



<795> FAQs

November 1, 2022

General

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

For FAQs on USP Compounding Standards, please see below:

- [General Chapter <795> Pharmaceutical Compounding—Nonsterile Preparations](#)
- [General Chapter <797> Pharmaceutical Compounding—Sterile Preparations](#)
- [General Chapter <800> Hazardous Drugs—Handling in Healthcare Settings](#)
- [General Chapter <825> Radiopharmaceuticals—Preparation, Compounding, Dispensing, and Repackaging](#)
- [Compounded Preparation Monographs \(CPMs\)](#)

2. Where can I find information about how to interpret and apply General Chapters?

The *General Notices and Requirements* describe the basic assumptions, definitions, and default conditions for the interpretation and application of *USP–NF* content. For example, Section 2.30. *Legal Recognition* describes the legal recognition of USP and NF. Section 3.10.30 *Applicability of Standards to the Practice of Compounding* describes when USP compounding practice standards are or are not applicable.

3. Can USP provide some clarity as to when a preparation needs to be prepared as sterile (CSP) as opposed to as nonsterile (CNSP)?

<795> and <797> both describe compounded preparations that are required to be sterile or can be prepared as nonsterile. In general, preparations designed to be delivered to any body space that does not normally freely “communicate” or have contact with the environment outside of the body, such as the bladder cavity or peritoneal cavity, are typically required to be sterile. Additionally, ophthalmic products and compounded aqueous inhalation solutions and suspensions are required to be sterile. Otic preparations are not required to be sterile unless being administered to a patient with a perforated eardrum. Irrigations for the mouth, rectal cavity, and sinus cavity are not required to be sterile, nor are nasal sprays.

Introduction and Scope

4. What is the definition of nonsterile compounding?

For purposes of General Chapter <795>, nonsterile compounding is defined as combining, admixing, diluting, pooling, reconstituting other than as provided in the manufacturer’s labeling, or otherwise altering a drug product or bulk drug substance to create a nonsterile preparation.



5. To whom do the standards in General Chapter <795> apply?

The chapter applies to all persons who prepare compounded nonsterile preparations (CNSPs) and all places where CNSPs are prepared for human and animal patients. This includes but is not limited to pharmacists, technicians, nurses, physicians, dentists, naturopaths, and chiropractors, in all places including but not limited to pharmacies, hospitals and other healthcare institutions, patient treatment sites, and physicians' practice sites. Personnel engaged in the compounding of CNSPs must additionally comply with laws and regulations of the applicable regulatory jurisdiction. Compounding of nonsterile hazardous drugs (HDs) must additionally comply with General Chapter <800> *Hazardous Drugs—Handling in Healthcare Settings*.

6. How do I know what are requirements versus recommendations in the chapter?

Generally, requirements in a General Chapter are conveyed by use of the term "must". Recommendations are conveyed by use of the terms "should" and "may".

7. What does "official date" mean?

The USP "official date" indicates the date by which affected users are expected to meet the requirements of a particular standard. Ensuring compliance with the requirements of these standards is the responsibility of the applicable regulatory jurisdiction. USP has no role in enforcement.

All text in the United States Pharmacopeia (USP) or National Formulary (NF) that has reached its official date is "official text." Although all text of the *USP–NF* that has reached its official date is "official text," not all official text states requirements with which compendial users must comply. Some official text is intended to assist or guide compendial users or to serve informational purposes.

8. When do the revisions to General Chapter <795> become official?

The revision of <795> published on November 1, 2022, will become "official" on November 1, 2023. The "official date" indicates the date by which affected users are expected to meet the requirements of a particular standard. However, ensuring compliance with the requirements of these standards is the responsibility of the applicable regulatory jurisdiction. Regulatory bodies such as state boards of pharmacy may have a different official date. USP has no role in enforcement.

9. Does the chapter apply for breaking or cutting a tablet into smaller portions?

No, breaking or cutting a tablet into smaller portions is not required to meet the standards in this chapter.

10. Does the chapter apply for reconstitution of conventionally manufactured nonsterile products (e.g., compounding kits)?

Reconstitution of a conventionally manufactured nonsterile product in accordance with the directions contained in the manufacturer approved labeling is not required to meet the standards in this chapter. Reconstitution that is not performed according to manufacturer approved labeling is considered nonsterile compounding and is subject to the requirements in the chapter. Compounding kits are within the scope of the chapter unless they are FDA-approved and reconstitution is performed in accordance with the directions contained in the manufacturer approved labeling.



11. Am I required to use purified water for reconstitution of a conventionally manufactured product?

Reconstitution of a conventionally manufactured nonsterile product in accordance with the directions contained in the manufacturer approved labeling is out of the scope of the chapter. As such, the chapter does not specify the quality of water to be used for reconstitution. Compounders can reach out to other resources, such as the regulatory bodies in their jurisdiction or the manufacturer of the products, for additional information.

12. Is administration out of the scope of the chapter?

The intent of the chapter is to establish minimum standards for practitioners when preparing compounded nonsterile preparations in order to minimize harm, including death, to human and animal patients. The scope of the chapter is intended to be limited to compounding and the standards are designed to help ensure a CNSP maintains its integrity up until the time when administration begins. Administration is out of scope of the chapter, and for purposes of <795>, is defined as the preparation of a single dose for a single patient when administration will begin within 4 hours

13. Does the chapter address compounded radiopharmaceutical dosage forms?

No. Compounding of radiopharmaceuticals is not required to meet the standards of this chapter as they are subject to the requirements in General Chapter <825> *Radiopharmaceuticals—Preparation, Compounding, Dispensing, and Repackaging*.

14. Are the temperatures in the chapter expressed in degrees Fahrenheit or Celsius?

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

15. Are products manufactured by 503B facilities or conventionally manufactured products considered active pharmaceutical ingredients (APIs)?

No. The term “API” refers to any substance or mixture of substances intended to be used in the compounding of a preparation, thereby becoming the active ingredient in that preparation and furnishing pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease in humans or animals or affecting the structure and function of the body. Also referred to as *Bulk drug substance*. A conventionally manufactured drug product is not an API but is typically manufactured from an API(s).

16. Why were the categories of compounding (simple, moderate, and complex) in the previous chapter eliminated in the new revision?

These categories of compounding were originally adapted from <1075> *Good Compounding Practices* in 2011. They often led to confusion among users on how to apply the criteria and the chapter did not provide standards on how to use these categories in applying the compounding standards.



17. Who can be the designated person(s)?

The designated person is one or more individuals assigned to be responsible and accountable for the performance and operation of the facility and personnel for the preparation of compounded nonsterile preparations (CNSPs). Facilities must determine whether they have one or more designated person, select the designated person, and determine how to allocate responsibility if there is more than one designated person.

18. Does the chapter apply for repackaging of a conventionally manufactured product?

No, repackaging of conventionally manufactured drug products is not required to meet the standards in this chapter (see <1178> *Good Repackaging Practices* for recommendations).

19. Please clarify the phrase, “variability from the intended strength of correct ingredients (e.g., $\pm 10\%$ of the labeled strength)”.

There may be variability from the labeled strength of a CNSP. The acceptable range is listed in the applicable monograph for official articles. The acceptable range is $\pm 10\%$ of the labeled strength for nonofficial articles (i.e., 90-110%).

20. This section defines altering a drug or bulk drug substance as nonsterile compounding. It is unclear whether flavoring a manufactured liquid would fall under this category or whether the preparation of premeasured kits, such as FIRST Magic Mouthwash and FIRST Omeprazole, would be required to meet the standards of this chapter.

Flavoring a manufactured product is compounding and must be conducted under compounding standards in accordance with the exemptions for compounding in the Federal Food, Drug, and Cosmetic Act, otherwise the drug product would be deemed adulterated under the Act. Compounding standards apply to the assembly of premeasured kits.

21. When repackaging capsules into unit dose containers using a robotic system, is the BUD limited to 180 days?

Repackaging nonsterile conventionally manufactured drug products is outside the scope of <795> so the BUD limits in *Table 4* do not apply. See <1178> *Good Repackaging Practices* for recommendations.

Personal Hygiene and Garbing

22. What garb is required for nonsterile compounding?

Gloves must be worn for all compounding activities. Other garb (e.g., shoe covers, head or hair covers, facial hair covers, face masks, and gowns) should be worn as required by the facility's standard operating procedures (SOPs). Garb is recommended for the protection of personnel and to minimize the risk of CNSP contamination. The garb must be appropriate for the type of compounding performed. The garbing requirements and frequency of changing the garb must be determined by the facility and documented in the facility's SOPs.



23. Are gloves required to be wiped or changed before beginning to compound a CNSP with different components?

The chapter recommends wiping or replacing gloves before beginning to compound a CNSP with different components to minimize the risk of cross-contaminating other CNSPs and contaminating other objects. General Chapter <795> does not describe the use of specific wipes or agents to use for wiping gloves. Facilities must determine whether gloves should be changed or replaced and the appropriate wipe/agent to use if they are wiped.

24. Can gowns be reused for multiple days if not soiled?

If gowns are worn, they may be re-used if not soiled. If gowns are visibly soiled or have tears or punctures, they must be changed immediately. Facilities must determine the frequency for changing gowns.

Buildings and Facilities

25. Is a compounding space required to be in an enclosed room (i.e., with walls and doors)?

No. While a room may be used as the compounding space, the chapter does not require a separate room. The chapter requires a space that is specifically designated for nonsterile compounding. A visible perimeter should establish the boundaries of the nonsterile compounding area.

26. What is considered an appropriate temperature range to store CNSPs or components?

The storage area must be maintained at a temperature that is appropriate for the CNSPs and components. The storage conditions for the CNSP would be dependent on the assigned beyond-use date (BUD) and CNSP-specific properties (see <795>, *10.2 Parameters to Consider in Establishing a BUD*). The storage conditions for components may be provided by the manufacturer or vendor on the labeling and/or specified in the USP monograph for that component (see also <659>).

27. Since reconstitution and repackaging are not considered compounding and are out of scope of the chapter, can they still be performed in the designated compounding space?

Yes, other activities may be performed in the compounding space when compounding is not occurring. The chapter requires that a compounding space be designated for nonsterile compounding, however, the space is not required to be dedicated for sole use in compounding. Other activities may occur in the compounding space, but they must not be occurring in the space at the same time as compounding.

Cleaning and Sanitizing

28. Can non-compounding personnel clean and sanitize the compounding space?

Facilities must determine the appropriate personnel for cleaning and sanitizing the compounding space. The chapter does not specify who may perform the cleaning and sanitization procedures. However, the chapter does specify that knowledge and competency must be demonstrated initially and at least every 12 months for those that are cleaning and sanitizing.

29. Is daily cleaning only required when nonsterile compounding has occurred?

Cleaning and sanitizing of the surfaces in the nonsterile compounding area(s) must occur on a regular basis at the minimum frequencies specified in *Table 1* or, if compounding is not performed daily, it must be performed before initiating compounding.

30. What is the difference between cleaning and sanitizing?

Cleaning is the process of removing substances (e.g., organic and inorganic material) from objects and surfaces, normally accomplished by manually or mechanically using water with detergents or enzymatic products. Sanitizing is the process of reducing, on inanimate surfaces, the number of all forms of microbial life including fungi, viruses, and bacteria.

31. Why does sterile compounding per <797> require cleaning daily, whereas for nonsterile compounding, cleaning is required at the beginning and end of a shift?

Cleaning and sanitizing of the surfaces in the nonsterile compounding area(s) must occur on a regular basis at the minimum frequencies specified in *Table 1* or, if compounding is not performed daily, it must be performed before initiating compounding.

Cleaning is required at the beginning and end of each shift in <795> due to the particle-generating nature of nonsterile compounding. Sterile compounding is less particle-generating than nonsterile, and compounders sanitize after preparing each batch of CSPs. There is greater risk of cross-contamination from particle-generation for nonsterile compounding.

32. If the dedicated compounding area is in the middle of a room (i.e., dedicated cart, island), does this mean we have to clean walls and storage shelving?

The designated person can define in an SOP what specifically constitutes the 'compounding area' that is specifically designated for nonsterile compounding. Defining the compounding area will determine what surfaces require cleaning and sanitizing per *Table 1*.

Equipment and Components

33. Are containment ventilated enclosures (CVEs) required for nonsterile compounding?

No. The chapter requires facilities to assess particle-generating activities (e.g., weighing, measuring, or other manipulation of components) to determine whether a closed-system processing device is needed. The chapter does not require a closed-system processing device but does require facilities to perform a process evaluation to determine whether a device is needed. A closed-system processing device reduces the potential exposure to personnel and contamination to the facility from airborne particles that weighing, measuring, or otherwise manipulating components could generate. A CVE is one example of a closed-system processing device; other examples include BSCs and single-use containment glove bags.

34. Why are APIs required to be obtained from an FDA-registered facility and components other than APIs only recommended to be obtained from an FDA-registered facility?

The Federal Food, Drug, and Cosmetic Act requires compounded preparations to be prepared from bulk drug substances that are obtained from FDA-registered facilities. The Expert Committee recognizes that there may be some components other than APIs that cannot be obtained from an FDA-registered facility, thus, it is a recommendation that these components be obtained from an FDA-registered facility but is not a requirement.

35. What does it mean when Purified Water is printed in italics?

It means the *Purified Water* is an official article and must meet the applicable monograph (e.g., Purified Water, USP).

36. When is the use of distilled water acceptable?

Purified Water, distilled water, or reverse osmosis water should be used for rinsing equipment and utensils. Note that *Purified Water* or better quality, e.g., *Sterile Water for Irrigation*, must be used for compounding CNSPs when formulations indicate the inclusion of water.

37. If Sterile Water for Irrigation is used as a component in a CNSP, what is the BUD of the Sterile Water for Irrigation once opened?

Purified Water or better quality, e.g., *Sterile Water for Irrigation*, must be used for compounding CNSPs when formulations indicate the inclusion of water. Since sterility is not required, *Sterile Water for Irrigation* may be used until its labeled expiration date if it is stored in its original container per the manufacturer's recommendations.

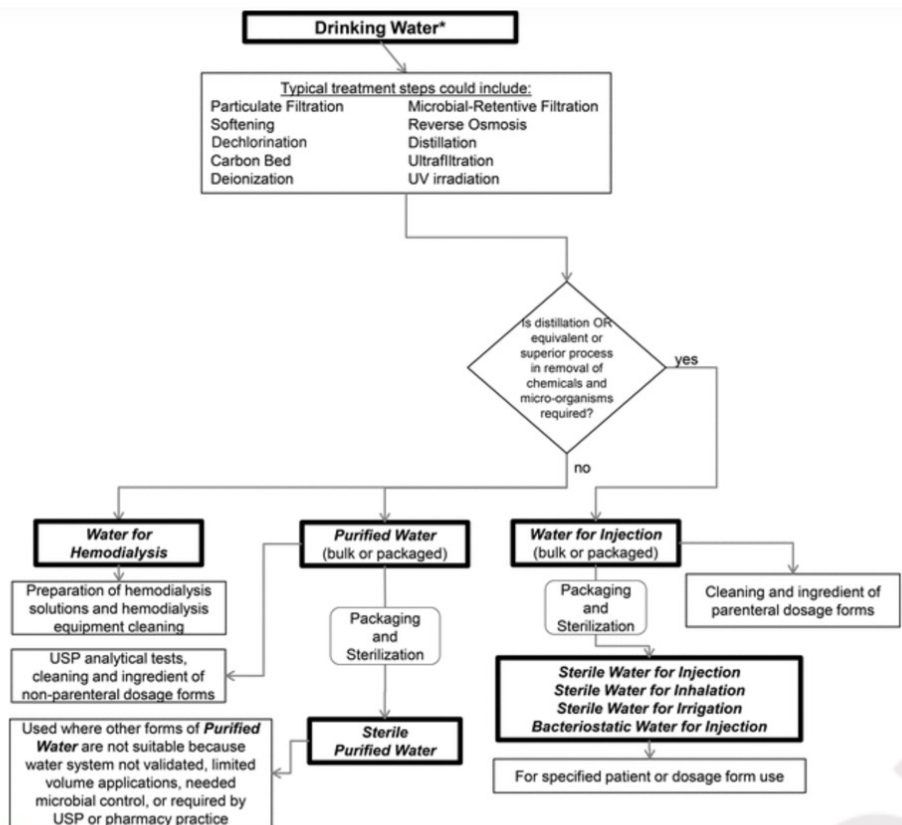
38. Our Board of Pharmacy inspector is questioning our use of Sterile Water for Irrigation in place of Purified Water in CNSPs. Does USP reference this in other general chapters?

Purified Water or better quality, e.g., *Sterile Water for Irrigation*, must be used for compounding nonsterile drug preparations when preparations indicate the inclusion of water. Per <1231> *Water for Pharmaceutical Purposes*, 3.2.4, *Sterile Water for Irrigation* may be used in other applications that do not have particulate matter specifications, including where *Purified Water* is indicated but where access to a validated water system is not practical.

39. FDA prescribing information for a specific brand of *Sterile Water for Irrigation* says, “*Sterile Water for Irrigation* is not potable water and is not intended for oral administration.” If *Sterile Water for Irrigation* is labeled as non-potable, may it be used as a component in a CNSP intended for oral administration?

Sterile Water for Irrigation, USP is prepared from *Water for Injection* that is sterilized and suitably packaged. It contains no antimicrobial agent or other added substance. *Water for Injection* is water purified by distillation or a purification process that is equivalent or superior to distillation in the removal of chemicals and microorganisms. It is prepared from water complying with the U.S. Environmental Protection Agency National Primary Drinking Water Regulations or with the drinking water regulations of the European Union or of Japan or with the World Health Organization’s Guidelines for Drinking Water Quality. Per <1231> *Water for Pharmaceutical Purposes*, *Sterile Water for Irrigation*, USP ‘may be used in other applications that do not have particulate matter specifications, where bulk *Water for Injection* or *Purified Water* is indicated but where access to a validated water system is not practical, or where somewhat larger quantities are needed than are provided as *Sterile Water for Injection*.’ However, if *Sterile Water for Irrigation* is labeled as non-potable, it must not be used in oral preparations.

Per <1231>



40. Is there any guidance on reverse osmosis (RO) systems, such as testing and maintenance requirements?

Water from RO systems that is used as a component in CNSPs must meet the monograph requirements for *Purified Water* including <643> *Total Organic Carbon* and <645> *Water Conductivity*. RO systems must be maintained per manufacturer’s recommendations.



41. Regarding the statement, “Once removed from the original container, any component not used in compounding (e.g., excess after weighing) should be discarded and not returned to the original container to minimize the risk of contaminating the original container”, given the risk of contamination that this could present, why isn’t the “should” a “must”?

There may be instances (e.g., drug shortages, controlled drugs) when discarding excess component is not possible. Personnel who perform weighing procedures must be trained and demonstrate knowledge and competency on handling components to minimize the risk of contamination, and avoid using excessive materials.

42. What organizations certify BSCs or CVEs?

The Compounding Expert Committee removed all references to specific professional organizations and facilities must determine the appropriate certification guide to use for certifying their equipment. Some examples of organizations that provide certification guidance include the Controlled Environment Testing Association (CETA), NSF International, and American Society of Heating, Refrigerating, and Air-Conditioning Engineers (ASHRAE).

43. Are these terms interchangeable: API, drug substance, drug product, active ingredient?

For the purposes of *USP* Chapters <795> and <797>, a bulk drug substance and an active pharmaceutical ingredient are the same. They are defined in the glossary of *USP* <795> and <797> as: Any substance or mixture of substances intended to be used in the compounding of a preparation, thereby becoming the active ingredient in that preparation and furnishing pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease in humans or animals or affecting the structure and function of the body.

A conventionally manufactured drug product is not an API but is typically manufactured from an API(s). There is no statutory or *USP* definition for active ingredient, but the term is used generically in *USP* when referring to the active ingredient in either a conventionally manufactured drug product or API (e.g., when labeling a CSP or a CNSP).

For the purposes of the *USP* Compounding Chapters, a drug product is the same as a conventionally manufactured product and defined as: A pharmaceutical dosage form, usually the subject of an application approved by the applicable national regulatory agency, that is manufactured under current good manufacturing practice conditions. Drug products and conventionally manufactured products are not CSPs or CNSPs.

Master Formulation and Compounding Records

44. Does a new master formulation record (MFR) need to be made for different batch sizes of final CNSP (e.g., same ointment of 120 grams and 60 grams)?

Yes, an MFR must be created for each unique preparation of a CNSP.



45. How specific must the description of the container closure be in the MFR?

A thorough description of the container closure would be considered best practice, which ideally would also include the material of composition that is in contact with the compounded preparation. The size of the container closure may vary depending on quantity of prescription dispensed. For example, “White opaque HDPE airless pump.” There should be enough detail so the selection of that container closure could be made by someone else.

Labeling

46. Are all CNSPs required to be labeled, regardless of whether they are dispensed?

Yes. CNSPs must be labeled with the information specified in 9. *Labeling* regardless of whether or not they are dispensed. Labeling provides the information of the package contents.

Establishing Beyond-Use Dates

47. What is water activity (a_w)?

Put simply, water activity is the measure of free water that is available to participate in chemical reactions such as hydrolysis or may provide an environment that can support microbiological growth. See <922> and <1112> for more detailed information.

48. Are compounders expected to measure the a_w of CNSPs to determine the BUD?

No, the chapter does not require compounders to measure a_w for CNSPs. a_w is intended to be used as a guide for assigning BUDs. General Chapter <795> provides examples of dosage forms that have an $a_w < 0.6$ and those that have an $a_w \geq 0.6$. Additionally, General Chapter <1112> *Application of Water Activity Determination to Nonsterile Pharmaceutical Products* provides a list of products and corresponding a_w in *Table 2*.

49. Why is the BUD for nonaqueous oral liquid dosage forms with an $a_w < 0.6$ (e.g., oral suspensions or solutions) limited to 90 days?

Although many nonaqueous preparations, including anhydrous oil preparations, may be stable for a long period of time, this is not consistently demonstrated for all nonaqueous formulations. For example, a stability-indicating assay of doxycycline compounded in oil exhibited degradation before 90 days. Additionally, there are other ingredients that may oxidize or otherwise react with the fatty acids in the oil. The chapter provides a conservative approach due to examples where preparations in oil are not stable for 180 days. Further, the chapter allows the BUD of CNSPs to be extended up to 180 days if there is a stability study using a stability-indicating assay (see <795>, *10.5 Extending BUDs for CNSPs*).



50. If a stability study shows that a CNSP is stable for longer than 180 days, can that BUD be assigned?

No. General Chapter <795> specifies that the BUD for CNSPs may be extended up to a maximum of 180 days if there is a stability study (published or unpublished) using a stability-indicating analytical method for the API(s), CNSP formulation, and material of composition of the container closure that will be used. If the CNSP is aqueous, the chapter additionally requires testing for antimicrobial effectiveness for extending BUDs beyond those contained in *Table 4* (see *10.5 Extending BUDs for CNSPs*).

However, if there is a *USP-NF* compounded preparation monograph for the CNSP, and the preparation is labeled to indicate that it meets the monograph specifications, the BUD must not exceed the BUD specified in the monograph. As stated in *General Notices 3.10*, monograph requirements supersede the requirements of General Chapters.

51. If I extend the BUD beyond those described in *Table 4. BUD Limit by Type of Preparation in the Absence of a USP-NF Compounded Preparation Monograph or CNSP-Specific Stability Information*, why does the CNSP have to be tested for antimicrobial effectiveness?

The chapter allows an extension of BUD if there is stability data supported by a stability-indicating study. Although the CNSP may be stable, the CNSP may be susceptible to microbial proliferation especially from prolonged and repeated use. Antimicrobial effectiveness testing is recommended and only needs to be performed once for a particular CNSP. If a range of concentration is used in the same CNSP formulation and stored under the same conditions, the antimicrobial effectiveness test can be conducted for the highest and lowest concentrations. The results can be extrapolated for the concentrations within the range studied (e.g., bracketed study design).

52. Is there a difference between testing stability with a strength (potency) over time or a stability-indicating method?

Yes, a strength (potency) over time test determines the amount of active ingredient in a preparation, however, it may not be able to separate the active ingredient from its degradation products and impurities for quantitation depending on the analytical methods used for the test. A stability-indicating method will be able to quantitate the active ingredient and its degradation products or related impurities in the preparation by separating the active ingredient from its degradation products and impurities, and to show a change in the concentration of the active ingredient with increasing storage time. A stability-indicating method is used to determine stability of a drug and used to establish the beyond-use date. (See article, "[Strength and Stability Testing for Compounded Preparations](#).")

53. What is the difference between a BUD and an expiration date?

Beyond-use dates (BUDs) and expiration dates are not the same. Expiration dates are assigned by manufacturers based on analytical and performance testing of the sterility, chemical and physical stability, and packaging integrity of the conventionally manufactured product, API, or added substance. Expiration dates are specific to a particular formulation in its container and at stated exposure conditions of illumination and temperature. Section *14.1 Terminology* in *USP <797>* and Section *10.1 Terminology* in *USP <795>* define an expiration date as: The time during which a product can be expected to meet the requirements of the *USP-NF* monograph, if one exists, or maintain expected quality provided it is kept under the specified storage conditions. Beyond-use dates are assigned by compounders and apply to CSPs and CNSPs. The *Terminology* sections in *USP <797>* and <795> define a BUD as: Either the date, or hour and date, after which a compounded preparation must not be used. The BUD is determined from the date and time that preparation of the compounded preparation is initiated.

54. What is the BUD of a stock solution with no API?

Section 10.4 states, For CNSPs prepared from one or more compounded components, the BUD should generally not exceed the shortest BUD of any of the individual compounded components. However, there may be acceptable instances when the BUD of the final CNSP exceeds the BUD assigned to compounded components (e.g., pH-altering solutions). If the assigned BUD of the final CSP exceeds the BUD of the compounded components, the physical, chemical, and microbiological quality of the final CSP must not be negatively impacted.

Examples of acceptable instances may include use of a pH-altering solution that has a 24 h BUD or preparing a methylcellulose or similar suspension (14 day BUD) for use during the same shift in CNSPs that are preserved (35 day BUD).

55. How may a BUD beyond USP <795> limits be assigned to a stock solution with no API?

Information may be found in the Stability Study Reference Document posted [here](#). In general, the following tests must be considered:

- Appearance (e.g., appearance, color, clarity, and particulates)
- Antimicrobial effectiveness testing (*USP* <51>) for aqueous preparations
- pH
- Microbiological tests for water-containing formulations ($a_w \geq 0.6$)
- <61> *Microbiological Examination of Nonsterile Products: Microbial Enumeration Tests*
- <62> *Microbiological Examination of Nonsterile Products: Tests for Specified Microorganisms*

56. How do I choose an appropriate preservative for my CNSP?

Preservative selection is dependent on the level of potential microbiological growth over the intended period of the BUD (amount of preservative in preparation must be sufficient to protect the preparation through the end of the BUD), the pH of the preparation being preserved (the preservative must have effectiveness at the pH of the preparation), specific microbiological organisms with which the preparation could be exposed (preservative system must be effective against the microbiological organism(s) that have a potential to propagate in the preparation), and chemical compatibility with the API and other excipients.

57. Given the water activity examples in Table 3, and the fact that these do not cover all formulation possibilities, how does a pharmacist determine total water activity of multi-ingredient compounds, and how should a pharmacist determine when water activity testing is needed?

Pharmacists can always reference <922> and <1112> for more information regarding a_w and its determination. The chapter does not require a compounded preparation to be tested for water activity, but a_w is the determining factor in categorizing a preparation as aqueous or nonaqueous. The table was meant to provide actual examples of formulations tested for water activity to assist the pharmacist in determining if a preparation would likely be squarely in the aqueous or nonaqueous category. It is also important to note that waters of hydration do not affect water activity. When in doubt, the best course of action to know water activity would be to test it. This is a one-time test for the specific preparation.



58. How is the BUD of a CNSP affected by pH-modifiers or other stock solutions that are used as components?

For CNSPs prepared from one or more compounded components, the BUD should generally not exceed the shortest BUD of any of the individual compounded components. However, there may be acceptable instances when the BUD of the final CNSP exceeds the BUD assigned to compounded components (e.g., pH-altering solutions). If the assigned BUD of the final CNSP exceeds the BUD of the compounded components, the physical, chemical, and microbiological quality of the final CSP must not be negatively impacted.

59. Must the stability studies used to extend BUDs to 180 days be published?

No. Any stability study that meets the requirements of a stability-indicating assay method can be used, whether published or unpublished, to extend beyond-use dates up to 180 days for a CNSP. To learn the requirements for a stability-indicating assay method, visit the Stability Study Reference Document posted [here](#).

60. When must <51> testing be performed?

<51> testing should be performed to verify a formulation for a multiple-dose preparation is capable of meeting the antimicrobial effectiveness testing requirements. Changes in package size, container closure system, or preparation components may necessitate repeating the <51> testing. Testing is not necessary for every batch.

61. Must antimicrobial effectiveness testing results be provided by an FDA-registered facility?

The designated person(s) may rely on antimicrobial effectiveness testing results provided by an FDA-registered facility or published in peer-reviewed literature as long as the CNSP formulation (including any preservative) and container closure materials of composition are the same as those tested (unless a bracketing study is performed). Outside of the United States, facilities must comply with the laws and regulations of the applicable regulatory jurisdiction.

62. Can unpublished antimicrobial effectiveness testing results be used?

Yes. Compounders are not required to perform their own *USP <51> Antimicrobial Effectiveness Testing* on each compound prepared. They may perform or contract the study themselves, or they may use published or unpublished peer-reviewed literature results or *USP <51>* results performed in an FDA-registered facility provided that the CNSP or CSP preparation (including any preservative) and container closure system are exactly the same as those that produced the preparation that produced the test results. Antimicrobial effectiveness testing may also be performed in what is known as a bracketing study by testing a low concentration and a high concentration of the active ingredient in the formulation to establish preservative effectiveness across various strengths of the same formulation. The concentration of all other ingredients (including preservatives) must be the same throughout the bracketing study.