March 17, 2022

[Submitted electronically via www.USP.org]
United States Pharmacopeia
12601 Twinbrook Pkwy
Rockville, MD 20852

RE: Proposed Revision to General Chapter <797>

ASHP is pleased to submit comments regarding the proposed revisions to USP General Chapter <797>. ASHP represents pharmacists who serve as patient care providers in acute and ambulatory settings. The organization's 60,000 members include pharmacists, student pharmacists, and pharmacy technicians. For more than 75 years, ASHP has been at the forefront of efforts to improve medication use and enhance patient safety. ASHP has a long history of supporting the safe practice of nonsterile and sterile compounded preparations.

ASHP commends the work of the Compounding Expert Committee and USP staff in revising General Chapter <797> and offers the following feedback on behalf of its members:

| Section | Comments or recommendations |
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| 1. Introduction and Scope | This section refers to "bulk drug substance," which is consistent with FDA guidance documents when referring to active pharmaceutical ingredients (API) in bulk form. The remainder of the chapter refers to bulk drug substances as API. For clarity, the Compounding Expert Committee should consider using the phrase "bulk drug substance" when referring to API in bulk form. |
| 1. Introduction and Scope | This section states "the requirements of the chapter must be followed to minimize harm, including death, to human and animal patients that could result from … 3) variability from the intended strength of correct ingredients …"<br><br>More emphasis should be placed on final product checking or verification to ensure CSPs are prepared correctly based on the formulation records. In 2019, the ASHP House of Delegates and Board of Directors approved a policy statement on the verification of compounded sterile preparations:<br><br><u>ASHP Policy Statement 1903: Compounded Sterile Preparation Verification</u><br><br>• To advocate that health systems adopt automation and information technology to facilitate in-process and final verification of compounded sterile preparations (CSPs) to ensure CSP quality; further,<br>• To advocate that, until such time as automation or technology can be implemented, independent in-process and final verification of CSPs be performed; further, |

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| | • To oppose the use of the syringe pull-back method or other proxy methods of CSP verification.<br><br>Proxy verification, known as the "syringe pull-back method" have been identified by the Institute for Safe Medication Practices as a dangerous practice that can allow errors to be missed.<br><br>ASHP recommends that the Compounding Expert Committee consider stronger controls for the verification of CSPs. |
| 1. Introduction and Scope | ASHP is pleased to see the re-addition of the new technologies statement. As written, the statement expressly prohibits the practice of drug-vial optimization (DVO), the practice of using a closed-system transfer device to extend the duration that a single-dose container may be used. The language also prevents any future device or technology from being used to extend the duration of vial use.<br><br>In 2018, the ASHP House of Delegates and Board of Directors approved a policy statement encouraging more research and requesting standards be developed to address DVO:<br><br><u>ASHP Policy Statement 1813: Use of Closed-System Transfer Devices to Reduce Drug Waste</u><br><br>• To recognize that a growing body of evidence supports the ability of specific closed-system transfer devices (CSTDs) to maintain sterility beyond the in-use time currently recommended by United States Pharmacopeia Chapter 797, when those CSTDs are used with aseptic technique and following current sterile compounding standards; further,<br>• To foster additional research on and develop standards and best practices for use of CSTDs for drug vial optimization; further,<br>• To educate healthcare professionals, especially pharmacists and pharmacy technicians, about standards and best practices for use of CSTDs in drug vial optimization.<br><br>ASHP recommends that the Compounding Expert Committee revise the wording in this section to allow new research, technologies, or devices not currently available that might further inform decisions around DVO or other methods of extending dating. |
| 1.3 Immediate-Use CSPs | ASHP members have expressed interest in further clarification about what specific training, and training intervals, should be required to demonstrate competency in aseptic processes for the preparation of CSPs for immediate use (bullet #3). Concern has been raised about regulators and accreditors requiring media-fill or glove-tip testing for clinicians who might prepare CSPs at the bedside for immediate use. |

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| 1.4 Preparation Per Approved Labeling | ASHP is concerned that the scope of USP Chapter <800> only includes compounding activities within the scope of USP Chapters <795> and <797>. Section 1.4 excludes CSPs prepared according to manufacturer labeling from the scope of <797> and therefore <800>, creating a substantial loophole for many antineoplastic and other hazardous drugs that may be prepared without a requirement to implement the containment strategies in USP Chapter <800>.<br><br>While ASHP recognizes that only preparations that meet the legal definition of compounding can remain in scope of <795> and <797>, we strongly recommend that the Compounding Expert Committee address this loophole through other means. |
| 2. Personnel Training and Evaluation | This section (as well as Section 1.1) mentions that any individual entering the sterile compounding area, whether preparing CSPs or not, must meet the requirements in *3. Personal Hygiene and Garbing*. This is not feasible for non-compounding personnel who may need to enter the compounding area for certification purposes, maintenance work, or other non-compounding activities.<br><br>ASHP recommends that the Compounding Expert Committee consider an accommodation for these isolated instances of entry into the compounding area and propose alternative strategies to mitigate the risk of environmental contamination in these cases. |
| 2.3 Competency Testing in Aseptic Manipulation | ASHP members have expressed concern about the requirement to perform aseptic manipulation competency every 6 months, citing time and financial burdens as well as technician shortages as barriers to implementation.<br><br>Similarly, members have also expressed concern with the need to complete surface sampling of the direct compounding area after each media-fill testing procedure is completed. This also increases the expense and time required for training and competency evaluation, especially at health-systems with a large number of personnel who perform sterile compounding. |
| 2.3 Competency Testing in Aseptic Manipulation | The section refers to successful completion of gloved fingertip/thumb sampling after media-fill testing as ≤ 3 cfu as a total from both hands. However, Table 1 in the same section states the action level is 3 cfu as a total from both hands. Please either correct the section to < 3 cfu, or correct Table 1 to state that the action level is either > 3 cfu or ≥ 4 cfu. |
| 3.1 Personnel Preparation | ASHP often receives questions seeking clarification about specific types of jewelry and cosmetics (e.g., semi-permanent cosmetics like eyelashes). ASHP recommends the Compounding Expert Committee develop an FAQ with more detail and examples about various cosmetics and piercings and best practices to prevent environmental contamination. |
| 3.3 Garbing Requirements | This section states that, for Category 1 CSPs, “all garb must be donned within the perimeter of the SCA.” |

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| | USP Chapter <800> requires a second pair of shoe covers be donned before entering the C-SEC (Section 7.3). (Per the USP Chapter <800> glossary, a C-SCA is a type of C-SEC). These two requirements are incompatible. |
| 4.2 Facility Design and Environmental Controls | This section refers to the temperature and humidity requirements for the cleanroom suite, but does not mention SCA. ASHP members have expressed interest in clarifying this section to address whether SCAs must also meet these temperature and humidity requirements. |
| 4.2 Facility Design and Environmental Controls | The Chapter <797> revisions are not consistent with Chapter <800> which allows the C-PEC to contribute to 100% of the ACPH. As written, the revision would require 50% to come from the buffer room, making sites re-engineer their HD buffer rooms to include exhaust if they were relying on the C-PEC for 100% of ACPH. This will result in expensive renovations and challenges with negative-pressure balancing and may not be possible depending on existing HVAC equipment and architecture.<br><br>ASHP asks the Compounding Expert Committee to further consider these requirements. |
| 4.2 Facility Design and Environmental Controls | ASHP is extremely concerned about limiting RABS located in SCAs to Category 1 CSPs with shortened BUDs.<br><br>The 2020 ASHP national survey of pharmacy practice in hospital settings found that only 42.8% of hospitals provide 24/7 services.[1] Further, 67 of 263 respondents (25.4%) to a compounding survey conducted by ASHP in 2019 indicated that their sterile compounding occurs exclusively within a RABS located within an SCA. Fifty-three of those 67 respondents (79%) indicated that the BUD change would impact their sterile compounding operation, with over half indicating that compounding by nurses in patient care areas would increase.<br><br>By limiting the BUD of CSPs prepared in a RABS within an SCA, the Expert Committee is likely increasing the amount of immediate-use compounding that will occur. This is directly counter to the intent of establishing standards for quality and safety of CSPs. ASHP strongly urges USP and the Expert Committee to consider the ramifications of limiting the BUDs of these CSPs.<br><br>1. Pedersen CA, Schneider PJ, Ganio MC, Scheckelhoff DJ. ASHP national survey of pharmacy practice in hospital settings: dispensing and administration—2020. *Am J Health-Syst Pharm*. 2021; 78:1074-1093. |
| Section 6.3 Monitoring Surfaces for Viable Particles | Table 6 lists cfu action levels for surface sampling, but lists "3" for ISO Class 5 spaces. Please clarify whether this should be "> 3","≥ 3", or some other representation of the action level. |
| Section 7.2 Cleaning Supplies | This section states that "in classified areas outside of the PEC, sterile cleaning and disinfecting agents should be used." ASHP members have expressed concern about the limited availability and the expense of sterile disinfecting agents, especially for |

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| | use outside of a PEC, and have recommended that this be revised so that the use of nonsterile one-step and sporicidal disinfectants is allowed. |
| Section 9.3 Components | ASHP recommends that the bullet "Must be obtained from an FDA-registered facility" be revised to match the proposed revisions to USP Chapter <795>: "In the United States, must be obtained from an FDA-registered facility." |

ASHP appreciates this opportunity to provide USP with feedback on the proposed revisions to General Chapter <797>. I have also appreciated the opportunity to provide direct feedback during public meetings of the Compounding Expert Committee while the chapter revisions and comments have been discussed.

We look forward to continuing to work with USP and the Compounding Expert Committee to protect patient and healthcare worker health and safety. Please contact me if you have any questions on ASHP's comments. I can be reached by telephone at 301-664-8617 or by email at mganio@ashp.org.

Sincerely,

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