



# New and Revised USP Compounding Standards

Summary of new and revised standards to help ensure quality compounded preparations and minimize harm to patients.

On June 1, 2019, updates to the USP General Chapters on compounding nonsterile medicines (USP <795> Pharmaceutical Compounding—Nonsterile Preparations), compounding sterile medicines (USP <797> Pharmaceutical Compounding—Sterile Preparations), and new standards for compounding radiopharmaceutical drugs (USP <825> Radiopharmaceuticals—Preparation, Compounding, Dispensing, and Repackaging) were published.

The revisions reflect advancements in science and clinical practice, clarification of topics that were frequently misconstrued, and incorporate input from over 8,000 public comments received during the public comment process.

## Mark Your Calendar:

The official date for the new and revised standards is **December 1, 2019**. USP General Chapter <800> (Hazardous Drugs — Handling in Healthcare Settings), which was published in February 2016, also goes into effect on December 1, 2019.

## Updates to USP <795> Pharmaceutical Compounding — Nonsterile Preparations

- ▶ Elimination of the **Categories of Compounding**, which formerly included simple, moderate, and complex. The categories of compounding did not impact how the standards were applied but frequently caused confusion on how to classify the preparations.
- ▶ Clarification of the scope of the chapter to include types of **Compounded Nonsterile Preparations (CNSP)** and to exclude specific practices including:
  - Administration
  - Nonsterile radiopharmaceuticals
  - Reconstitution
  - Repackaging
  - Splitting tablets
- ▶ Addition of cross-references to <800> *Hazardous Drugs — Handling in Healthcare Settings* for standards related to hazardous drugs.

### What is Compounding?

Compounding is the act of combining or altering ingredients to create medicines to meet the unique medical needs of individual patients.

### Medicines that are intended to be nonsterile include the following preparations:

- ▶ Solid oral
- ▶ Liquid oral
- ▶ Rectal
- ▶ Vaginal
- ▶ Topical (e.g. creams, gels, ointments)
- ▶ Nasal and sinus intended for local application (e.g. nasal sprays, nasal irrigation)
- ▶ Otic



- ▶ Inclusion of new provisions for equipment for weighing, measuring, or otherwise manipulating components that could generate airborne particles. Facilities **must assess these activities to determine whether a closed system processing device** is required to reduce potential exposure to personnel or contamination of the facility or CNSP. Examples of closed system processing devices include:
  - Containment ventilated enclosures (CVEs)
  - Biological safety cabinets (BSCs)
  - Single-use containment glove bags
- ▶ Revision of the **Beyond-Use Date (BUD)** criteria to take into consideration both stability and water activity to assess the susceptibility of CNSPs to microbial contamination and potential for degradation due to hydrolysis. The BUD provisions additionally addresses CNSPs requiring shorter BUDs and BUDs for CNSPs that may be extended (e.g. CNSPs with a *USP-NF* monograph or stability information).

## Updates to USP <797> Pharmaceutical Compounding — Sterile Preparations

- ▶ Inclusion of standards for specific practices, including:
  - Repackaging, which must be performed in accordance with the requirements in the chapter.
  - Expanded previous provisions related to preparation of **allergenic extract** prescription sets.
  - Addition of cross-references to <800> *Hazardous Drugs — Handling in Healthcare Settings* for standards related to hazardous drugs.
  - Removal of standards related to sterile **radiopharmaceuticals** and addition of cross-reference to a new chapter, <825> *Radiopharmaceuticals — Preparation, Compounding, Dispensing, and Repackaging*.
- ▶ Addition of provisions for **administration** and **preparation per approved labeling**, which are out of the scope of the chapter if certain conditions are met.
- ▶ Revision of the provisions for immediate use **Compounded Sterile Preparations (CSPs)**, which may be prepared with no more than 3 different sterile products and administration is required to begin **within 4 hours** (previously 1 hour) following the start of preparation. The provision does not address administration time (e.g., infusion time).
- ▶ Revision of the microbial contamination risk levels (i.e. low-, medium-, and high-risk level) to **Category 1** and **Category 2 CSPs**. Category 1 and Category 2 are distinguished primarily based on the conditions under which they are made, the probability for microbial growth, and the time period within which they must be used.
- ▶ Revision of the Facilities and Engineering Controls requirements to better describe the types of primary engineering controls (PECs) and their placement. New requirement to place **Compounding Aseptic Isolator (CAI)** and **Compounding Aseptic Containment Isolator (CACI)** in a cleanroom suite to prepare Category 2 CSPs, which has longer BUDs to minimize the risk of contamination. Movement of materials in and out of the CAI/CACI in unclassified air carries a higher risk of contamination and thus placement of the CAI and CACI in classified areas helps mitigate the risks for CSPs with longer Category 2 BUDs.
- ▶ Update to require **monthly surface sampling**, whereas previously surface sampling was required “periodically” and interpreted differently among healthcare facilities. Monthly surface sampling provides a measure of control and provides additional monitoring in between semi-annual (e.g. every 6 months) viable air monitoring and certification requirements.

### Medicines that are intended to be sterile include the following:

- ▶ Injections, including infusions
- ▶ Irrigations for internal body cavities (e.g. any space that does not normally communicate with the environment outside of the body such as the bladder cavity or peritoneal cavity)
- ▶ Ophthalmic dosage forms
- ▶ Pulmonary inhalation preparations
- ▶ Baths and soaks for live organs and tissues
- ▶ Implants



- ▶ Addition of a new requirement for **Master Formulation Records** (for CSPs prepared for more than one patient and for CSPs prepared from nonsterile ingredient(s)) and **Compounding Records** (for all CSPs). A prescription, medication order, or label may serve as the compounding record provided that it contains all of the information specified in the chapter.
- ▶ Addition of new provisions related to establishing **Beyond-Use Dates (BUDs)** based on several factors including the environment in which the CSPs are prepared, aseptic processing and sterilization method, starting components, sterility testing, and storage conditions.
  - Category 1 CSPs are typically prepared in an unclassified Segregated Compounding Area (SCA) and have shorter BUDs.
  - Category 2 CSPs are prepared in a cleanroom suite and have longer BUDs.

## New USP <825> Radiopharmaceuticals — Preparation, Compounding, Dispensing, and Repackaging

- ▶ Inclusion of regulatory requirements for **handling radioactive materials** necessary to balance patient safety with radiation safety of workers and others by following the radiation protection principles.
- ▶ Provisions related to **Beyond Use Dates (BUDs)** that are generally shorter, due to the short half-lives of the radioactive materials.
- ▶ Considerations for the **radiolabeling** of white blood cells and red blood cells requiring language for blood handling and specific facility requirements.
- ▶ Inclusion of practices which are **different than <797>**:
  - Retraining/reevaluation requirements for sterility assurance practices.
  - Temperature requirement for the buffer room due to the storage of radionuclide generators and other radiopharmaceuticals in the buffer room.
- ▶ Addition of standards which are **out of scope in <795> or <797>**:
  - Activities such as preparation, preparation with minor deviations, dispensing and repackaging for radionuclide generator storage and elution.
  - Radioactivity measuring devices, radiation detection devices, and other radiation/radioactivity supplies and equipment required to be present and used.
  - Dose-pooling, dose-splitting, kit-splitting, and other manipulations often necessary for radiopharmaceuticals.
  - Immediate Use standards for radiopharmaceuticals related to preparation and dispensing of short-lived radionuclides, which require manipulations.
  - Some radiopharmaceuticals that have unique product-administration requirements, such as direct infusion generators.
  - Intravascular radioactive devices (radioactive microspheres).

### Medicines, which have radioactivity, used for diagnostic or therapeutic purposes, including:

- ▶ Fludeoxyglucose F 18 Injection
- ▶ Rubidium Chloride Rb 82 Injection
- ▶ Sodium Pertechnetate Tc 99m Injection
- ▶ Technetium Tc 99m Red Blood Cells Injection
- ▶ Technetium Tc 99m Mebrofenin Injection

Explore USP Education to better understand the new and revised compounding standards at [www.usp.org/compounding](http://www.usp.org/compounding).

For any technical questions, email [CompoundingSL@usp.org](mailto:CompoundingSL@usp.org) to access USP's Healthcare Quality and Safety team.