



Decision on Appeal to USP <825>

USP's Chemical Medicines Monographs 4 Expert Committee (CHM4 EC) has issued a decision on the appeal of USP General Chapter <825> Radiopharmaceuticals – Preparation, Compounding, Dispensing, and Repackaging. USP remains committed to keeping stakeholders and the general public informed of the progress of this standard.

Background

On June 1, 2019, USP published a new standard for compounding radiopharmaceutical drugs, [USP General Chapter <825> Radiopharmaceuticals – Preparation, Compounding, Dispensing, and Repackaging](#), which is intended to provide the minimum standards for the preparation, compounding, dispensing, and repackaging of sterile and nonsterile radiopharmaceuticals. The addition of this new standard represents significant 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. The creation of this chapter reflects advancements in science and clinical practice, clarification of sections that were frequently misconstrued, and input from more than 1,600 public comments received. Over the course of the development process for <825>, the CHM4 EC considered all input and worked towards preserving patient access to quality radiopharmaceuticals while minimizing the risk of harm.

After <825> was published, USP received an appeal to this chapter. In accordance with [USP's Bylaws](#), the CHM4 EC worked with a sense of urgency to consider and issue a decision on this information. See this [link](#) for further information about USP's formal appeals process. A summary of key provisions appealed and the decision of the CHM4 EC are provided below.

Appeal Topics and CHM4 EC Decisions

Key topics covered in the appeal of <825> include:

- ▶ Compounding from sterile substances
- ▶ Beyond-Use Date (BUD) provisions in <825>
- ▶ Applicability of <825> within the radiopharmaceutical regulatory context

Compounding from Sterile Substances

After careful consideration and deliberation, the CHM4 EC decided to:

- ▶ Maintain the use of sterile substances in compounding
 - Compounding from sterile substances poses less risk and is consistent with FDA's stance concerning compounding from sterile conventionally manufactured products.
 - The BUDs listed in Table 7 are the maximum values assigned in the absence of sterility testing; however, BUDs can be prolonged with proper validation of sterility through collection of appropriate data.



BUD Provisions

The appeal questioned the BUD approaches in the new chapter. In response to the appeal, the CHM4 EC decided to:

- ▶ Maintain the BUD framework for radiopharmaceutical compounding
 - Radiopharmaceutical compounding differs from compounding sterile preparations because the use of radiation shields may disrupt laminar flow and interfere with bathing critical sites with first air. The shorter radiopharmaceutical BUDs in <825> take into account the impact of radiation shielding on air quality. The CHM4 EC emphasizes that <825> does permit extension of BUDs when supporting sterility and stability testing is available.
 - BUDs for radiopharmaceuticals take into consideration additional factors such as the half-life of radionuclides, changes in radionuclidic purity, and the radiolytic decomposition of formulation components, all of which must be supported with validation data.
 - Although the CHM4 EC chose not to incorporate the consideration of storage conditions into the current chapter, the Committee agreed to consider their inclusion in future revisions when supporting data become available.

Applicability of <825> Within the Radiopharmaceutical Regulatory Context

The CHM4 EC was asked to review and reconsider the inclusion of the final sentence of <825> Section 11. *Compounding*:

“Radiopharmaceuticals that are essentially copies of marketed FDA-approved radiopharmaceuticals must not be compounded unless there is a change that produces a clinical difference for an identified individual patient, as determined by a prescriber.”

In response, the CHM4 EC decided to:

- ▶ Maintain the current statement
 - The CHM4 EC recognized that <825> reflects FDA’s position in its final guidance for industry and provides salient information for regulated entities, reducing their regulatory burden. The statement addresses patient safety and serves as a point of emphasis for nuclear pharmacies required to comply with federal law.
 - <825> does not apply to radiopharmaceuticals produced in section 503B facilities, i.e., registered outsourcing facilities.

The CHM4 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 CHM4 EC is committed to further engagement with stakeholders to develop additional resources.