Decisions on Appeals to USP <795> and <797>

USP's Compounding Expert Committee (CMP EC) has issued decisions on appeals to recent revisions to General Chapters <795> Pharmaceutical Compounding – Nonsterile Preparations and <797> Pharmaceutical Compounding – Sterile Preparations. USP remains committed to keeping stakeholders and the general public informed of the progress of these standards, which are anticipated to become official on December 1, 2019.

Background

On June 1, 2019, USP published major revisions to General Chapters <795> and <797>, which are intended to minimize the risk of patient harm in the areas of nonsterile and sterile compounding. The revisions represent more than nine years of deliberation and stakeholder engagement in the form of public comment review, roundtables, workshops, open face-to-face meetings, and open microphone sessions. USP received diverse input and participation from pharmacists, practitioners, representatives from healthcare organizations, academicians, federal and state regulators, and many others. Changes to these chapters reflect advancements in science and clinical practice, clarification of sections that were frequently misconstrued, and input from more than 6,400 public comments received. Over the course of the revision process for both <795> and <797>, the CMP EC considered all input and worked towards achieving patient access to quality compounded preparations while minimizing the risk of harm.

After the revisions were published, USP received appeals to these chapters. In accordance with USP's Bylaws, the CMP EC worked with a sense of urgency to reconsider and issue decisions on these challenges. In light of the significant work that the CMP EC has undertaken to date on the revision to <795> and <797>, the Committee was prepared to evaluate the appeals expeditiously. See this link for further information about USP's formal appeals process. A summary of key provisions appealed and the decisions of the CMP EC are provided below.

Appeal Topics and CMP EC Decisions

Key topics covered in the appeals to <795> and <797> included:

- Beyond-Use Date (BUD) provisions in <795> and <797>
- Removal of Alternative Technology provision from <797>
- Applicability of <795> and <797> to veterinary practitioners

BUD Provisions

Several appeals challenged the BUD approaches in the revised chapters. In response to these appeals, the CMP EC decided to:

- Maintain the BUD framework for compounded nonsterile preparations (CNSPs) in <795>
    - Stability-indicating assays will be required to extend BUDs based on their ability to quantitate the active ingredient and its degradation products or related impurities.
    - The BUDs in Table 3, which are assigned based on the consideration of stability, compatibility, and microbial proliferation in the CNSP, will be maintained. The BUD framework takes into consideration water activity and the susceptibility of some oils or fatty acid bases (e.g., nonaqueous formulations) to be reactive to certain substances.

- Maintain the BUD provisions for compounded sterile preparations (CSPs) in <797> with the commitment to develop resources for extending BUDs to include stability, sterility, and monitoring (personnel and environmental) considerations.
    - The maximum BUDs in Table 11 for Category 2 CSPs are intended to mitigate the risk of inadvertent contamination or the risk of not sterilizing the CSP. Contaminated vials stored for longer periods of time allow for microbial proliferation and increased risk of harm to patients. The CMP EC determined that extending BUDs for CSPs may need additional testing such as stability, sterility, endotoxin, container-closure integrity, and particulate matter, in addition to personnel and environmental monitoring which are specific to each facility.

See USP's BUD Fact Sheet for further information about the approach to BUDs in revised <795> and <797>.

Alternative Technology Provision

The CMP EC was asked to reinstate the following specific provision (Alternative Technology provision) in <797> to provide greater flexibility for modalities used in pharmacy compounding:

> *"The use of technologies, techniques, materials, and procedures other than those described in this chapter is not prohibited so long as they have been proven to be equivalent or superior with statistical significance to those described herein."*

In response to this request, the CMP EC decided to:

- Reinstate the Alternative Technology Provision from the 2008 Version of <797>
    - The CMP EC recognized that <797> may not capture all modalities used in pharmacy compounding. However, the CMP EC also intends to publish a Frequently-Asked-Question (FAQ) to clarify that the reinstatement of the Alternative Technology provision is not intended to permit BUD extension or to extend the time during which single-dose containers may be used.

Applicability to Veterinary Practitioners

The CMP EC was asked to postpone the applicability of <795> and <797> with respect to veterinary practitioners until such time that USP publishes a veterinary-specific compounding chapter. In response to this request, the CMP EC decided:

- Not to Postpone these Chapters and to Maintain Veterinary References
    - <795> and <797> do not state compendial requirements for animal drug compounding under federal law. Section 503A of the Federal Food, Drug and Cosmetic Act, which makes <795> and <797> applicable to pharmacy compounding, applies only to pharmaceuticals for human use.
    - <795> and <797> contain provisions that are intended to be relevant and useful for veterinary practitioners. For this reason, it is the CMP EC's view that continued reference to veterinarians in both <795> and <797> may serve value, from a best practice standpoint. The requirements of these chapters are relevant to ensuring quality CSPs for both human and animal patients.

The CMP EC's decisions do not foreclose the possibility of future revisions to these chapters. Standards in the *USP-NF* are in continuous revision, and the CMP EC is committed to further engagement with stakeholders to develop additional resources, including those for extending BUDs.