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Alliance for Pharmacy Compounding

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Eamon D. Briggs
Deputy General Counsel
Texas State Board of Pharmacy
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Dear Mr. Briggs,

On behalf of the Alliance for Pharmacy Compounding, we appreciate the opportunity to comment on the proposed sterile compounding rule changes outlined in Texas Pharmacy Rule §291.133.

We commend the Texas State Board of Pharmacy for its commitment to high standards for patient safety and quality in sterile compounding. The Board's efforts to align many of these rules with the latest U.S. Pharmacopeia (USP) standards while considering the practical implications of those changes on compounding pharmacies and patients is appreciated.

Comments on Proposed Definitions

- Anteroom: The definition states that "The anteroom is the transition room between the unclassified area of the pharmacy and the buffer room." However, that definition may inadvertently include classified gowning rooms that some pharmacies use as transition spaces. Facilities may have more than two rooms, with one designated as the anteroom and another as the buffer room. In a facility with a three-room setup, the second room may serve as the anteroom without directly transitioning between the unclassified area of the pharmacy and the buffer room. Instead, it may act as an intermediary space, such as a classified gowning room. We recommend refining the definition to account for classified gowning rooms serving this purpose.
- Aseptic Processing: For clarity and consistency, the definition should align with USP's phrasing: *"A method by which separate, sterile components (e.g., drugs, containers, or closures) are brought together under conditions that maintain their sterility. The components can either be purchased as sterile or, when starting with nonsterile components, can be separately sterilized prior to combining (e.g., by membrane filtration*

or by autoclave).” The current proposed definition references the sterilization of both the packaging and the preparation. However, in aseptic processing, the compounder may not be responsible for the sterilization of any component. While the wording in the proposed Texas definition may aim to address the sterilization of container-closure systems and drug products by manufacturers, it leaves room for misinterpretation.

- Biological Safety Cabinet: The proposed definition should match USP’s: *“A ventilated cabinet with an open front and inward and downward unidirectional HEPA-filtered airflow and HEPA-filtered exhaust. A BSC used to prepare a CSP must be capable of providing an ISO Class 5 or better environment for preparation of the CSPs.”*
- Clean Room: We question the need for definitions of both a buffer room and a clean room. It appears that a “clean room” as described is similar to what USP defines as a classified area: an area that maintains an air quality classification based on the ISO standards required in this chapter (see also the definition for *ISO class*.) We recommend removing “clean room” from the definition section, as this term is commonly used as a synonym for “buffer room.” We also recommend utilizing the term “classified area,” to align with USP’s definition.
- Compounding Aseptic Containment Isolator: This definition includes microbial retentive filtration but omits particulate filtration. The USP defines HEPA filtration as being, using, or containing a filter designed to remove 99.97% of airborne particles measuring 0.3-micron or greater in diameter passing through it.
- Critical Sites: Adding “and” to the phrase “microbial and particulate contamination” would enhance clarity and accuracy.
- Multiple-Dose Container: The definition should explicitly include sterile ophthalmic eye dropper containers. Additionally, the text should be amended to indicate that the beyond-use date may not exceed the original expiration date of a commercially available product.

Media-Fill and Gloved Fingertip Testing

We are concerned about the removal of the requirement for media-fill testing under the most challenging or stressful conditions for Category 3 compounding, while retaining this requirement for Category 1 and 2 compounding. Media-fill testing is a cornerstone of ensuring quality and sterility in compounding, and its omission for Category 3 compounds may compromise patient safety.

We support the proposed rule requiring gloved fingertip testing and gowning observations every 12 months for supervisory personnel who do not actively compound. This distinction acknowledges their roles and appropriately tailors the requirements.

Beyond-Use Dates and Batch Sizes

The allowance of up to a 180-day beyond-use-date for nonaqueous Category 3 sterile compounds demonstrates a forward-thinking perspective that recognizes stability science and

practical patient care needs. This 180-day BUD would be allowed based on documented "current literature supporting stability and sterility." However, sterility can only be supported by the testing of each particular batch and formulation specific container closure integrity testing.

The proposed increase in batch size to 750 units is an improvement over the 250 maximum batch size in USP <797>, and we appreciate the Board's recognition of the need for scalability in sterile compounding. However, we continue to encourage the Board and other regulators to allow pharmacies to determine batch sizes and assign beyond-use dates based on data, rather than imposing an arbitrary limit. This would align with scientific principles, potential for advancing technology, and ensure flexibility for pharmacies to meet diverse patient needs.

Additional Comments on Sterile Compounding Practices

- Sterility testing: The proposed flat 5 percent batch testing requirement deviates from USP <71> and <797>, which use batch-size-specific testing. We recommend adopting USP's approach for batches up to 250 units and applying the 5 percent rule only for larger batches.
- Component Sourcing: We support the flexibility to source components from non-FDA-registered facilities provided a Certificate of Analysis is available and the pharmacist deems the ingredient appropriate.
- Filter Integrity Testing: This requirement for Category 2 and 3 compounding is an important safeguard and we are pleased to see its inclusion.
- Hazardous Drug Compounding: The provisions for protecting employee safety without fully adopting USP <800> strike a reasonable balance between safety and feasibility.
- Copies of FDA-Approved Drug Products: We support the provision in the proposed rules that would allow pharmacists to compound copies of commercially available drug products that are not reasonably available, even if those products are not on the FDA's drug shortage list. This flexibility is important for addressing patient needs in real-time.
- Component Selection: Some active pharmaceutical ingredients (APIs), such as ketotifen EP, do not have USP/NF, CP, AR, ACS, or FCC grades. Current regulations must account for APIs that are allowed under federal law and FDA guidance. Without this flexibility, Texas licensed pharmacies will not be able to compound all medications that should be available to patients. We recommend aligning with section 503A of the Food, Drug, and Cosmetic Act with regard to component selection.

Some other comments

- The proposed rules reference a buffer room that is not physically separated from the anteroom, relying on the principle of displacement airflow as defined in the previous version of USP <797>. However, the current version of USP <797> no longer includes this concept. We recommend removing this outdated reference. The clean room required for compounding Category 1 and Category 2 preparations indicates there must be some demarcation designation that delineates the anteroom from the buffer room. This could

be read that a line of demarcation would be sufficient to comply, but we would expect a full physical separation (wall with a door) would be required.
- We recommend requiring sterile one-step disinfectants and sporicidal cleaners, as they are required for use in an ISO 5 environment by USP and FDA.
- In the section on handwashing, it appears that the personnel going into the buffer room is doing so before donning gloves, which should be performed while still in the anteroom.
- Filter integrity testing should be performed on each filter if multiple filters are required to be used for sterilization. This is not discussed in the proposed regulations.

In conclusion, we thank the Board for its thoughtful approach to these complex issues and for the opportunity to provide input. We urge the Board to align its regulations with national standards, ensure flexibility in compounding practices, and balance safety with practical implementation. APC stands ready to assist the Board in further refining these rules to ensure patient access to high-quality compounded medications.

Sincerely,

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The Alliance for Pharmacy Compounding is the voice for pharmacy compounding, representing more than 600 compounding small businesses – including compounding pharmacists and technicians in both 503A and 503B settings – as well as prescribers, educators, researchers, and suppliers.