



Commentary

USP–NF 2023 Issue 1

November 1, 2022

In accordance with USP’s Rules and Procedures of the Council of Experts (“Rules”), and except as provided in Section 7.02 Accelerated Revision Processes, USP publishes proposed revisions to the *United States Pharmacopeia and the National Formulary (USP–NF)* for public review and comment in the *Pharmacopeial Forum (PF)*, USP’s free bimonthly journal for public notice and comment. After comments are considered and incorporated as the Expert Committee deems appropriate, the proposal may advance to official status or be re-published in *PF* for further notice and comment, in accordance with the Rules. In cases when proposals advance to official status without re-publication in *PF*, a summary of comments received, and the appropriate Expert Committees responses are published in the Revisions and Commentary section of USP.org at the time the official revision is published.

The *Commentary* is not part of the official text and is not intended to be enforceable by regulatory authorities. Rather, it explains the basis of Expert Committees’ responses to public comments on proposed revisions. If there is a difference between the contents of the *Commentary* and the official text, the official text prevails. In case of a dispute or question of interpretation, the language of the official text, alone and independent of the *Commentary*, shall prevail.

For further information, contact:
USP Executive Secretariat
United States Pharmacopeia
12601 Twinbrook Parkway
Rockville, MD 20852-1790 USA

Comments were received for the following when they were proposed in Pharmacopeial Forum:

General Chapter

<795> Pharmaceutical Compounding – Nonsterile Preparations

Sections:

[General Comments](#)

[Introduction and Scope](#)

[Personnel Training and Evaluation](#)

[Personal Hygiene and Garbing](#)

[Buildings and Facilities](#)

[Cleaning and Sanitizing](#)

[Equipment and Components](#)

[Master Formulation and Compounding Records](#)

[Release Inspections and Testing](#)

[Labeling](#)

[Establishing Beyond-Use Dates](#)

[SOPs](#)

[Quality Assurance and Quality Control](#)

[CNSP Packaging and Transporting](#)

[Documentation](#)

[Glossary](#)

General Chapter/Section(s): <795> Pharmaceutical Compounding – Nonsterile Preparations
Expert Committee: Compounding
No. of Commenters: 73

General Comments

Comment Summary #1: The commenter recommended including a table of contents as part of the final chapter.

Response: Comment partially incorporated. While a table of contents cannot be added as a part of the chapter, per *USP Style Guide*, a table of contents is included as a part of the *USP-NF* platform.

Comment Summary #2: Commenters recommended implementing a delayed implementation date.

Response: Comment incorporated. The implementation date for the chapter is November 1, 2023.

Comment Summary #3: The commenter recommended providing clear procedures in tables to ease compliance.

Response: Comment partially incorporated. The information included in the chapter sets forth the minimum standards and details as appropriate. Tables were added and some were modified throughout the text for added clarity as appropriate. This chapter leaves specific procedures up to facilities to determine in their SOPs, as outlining them in the chapter is more specific than the minimum standards in the chapter.

Comment Summary #4: The commenter recommended details be included in the chapter text rather than clarified in FAQs posted to the USP website to provide a clear minimum standard of quality.

Response: Comment partially incorporated. The information included in the chapter sets forth the minimum standards and details as appropriate. Additional information is included in the FAQs to assist with implementation.

Comment Summary #5: The commenter recommended including a section on compounding for animal patients.

Response: Comment not incorporated. The chapter describes the minimum standards to be followed for the preparation of CNSPs (Compounded nonsterile preparations) for humans and animals.

Comment Summary #6: The commenter indicated that due to the diversity of veterinary practice settings within which veterinary care is delivered, a veterinary-specific chapter should be developed.

Response: Comment not incorporated. The Compounding Expert Committee (EC) is committed to ongoing engagement on the application of these standards to veterinary medicine. Ensuring compliance with the requirements of the chapter is the responsibility of the applicable regulatory jurisdiction.

Comment Summary #7: The commenter recommended that the requirement for adherence to USP monographs be removed for veterinary compounding.

Response: Comment not incorporated. The Compounding Expert Committee is committed to ongoing engagement on the application of these standards to veterinary medicine. Ensuring compliance with the requirements of the chapter is the responsibility of the applicable regulatory jurisdiction.

Comment Summary #8: The commenter recommended initiating educational efforts for veterinary medicine and compounding.

Response: Comment partially incorporated. The Compounding Expert Committee is committed to ongoing engagement on the application of these standards to veterinary medicine. Ensuring compliance with the requirements of the chapter is the responsibility of the applicable regulatory jurisdiction.

Comment Summary #9: The commenter recommended including clarification regarding areas of potential regulatory interaction or conflict for veterinary compounding.

Response: Comment not incorporated. USP has no role in enforcement. Ensuring compliance with the requirements of the chapter is the responsibility of the applicable regulatory jurisdiction.

Comment Summary #10: The commenter indicated compounding veterinarians have a funding structure that differs from that for human health and there should be a tiered approach to standard development to accommodate this divergent funding structure.

Response: Comment not incorporated. This is out of scope of the chapter. USP has no role in enforcement or funding. The Compounding Expert Committee is committed to ongoing engagement on the application of these standards to veterinary medicine. Ensuring compliance with the requirements of the chapter is the responsibility of the applicable regulatory jurisdiction.

Comment Summary #11: The commenter recommended including a statement that the compounder is solely responsible for the finished preparation.

Response: Comment not incorporated. The compounding facility's leadership and all personnel involved in preparing, storing, packaging, dispensing, and transporting CNSPs are responsible for 1) ensuring that the applicable practices and quality standards in this chapter are continually and consistently applied to their operations, and 2) proactively identifying and remedying potential problems within their operations. Personnel engaged in the compounding and dispensing of CNSPs must also comply with laws and regulations of the applicable regulatory jurisdiction. The compounding facility must designate one or more individuals to be responsible and accountable for the performance and operation of the facility and personnel for the preparation of CNSPs.

Comment Summary #12: The commenter recommended including a statement in the chapter that at the time of dispensing the prescription, the patient or the patient's agent shall be counseled about proper use, storage, handling, and disposal of the compounded preparation.

Response: Comment not incorporated. USP has no role in enforcement. Ensuring compliance with the requirements of the chapter is the responsibility of the applicable regulatory jurisdiction.

Comment Summary #13: The commenter recommended that if the comments for the chapter appearing in PF 47(6) result in substantial changes to the proposal, that it be re-published in a subsequent PF.

Response: Comment not incorporated. No additional comment period was deemed to be necessary at this time.

Comment Summary #14: The commenter requested a 90-180-day extension for the public comment period for the chapter.

Response: Comment partially incorporated. The public comment period deadline was extended from January 31, 2022, to March 17, 2022, to bring the total public comment period to over 6 months.

Comment Summary #15: The commenter suggested that the chapter be structured by requirements for low-volume versus high-volume nonsterile compounding.

Response: Comment not incorporated. The requirements of the chapter must be followed to minimize harm to human and animal patients that could result from excessive microbial contamination, variability from the intended strength of correct ingredients, physical and chemical incompatibilities, chemical and physical contaminants, and/or use of ingredients of inappropriate quality, regardless of the volume of compounding done in a facility.

Comment Summary #16: The commenter indicated support for the organization and clarity of the chapter.

Response: Comment incorporated. The language for clarification and organization was maintained and additional clarification added as deemed necessary.

Comment Summary #17: The commenter indicated support for the webinars and supporting documents providing further information regarding water activity.

Response: Comment incorporated. The expert committee will consider future resources and stakeholder engagement sessions to support understanding of the standards.

Comment Summary #18: The commenter indicated the chapter revisions are not necessary.

Response: Comment not incorporated. The chapter was revised to improve clarity and to respond to stakeholder input.

1. Introduction and Scope

Expert Committee-Initiated Change #1: A sentence was added to the chapter to clarify that administration, including crushing a tablet(s) or opening a capsule(s) to mix with food or liquids to facilitate patient dosing, is not subject to the requirements of the chapter. A statement was added to say, "Refer to facility SOPs for additional safe practices (e.g., labeling)".

Expert Committee-Initiated Change #2: A statement was added to Section 1.1.2 *Practices not subject to the requirements in this chapter*, to state that handling of nonsterile hazardous drugs (HDs) should additionally comply with <800>.

Expert Committee-Initiated Change #3: Language about the responsibilities of the designated person(s) was separated into its own subsection 1.1.4 *Oversight by designated person(s)*.

Expert Committee-Initiated Change #4: Language was revised from "an SOP" to "the facility's SOPs" for consistency with language throughout the chapter.

Comment Summary #19: The commenter indicated that it is unclear whether adding flavoring to a conventionally manufactured product would fall under the definition of nonsterile compounding.

Response: Comment not incorporated. Compounding is defined as the process of 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.

Comment Summary #20: Commenters indicated that excluding flavoring of conventionally manufactured products and the preparation of premeasured kits should not be required to meet the standards of the chapter.

Response: Comment not incorporated. Flavorings are organic chemicals with reactive functional groups including acids, alcohols, aldehydes, amides, amines, esters, ketones, and lactams. Flavorings are not always labeled with their full ingredients and may contain solvents. Minor components in a flavoring system can impact the stability of a CNSP. Impacts on stability can lead to degradation, production of harmful impurities, and/or reduced bioavailability. Flavorings can impact levels of impurities while having no impact on assay values.

Comment Summary #21: The commenter indicated addition of flavoring agents should not invalidate stability-indicating studies performed on non-flavored or alternate-flavored compounds and should provide stakeholders with a list of flavor/API combinations that are known to cause short product stability.

Response: Comment not incorporated. Flavorings are organic chemicals with reactive functional groups including acids, alcohols, aldehydes, amides, amines, esters, ketones, and lactams. Flavorings are not always labeled with their full ingredients and may contain solvents. Minor components in a flavoring system can impact the stability of a CNSP. Impacts on stability can lead to degradation, production of harmful impurities, and/or reduced bioavailability. Flavorings can impact levels of impurities while having no impact on assay values. There is a wide range of flavorings, and the EC is unable to capture all information about combinations known to impact or not impact stability.

Comment Summary #22: The commenter indicated that clarification is needed regarding the acceptable range of variability from the labeled strength of a CNSP.

Response: Comment not incorporated. The acceptable range is $\pm 10\%$ of the labeled strength for nonofficial articles (i.e., 90-110%).

Comment Summary #23: The commenter indicated that a sentence should be included in the chapter to state that compounding is an integral part of pharmacy practice and essential to provision of healthcare, to avoid the topic of compounding from being removed from pharmacy school curricula.

Response: Comment not incorporated. Inclusion of this sentence may incorrectly imply that the chapter only applies to pharmacy practice. The proposed statement is editorial.

Comment Summary #24: The commenter indicated that chapter text may be interpreted differently than intended by regulators.

Response: Comment not incorporated. USP has no role in enforcement. Ensuring compliance with the requirements of the chapter is the responsibility of the applicable regulatory jurisdiction. The EC compiles FAQs to further clarify the intent of the chapter as deemed necessary.

Comment Summary #25: Commenters indicated that the categorization of nonsterile compounding should continue to be identified as simple, moderate, and complex.

Response: Comment not incorporated. Designating nonsterile compounding as simple, moderate, or complex does not reflect the training needed or the true complexity of the processes being performed. Many examples of compounding stakeholders would describe as simple are actually considered to be moderate under the previous chapter. Regardless of the perceived ease of the processes being performed, stability of the CNSP needs to be considered.

Comment Summary #26: Commenters indicated that while the chapter indicates that compounded otic preparations, excluding use in perforated eardrums, must comply with the chapter, personnel may not know if the eardrum is perforated or non-perforated at the time of administration.

Response: Comment not incorporated. Otic preparations are required to be sterile if being administered to a patient with a perforated eardrum. Diagnosing and prescribing are out of scope of this chapter. USP has no role in enforcement. Ensuring compliance with the requirements of the chapter is the responsibility of the applicable regulatory jurisdiction.

Comment Summary #27: The commenter requested clarification that facilities should apply any necessary containment strategies when reconstituting, repackaging, and splitting tablets.

Response: Comment partially incorporated. A statement was added to say that handling of nonsterile HDs should additionally comply with <800>.

Comment Summary #28: The commenter indicated support for the statement in the chapter that compounding of nonsterile radiopharmaceuticals is not required to meet the standards in this chapter and is subject to the requirements in *Radiopharmaceuticals – Preparation, Compounding, Dispensing, and Repackaging* <825>.

Response: Comment partially incorporated. This sentence was revised to say that “compounding of nonsterile radiopharmaceuticals is subject to the requirements in *Radiopharmaceuticals – Preparation, Compounding, Dispensing, and Repackaging* <825>, within the list of practices not subject to the requirements in this chapter.” This revision was made to avoid redundancy.

Comment Summary #29: The commenter recommended stating to, “refer to *Good Repackaging Practices* <1178> which is informational only and consult with the regulators in the jurisdiction to ensure your practice meets expectations”.

Response: Comment partially incorporated. The text was edited to “see *Good Repackaging Practices* <1178> for recommendations.”

Comment Summary #30: The commenter asked to clarify if repackaging a final compounded nonsterile preparation (CNSP) would be considered compounding.

Response: Comment not incorporated. Additional text to address repackaging a final CNSP was not added as this would be a component of dispensing.

Comment Summary #31: The commenter indicated that they repackage conventionally manufactured final dosage forms into unit dose packaging for use in a robot system, and that a maximum 180-day limit would lead to increased drug waste and disallow them from using a robot system.

Response: Comment not incorporated. Repackaging conventionally manufactured drug products is out of scope of this chapter and not subject to the requirements of this chapter.

Comment Summary #32: The commenter indicated that the statement describing the personnel and settings affected saying, “includes but is not limited to”, is unclear about the applicability of the chapter and suggested removing “not limited to” and listing those the chapter applies to.

Response: Comment not incorporated. The chapter applies to all persons who prepare CNSPs and all places where CNSPs are prepared. The applicability of the chapter is not limited to those individually specified.

Comment Summary #33: The commenter indicated that the language describing the designated person is resource intensive and recommended revising to designated panel or committee.

Response: Comment not incorporated. The chapter describes the responsibilities of the designated person(s) as one or more individuals assigned to be responsible and accountable for the performance and operation of the facility and personnel as related to the preparation of CNSPs.

Comment Summary #34: The commenter indicated that preparation of a single dose for multiple non-human patients when administration will begin within 4 hours of beginning the preparation should not be required to meet the standards of the chapter.

Response: Comment not incorporated. Administration is defined in the chapter as the preparation of a single dose for a single patient when administration will begin within 4 hours. The requirements of this chapter are equally relevant to CNSPs for human and animal patients. USP has no role in the enforcement of compounding chapters. Pursuant to *General Notices, 2.30 Legal Recognition*, ensuring compliance with USP standards is the responsibility of regulatory bodies. Regulators may choose to enforce the requirements of <795> with respect to veterinary practice settings.

2. Personnel Training and Evaluation

Expert Committee-Initiated Change #1: “Assigned” was added to all instances of “trainer” throughout the chapter.

Expert Committee-Initiated Change #2: Instances of “knowledge competency” were corrected to state “knowledge and competency”.

Expert Committee-Initiated Change #3: Language was revised for clarity regarding the designated person(s) being responsible for creating and implementing a training program that describes the required training, the frequency of training, and the process for evaluating the competency of personnel.

Comment Summary #35: Commenters indicated that if personnel are able to demonstrate competency at least every 12 months, they should not be required to undergo re-training every 12 months.

Response: Comment not incorporated. USP has no role in enforcement. Ensuring compliance with the requirements of the chapter is the responsibility of the applicable regulatory jurisdiction.

The chapter requires facilities to develop SOPs on all aspects of the compounding operation, and this is a topic that may be described in the facility's SOPs.

Comment Summary #36: The commenter recommended clarifying if all compounders, including those with prior experience, need to be formally trained with documentation.

Response: Comment not incorporated. USP has no role in enforcement. Ensuring compliance with the requirements of the chapter is the responsibility of the applicable regulatory jurisdiction.

Comment Summary #37: Commenters recommended removing the requirement for compounders to read and understand the chapter, other applicable standards, and other relevant literature.

Response: Comment incorporated. The language was revised to require training procedures to include understanding the requirements in the chapter.

Comment Summary #38: Commenters indicated facilities should be able to customize the type of evaluations for their personnel, not all personnel involved in the direct oversight of compounding actively compound, and other personnel that enter the compounding area that are not compounding personnel should not be required to complete the same training and evaluation requirements as compounding personnel.

Response: Comment partially incorporated. Language was revised to state that that before beginning to compound CNSPs independently or have direct oversight of compounding personnel, personnel must complete training and be able to demonstrate knowledge of principles and competency of skills for performing nonsterile manipulations as applicable to their assigned tasks.

Comment Summary #39: Commenters indicated that not all personnel involved in the direct oversight of compounding actively compound.

Response: Comment incorporated. Language was revised to state that that before beginning to compound CNSPs independently or have direct oversight of compounding personnel, personnel must complete training and be able to demonstrate knowledge of principles and competency of skills for performing nonsterile manipulations as applicable to their assigned tasks.

Comment Summary #40: The commenter recommended revising text to clarify that training and evaluation requirements apply for personnel involved in, or the direct oversight of, the compounding CNSPs.

Response: Comment incorporated.

Comment Summary #41: The commenter recommended removing the requirement that compounding personnel demonstrate competency in the principles and hands-on skills of nonsterile manipulations as applicable to their assigned tasks.

Response: Comment not incorporated. The language was clarified to say that personnel must complete training and be able to demonstrate knowledge of principles and competency of skills for performing nonsterile manipulations as applicable to their assigned tasks.

Comment Summary #42: The commenter indicated that the requirements for personnel training and evaluation will have a significant impact on abilities of low-volume compounding pharmacies.

Response: Comment partially incorporated. The requirements for personnel training and evaluation were revised to clarify to which personnel the requirements apply.

3. Personal Hygiene and Garbing

Expert Committee-Initiated Change #1: Language was revised to specify that garb (e.g., shoe covers, head or hair covers, facial hair covers, face masks, and gowns) must be appropriate for the type of compounding performed and should be worn as needed for the protection of personnel from chemical exposures and for prevention of CNSP contamination, rather than stating as "preparation contamination".

Expert Committee-Initiated Change #2: A statement was removed stating that if used, gloves, shoe covers, head or hair covers, facial hair covers, and face masks may not be re-used and must be replaced with new ones. Clarification was added to state that when personnel exit the compounding area, garb, except for gowns should be discarded.

Expert Committee-Initiated Change #3: Language regarding garb and glove requirements was revised for clarity and to harmonize with comparable language in <797>.

Expert Committee-Initiated Change #4: Language was revised for clarity stating that because of the risk of contaminating the CNSP and the environment, the designated person(s) is responsible for evaluating whether individuals should be excluded from working in compounding areas until potentially contaminating conditions have resolved.

Comment Summary #43: Commenters recommended changing “must” to “should” regarding personnel being required to remove personal outer garments, removing all exposed jewelry, and removing earbuds or headphones.

Response: Comment not incorporated. The chapter states that the designated person(s) may permit accommodations provided that the quality of the environment and CNSP will not be affected.

Comment Summary #44: The commenter indicated there is a lack of scientific justification to support revisions to the garbing competency.

Response: Comment not incorporated. Garbing competency evaluations are not required by <795>.

Comment Summary #45: The commenter recommended the chapter state that gloves be replaced before beginning a CNSP that has different components, rather than being wiped or replaced.

Response: Comment not incorporated. In some circumstances there may difficulty replacing gloves each time before beginning a CNSP with different components, such as garbing shortages. Personnel should at least wipe the gloves before beginning a CNSP with different components.

Comment Summary #46: The commenter recommended that hands and gloves should be wiped each time before bringing them out of the powder containment hood, and that equipment and components should be wiped down before being brought out of the powder containment hood.

Response: Comment not incorporated. The chapter requires facilities to develop SOPs on all aspects of the compounding operation, and this is a topic that may be described in the facility’s SOPs. Information on the handling of hazardous drugs is in <800>. For nonsterile compounding, gloves should be wiped or replaced before beginning a CNSP that has different components.

Comment Summary #47: The commenter recommended the chapter state that gloves must be wiped or replaced before beginning a CNSP that has different components.

Response: Comment not incorporated. The chapter requires facilities to develop SOPs on all aspects of the compounding operation, and this is a topic that may be described in the facility’s SOPs.

Comment Summary #48: The commenter recommended the chapter state gloves should be wiped with IPA or replaced before beginning a CNSP that has different components.

Response: Comment not incorporated. Other solvents or materials may be appropriate for wiping gloves. The chapter requires facilities to develop SOPs on all aspects of the compounding operation, and this is a topic that may be described in the facility’s SOPs.

Comment Summary #49: The commenter recommended the chapter state to wipe gloves with isopropyl alcohol and paper towel(s) when exiting the hood to reduce contamination of other areas and objects.

Response: Comment not incorporated. Other solvents or materials may be appropriate for wiping gloves. The chapter requires facilities to develop SOPs on all aspects of the compounding operation, and this is a topic that may be described in the facility's SOPs.

Comment Summary #50: The commenter indicated support for the chapter not requiring hands and arms be washed up to the elbow.

Response: Comment incorporated. Language was not revised to include a requirement for hands and arms be washed up to the elbow.

Comment Summary #51: The commenter indicated it is redundant for hand hygiene procedures to require drying hands completely with disposable towels or wipers, and then allowing hands to dry thoroughly before donning gloves.

Response: Comment incorporated. The hand hygiene procedures were revised to dry hands completely with disposable towels or wipers, and then don gloves.

Comment Summary #52: The commenter indicated the chapter does not provide any information regarding re-use of gowns.

Response: Comment not incorporated. The chapter requires facilities to develop SOPs on all aspects of the compounding operation, and this is a topic that may be described in the facility's SOPs. The chapter requires garbing requirements and frequency of changing garb be determined by the facility and documented in the facility's SOPs.

Comment Summary #53: The commenter indicated lab coats must not be used and that either disposable gowns, or not using gowns more than daily, should be required.

Response: Comment not incorporated. The chapter requires facilities to develop SOPs on all aspects of the compounding operation, and this is a topic that may be described in the facility's SOPs. The chapter requires garbing requirements and frequency of changing garb be determined by the facility and documented in the facility's SOPs.

Comment Summary #54: The commenter recommended allowing face masks to be reusable in accordance with the manufacturer's recommendations.

Response: Comment partially incorporated. Revisions were included for clarification to state that when personnel exit the compounding area, garb, except for gowns, should be discarded. The chapter requires facilities to develop SOPs on all aspects of the compounding operation, and this is a topic that may be described in the facility's SOPs. The chapter requires garbing requirements and frequency of changing garb be determined by the facility and documented in the facility's SOPs.

Comment Summary #55: The commenter indicated that clarification is needed regarding who should determine what is appropriate garb for various compounding activities for nonsterile preparations.

Response: Comment not incorporated. The chapter requires facilities to develop SOPs on all aspects of the compounding operation, and this is a topic that may be described in the facility's SOPs. The chapter requires garbing requirements and frequency of changing garb be determined by the facility and documented in the facility's SOPs.

4. Buildings and Facilities

Expert Committee-Initiated Change #1: Language was revised for clarity stating that the method of designation for a compounding area must be described in the facility's SOPs.

Expert Committee-Initiated Change #2: All instances of "compounding space" were changed to "compounding area".

Expert Committee-Initiated Change #3: Language was revised for clarification to state that an easily accessible sink must be available.

Comment Summary #56: Commenters recommended including information regarding monitoring of relative humidity.

Response: Comment not incorporated. The chapter requires facilities to develop SOPs on all aspects of the compounding operation, and this is a topic that may be described in the facility's SOPs. The requirements for relative humidity may be determined by the applicable regulatory jurisdiction(s). USP has no role in enforcement.

Comment Summary #57: Commenters recommended requiring that space be designated for nonsterile compounding while nonsterile compounding is occurring, rather than only designated for nonsterile compounding.

Response: Comment partially incorporated. Language was revised to say that an area must be designated for nonsterile compounding, revised from "specifically designated". The method of designation must be described in the facility's SOPs, and other activities must not be occurring in the compounding area at the same time as compounding.

Comment Summary #58: The commenter recommended requiring facilities engaging in complex nonsterile compounding to have a dedicated room for compounding.

Response: Comment not incorporated. Space is limited for many pharmacy spaces. The chapter requires that an area be designated for nonsterile compounding. The method of designation must be described in the facility's SOPs, and other activities must not be occurring in the compounding area at the same time as compounding.

Comment Summary #59: The commenter recommended clarifying if a designated compounding surface or cart is sufficient as a compounding space.

Response: Comment not incorporated. The chapter requires that an area be designated for nonsterile compounding. The method of designation must be described in the facility's SOPs, and other activities must not be occurring in the compounding area at the same time as compounding. The chapter requires facilities to develop SOPs on all aspects of the compounding operation, and this is a topic that may be described in the facility's SOPs. USP has no role in enforcement. Ensuring compliance with the requirements of the chapter is the responsibility of the applicable regulatory jurisdiction.

Comment Summary #60: The commenter indicated support for language indicating that spaces within a veterinary practice setting may accommodate activities other than compounding, as long as other activities are not occurring in the same place at the same time.

Response: Comment incorporated. Language was maintained indicating that an area must be designated for nonsterile compounding. The method of designation must be described in the facility's SOPs, and other activities must not be occurring in the compounding area at the same time as compounding.

Comment Summary #61: The commenter indicated that there are veterinary practice settings where other activities will unavoidably occur in the compounding area at the same time as compounding.

Response: Comment not incorporated. USP has no role in enforcement. Ensuring compliance with the requirements of the chapter is the responsibility of the applicable regulatory jurisdiction.

Comment Summary #62: The commenter recommended waiving the no carpeting requirement for simple, nonsterile compounding, and including clarification regarding a floor mat would be acceptable.

Response: Comment partially incorporated. The statement was revised to state that there should not be carpet in the compounding area.

Comment Summary #63: Commenters recommended removing the requirement that there be no carpet in the compounding space.

Response: Comment partially incorporated. The statement was revised to state that there should not be carpet in the compounding area.

Comment Summary #64: The commenter indicated that documenting room temperatures would be difficult for community retail pharmacies engaging in occasional compounding.

Response: Comment not incorporated. Temperatures need to remain within the appropriate range for drugs. Temperatures must be monitored either manually at least once daily on days that the facility is open, or continuously with a temperature recording device.

Comment Summary #65: The commenter recommended clarifying that rinsing with purified water should be completed after cleaning equipment.

Response: Comment not incorporated. The chapter requires facilities to develop SOPs on all aspects of the compounding operation, and this is a topic that may be described in the facility's SOPs.

Comment Summary #66: The commenter recommended clarifying if purified water, distilled water, or reverse osmosis water "must" or "should" be used for rinsing equipment and utensils.

Response: Comment not incorporated. The chapter states that purified water, distilled water, or reverse osmosis water should be used for rinsing equipment and utensils.

Comment Summary #67: The commenter indicated that there are veterinary practice settings where personnel will not have access to purified water, distilled water, or water obtained via reverse osmosis to be used for rinsing equipment.

Response: Comment not incorporated. The chapter states that purified water, distilled water, or reverse osmosis water "should" be used for rinsing equipment and utensils. USP has no role in enforcement. Ensuring compliance with the requirements of the chapter is the responsibility of the applicable regulatory jurisdiction.

Comment Summary #68: The commenter indicated that there are veterinary practice settings where personnel will not have access to hot and cold water.

Response: Comment not incorporated. USP has no role in enforcement. Ensuring compliance with the requirements of the chapter is the responsibility of the applicable regulatory jurisdiction.

5. Cleaning and Sanitizing

Comment Summary #69: The commenter recommended removing the requirement to clean and sanitize ceilings in nonsterile compounding area(s).

Response: Comment not incorporated. The chapter does not state a minimum frequency for cleaning and sanitizing ceilings in nonsterile compounding area(s) but does require cleaning and sanitizing when visibly soiled and when surface contamination (e.g., from splashes) is known or suspected.

Comment Summary #70: The commenter recommended ceilings be required to be cleaned and sanitized every 3 months, after spills, and when surface contamination (e.g., from splashes) is known or suspected, to match the frequency to which walls are required to be cleaned and sanitized.

Response: Comment not incorporated. The minimum frequency for cleaning and sanitizing walls in nonsterile compounding area(s) was revised to as when visibly soiled, after spills, and when surface contamination (e.g., from splashes) is known or suspected.

Comment Summary #71: The commenter indicated clarity is needed for if the requirements for cleaning and sanitizing storage shelving applies to shelf/shelves where compounding ingredients are stored in the designates space for compounding or shelf/shelves of the entire pharmacy where compounding ingredients may be stored.

Response: Comment not incorporated. *Table 1* states it includes the minimum frequency for cleaning and sanitizing in nonsterile compounding area(s). An area must be designated for nonsterile compounding. The method of designation must be described in the facility's SOPs.

Comment Summary #72: Commenters suggested requiring cleaning and sanitizing of work surfaces only on days when compounding occurs.

Response: Comment incorporated. At minimum, work surfaces are required to be cleaned and sanitized at the beginning and end of each shift on days when compounding occurs, after spills,

and when surface contamination (e.g., from splashes) is known or suspected, and between compounding CNSPs with different components.

Comment Summary #73: The commenter suggested requiring cleaning and sanitizing of work surfaces at the end of the compounding day for non-continuous compounding locations operations.

Response: Comment not incorporated. At minimum, work surfaces are required to be cleaned and sanitized at the beginning and end of each shift on days when compounding occurs, after spills, and when surface contamination (e.g., from splashes) is known or suspected, and between compounding CNSPs with different components.

Comment Summary #74: The commenter suggested requiring cleaning and sanitizing of work surfaces in between weighing of different components.

Response: Comment not incorporated. At minimum, work surfaces are required to be cleaned and sanitized at the beginning and end of each shift on days when compounding occurs, after spills, and when surface contamination (e.g., from splashes) is known or suspected, and between compounding CNSPs with different components.

Comment Summary #75: The commenter recommended limiting the requirement for a minimum frequency for cleaning and sanitizing walls in nonsterile compounding area(s) to the walls located adjacent to the compounding areas.

Response: Comment not incorporated. *Table 1* states it includes the minimum frequency for cleaning and sanitizing in nonsterile compounding area(s). An area must be designated for nonsterile compounding. The method of designation must be described in the facility's SOPs.

Comment Summary #76: The commenter recommended clarifying the requirement to clean walls and storage shelving in nonsterile compounding area(s) if the compounding area is in the middle of the room (i.e., a dedicated cart).

Response: Comment not incorporated. An area must be designated for nonsterile compounding. The method of designation must be described in the facility's SOPs.

Comment Summary #77: The commenter recommended removing sanitizing from *Table 1. Minimum Frequency for Cleaning and Sanitizing in Nonsterile Compounding Area(s) – Surfaces due to the term being removed in <797>*.

Response: Comment not incorporated. Sterile environments require different agents to maintain sterility. USP has no role in enforcement. Ensuring compliance with the requirements of the chapter is the responsibility of the applicable regulatory jurisdiction. The chapter requires facilities to develop SOPs on all aspects of the compounding operation, and this is a topic that may be described in the facility's SOPs.

Comment Summary #78: Commenters recommended revising the requirement that each occurrence of cleaning and sanitizing be documented to be required daily.

Response: Comment partially incorporated. The requirement was revised as applicable cleaning and sanitizing must be documented daily on days when compounding occurs. This information may be included in the facility's SOPs.

Comment Summary #79: Commenters suggested requiring cleaning and sanitizing of the floors in nonsterile compounding area(s) weekly, after spills, and when surface contamination is known or suspected.

Response: Comment partially incorporated. At minimum, floors in nonsterile compounding area(s) are required to be cleaned and sanitized daily on days when compounding occurs, after spills, and when surface contamination (e.g., from splashes) is known or suspected.

Comment Summary #80: The commenter suggested requiring cleaning of floors in nonsterile compounding area(s) at a minimum frequency of at the beginning and end of each shift, after spills, and when surface contamination is known or suspected, and in between compounding CNSPs with different requirements.

Response: Comment not incorporated. At minimum, floors in nonsterile compounding area(s) are required to be cleaned and sanitized daily on days when compounding occurs, after spills, and when surface contamination (e.g., from splashes) is known or suspected.

Comment Summary #81: The commenter indicated that due to the diversity of veterinary practice settings, cleaning requirements are unable to be implemented for such practices.

Response: Comment not incorporated. The Compounding Expert Committee is committed to ongoing engagement on the application of these standards to veterinary medicine. USP has no role in enforcement. Ensuring compliance with the requirements of the chapter is the responsibility of the applicable regulatory jurisdiction.

Comment Summary #82: Commenters recommended requiring cleaning and sanitizing of walls in nonsterile compounding area(s) when visibly soiled and when surface contamination is known or suspected.

Response: Comment incorporated.

6. Equipment and Components

Expert Committee-Initiated Change #1: Specifying a particular organization for guidelines to certify BSCs or CVEs was removed as there may be other organizations that prepare such guidelines.

Expert Committee-Initiated Change #2: Language about component receipt was revised to state that the following information must be documented according to the facility's SOPs: receipt date, quantity received, supplier name, lot number, expiration date, and results of any in-house or third-party testing performed.

Expert Committee-Initiated Change #3: Language was revised for clarity to state that the management and documentation of nonhazardous component spills and disposal must be described in the facility's SOPs.

Expert Committee-Initiated Change #4: Language was revised for clarity regarding APIs used as components being required to have a COA that includes specifications (e.g., compendial requirements for quality) and test results for the component that show the API meets expected quality.

Comment Summary #83: The commenter indicated support for language indicating the compounder must assess whether weighing, measuring, or otherwise manipulating components that could generate airborne chemical particles should be performed in a closed-system processing device.

Response: Comment incorporated. Language was maintained indicating that these activities must be evaluated to determine if they must be performed in a closed-system processing device to reduce the potential exposure to personnel or contamination of the facility or CNSPs.

Comment Summary #84: Commenters recommended clarifying the meaning of the chapter requirement that weighing, measuring, or otherwise manipulating components that could generate airborne chemical particles must be assessed to determine if these activities must be performed in a closed-system processing device, and if a documented risk assessment for all nonsterile drug compounding would need to be developed.

Response: Comment not incorporated. The chapter requires facilities to develop SOPs on all aspects of the compounding operation, and this is a topic that may be described in the facility's SOPs. Information on the handling of hazardous drugs is in <800>.

Comment Summary #85: Commenters recommended requiring that weighing, measuring, or otherwise manipulating components that could generate airborne chemical particles be performed in a closed-system processing device.

Response: Comment not incorporated. The chapter requires facilities to develop SOPs on all aspects of the compounding operation, and this is a topic that may be described in the facility's SOPs. Information on the handling of hazardous drugs is in <800>.

Comment Summary #86: Commenters recommended requiring that weighing, measuring, or otherwise manipulating components that could generate airborne chemical particles be performed in a closed-system processing device, or be assessed to determine if these activities must be performed in a closed-system processing device.

Response: Comment not incorporated. The chapter requires facilities to develop SOPs on all aspects of the compounding operation, and this is a topic that may be described in the facility's SOPs. Information on the handling of hazardous drugs is in <800>.

Comment Summary #87: The commenter indicated that in veterinary practices the majority of compounding is performed using FDA-approved drugs, which poses lesser risk than compounding from bulk drug substances.

Response: Comment not incorporated. Compounding using conventionally manufactured products is within the scope of compounding. Compounding is defined as the process of 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. While FDA-approved drugs are stable on their own, when combined with other ingredients the components may no longer be stable or effective. There is risk of contamination when compounding with bulk substances or commercial drugs.

Comment Summary #88: The commenter recommended removing the requirement that a facility must have a readily accessible spill kit in the compounding area.

Response: Comment not incorporated. Many drugs can be hazardous and cause harm without appropriate precautions.

Comment Summary #89: Commenters suggested requiring cleaning of the containment ventilated enclosure (CVE) and/or biological safety cabinet (BSC) only on days when compounding occurs.

Response: Comment incorporated. At minimum, a CVE and BSC are required to be cleaned and sanitized at the beginning and end of each shift on days when compounding occurs, after spills, and when surface contamination (e.g., from splashes) is known or suspected.

Comment Summary #90: The commenter recommended aligning the cleaning frequency of CVEs, BSCs, and other devices with the requirements in <797>, to be cleaned daily.

Response: Comment partially incorporated. At minimum, a CVE and BSC are required to be cleaned and sanitized at the beginning and end of each shift on days when compounding occurs, after spills, and when surface contamination (e.g., from splashes) is known or suspected.

Comment Summary #91: The commenter suggested clarifying what type of cleaning agents should be used to clean and sanitize compounding tools between uses and including information on hazardous drug decontamination prior to cleaning equipment.

Response: Comment not incorporated. Information on the handling of hazardous drugs is in <800>. Requirements for cleaning agents is the purview of the applicable regulatory jurisdiction(s). USP has no role in enforcement.

Comment Summary #92: The commenter suggested clarifying if household cleaning and sanitizing agents meet the requirements of the chapter for cleaning and sanitizing.

Response: Comment not incorporated. Cleaning and sanitizing agents are tested for specific uses. Designation as industrial versus household-use is indicated by EPA-registration in the U.S. EPA-registration is not a requirement for cleaning and sanitizing agents in <795>. Ensuring compliance with the requirements of the chapter is the responsibility of the applicable regulatory jurisdiction. USP has no role in enforcement. The chapter requires facilities to develop SOPs on

all aspects of the compounding operation, and this is a topic that may be described in the facility's SOPs.

Comment Summary #93: The commenter recommended clarifying how stakeholders can verify that a vendor is an FDA-registered facility.

Response: Comment not incorporated. USP has no role in enforcement. Ensuring compliance with the requirements of the chapter is the responsibility of the applicable regulatory jurisdiction.

Comment Summary #94: The commenter indicated that a statement indicating that if an API cannot be obtained from an FDA-registered facility, the designated person(s) must select a component that is suitable for the intended use, seems out of place where it is located in the text describing all components other than APIs. The commenter recommended revising the text to indicate that if components other than APIs cannot be obtained from an FDA-registered facility, the designated person(s) must select a component that is suitable for the intended use.

Response: Comment partially incorporated. The text was revised to state that in the United States, all components other than APIs should be manufactured by an FDA-registered facility, and if a component cannot be obtained from an FDA-registered facility, the designated person(s) must select a component that is suitable for the intended use.

Comment Summary #95: The commenter recommended revising the statement indicating that if an API cannot be obtained from an FDA-registered facility, the designated person(s) must select a component that is suitable for the intended use, to say state that if "a component" cannot be obtained from an FDA-registered facility, the designated person(s) must select a component that is suitable for the intended use.

Response: Comment incorporated.

Comment Summary #96: The commenter recommended that a certificate of analysis not be required for component selection or receipt, or that labeling of the conventionally manufactured product may be used as an alternative to a certificate of analysis.

Response: Comment not incorporated. USP has no role in enforcement. Ensuring compliance with the requirements of the chapter is the responsibility of the applicable regulatory jurisdiction.

Comment Summary #97: The commenter indicated that the documentation requirements for component receipt would be difficult for community retail pharmacies engaging in occasional compounding.

Response: Comment partially incorporated. The chapter was revised to require that the information must be documented according to the facility's SOPs.

Comment Summary #98: The commenter recommended revising the text for the documentation requirements for component receipt to state that the information must be documented as described in the documentation section of the chapter.

Response: Comment incorporated. The chapter was revised to require that the information be documented (see 14. Documentation) according to the facility's SOPs.

Comment Summary #99: The commenter recommended revising "any other lots" of an ingredient found to be of unacceptable quality to "all lots", for clarification.

Response: Comment not incorporated. The language as written was determined to convey the intent more accurately.

Comment Summary #100: The commenter recommended the chapter require if the correct identity, strength, purity, and quality of components intended for preparation of CNSPs cannot be predicted, or expected, the components must be immediately rejected, rather than if the correct identity, strength, purity, and quality of components intended for preparation of CNSPs cannot be "confirmed".

Response: Comment partially incorporated. The text was revised to state that if the identity, strength, purity, and quality of components intended for preparation of CNSPs cannot be verified (e.g., containers with damaged or incomplete labeling), the components must be immediately rejected.

Comment Summary #101: The commenter recommended revising “should” to “must” regarding, “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”.

Response: Comment not incorporated. 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 to avoid using excessive materials.

Comment Summary #102: The commenter indicated that the chapter stating that once removed from the original container, any component not used in compounding should be discarded and not returned to the original container, can lead to logistical difficulties for compounders regarding controlled components and weighing topical creams.

Response: Comment not incorporated. This text in the chapter states that once removed from the original container, any component not used in compounding “should” be discarded and not returned to the original container. 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 to avoid using excessive materials.

Comment Summary #103: The commenter indicated that <800> does not require spill kits to be labeled with contents and recommended to add this requirement to <800>.

Response: Comment partially incorporated. This requirement was removed from <795> for consistency.

Comment Summary #104: The commenter recommended removing the requirement the facility must document the review and update of its chemical hazard and disposal information at least every 12 months and instead require that the facility maintain the most updated chemical hazard and disposal information.

Response: Comment incorporated. The text was revised to state that the facility must maintain current chemical hazard and disposal information (e.g., SDSs).

Comment Summary #105: The commenter recommended that the chapter should require the beyond-use date of bulk APIs repackaged into smaller containers to be limited to harmonize with requirements in <7>.

Response: Comment not incorporated. The requirements for this in <7> are regarding dispensing drugs and for variable environmental conditions after dispensing.

7. Master Formulation and Compounding Records

Expert Committee-Initiated Change #1: “Compounding record” was defined at the first instance as “CR” and then “CR” was used throughout.

Comment Summary #106: Commenters recommended that master formulation records should only be required for anticipatory compounding, and a compounding record is sufficient for patient-specific CNSPs.

Response: Comment not incorporated. The master formulation record is a detailed record of procedures that describes how the CNSP is to be prepared and therefore must be created for each unique formulation of a CNSP.

Comment Summary #107: The commenter recommended clarifying if studies must be conducted for each formulation that does not have a published reference other than <795>.

Response: Comment not incorporated. It is common practice to reference <795> if it is the reference used to establish the BUD.

Comment Summary #108: Commenters recommended clarifying how specific the information regarding the container closure system(s) in the master formulation must be.

Response: Comment not incorporated. This information may vary depending on the volume of compounding in the facility. The chapter requires facilities to develop SOPs on all aspects of the compounding operation, and this is a topic that may be described in the facility's SOPs.

Comment Summary #109: The commenter recommended requiring that a master formulation record include the container closure system(s) only if applicable.

Response: Comment not incorporated. The container closure system is the packaging system components that together contain and protect the dosage form, including primary packaging system components and secondary packing system components if the latter are intended to provide additional protection.

Comment Summary #110: The commenter recommended requiring compounding records to include the electronic weight measurement if used and require weights and measurements to be verified by a second person.

Response: Comment not incorporated. Some facilities have weight systems that include electronic transmission from the balance. Ensuring compliance with the requirements of the chapter is the responsibility of the applicable regulatory jurisdiction. The chapter requires facilities to develop SOPs on all aspects of the compounding operation, and this is a topic that may be described in the facility's SOPs.

Comment Summary #111: Commenters recommended removing the statement that the compounding record must include the time of preparation of the CNSP.

Response: Comment partially incorporated. The language was revised to state the compounding record must include the date, or date and time, of preparation of the CNSP.

Comment Summary #112: Commenters recommended removing the statement that the compounding record must include results of quality control procedures due to this being observed at final verification.

Response: Comment not incorporated. The compounder needs to be aware of what to expect as part of the quality control results. The chapter requires facilities to develop SOPs on all aspects of the compounding operation, and this is a topic that may be described in the facility's SOPs.

8. Release Inspections and Testing

Expert Committee-Initiated Change #1: The structure and language of the section was revised to harmonize more closely with the comparable section in <797>.

Comment Summary #113: The commenter indicated that all rejected CNSPs do not need to be segregated before disposal.

Response: Comment not incorporated. Segregating from active stock allows personnel to investigate causes for the failure.

Comment Summary #114: The commenter indicated that it would be more appropriate for visual inspection of container closure integrity to be a part of final verification of the prescription than being documented in the compounding log.

Response: Comment not incorporated. All release inspections must be included in the facility's documentation. The chapter requires facilities to develop SOPs on all aspects of the compounding operation, and this is a topic that may be described in the facility's SOPs.

Comment Summary #115: The commenter indicated that requiring documentation of checks, inspections, and any other tests on the MFR is complicated for compounders preparing CNSPs in batches for multiple orders.

Response: Comment not incorporated. This information is documented in the compounding record. All release inspections must be included in the facility's documentation. The chapter requires facilities to develop SOPs on all aspects of the compounding operation, and this is a topic that may be described in the facility's SOPs.

Comment Summary #116: The commenter recommended clarifying who is permitted to perform release inspections.

Response: Comment not incorporated. The personnel may differ depending on which part of release inspections is being done. All release inspections must be included in the facility's documentation. The chapter requires facilities to develop SOPs on all aspects of the compounding operation, and this is a topic that may be described in the facility's SOPs.

Comment Summary #117: The commenter recommended clarifying if repackaging finished CNSPs is considered compounding.

Response: Comment not incorporated. This would be a part of dispensing. USP has no role in enforcement. Ensuring compliance with the requirements of the chapter is the responsibility of the applicable regulatory jurisdiction.

9. Labeling

Expert Committee-Initiated Change #1: Language was revised to state that every CNSP, rather than every dispensed CNSP, must be labeled with appropriate, legible identifying information to prevent errors during storage, dispensing, and use, as not every CNSP is dispensed when compounded.

Expert Committee-Initiated Change #2: Language was revised for clarification and harmonization with <797> to state that labeling on the dispensed CNSP should display the compounding facility name, and contact information if the CNSP is to be sent outside of the facility or healthcare system in which it was compounded.

Comment Summary #118: The commenter recommended removing the statement, "All labels must also comply with laws and regulations of the applicable regulatory jurisdiction", as this is redundant from the statement earlier in the section, "All labeling must be in compliance with laws and regulations of the applicable regulatory jurisdiction".

Response: Comment incorporated.

Comment Summary #119: The commenter indicated a potential editorial error that the word "confirms" should be "conforms".

Response: Comment incorporated.

Comment Summary #120: The commenter recommended requiring route of administration on the label on each immediate container of the CNSP.

Response: Comment not incorporated. There is limited space available on the label of the immediate container.

Comment Summary #121: The commenter recommended revising "should" to "must" regarding, "The labeling on the CNSP should display the following information:".

Response: Comment not incorporated. The requirements for information included in labeling is the purview of the applicable regulatory jurisdiction(s). USP has no role in enforcement.

Comment Summary #122: The commenter indicated that it is unclear if patient-specific CNSP labels or batched CNSPs are required to be labeled as being compounded.

Response: Comment partially incorporated. Language was clarified to specify the labeling on the dispensed CNSP should display this information.

Comment Summary #123: The commenter indicated that the chapter does not address labeling for CNSPs to be used as ingredients in future preparations.

Response: Comment not incorporated. "Dispensed" was removed from the statement, "Every dispensed CNSP must be labeled with appropriate, legible identifying information to prevent errors during storage, dispensing, and use", for clarification.

Comment Summary #124: The commenter indicated that clarification may be needed regarding the due diligence required of the designated person(s) in determining if there is existing stability data that would require a shorter BUD for a CNSP.

Response: Comment not incorporated. The chapter requires facilities to develop SOPs on all aspects of the compounding operation, and this is a topic that may be described in the facility's SOPs.

10. Establishing Beyond-Use Dates

Expert Committee-Initiated Change #1: Language revised for clarity stating that CNSPs with an $a_w \geq 0.6$, and a CNSPs within the limits of *Table 4*, should contain suitable antimicrobial agents to protect against the proliferation of bacteria, yeast, and mold contamination that may be inadvertently introduced anytime during the compounding process or throughout the CNSPs under appropriate handling and storage conditions, and that all CNSPs with an extended CNSPs must follow 10.5 Extending CNSPs for CNSPs.

Expert Committee-Initiated Change #2: "Troche (gelatin)" and "Troche (glycol based)" were revised for clarity to be "Troche or lozenge (gelatin based)" and "Troche or lozenge (glycol based)".

Expert Committee-Initiated Change #3: "Water activity" was defined at the first instance as " a_w " and then " a_w " was used throughout.

Expert Committee-Initiated Change #4: A statement was removed stating that BUDs indicate the days after the CNSP is prepared and beyond which the CNSP must not be used, as this is stated elsewhere in the section.

Expert Committee-Initiated Change #5: Language was revised for clarity stating that compounders must consider parameters that may affect "quality", rather than "stability".

Expert Committee-Initiated Change #6: The description of the glycol-based troche was clarified to be polyethylene glycol.

Expert Committee-Initiated Change #7: Language was revised for clarity regarding antimicrobial effectiveness testing bracketing studies.

Comment Summary #125: Commenters indicated that the beyond-use date parameters in the chapter are arbitrary, and the compounder should be permitted to use their professional judgement to extend BUDs if reasonable.

Response: Comment not incorporated. The EC has taken a risk-based approach to determining the maximum BUD limits to balance the risk of having less information than would be available in a current good manufacturing practices (CGMP) stability study, with the known stability characteristics and acute, personalized needs of patients. The EC considered the large diversity of compounding environments, formulations, compounder experience, and raw materials as part of this approach.

Comment Summary #126: The commenter indicated concern with extending BUDs for drugs compounded without following CGMP requirements.

Response: Comment not incorporated. The Compounding Expert Committee revised the chapter based on stakeholder input, and the chapter describes a minimum standard to be followed when preparing CNSPs that encompasses a wide variety of practice sites. The EC has taken a risk-based approach to determining the maximum BUD limits to balance the risk of having less information than would be available in a current good manufacturing practices (CGMP) stability study, with the known stability characteristics and acute, personalized needs of patients. The chapter does not prohibit compounders from going beyond the requirements in the chapter.

Comment Summary #127: The commenter indicated that relying on stability studies to support extended BUDs for compounded drugs is not valid for a given product made by a pharmacy because there may be undetermined differences in the active pharmaceutical ingredients and excipients, formulation, compounding process, and packaging of the preparation. The

commenter also indicated that regulators will need information outside of the chapter to determine if private analytical methods and studies are suitable for their intended use.

Response: Comment not incorporated. The chapter describes a minimum standard to be followed when preparing CNSPs that encompasses a wide variety of practice sites. The EC has taken a risk-based approach to determining the maximum BUD limits to balance the risk of having less information than would be available in a current good manufacturing practices (CGMP) stability study, with the known stability characteristics and acute, personalized needs of patients. The chapter does not prohibit compounders from going beyond the requirements in the chapter. The EC has also developed and posted supplementary materials describing stability studies, and has engaged with regulators regarding the ability to assess stability studies and no major concerns were shared regarding requiring additional information to determine if stability studies are suitable.

Comment Summary #128: Commenters indicated that stability testing per ingredient to extend BUDs is unattainable for compounders financially.

Response: Comment not incorporated. The EC has taken a risk-based approach to determining the maximum BUD limits to balance the risk of having less information than would be available in a current good manufacturing practices (CGMP) stability study, with the known stability characteristics and acute, personalized needs of patients. Nonaqueous oral liquids are the only dosage form with a shorter BUD limit (90 days) than designated by the previous chapter in the absence of a *USP–NF* compounded preparation monograph or CNSP-specific stability information.

Comment Summary #129: Commenters indicated that compounders should have the ability to cite scholarly research for BUDs that have been previously tested if compounded in the same manner.

Response: Comment not incorporated. The chapter permits extending BUDs using 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, up to a maximum of 180 days. 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. The EC has taken a risk-based approach to determining the maximum BUD limits to balance the risk of having less information than would be available in a current good manufacturing practices (CGMP) stability study, with the known stability characteristics and acute, personalized needs of patients. The EC considered the large diversity of compounding environments, formulations, compounder experience, and raw materials as part of this approach.

Comment Summary #130: Commenters indicated that the beyond-use date parameters for oral nonaqueous dosage forms are arbitrary and should have a BUD limit of 180 days without a stability study due to financial impact.

Response: Comment not incorporated. Nonaqueous oral liquids were given a BUD limit of 90 days in the absence of a *USP–NF* compounded preparation monograph or CNSP-specific stability information due to known stability concerns for nonaqueous preparations. The chapter permits extending BUDs using 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, up to a maximum of 180 days. 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. The EC has taken a risk-based approach to determining the maximum BUD limits to balance the risk of having less information than would be available in a current good manufacturing practices (CGMP) stability study, with the known stability characteristics and acute, personalized needs of patients. The EC considered the large diversity of compounding

environments, formulations, compounding experience, and raw materials as part of this approach.

Comment Summary #131: Commenters indicated that limiting nonaqueous dosage forms to 180 days will negatively impact treatment of veterinary patients due to increased product turnover.

Response: Comment not incorporated. The BUD limits are primarily determined based on whether a compounded preparation is aqueous or nonaqueous in the absence of a *USP–NF* compounded preparation monograph or CNSP-specific stability information due to known stability concerns for nonaqueous preparations. Drug degradation via hydrolysis was a factor the EC considered in taking a risk-based approach for determining the maximum BUD limits. The chapter permits extending BUDs using 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, up to a maximum of 180 days. 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.

Comment Summary #132: Commenters suggested differentiating BUD limits based on route of administrations and revising the BUD limit for preserved topical water-containing topical dosage forms to be 180 days with supporting stability data.

Response: Comment not incorporated. The BUD limits are primarily determined based on whether a compounded preparation is aqueous or nonaqueous in the absence of a *USP–NF* compounded preparation monograph or CNSP-specific stability information due to known stability concerns for nonaqueous preparations. Drug degradation via hydrolysis was a factor the EC considered in taking a risk-based approach for determining the maximum BUD limits. The chapter permits extending BUDs using 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, up to a maximum of 180 days. 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.

Comment Summary #133: The commenter suggested including language stating the compounder shall use his or her compounding education and experience in considering stability factors for assigning BUDs.

Response: Comment not incorporated. The chapter permits extending BUDs using 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, up to a maximum of 180 days. 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. The EC has posted the informational document *Stability Study Reference Document for the 2021 Proposed Revisions to <795> and <797>* for additional information for stability factors to be considered in assigning BUDs.

Comment Summary #134: The commenter suggested moving language from *10.2 Parameters to Consider in Establishing a BUD* to *13. CNSP Packaging and Transporting* regarding compounders considering compatibility of the container closure system with the finished preparation and degradation of the container closure system in when establishing BUDs.

Response: Comment not incorporated. Compatibility of the container closure system with the finished preparation and degradation of the container closure system are parameters that compounders must consider when establishing a BUD. Personnel should select and use packaging materials that will maintain the physical and chemical integrity and stability of the

CNSPs. Packaging materials must protect CNSPs from damage, leakage, contamination, and degradation, while simultaneously protecting personnel from exposure.

Comment Summary #135: The commenter recommended revising “should” to “must” in the sentence, “BUDs for CNSPs should be established conservatively to ensure that the preparation maintains its required characteristics to minimize the risk of contamination or degradation”.

Response: Comment not incorporated. The chapter reinforces that a shorter BUD must be assigned when the physical and chemical stability of the CNSP is less than the BUD limit stated in *Table 4. BUD Limit by Type of Preparation in the Absence of a USP–NF Compounded Preparation Monograph or CNSP-Specific Stability Information*.

Comment Summary #136: The commenter recommended including, “Composition of the closure systems (e.g., type of glass, resin in the container or cap contact surface)”, as a parameter that compounders must consider in establishing a BUD for a CNSP.

Response: Comment not incorporated. This recommendation is inconsistent with language in compounded preparation monographs. The chapter requires compounders to consider parameters including compatibility of the container closure system with the finished preparation (e.g., leachables, interactions, adsorption, and storage conditions), and degradation of the container closure system, when establishing a BUD for a CNSP.

Comment Summary #137: The commenter indicated support for including the concept of water activity.

Response: Comment incorporated. The concept of using water activity as a guide for assigning BUDs was maintained.

Comment Summary #138: Commenters recommended providing additional directions or methods of assigning a BUD due to the difficulty of determining water activity of a CNSP with multiple ingredients.

Response: Comment partially incorporated. Language was added to the chapter to clarify that compounders are not required to measure water activity for CNSPs. Water activity is intended to be used as a guide for assigning BUDs. The chapter provides examples of dosage forms that have a water activity < 0.6 and those with a water activity ≥ 0.6.

Comment Summary #139: Commenters recommended clarifying how to determine water activity, and when water activity must be measured.

Response: Comment partially incorporated. Language was added to the chapter to clarify that compounders are not required to measure water activity for CNSPs. Water activity is intended to be used as a guide for assigning BUDs. The chapter provides examples of dosage forms that have a water activity < 0.6 and those with a water activity ≥ 0.6. <922> and <1112> provide further information regarding water activity and its determination.

Comment Summary #140: The commenter recommended removing the water activity and antimicrobial effectiveness testing requirements.

Response: Comment not incorporated. Language was added to the chapter to clarify that compounders are not required to measure water activity for CNSPs. Water activity is intended to be used as a guide for assigning BUDs. The chapter provides examples of dosage forms that have a water activity < 0.6 and those with a water activity ≥ 0.6. The chapter states that aqueous dosage forms should contain suitable antimicrobial agents and that careful consideration should be taken when selecting a preservative to ensure microbiological effectiveness and stability.

Comment Summary #141: The commenter recommended defining preserved vs non-preserved.

Response: Comment not incorporated. This information is more specific than the minimum standards described in the chapter.

Comment Summary #142: The commenter recommended stating that the presence of preservatives is not used to determine BUDs.

Response: Comment not incorporated. Personnel must consider many parameters that may affect quality when establishing a BUD for a CNSP, including the potential for microbial proliferation.

Comment Summary #143: Commenters recommended differentiating BUDs for topical and oral aqueous formulations.

Response: Comment not incorporated. CNSPs with a higher water activity have increased potential for microbial growth which can also impact potency. Skin may not be intact when using topical formulations.

Comment Summary #144: The commenter indicated that when compounding together two conventionally manufactured products the BUD should be based on the expiration date.

Response: Comment not incorporated. An expiration date identifies the time during which a conventionally manufactured product, API, or added substance can be expected to meet the requirements of a compendial monograph, if one exists, or maintain expected quality, provided it is kept under the prescribed storage conditions. When the product is compounded, the conditions have been modified and may affect the stability. BUDs for CNSPs should be established conservatively to ensure that the preparation maintains its required characteristics to minimize the risk of contamination or degradation.

Comment Summary #145: The commenter indicated that all non-aqueous dosage forms that are preserved and protected from oxidation should be assigned a BUD of 180 days.

Response: Comment not incorporated. Nonaqueous dosage forms are typically nonpreserved. Nonaqueous dosage forms are not inert and can be reactive.

Comment Summary #146: The commenter indicated that the BUD limit for preserved aqueous dosage forms without stability data should be limited to 14 days.

Response: Comment not incorporated. The BUD limits are primarily determined based on whether a compounded preparation is aqueous or nonaqueous in the absence of a *USP–NF* compounded preparation monograph or CNSP-specific stability information due to known stability concerns for nonaqueous preparations. Drug degradation via hydrolysis was a factor the EC considered in taking a risk-based approach for determining the maximum BUD limits. A shorter BUD must be assigned when the physical and chemical stability of the CNSP is less than the BUD limits in *Table 4*.

Comment Summary #147: The commenter recommended including storage conditions for non-preserved preparations that are unable to be refrigerated due to chemical stability concerns.

Response: Comment not incorporated. The chapter states that when preservatives are contraindicated in a CNSP, storage of the preparation in a refrigerator is required if such storage does not change the physical or chemical properties of the CNSP. A shorter BUD must be assigned when the physical and chemical stability of the CNSP is less than the BUD limit stated in *Table 4. BUD Limit by Type of Preparation in the Absence of a USP-NF Compounded Preparation Monograph or CNSP-Specific Stability Information*.

Comment Summary #148: The commenter recommended clarifying if the only opportunity to compound without preservatives is when clinically contraindicated.

Response: Comment incorporated. The language was revised to state that when preservatives are contraindicated in a CNSP, storage of the preparation in a refrigerator is required if such storage does not change the physical or chemical properties of the CNSP.

Comment Summary #149: The commenter recommended clarifying if a non-preserved, nonaqueous formulation would require refrigeration.

Response: Comment not incorporated. Nonaqueous dosage forms are typically nonpreserved. The chapter states that when preservatives are contraindicated in a CNSP, storage of the preparation in a refrigerator is required if such storage does not change the physical or chemical properties of the CNSP. A shorter BUD must be assigned when the physical and chemical

stability of the CNSP is less than the BUD limit stated in *Table 4. BUD Limit by Type of Preparation in the Absence of a USP-NF Compounded Preparation Monograph or CNSP-Specific Stability Information*.

Comment Summary #150: The commenter recommended revising the order and numbering of the tables in *10.3 Establishing a BUD for a CNSP* as *Table 4* is referenced before *Table 3*.

Response: Comment not incorporated. *Table 3* describes representative examples of measured water activities that can be applied when determining whether CNSPs are aqueous or nonaqueous to establish BUDs per the limits in *Table 4*.

Comment Summary #151: The commenter recommended requiring a one-time <51> test at the end of the BUD for preserved aqueous dosage forms.

Response: Comment not incorporated. The chapter states that aqueous dosage forms should contain suitable antimicrobial agents and that careful consideration should be taken when selecting a preservative to ensure microbiological effectiveness and stability.

Comment Summary #152: The commenter recommended clarifying whether for a CNSP to be considered a preserved dosage form, a separate preserving agent must be added to the preparation.

Response: Comment not incorporated. The chapter states that aqueous dosage forms should contain suitable antimicrobial agents and that careful consideration should be taken when selecting a preservative to ensure microbiological effectiveness and stability. A shorter BUD must be assigned when the physical and chemical stability of the CNSP is less than the BUD limits in *Table 4*. When the BUD of the CNSP is extended beyond the BUDs in *Table 4*, an aqueous CNSP must be tested for antimicrobial effectiveness.

Comment Summary #153: The commenter recommended clarifying how to determine that an aqueous solution is preserved.

Response: Comment not incorporated. The chapter states that aqueous dosage forms should contain suitable antimicrobial agents and that careful consideration should be taken when selecting a preservative to ensure microbiological effectiveness and stability. A shorter BUD must be assigned when the physical and chemical stability of the CNSP is less than the BUD limits in *Table 4*. When the BUD of the CNSP is extended beyond the BUDs in *Table 4*, an aqueous CNSP must be tested for antimicrobial effectiveness.

Comment Summary #154: The commenter indicated that the footnote for *Table 4* describing other nonaqueous dosage forms is not an all-inclusive list of other nonaqueous dosage forms.

Response: Comment incorporated. The footnote was revised to provide the other nonaqueous dosage forms as examples.

Comment Summary #155: The commenter recommended clarifying if compounders must have chemical and physical data to support using the BUD limits in *Table 4*.

Response: Comment partially incorporated. A footnote was added to *Table 4* to clarify that a shorter BUD must be assigned when the physical and chemical stability of the CNSP is less than the BUD limits in *Table 4*. The chapter states that when compounding from a USP–NF compounded preparation monograph for the CNSP, the BUD must not exceed the BUD specified in the monograph. The chapter permits extending BUDs using 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, up to a maximum of 180 days.

Comment Summary #156: The commenter requested clarifying how specific information about the container closure needs to be when using stability information to extend BUDs up to a maximum of 180 days with a stability study.

Response: Comment partially incorporated. The text was revised to clarify that if there is a stability study using a stability-indicating analytical method for the API(s), CNSP formulation, and material of composition of the container closure that will be used, then the BUD indicated by

the study may be used in lieu of the BUDs specified in *Table 4* for aqueous and nonaqueous dosage forms, up to a maximum of 180 days.

Comment Summary #157: The commenter recommended stating “type of container closure” instead of “particular container closure system” and “container closure materials of composition” regarding antimicrobial effectiveness testing conducted for each formulation, or antimicrobial effectiveness testing results provided by an FDA-registered facility or published in peer-reviewed literature for extending BUDs for CNSPs with stability information.

Response: Comment not incorporated. The text was revised to clarify that the designated person(s) may rely on antimicrobial effectiveness testing that is conducted (or contracted for) once for each formulation in the particular container closure system—including materials of composition of the container closure system—in which it will be packaged. Alternatively, 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).

Comment Summary #158: Commenters indicated that stability-indicating analytical methods are not superior in outcomes to traditional potency testing and other conservative measures.

Response: Comment not incorporated. The chapter permits extending BUDs using 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, up to a maximum of 180 days. 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.

Comment Summary #159: Commenters indicated that minor deviations from a stability study should not disallow use of the study to extend BUDs for CNSPs.

Response: Comment not incorporated. Deviations in formulations can have significant impacts on stability and potency. The chapter permits extending BUDs using 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, up to a maximum of 180 days. 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.

Comment Summary #160: The commenter indicated that the use of unpublished stability studies to extend BUDs for CNSPs should not be permitted by the chapter.

Response: Comment partially incorporated. The text was revised to clarify that if there is a stability study a stability-indicating analytical method for the API(s), CNSP formulation, and material of composition of the container closure that will be used, then the BUD indicated by the study may be used in lieu of the BUDs specified in *Table 4* for aqueous and nonaqueous dosage forms, up to a maximum of 180 days. The study referenced can be published or unpublished (e.g., in-house data, studies from member-only organizations that have not been published).

Comment Summary #161: The commenter indicated that the chapter should not require bracketing to establish preservatives effectiveness across various strengths of the same formulation.

Response: Comment not incorporated. The chapter requires that when the BUD of the CNSP is extended beyond the BUDs in *Table 4*, an aqueous CNSP must be tested for antimicrobial effectiveness. The chapter allows bracketing as an option to establish preservative effectiveness across various strengths of the same formulation.

Comment Summary #162: The commenter recommended that requirements be added for <60>, <61>, and <62> testing for batches of CNSPs assigned BUDs extended beyond those in *Table 4*.

Response: Comment not incorporated. This information is more specific than the minimum standards described in the chapter.

Comment Summary #163: Commenters recommended including requirements or a reference for completing stability-indicating methods.

Response: Comment not incorporated. This information is more specific than the minimum standards described in the chapter. The Compounding Expert Committee will consider development of additional resources to support understanding of the standards. The Compounding Expert Committee will consider the development of a standard related to stability-indicating methods.

Comment Summary #164: The commenter indicated that if a stability-indicating study indicates stability beyond 180 days, that BUD should be allowable up to a limit of 365 days.

Response: Comment not incorporated. A diversity of practice settings, environments, processes, raw materials, analytical approaches, and few cases in practice which require greater than a 6-month supply resulted in the limit of 180 days. The chapter permits extending BUDs using 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, up to a maximum of 180 days. 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.

Comment Summary #165: The commenter recommended clarifying what resources of stability information are allowable to extend BUDs for CNSPs.

Response: Comment partially incorporated. The text was revised to clarify that if there is a stability study using a stability-indicating analytical method for the API(s), CNSP formulation, and material of composition of the container closure that will be used, then the BUD indicated by the study may be used in lieu of the BUDs specified in *Table 4* for aqueous and nonaqueous dosage forms, up to a maximum of 180 days.

Comment Summary #166: The commenter recommended clarifying if extending BUDs according to 10.5 is meant to be additive to the BUD limits in *Table 4*.

Response: Comment incorporated. The text was revised to clarify that if there is a stability study using a stability-indicating analytical method for the API(s), CNSP formulation, and material of composition of the container closure that will be used, then the BUD indicated by the study may be used in lieu of the BUDs specified in *Table 4* for aqueous and nonaqueous dosage forms, up to a maximum of 180 days.

Comment Summary #167: Commenters recommended the chapter allow applying stability studies with any pharmaceutical equivalent to the API, as defined by the FDA, to extend BUDs for CNSPs.

Response: Comment not incorporated. Text was added to the definition of API to clarify that API is also referred to as bulk drug substance, and that a conventionally manufactured drug product is not an API but is typically manufactured from an API(s).

Comment Summary #168: The commenter indicated 35 days is an arbitrary BUD limit for preserved aqueous dosage forms, and that a longer BUD should be allowable if based on stability information.

Response: Comment not incorporated. The chapter permits extending BUDs using 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, up to a maximum of 180 days. 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. The EC has taken a risk-based approach to determining the maximum BUD limits to balance the risk of having less information than would be available in a current good manufacturing practices (CGMP) stability study, with the known stability characteristics and acute, personalized needs of patients. The EC considered the large diversity of compounding environments, formulations, compounding experience, and raw materials as part of this approach.

Comment Summary #169: Commenters indicated that when compounding with vehicles that have completed antimicrobial effectiveness testing, then BUDs may be extended.

Response: Comment not incorporated. <51> testing done on individual conventionally manufactured vehicles applies to the antimicrobial effectiveness of the vehicle. When the product is compounded with any other component, the conditions have been modified and may affect the stability of the preservative system.

Comment Summary #170: Commenters recommended changing “must” to “should” regarding <51> testing being required for an aqueous CNSP with a BUD extended beyond the BUDs in *Table 4*.

Response: Comment not incorporated. When the BUD of the CNSP is extended beyond the BUDs in *Table 4*, an aqueous CNSP must be tested for antimicrobial effectiveness. To extend a BUD to up to 180 days, the compounding must ensure that the CNSP has an effective preservative system to prevent microbial overgrowth. The chapter states that aqueous dosage forms should contain suitable antimicrobial agents and that careful consideration should be taken when selecting a preservative to ensure microbiological effectiveness and stability. A shorter BUD must be assigned when the physical and chemical stability of the CNSP is less than the BUD limits in *Table 4*.

11. SOPs

Expert Committee-Initiated Change #1: Language was revised to refer to SOPs as “the facility’s SOPs” for consistency with language throughout the chapter.

Comment Summary #171: The commenter indicated a list of required SOPs in the chapter would be helpful.

Response: Comment not incorporated. USP has no role in enforcement. Ensuring compliance with the requirements of the chapter is the responsibility of the applicable regulatory jurisdiction. The chapter requires facilities to develop SOPs on all aspects of the compounding operation, and this is a topic that may be described in the facility’s SOPs.

12. Quality Assurance and Quality Control

Expert Committee-Initiated Change #1: The structure and language of the section was revised to harmonize more closely with the comparable section in <797>. The section about complaint handling and adverse event reporting was combined with this section.

Comment Summary #172: The commenter indicated that regarding quality control being described as the sampling, testing, and documentation of results that, taken together, ensure that specifications have been met before release of the CNSP, “sampling” and “testing” is unclear.

Response: Comment not incorporated. Requirements for a quality assurance program is described in <1163> *Quality Assurance in Pharmaceutical Compounding*.

Comment Summary #173: The commenter recommended adding, “All adverse events need to be reported to the FDA.”

Response: Comment not incorporated. This chapter is also used outside of the United States. The chapter requires that adverse event potentially associated with the quality of CNSPs to be

reported in accordance with the facility's SOPs and all laws and regulations of the applicable regulatory jurisdiction.

13. CNSP Packaging and Transporting

Comment Summary #174: The commenter indicated that personnel should be required to select and use packaging materials that will maintain the physical and chemical integrity and stability of the CNSPs, rather than this being a recommendation.

Response: Comment not incorporated. For personnel to be required to select and use packaging materials that will maintain the physical and chemical integrity and stability of the CNSP, the compounding would be required to test and document for each of these considerations. The chapter states that personnel should select and use materials that will maintain the integrity and stability of the CNSP, allowing for professional judgement regarding these considerations.

14. Documentation

Comment Summary #175: Commenters requested that compounding records for a particular CNSP be retained for 2 years, rather than 3 years, after preparation.

Response: Comment incorporated.

Comment Summary #176: The commenter requested including a list of the SOPs that must be included in the facility's written or electronic documentation.

Response: Comment not incorporated. USP has no role in enforcement. Ensuring compliance with the requirements of the chapter is the responsibility of the applicable regulatory jurisdiction. The chapter requires facilities to develop SOPs on all aspects of the compounding operation, and this is a topic that may be described in the facility's SOPs.

Glossary

Expert Committee-Initiated Change #1: Minor editorial changes were made.

Expert Committee-Initiated Change #2: A definition for "Administration" was added to the glossary.

Expert Committee-Initiated Change #3: A definition was added for "Assigned trainer" and harmonized with <797>.

Expert Committee-Initiated Change #4: The definition for "Beyond-use date (BUD)" was revised for clarity and harmonized with <797>.

Expert Committee-Initiated Change #5: The definition for "Biological safety cabinet (BSC)" was revised to include that Class II BSCs are further divided into types, including Type C1.

Expert Committee-Initiated Change #6: The definition for "Cleaning" was revised for clarity and harmonized with <797>.

Expert Committee-Initiated Change #7: A definition for "Cleaning agent" was added and harmonized with <797>.

Expert Committee-Initiated Change #8: A definition for "Closed-system processing device" was added to the glossary.

Expert Committee-Initiated Change #9: The definition for "Compounded nonsterile preparation (CNSP)" was revised for clarity.

Expert Committee-Initiated Change #10: The definition for "Compounding area" was revised for clarity and harmonized with <797>.

Expert Committee-Initiated Change #11: The definition of “Conventionally manufactured product” was revised to say, “an application approved by the applicable national regulatory agency”, as this is a globally used chapter.

Expert Committee-Initiated Change #12: The definition for “Designated person(s)” was revised for clarity and harmonized with <797>.

Expert Committee-Initiated Change #13: The definition for “FDA” was harmonized with <797>.

Expert Committee-Initiated Change #14: A definition for “Formulation” was added and harmonized with <797>.

Expert Committee-Initiated Change #15: The definition for “Label” was revised for clarity and harmonized with <797>.

Expert Committee-Initiated Change #16: The definition for “Labeling” was revised for clarity and harmonized with <797>.

Expert Committee-Initiated Change #17: A definition for “Monograph” was added and harmonized with <797>.

Expert Committee-Initiated Change #18: A definition was added for “Oversight”.

Expert Committee-Initiated Change #19: The definition for “Quality assurance (QA)” was harmonized with <797>.

Expert Committee-Initiated Change #20: The definition of “Quality control (QC)” was clarified to say, “The sampling, testing, and documentation of results that, taken together, ensure that specifications have been met for the CNSP.”

Expert Committee-Initiated Change #21: A definition for “Verify” was added and harmonized with <797>.

Comment Summary #177: The commenter recommended adding a definition for “expiration date” to the glossary.

Response: Comment not incorporated. Expiration dates are described within the chapter.

Comment Summary #178: The commenter recommended modifying the definition of “sanitizing agent” so that isopropyl alcohol may be used for cleaning and sanitizing purposes.

Response: Comment partially incorporated. The definition for sanitizing agent was revised as, “An agent for reducing, on inanimate surfaces, the number of microorganisms (e.g., 70% isopropyl alcohol).”