacturers or from Section 503B outsourcing facilities<sup>1</sup> are often centrally compounded by hospital and health system pharmacies and distributed so they can be available in a timely manner for special patient populations, including those in the neonatal intensive care unit, for cancer patients and for dialysis patients. Finally, in many health systems, such centralized compounding pharmacies help supply sterile compounded drugs to their small hospitals that do not have pharmacy services available on a 24/7 basis.

Finalizing an arbitrary one-mile radius limitation would have a negative impact on patient quality of care by forcing many health systems back to the older system of each individual hospital or outpatient facility within the system carrying out its own compounding in less structured settings or shifting to bedside compounding in hospitals without 24/7 pharmacy services. This could result in sterile compounded drugs being prepared by less experienced staff, potentially reducing quality and patient safety. It would also undermine existing hospital and health system care delivery models that have already been assessed and approved by the States' Boards of Pharmacy.

Alternatively, the FDA has suggested that in the event that their one-mile radius limit proves to be inadequate, obtaining compounded drugs from 503B outsourcing facilities is an option for

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<sup>1</sup> Outsourcing facilities, defined in Section 503B of the FD&C Act, are a new category of compounders created by the Drug Quality and Security Act (DQSA) of 2013. These facilities may send prescription drugs to health care facilities without obtaining prescriptions for identified individual patients. However, they must comply with several of the same FD&C Act requirements as drug manufacturers, including CGMP, and are subject to a risk-based FDA inspection schedule.

hospitals and health systems. However, while hospitals and health systems can and do obtain many products from 503B outsourcing facilities, they cannot be relied upon exclusively for all of the system's compounding needs. For instance, the number of currently registered outsourcing facilities do not have the capacity to serve all the nation's hospitals. This is evidenced by the long wait and turnaround times that hospitals are reporting for compounded products that they require on short notice. Hospitals report that it can take several days to receive ordered products from an outsourcing facility. Second, outsourcing facilities do not produce all the specialized compounded products hospitals need for patient care. They typically make large batches of compounded drugs and are not equipped to provide small amounts of tailor-made products to hospitals and health systems. Finally, when there is a drug shortage, outsourcing facilities often cannot provide the needed product. By contrast, hospitals and health systems have processes in place to help stretch the supply of compounded drugs that are in short supply. Therefore, hospitals and health systems cannot exclusively rely on 503B outsourcing facilities for all their compounding needs.

Finally, the FDA also suggests that a hospital or health system pharmacy can register as a 503B outsourcing facility if it intends to provide non-patient-specific compounded drugs to its facilities, such as other hospitals or clinics, outside the one-mile radius limitation. However, this option may be infeasible if the FDA finalizes its Draft Facility Definition Guidance. The agency's proposed policy would require that any compounded product produced "at the same street address, or in the same building, or in buildings located in close proximity to one another" as a registered 503B outsourcing facility to meet 503B standards. As the FDA is aware, some critical 503A drugs cannot be compounded in accordance with 503B's CGMP requirements. Hospitals must have a 503A compounding pharmacy available in order to be able to prepare and dispense such compounded products quickly to ensure that patients have timely access to treatment. Therefore, it is critical that health system pharmacies be able to retain their state license to provide traditional compounding to their own patients under 503A.

**For all these reasons, the AHA strongly recommends that the FDA remove the arbitrary one-mile radius limitation and replace it with an alternative approach that would support the existing hospital and health system care delivery model and also put into place widely-vetted, evidence-based limits on anticipatory compounding in hospitals and health systems to ensure safe, high-quality patient care.**

**Specifically, instead of the one-mile radius limitation, the AHA recommends that the FDA allow hospitals and health systems to use the beyond-use date (BUD) timeframes contained in USP Chapter 797 Pharmaceutical Compounding—Sterile Preparations and USP Chapter 800 Hazardous Drugs—Handling in Healthcare Settings.<sup>2</sup>** We believe that limiting the distribution of non-patient-specific sterile compounded drugs in hospitals and health systems

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<sup>2</sup> USP Chapter 797 describes the procedures and requirements for compounding sterile preparations in order to ensure conditions and practices that prevent harm to patients from: microbial, chemical, or physical contamination; excessive bacterial endotoxins; variations in product strength; or poor quality ingredients. Further, it requires that all personnel involved in sterile compounding undergo specific training and testing. USP Chapter 800 describes the standards for the handling and administration of hazardous drugs, including consideration of patient safety, worker safety, and environmental protection.

based on these BUDs addresses the FDA's concerns regarding the risk and quality associated with compounded products. A BUD is the date or time after which administration of a compounded sterile product must not be initiated. As described in USP Chapter 797, the BUD is determined from the date or time the preparation is compounded, its chemical stability, and sterility limits. Both the stability of the components and the sterility limits must be taken into consideration when determining BUDs, and the BUD must be the shorter of the sterility dating or chemical stability dating. Therefore, this approach would limit the amount of a compounded drug that could be created and distributed without a prescription and would ensure its timely use. As intended by the Drug Quality and Security Act (DQSA), it would also preserve State Board of Pharmacy oversight of hospital and health system compliance with the USP standards. TJC and CMS also explicitly require hospital and health system compliance with the relevant USP chapters on compounding. In fact, the CMS State Operations Manual "Survey Protocol, Regulations and Interpretive Guidelines for Hospitals" states, "all compounding of medications used or dispensed by the hospital must be performed consistent with standards of practice equivalent to or more stringent than those described in the compounding-related chapters in the United States Pharmacopeia and the National Formulary (USP-NF) published by the USP, which are recognized as authoritative guidance regarding minimum standards of safe practice applicable to both sterile and non-sterile compounding."

**Furthermore, to assure that this practice would be appropriately constrained to prevent hospitals and health systems from behaving in ways that resemble manufacturing, we also support retaining the FDA's proposed requirements that non-patient-specific compounded drugs "are distributed only to health care facilities that are owned and controlled by the same entity that owns and controls the hospital pharmacy" and that "the drug products are only administered within the health care facilities to patients within the health care facilities, pursuant to a patient-specific prescription or order."**

Health System Definition. The FDA also requests assistance in further defining a "health system" and determining when a health system and its associated health care entities are under "common control". **We suggest that the agency adopt an expanded version of the definition of health system that is used in Section 506F of the FD&C Act.** Section 506F defines a health system as "a collection of hospitals that are owned and operated by the same entity and that share access to databases with drug order information for their patients." However, because health systems often include other types of health care facilities that should continue to benefit from access to safe, high quality sterile compounded drugs prepared by a system's centralized compounding pharmacy, **we support a more expansive definition that includes not only hospitals but also other health system facilities, such as provider-based infusion centers, ambulatory surgical centers and other health care facilities that are owned and operated by the same entity.**

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Thank you again for the opportunity to comment. If you have any questions, please contact me or Roslyne Schulman, director for policy development, at (202) 626-2273 or [rschulman@aha.org](mailto:rschulman@aha.org).

Sincerely,

/s/

Ashley Thompson

Senior Vice President

Public Policy Analysis and Development