Frequently Asked Questions on USP Compounded Preparation Monographs (CPMs)

USP provides answers to Frequently Asked Questions (FAQs) as a service to stakeholders and others who are seeking information regarding USP's organization, standards, standards-setting process, and other activities. These are provided for informational purposes only, and should not be construed as an official interpretation of USP text, or be relied upon to demonstrate compliance with USP standards or requirements.

1. What is a USP Compounded Preparation Monograph (CPM)?

A USP CPM is an official documentary standard which provides specific formulations for patients for whom there are no suitable commercially available products. The CPMs include the formula (components and quantities), compounding instructions, and beyond-use dates (BUD) established by stability-indicating studies. CPMs additionally contain an assay, specific tests (and acceptance criteria), and other requirements related to packaging, storage, and labeling of the compounded preparation.

2. How do I access the CPMs?

USP CPMs are available through the purchase of an annual subscription to the *USP-NF* or USP Compounding Compendium. You can view a list of available CPMs, those under development as well as unsuccessful studies here.

3. How are CPMs developed?

There are two pathways for CPM creation: (1) contract laboratory studies funded by USP for formulations developed by the Compounding Expert Committee, and (2) donations received through the USP CPM Donation Program. Compounders, entities in academia, compounder member support organizations, drug manufacturers and other stakeholders who have the data necessary for the creation of a monograph are invited to donate this information to USP to support CPM development. Supporting scientific data from both USP contracted studies, and the Donation Program is provided to the Compounding Expert Committee for analysis and evaluation in the USP standard-setting process.

4. How can I participate in the CPM Donation Program?

USP requests submissions of compounded preparations and supporting scientific information to create CPMs that address unmet health needs of patients. The scientific information should include the formulation, compounding procedures, stability-indicating assays, stability test results, packaging, labeling and storage instructions, and any other relevant information. To submit donations to the monograph donation process, please email CPMDonate@usp.org. More details about the Donation Program can be found here.

5. How are beyond-use dates (BUDs) in CPMs established?

The BUDs in USP CPMs are based on quality attributes (e.g., sterility, antimicrobial effectiveness) and a stability study supported by a stability-indicating assay specifically developed and validated for the compounded formulation using the criteria described in General Chapter <1225> *Validation of Compendial Procedures*.

6. What is a validated stability-indicating assay?

A validated stability-indicating assay is one that can distinguish between the active pharmaceutical ingredient (API), its degradation products, and other excipients present in the formulation, in order to accurately determine the strength of the API. During the development of the assay, forced-degradation of the API is performed using various stress conditions such as heat, illumination, and acid-base catalyzed hydrolysis or other degradation. Peak purity analyses are then carried out during validation as part of the specificity test of the forced-degradation samples. Method validation criteria are described in General Chapter <1225> *Validation of Compendial Procedures*. Also, a detailed discussion of the difference between strength and stability testing can be found here.

7. How does the Compounding Expert Committee determine which compounded preparations to prioritize for CPM development?

The process of creating CPMs begins with identifying a public health need. USP applies the following criteria to prioritize formulas for development:

- Medications with the highest public health impact (i.e., affecting major population groups, disease states, and access needs)
- Medications essential to treat pediatric and geriatric patients where there are unmet needs
- Medications that meet the unique unmet needs of animal patients
- Medications that need to be formulated to avoid allergic reactions and to be suitable for administration to patients with specific genetic anomalies
- Medications for currently unmet clinical and therapeutic needs that may arise during chronic shortages of conventionally manufactured products

8. Which BUD do I apply if the CPM BUD is different from those in <795> or <797>?

The BUDs stated in USP Chapters <795> and <797> are often referred to as "default dates," meaning that these BUDs can be applied in the absence of stability information, unless otherwise indicated (e.g., drugs or chemicals known to be more liable to decomposition will require shorter BUDs). A CPM is supported by additional studies to support a different BUD. Where the requirements in a CPM differ from an applicable general chapter, the monograph requirements apply and supersede the general chapter (see *General Notices 3.10. Applicability of Standards*). Thus, when the CPM contains a BUD that is different than those stated in <795> and <797>, for nonsterile and sterile compounding, respectively, the BUD in the CPM can be applied provided that all the CPM requirements are met.

9. Is there any testing required if I use the CPM?

A conservative approach should be taken when assigning BUDs for nonsterile and sterile preparations. The BUD in a CPM can only be applied if the preparation has passed the specific tests in the monograph (e.g., sterility test and bacterial endotoxins test). Otherwise, the default BUDs in <795> and <797> must be assigned.

10. Am I required to use USP or NF grade components when compounding according to a CPM?

Compounders must select components that are suitable for their intended use. The FD&C Act specifies that a bulk drug substance used in compounding must comply with the standards of an applicable USP or NF monograph, if a monograph exists. For other ingredients (e.g., non-APIs), a USP, NF, or FCC substance is recommended as the source of ingredient for compounding (see <795> *Component Selection, Handling, and Storage*).

11. May I deviate from the formulation provided in the CPM (e.g., different concentration, addition of flavoring, use of tablets instead of API, use of different manufacturer of tablet)?

The CPM contains a BUD and assay specific for the formulation provided. Some deviations from the formulation may impact stability and BUD, while other deviations may not have an impact. Flavors, for example, are organic chemicals with reactive functional groups including acids, alcohols, aldehydes, amides, amines, esters, ketones, and lactams. Since the outcome of any deviation is unpredictable without assay data, use the default BUD for the preparation, unless bracketing provisions are provided in the CPM.

12. What is a bracketing study design and how do I use a CPM where two concentrations are given in the same formulation?

A bracketing study is where a particular formulation is studied for stability and sterility (if applicable) at a low concentration and at a high concentration. The stability of the formulation can be extrapolated based on the study of the low and high concentration. Thus, compounders can apply the BUD for concentrations of the preparation within the range specified in the CPM, provided that all other monograph requirements are met.

13. The temperature given in the CPM does not contain units. Is it in Fahrenheit or Celsius?

Unless otherwise specified, all temperatures in the *USP-NF* are expressed in degrees centigrade (Celsius) (see General Notices 8.180 *Temperatures*).

14. Where can I find failed studies?

Occasionally, the Compounding Expert Committee determines that the results of a stability study are not satisfactory to support the development of a CPM. USP compiles the list of failed studies that have been studied by contract laboratories for information purposes only. The list includes the details of the formulation, relevant assay information, and reason for failure. USP encourages any parties who have successfully studied these or other preparations to consider donating them to USP for CPM development.

15. Where can I find FAQs and other information on USP Compounding Standards?

For FAQs on other USP Compounding Standards, please see below:

- USP General Chapter <795> *Pharmaceutical Compounding – Nonsterile Preparations*
- USP General Chapter <797> *Pharmaceutical Compounding – Sterile Preparations*
- USP General Chapter <800> *Hazardous Drugs – Handling in Healthcare Settings*
- USP General Chapter <825> *Radiopharmaceuticals – Preparation, Compounding, Dispensing, and Repackaging*