December 3, 2021

Janet Woodcock, MD
Acting Commissioner
U.S. Food and Drug Administration
5630 Fishers Lane
Rockville, MD 20852

SUBJECT: [Docket No. FDA–2016–D–0271], Hospital and Health System Compounding Under Section 503A of the Federal Food, Drug, and Cosmetic Act; Revised Draft Guidance for Industry; (Vol 86, No 192), October 7, 2021

Dear Acting Commissioner Woodcock:

On behalf of our more than 400 hospital and health system members, the California Hospital Association (CHA) appreciates the opportunity to provide comments on the Food and Drug Administration's (FDA) revised draft guidance on Hospital and Health System Compounding Under Section 503A of the Federal Food, Drug, and Cosmetic (FD&C) Act.

California's hospital and health system compounding pharmacies are vital to ensuring our patients have access to high-quality, safe, and timely medications — including sterile and non-sterile compounded medications. We appreciate the FDA's ongoing to work to ensure that its regulatory framework supports this access to patients in all settings. **In particular, we applaud the agency for considering stakeholder feedback and revising its earlier 2016 draft guidance to eliminate the previously proposed policy that would have established a one-mile radius requirement as criteria for medication distribution by a hospital or health system.** The arbitrary one-mile policy was not reflective of the structure of health systems that operate under a centralized compounding model and would have reduced timely access to necessary medications, resulting in negative impacts to patient safety and quality of care.

However, CHA is concerned that the FDA's continued focus on hospitals and health systems relying on outsourcing facilities could exacerbate drug shortages, further stress the workforce, and delay — and potentially decrease — the quality of patient care. Specifically, we are concerned that the proposed policy that would require compounded drug products to be administered or discarded within 24 hours of transfer out of the pharmacy could result in unintended consequences for patient access to compounded medications. While we understand that Section 503A of the FD&C Act requires that non-patient-specific compounded drugs be subject to certain limitations, we believe that the proposed 24-hour policy is another arbitrary limit that does not reflect the existing standards that hospital and health system pharmacies strictly follow.
The United States Pharmacopeia (USP) develops standards for preparing compounded sterile medications to help ensure patient benefit and reduce risks. The standards include environmental, personnel, and end-product validation processes to ensure medication quality and safety. Health system pharmacies must comply

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with USP standards to meet the requirements of State Boards of Pharmacy, the Centers for Medicare & Medicaid Services (CMS), and other accrediting bodies such as The Joint Commission (TJC). The FDA has also endorsed USP standards and references them throughout section 503A of the FD&C Act. USP chapters 71, 85, 795, and 797 establish evidence-based, beyond use date (BUD) time frames for sterile and non-sterile compounding. The FDA's proposed 24-hour cutoff from time of transfer out of pharmacy does not align with established BUDs for sterile compounded drug products established by USP 797 (i.e., 24 hours at room temperature or nine days refrigerated for medium-risk compounded sterile preparations).

In lieu of the FDA's arbitrary 24-hour policy, we urge the agency to further revise its guidance to specify that hospital and health system compounding pharmacies should follow the established BUDs that comply with USP 797 standards. We are most concerned that the proposed policy threatens the safety and quality care to patients in the emergency department, operating rooms, and intensive care units, where medications need to be immediately available to prevent harm. We also believe that limiting the distribution of non-patient-specific sterile compounded drugs in hospitals and health systems based on these BUDs addresses the FDA's concerns about the risk and quality associated with compounded products. And we are concerned that if the FDA does not eliminate the 24-hour requirement, several unintended consequences will result, including exacerbating drug shortages due to waste and increasing the burden on an already stressed workforce by requiring the daily compounding of medications.

As the FDA continues to refine and finalize its guidance, we urge the agency to consider the important role of hospital and health system compounding pharmacies. While hospitals and health systems can and do obtain many products from 503B outsourcing facilities, they cannot solely be relied upon to support a community's compounding needs. California has a longstanding history of exceptional pharmaceutical practices driven by a proactive, multidisciplinary, evidenced-based approach between hospitals and health systems and the California State Board of Pharmacy, and the state has long embraced a three-pronged framework for purchasing and processing sterile and non-sterile compounded products through hospital pharmacies, central fill pharmacies, and 503B manufacturers. We believe development of a federal regulatory framework that compliments state efforts is essential to ensuring that all hospitals have access to essential sterile and non-sterile compounded medications. The FDA is an important partner in this process, and we look forward to collaborating with other stakeholders to ensure that a federal framework balances patient safety with the need for timely access to medication, without creating inappropriate regulatory barriers to providing care.

In addition to these overarching comments, CHA has prepared the attached grid with specific recommendations for revisions to the language included in the FDA's draft guidance. CHA appreciates the opportunity to provide feedback to the FDA on its draft guidance. If you have any questions, please contact me at mhoward@calhospital.org or (202) 488-3742, or my colleague Sheree Lowe, vice president, policy, at slowe@calhospital.org or (916) 552-7576.

Sincerely,

/s/
Megan Howard
Vice President, Federal Policy

Attachment: Recommended Revisions to the FDA Draft Guidance

California Hospital Association

Docket No. FDA–2016–D–0271
Food and Drug Administration Hospital and Health System Compounding Under Section 503A of the Federal Food, Drug, and Cosmetic (FD&C) Act
Draft Guidance for Industry – Comments

Proposed Language	**Recommendation/Comments:**
II. Lines 52-53 **Compounding Under Section 503A of the FD&C Act** Section 503A of the FD&C Act describes the conditions that must be satisfied for human drug products compounded by a licensed pharmacist in a State Licensed pharmacy or federal facility or by a licensed physician, to be exempt from certain provisions of the FD&C Act	**Recommendation:** Revise the proposed language to: "Section 503A of the FD&C Act describes the conditions that must be satisfied for human drug products compounded by a licensed pharmacist or a pharmacy technician under the direct supervision of a licensed pharmacist, in a State Licensed pharmacy…"
II. Lines 68-70 One of the conditions that must be met for a compounded drug product to qualify for the exemptions under section 503A of the FD&C Act is that it is compounded by a licensed pharmacist in a State Licensed pharmacy or Federal facility, or by a licensed physician.	"One of the conditions that must be met for a compounded drug product to qualify for the exemptions under section 503A of the FD&C Act is that it is compounded by a licensed pharmacist or a pharmacy technician under the direct supervision of a licensed pharmacist, in a State Licensed pharmacy…"
II. Lines 86-89 Another of the conditions in section 503A of the FD&C Act is that the drug product must be compounded by a licensed pharmacist or licensed physician that "does not compound	"Another of the conditions in section 503A of the FD&C Act is that the drug product must be compounded by a licensed pharmacist or a pharmacy technician

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regularly or in inordinate amounts (as defined by FDA any drug products that are essentially copies of a commercially available drug product **II. Lines 117-118** In addition, licensed pharmacists and licensed physicians who compound drug products in accordance with section 503A of the FD&C Act	under the direct supervision of a licensed pharmacist, or licensed physician that…" "In addition, licensed pharmacists, or a pharmacy technician under the direct supervision of a licensed pharmacist, and licensed physicians who compound drug products in accordance with section 503A of the FD&C Act…" **Comments**: The current draft guidance excludes the compounding by pharmacy technicians. Most sterile products compounded in the hospital setting are compounded by pharmacy technicians under direct supervision of a licensed pharmacist. The pharmacy technician performs the sterile compounding, and the pharmacist performs a verification to validate the accuracy and quality of the sterile compound.
II-C lines 157-162 **Compounding by Hospitals and Health Systems** To the extent that hospitals and health systems have a need for compounded drug products, FDA encourages them to obtain such products from outsourcing facilities. Compounders that elect to become outsourcing facilities must register with FDA, are subject to CGMP requirements, and are inspected by FDA according to a risk-based schedule (section 503B of the FD&C Act). This helps to mitigate the risk that their drug products will be contaminated or otherwise made under substandard conditions. **II-C-1 lines 212-214** We encourage hospitals and health systems to look to outsourcing facilities, or to register their pharmacies as outsourcing facilities, when they wish to obtain non-patient-specific compounded drug products	**Recommendation:** Revise proposed language to: "To the extent that hospitals and health systems have a need for compounded drug products, FDA encourages them to either obtain such products from outsourcing facilities or comply with the United States Pharmacopoeia (USP) standards and respective state board of pharmacy regulations when preparing compounded drug products." **Comments**: While hospitals and health systems can and do obtain many products from 503B outsourcing facilities, they cannot solely be relied upon to support a community's compounding needs. Should health systems solely rely on outsourcing facilities for their compounding needs, their personnel's compounding capability will diminish over time such that during compounder shortages, the health system is unable to meet patient care needs. To manage the increased acuity of patients, it is essential for health systems to provide sterile compounding services. Health system pharmacies must comply with USP standards to meet the requirements of State Boards of Pharmacy, the Centers for Medicare & Medicaid Services (CMS), and other accrediting bodies such as The Joint Commission. In addition, as indicated in CMS' interpretive guidance for surveyors (S&C 16-01-Hospital), under the current Conditions of Participation hospitals cannot be required to use

III-A-2 lines 399-402 The above policy is intended to focus FDA's regulatory efforts. FDA encourages hospitals and health systems to obtain any non-patient-specific compounded drug products they may need from outsourcing facilities where that is possible, and to consider registering their pharmacies as outsourcing facilities.	only registered outsourcing facilities when obtaining compounded medications from an external source.
III – A- 1 Lines 343-356 **Part 1: Circumstances When FDA Generally Does Not Intend To Take Action** (2) The compounded drug products are used or discarded within 24 hours of transfer out of the pharmacy.[23] Footnote (page 10) [23]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.	**Recommendation:** Revise proposed language to: "(2) The compounded drug products are used or discarded within ~~24 hours of transfer out of the pharmacy~~ the established beyond-use-dates that comply with the United States Pharmacopoeia (USP 797) standards. **Comments:** The proposed 24-hour policy is arbitrary and could result in unintended consequences for patient safety and quality of care. We urge the FDA to instead follow the evidence-based standards of the USP 797 beyond-use-date standards.
III-A-2 lines 376-385 • **Non-patient-specific compounded drug products not for emergency uses.** Drug products are compounded and sent out of the pharmacy before the receipt of a patient- specific prescription in an amount that exceeds the amount needed for ***emergency*** situations (e.g., immediate administration for unplanned procedures in emergency or operating rooms).	**Recommendation:** **Non-patient-specific compounded drug products not for emergency uses.** Drug products are compounded and sent out of the pharmacy before the receipt of a patient-specific prescription in an amount that exceeds the amount needed for timely treatment of hospitalized patients and which have been approved for availability in patient care areas by the Medical Staff Committee and/or Pharmacy & Therapeutics (P&T) Committee. ~~***emergency*** situations (e.g.,~~

• **Routine, large amounts of non-patient-specific compounded drug products.** The pharmacy routinely compounds a large total number of compounded drug products that are sent out of the pharmacy before the receipt of valid prescriptions or orders for individually identified patients.	~~immediate administration for unplanned procedures in emergency or operating rooms) continuity of care~~ • **Routine, large amounts of non-patient-specific compounded drug products.** The pharmacy routinely compounds a large total number of compounded drug products that are sent out of the pharmacy before the receipt of valid prescriptions or orders for individually identified patients in excess of quantities needed for timely treatment of hospitalized patients and which have been approved for availability in patient care areas by the Medical Staff Committee and/or Pharmacy & Therapeutics (P&T) Committee. **Comments:** Sec. 503A(a)(2) allows for limited quantities of drug products to be compounded before receipt of a valid prescription order when there's an established relationship between the pharmacist and the physician. In health systems such relationship exists, and health system pharmacies should be able to compound a limited amount of drug products in anticipation of prescriptions and to prevent delays in emergency departments, operating rooms, and patient care areas per the current FDA regulations. Limiting this practice to emergency situations would negatively impact routine patient care and patient clinical status.
III-B lines 407-429 **B. Hospital and Health System Compounding of Drug Products That Are Essentially Copies Under Section 503A of the FD&C Act** At this time and based on the Agency's current understanding of risks, FDA generally does not intend to take action against a hospital or health system pharmacy that is not an outsourcing facility for compounding a drug product regularly or in inordinate amounts that is essentially a copy of a commercially available drug product when the following circumstances are present: • The compounded drug product is administered only to patients within the hospital or health system. • The pharmacy obtains from the prescriber a statement that: specifies a change between the compounded drug product and the commercially available drug product; indicates that the compounded drug product will be administered only to patients for whom the change produces a significant difference from the	**Recommendation:** **B. Hospital and Health System Compounding of Drug Products That Are Essentially Copies Under Section 503A of the FD&C Act** At this time and based on the Agency's current understanding of risks, FDA generally does not intend to take action against a hospital or health system pharmacy that is not an outsourcing facility for compounding a drug product regularly or in inordinate amounts that is essentially a copy of a commercially available drug product when the following circumstances are present: • The compounded drug product is administered only to patients within the hospital or health system. • The pharmacy obtains from the prescriber or Medical Staff Committee (e.g., P&T Committee) a statement that: specifies a change between the compounded drug product and the commercially available drug product; indicates that the compounded drug product will be administered only to patients for whom the change produces a significant difference from the commercially available drug product; and describes the intended patient population for the compounded drug product.

commercially available drug product; and describes the intended patient population for the compounded drug product. • A statement is on file for each prescriber that covers each drug product that is compounded. • The statement is maintained in the hospital or health system pharmacy to address routine orders for patients for whom the change produces a significant difference.	~~• A statement is on file for each prescriber that covers each drug product that is compounded~~. • The statement is maintained in the hospital or health system pharmacy to address routine orders for patients for whom the change produces a significant difference. **Comments:** Health systems often have several prescribers caring for the same patient populations and requiring individual statements from each prescriber would create an undue documentation and workflow burden for the pharmacy and the health system to manage. Furthermore, as stated in lines 281-290, health systems have medical staff P&T committees that are approved by the Medical Executive Committee and are responsible for developing, implementing, and periodically reviewing and revising medication-use policies and procedures. A statement from the P&T Committee should prove sufficient to meet the intent of this section and negate the need for individual prescriber statement.