July 30, 2018

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

RE: Proposed Revision to General Chapter <795>

ASHP is pleased to submit comments regarding the proposed revisions to USP General Chapter <795>. ASHP represents pharmacists who serve as patient care providers in acute and ambulatory settings. The organization's 45,000 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.

Line(s)	Comments or recommendations
162-163	70% isopropyl alcohol may degrade some non-disposable garb. Recommend incorporating language similar to 210-212 "agents must be selected and used with consideration of compatibilities, effectiveness, and the potential to leave residues".
232-236	Strictly following the definitions in the Glossary section, this would not apply to opened capsules or crushed tablets. It would be helpful to have this explicitly stated in the Chapter to avoid confusion by regulators and enforcement entities.
232-236	ASHP asks the Expert Committee to weigh the benefits of a CVE for compounding powder forms of non-hazardous API and added substances against the possible impact this requirement may have on accessibility to compounded nonsterile preparations. Not all facilities will have the physical space or resources for a CVE, which could make it difficult for patients to access specific CNSPs. We ask that the committee consider the possibility of an assessment of risk based on frequency or volume of compounding using powder forms of non-hazardous API or added substances in determining whether a CVE is mandatory.
278	ASHP asks for further guidance on what qualifies as an "equivalent quality of water". As currently worded, a higher quality of water (per USP General Chapter <1231>) would not be appropriate for reconstitution of conventionally manufactured nonsterile products.
296-300	This paragraph requires examination of "other lots" of an ingredient found to be of unacceptable quality, but does not address other containers of the same lot as the ingredient found to be of unacceptable quality. "Any other" (line 298) can be changed to "all" in order to add clarity.
394	Some requirements in Section 9 (Labeling), such as specific handling instructions and warning statements, should be consistent for a CNSP and should be a required part of the Master

	Formulation Record for that CNSP.
409	BUD assignment and storage requirements, as well as reference sources of the BUD assignment and storage requirements, are part of the Master Formulation Record. These should not need to be repeated on the Compounding Record. The Compounding Record should instead reflect the BUD calendar date (as opposed to number of days) assigned to the specific CNSP.
535	Table 3 lists the BUD of preserved aqueous solutions, but does not provide guidance on what is considered preserved. General Chapter <51> establishes a standard for effectiveness testing of preservatives, but Table 3 applies when there is no other stability study. Further, line 561 indicates that General Chapter <51> requirements must be met to extend the BUD past the 30-day preserved aqueous dosage form BUD, implying that no such requirement is needed to assign 30 days. Some ingredients used for compounding oral suspensions or solutions contain preservatives. The USP NF monographs for Vehicles for Oral Solution and Vehicles for Oral Suspension also contain preservatives. Final CNSPs using these vehicles may contain preservatives, but are they preserved? ASHP asks the expert committee to provide further guidance on what qualifies as a preserved aqueous solution that can be assigned a 30-day BUD without General Chapter <51> testing.
535	ASHP is unable to find any evidence, guidance, or science behind limiting non-preserved aqueous dosage forms to a 14-day BUD. While Aw may be a factor in potential API degradation due to hydrolysis, the assignment of a 30-day BUD for preserved aqueous dosage forms indicates that hydrolysis is not a limiting factor up to that time. Microbial proliferation depends on temperature, pH, and aW among other variables, including the type of microorganism. The assignment of a 14-day BUD under refrigerated conditions is limiting and may not be possible depending on the chemical properties of the CNSP at cold temperatures. The 14-day BUD may cause access issues with patients who have to pay multiple copayments or rural patients who must visit a pharmacy multiple times a month for refills. A 30-day BUD would alleviate these issues. ASHP asks that the expert committee take these factors into consideration when establishing the BUD for non-preserved aqueous CNSPs. Whether the committee decides to keep the 14-day BUD under refrigerated temperatures or not, we ask that further scientific documentation or resources be made available to improve the understanding of and compliance with these BUDs.
539-541	ASHP recognizes that Aw is not the only factor in determining the ability for microbes to proliferate. Other factors, such as temperature and pH can have an equally significant impact on the prevention of microbial proliferation. However, we recognize that Aw is the most reasonable and accessible estimation of microbial proliferation and we support the use of Aw for this purpose.

ASHP appreciates this opportunity to provide USP with feedback on the proposed revisions to General Chapter <795>. 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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