California State Board of Pharmacy
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Business, Consumer Services and Housing Agency
Department of Consumer Affairs
Gavin Newsom, Governor

Enforcement and Compounding Committee Report
February 15, 2022

Maria Serpa, Licensee Member, Chair
Jignesh Patel, Licensee Member, Vice-Chair
Renee Barker, Licensee Member
Indira Cameron-Banks, Public Member
Seung Oh, Licensee Member, President
Ricardo Sanchez, Public Member

I. Call to Order, Establishment of Quorum, and General Announcements

II. Public Comments on Items Not on the Agenda/Agenda Items for Future Meetings

Note: The Committee may not discuss or take action on any matter raised during this public comment section that is not included on this agenda, except to decide whether to place the matter on the agenda of a future meeting. [Government Code sections 11125, 11125.7(a)]

III. Discussion, Consideration and Approval of Draft Minutes from the January 23, 2023, Enforcement and Compounding Committee Meeting

Attachment 1 includes a copy of the draft minutes.

IV. Presentation on US Pharmacopeia (USP) General Chapter 795, Pharmaceutical Compounding – Nonsterile Preparations

USP Chapter 795 provides standards for compounding nonsterile medications to help ensure patient benefit and reduce risks such as contamination, infection, or incorrect dosing. Consist with action taken by the USP Compounding Expert Committee, USP Chapter 795 shall become official on November 1, 2023.

To assist with implementation, USP has published FAQs on the Chapter available on its website and information on adding flavor to conventionally manufactured nonsterile products.

During the meeting members will receive a brief overview of the provisions established in the Chapter.

A copy of the FAQs, information regarding flavoring agents, and presentation slides is provided in **Attachment 2**.

V. Discussion, Consideration and Possible Action on Proposed Changes to Regulations Related to Pharmaceutical Compounding of Nonsterile Preparations (Amend Title of 45 and Repeal Sections 1735, 1735.1, 1735.3, 1735.4, 1735.5, 1735.6, 1735.7, to amend section 1735.2, and adopt new titles and sections 1735, 1735.1, 1735.3, 1735.4, 1735.5, 1735.6, 1735.7, 1735.8, 1735.9, 1735.10, 1735.11, 1735.12, 1735.13 and 1735.14 of Division 17 of Title 16 of the California Code of Regulations

Relevant Law

Business and Professions Code (BPC) section 4126.8 generally provides that compounding of drug preparations shall be consistent with standards established in the pharmacy compounding chapters of the current version of the United States Pharmacopeia-National Formulary, including relevant testing and quality assurance. Further, the Board may adopt regulations to impose additional standard for compounding drug preparations.

BPC section 4341 provides authority for the Board to institute any action or actions as may be provided by law and that, in its discretion, are necessary, to prevent the sale of pharmaceutical preparations and drugs that do not conform to the standard and tests as to quality and strength, provided in the latest edition of the United States Pharmacopeia or the National Formulary, or that violate any provision of the Sherman Food, Drug, and Cosmetic Act.

Background

In anticipation of the upcoming official date of Chapter 795, it is appropriate to review the Board's regulations to determine, in the interest of patient safety, where changes are appropriate.

For Committee Consideration and Discussion

During the meeting members will have the opportunity to consider draft regulation language developed by staff to replace existing regulations.

A copy of the regulation language is provided in **Attachment 3**.

VI. Future Committee Meeting Dates

- March 23, 2023, in person and via WebEx
- April 13, 2023, via WebEx
- July 18, 2023, in person and via WebEx
- October 19, 2023, in person and via WebEx

VII. Adjournment

Attachment 1

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Business, Consumer Services and Housing Agency
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DRAFT ENFORCEMENT AND COMPOUNDING COMMITTEE MEETING MINUTES

DATE: January 23, 2023

LOCATION: Pursuant to the provisions of Government Code section 11133, neither a public location nor teleconference locations are provided.

COMMITTEE MEMBERS PRESENT: Maria Serpa, Licensee Member, Chair
Renee Barker, Licensee Member
Seung Oh, Licensee Member
Ricardo Sanchez, Public Member

COMMITTEE MEMBERS NOT PRESENT: Indira Cameron-Banks, Public Member
Jig Patel, Licensee Member, Vice Chair

STAFF MEMBERS PRESENT: Anne Sodergren, Executive Officer
Eileen Smiley, DCA Staff Counsel
Debbie Damoth, Executive Manager Specialist

I. Call to Order, Establishment of Quorum, and General Announcements

Chairperson Maria Serpa called the meeting to order at 9:00 a.m. Dr. Serpa reminded all present that the Board is a consumer protection agency. Dr. Serpa advised the meeting was being conducted with participation through WebEx and being webcast. The meeting moderator provided updated WebEx instructions.

Chairperson Serpa took roll call. Members present included: Renee Barker, Licensee Member; Seung Oh, Licensee Member; Ricardo Sanchez, Public Member; and Maria Serpa; Licensing Member. A quorum was established.

II. Public Comments on Items Not on the Agenda/Agenda Items for Future Meetings

Members of the public were provided the opportunity to provide comments for items not on the agenda.

A representative of the CRA/NACDS raised an issue that state of emergency would be ending February 28, 2023, and all Department of Consumer Affairs (DCA) waivers would be ending on that date not including Board of Pharmacy waivers that end at the end of May 2023. The representative added the DCA waiver that allows pharmacy technicians to perform COVID immunization and testing expires February 28, 2023. However, the federal Public Readiness and Emergency Preparedness (PREP) Act allows pharmacy technicians to perform COVID immunizations and testing as well as flu vaccines that won't expire until the end of October 2024. The representative requested confirmation from the Board as to whether the Board recognizes the PREP Act preemption and will continue to allow pharmacy technicians to administer COVID testing and COVID and flu vaccines. The representative noted there were references to the PREP Act in state documentation including the Department of Public Health. The representative stated understanding that the Board is pursuing a legislative proposal that would allow for expanded pharmacy technician duties but noted there was a significant amount of time between the end of the state of the emergency and when the legislation would go into effect, if approved, and would like to ensure pharmacy technicians can do the testing and immunization until the PREP Act expires. The representative added this would be a significant impact to services if the services cannot be provided through the end of the PREP Act. If that was the case, the representative requests adding the issue to the February 2023 agenda.

Members were surveyed to see if an item should be added to a future agenda to the Committee or Board; however, no comments were made.

III. Approval of October 4, 2022, Enforcement and Compounding Committee Meeting Minutes

Chairperson Serpa referenced the draft minutes for the October 4, 2022, Enforcement and Compounding Committee Meeting.

Members were provided an opportunity to provide comments on the draft minutes; however, no comments were made.

Motion: Approve the October 4, 2022, Committee Meeting Minutes as presented in the meeting materials

M/S: Oh/Sanchez

Members of the public were provided with an opportunity to provide public comment; however, no comment was provided.

Support: 4 Oppose: 0 Abstain: 0 Not Present: 2

Committee Member	Vote
Barker	Support
Cameron-Banks	Not Present
Oh	Support
Patel	Not Present
Sanchez	Support
Serpa	Support

IV. Discussion and Consideration and Possible Action on Self-Assessment Forms

Chairperson Serpa advised the dynamic nature of the pharmacy law generally results in the need to update the self-assessment forms on an annual basis to incorporate law changes made at either the state or federal level. Dr. Serpa referred to the meeting materials containing four self-assessments provided for review. Staff was recommending action on only one of the self-assessment forms, 17M-112 related to Automated Drug Delivery Systems noting staff recommended that the remainder of the forms be completed through a section 100 regulation change as the proposed changes to the forms themselves do not create a requirement, but rather include a new, update or repealed legal requirement that licensees must follow. Dr. Serpa advised should the Committee agree with this approach, moving forward, the executive officer will be able to move forward with updating these forms through this streamlined process. Dr. Serpa spoke in support of this approach and would offer, as the Chairperson to review proposed changes before future updates are made via the section 100 process.

Chairperson Serpa reviewed the proposed changes and agreed with staff recommendation offered for self-assessments included as agenda item IV a-c, including the Community Pharmacy/Hospital Outpatient Self-Assessment, Hospital Pharmacy Self-Assessment and Wholesaler/Third Party Logistics Provider Self-Assessment.

Chairperson Serpa provided members an opportunity to comment on both the recommendation offered to use the section 100 process as a means to update these three forms as well as recommended changes on the forms themselves. Dr. Serpa noted that the meeting materials and slides summarize the changes offered in these forms.

Members were provided the opportunity to comment.

Member Oh requested clarification on the Community Pharmacy Self-Assessment/Hospital Outpatient Pharmacy Self-Assessment. Dr. Oh noted in added 1.24 about temporary closure might cause confusion when a pharmacy is closed for a pharmacist's lunch break. Dr. Oh requested that it was clarified this closure was for temporary closure of a pharmacy facility and did not include closure of the pharmacy for lunch breaks.

Member Oh commented on the language in 22.3.7 about inventory reconciliation that "An inventory reconciliation report must be prepared for any identified controlled substances lost no later than three months after discovery of the reportable loss." was a very legal nuance. Dr. Oh wanted to emphasize the discovery of the reportable loss so to make it clear that it is for "reportable" loss and not all loss. Dr. Oh noted the term "loss" was confusing to pharmacists and wanted to clarify it was for "reportable" loss. Dr. Oh also commented on 22.3.8 about "inventory activities" which was different from reconciliation.

Member Oh commented 22.5 was supposed to be removed and incorporated in 22.3.9 noting both were not correct. Dr. Oh added the Hospital Pharmacy Self-Assessment was correct.

Member Oh commented that the sections being removed were still helpful and was hopeful the information could still be left on the website as optional for the blood products.

Chairperson Serpa would work with staff to combine 22.5 and 22.3.9. Dr. Serpa was not sure how to provide 27 and suggested possibly as an FAQ. Dr. Serpa noted the intent was to remove the details but keep the references as previous public comment indicated it didn't apply to everyone. Dr. Oh inquired how many pharmacies provided bloodborne products and how many remote dispensing pharmacies there were in California. Ms. Sodergren provided there were few remote dispensing pharmacies and given the number in California, staff's recommendation was to remove the text but keep the reference. Ms. Sodergren stated the Board can add information and create links to the Board's website for more information if the Committee desired. Dr. Oh stated it was acceptable to not do that.

Chairperson Serpa was not sure how to make Dr. Oh's first two comments clearer other than bolding/highlighting. Dr. Oh hoped the first sentence could be clearer regarding the intent of the regulation for closure and reconciliation. Dr. Serpa agreed when going through the Section 100 process to be mindful of the issues.

Members of the public were provided an opportunity to comment.

A member of the public inquired what was defined as considered a loss related to inventory reconciliation. Dr. Serpa referred to 21.14 that specified the regulatory language.

A representative from CVS Health commented there was a mention on community form concerning remote work that may be premature to address. The representative was also curious why it was not consistent with Hospital Self-Assessment Form based on the Board's recent interpretation that drastically restricts remote work also pertains to hospitals.

A retired pharmacist commented meeting participants may not understand the Section 100 process and suggested discussion. Counsel Smiley advised the information covered in the Chairperson's opening remarks; no additional information was required.

Chairperson Serpa reviewed the proposed changes and agreed with the changes and the possible motion offered in the meeting materials related to the automated drug delivery system self-assessment. Dr. Serpa noted the meeting materials and slide highlight the changes.

Chairperson Serpa advised the Committee must address this self-assessment differently than the prior three, because the regulation section, CCR section 1715.1 that includes this self-assessment for, and the form itself are currently going through the rulemaking process. Dr. Serpa advised the comment period closed on December 27, 2022, and comments received during the comment period would be considered by the full Board during the February 2022 Board Meeting.

Chairperson Serpa provided the review and discussion was limited to just the new changes being recommended noting the changes were highlighted in the meeting materials and were reflected in the form. Dr. Serpa added deleted text was shown by italicized double strikethrough and added language is shown as italicized wavy underline. Dr. Serpa noted easy examples to highlight both were included on the first page of the form where the "note" and text added shown as italicized and wavy underline was a new change for our consideration and the update to the revision date at the bottom of the form is an example of deleted text. Dr. Serpa noted because the Board would be considering the comments

received during the comment period, to ensure compliance with the government code, it was very important that comments were limited to only the new changes.

Members were provided the opportunity to provide comment.

Member Oh requested clarification on the Note on page 1 that confirmed one for was required for an entity with many non-licensed ADDS in a hospital.

Motion: Recommend approval of the proposed amendments to self-assessment form 17M-112 and incorporate the proposed amendments into the rulemaking package and initiate a 15-day comment period, authorize the Executive Officer to take all steps necessary to complete the rulemaking, make any non-substantive changes to the package, and adopt self-assessment form 17M-112.

M/S: Oh/Barker

Members of the public were provided the opportunity to comment; however, comments were not made.

Support: 4 Oppose: 0 Abstain: 0 Not Present: 2

Committee Member	**Vote**
Barker	Support
Cameron-Banks	Not Present
Oh	Support
Patel	Not Present
Sanchez	Support
Serpa	Support

V. Discussion and Consideration of Barriers to Timely Case Resolutions

Chairperson Serpa recalled one of the Committee's strategic objectives was to determine and reduce barriers to timely case resolutions to improve consumer protections. Dr. Serpa provided there were many steps involved in an investigation

and the egregiousness of the violations, if any, would in large part determine the outcome of the matter. Dr. Serpa noted later in the meeting, the Committee will be discussing enforcement statistics but would like to highlight that only about 7 percent of the Board's investigations result in referral to the Office of the Attorney General for discipline. Dr. Serpa highlighted this as there appears to be a perception that the formal discipline taken by the Board constitutes a significant portion of its investigations; however, the data tells otherwise. Dr. Serpa added when aggregated data for investigations was considered, investigation timeframes were currently the longest step.

Chairperson Serpa referred to information included in the meeting materials and on the meeting slide were recommendations offered by staff that would remove barriers:

- Amend BPC 4081 to require maintenance and release of staffing schedules, job duty statements, consultant reports, and policies and procedures related to pharmacy personnel and pharmacy operations as part of the records that must be maintained; and
- Amend BPC 4105 to require maintenance and release of staffing schedules, job duty statements, consultant reports, and policies and procedures related to pharmacy personnel and pharmacy operations as part of the records that must be readily retrievable.

Chairperson Serpa noted that the barriers identified and changes offered appear to be consistent with the policy of the legislature and believed the changes were appropriate. Dr. Serpa agreed with the staff recommendations and thanked supervising inspector staff for bringing these recommendations to the Committee for consideration. Dr. Serpa supported staff drafting statutory language for future consideration.

Members were provided the opportunity to comment; however, no comments were made.

Members of the public were provided the opportunity to comment; however, no comments were made.

Chairperson Serpa noted Committee consensus and agreed to work with staff to bring statutory language to a future meeting.

VI. Overview of Federal Requirements for Compounding under the Provisions of 503A

Chairperson Serpa advised licensees of the Board generally must comply with a myriad of state and federal laws noting at times, a licensee may be so focused on a specific section of the law that they may forget the larger picture and other

provisions of law that may be relevant. Dr. Serpa noted this was seen in several areas of pharmacy practice but it was quite pronounced in compounding. Dr. Serpa advised to serve as a reminder of some of the federal legal requirements for compounding, Board Counsel Eileen Smiley provided an overview of the requirements for authorized individuals for qualify for some exemptions to federal law under provisions of section 503A.

Ms. Smiley provided an overview of federal requirements for compounding and the need for exemptions for compounding. Ms. Smiley reviewed the 503A exemption and provided a summary of the 503A exemption. Ms. Smiley reviewed how state requirements also apply.

Members were provided the opportunity to comment; however, no comments were made.

Members of the public were provided the opportunity to comment. Ms. Smiley reminded participants that pending enforcement issues would not be discussed. However, no public comments were made.

Chairperson Serpa thanked Ms. Smiley for her presentation.

The Committee took a break from 9:54 a.m. – 10:01 a.m. Chairperson Serpa took roll call. Members present included: Renee Barker, Licensee Member; Seung Oh, Licensee Member; and Maria Serpa; Licensing Member. A quorum was not established. As indicated on the agenda, in the event a quorum of the Committee was unable to attend the meeting, or the Committee was unable to maintain a quorum once the meeting is called to order, the members present may, at the Chair's discretion, continue to discuss items from the agenda and make recommendations to the full board at a future meeting.

Member Sanchez arrived at 10:06 a.m. A quorum was established.

VII. Presentation on USP General Chapter 825, Regarding Radiopharmaceuticals

Chairperson Serpa advised the Committee would hear a presentation from Supervising Inspector Christine Acosta on the new USP 825 Chapter related to Radiopharmaceuticals. Dr. Serpa noted the provisions of this chapter become effective November 1, 2023.

Supervising Inspector Christine Acosta reviewed definitions, generators, PECs, and conventionally manufactured kits, preparation, and dispensing. Dr. Acosta reviewed 1. Introduction; 1.1 Nonsterile Radiopharmaceuticals; 1.2 Sterile Radiopharmaceuticals; 2. Radiation Safety Considerations; 2.4 Radiation Contamination Control; 4. Personnel Qualifications, Training and Hygiene; 4.1

Aseptic Qualifications; 4.2 Re-Evaluations, Retraining and Requalification; 4.5 Hand Hygiene and Garbing for Buffer Areas and Segregated Radiopharmaceutical Processing Area; 5.1 Facility Design and Environmental Controls; 5.2 Creating Areas to Achieve Easily Cleanable Conditions; 5.3 Water Sources; 5.7 Environmental Controls; 6. Microbiological Air and Surface Monitors; 6.1 General Monitoring Requirements; 6.2 Monitoring Air Quality for Viable Airborne Particulates; 6.3 Monitoring Surfaces for Viable Particles; 7. Cleaning and Disinfecting; 8. Assigning BUD, Sterility BUD; 9. Documentation; 10.2 Preparation with Minor Deviations; 10.3 Preparation of Radiolabeled Blood Components; 11.1 Compounding Nonsterile Radiopharmaceuticals; 11.2 Sterile Compounding; 12.1 Dispensing and Radioassay; 12.2 Labeling; 13. Repackaging; and 14. Quality Assurance and Quality Control.

Members were provided the opportunity to comment.

Member Barker inquired about the qualifications for the workers in 4.1 Aseptic Qualification that Qualifications may be conducted at a different site if all SOPs are identical for the applicable job function. Dr. Barker noted that it varies from how training for sterile compounding. Dr. Acosta provided in the scope of radiopharmaceutical, the primary engineering control (PEC) will always be a biological safety cabinet where it could be different in a hospital practice setting using different PECs. Dr. Acosta advised for aseptic technique that was carried over also because there are only 3-4 different companies that do this and trained staffing is limited. However, it was possible this presents a risk to the consumer.

Member Barker mentioned having experience with someone who was learning aseptic technique but trying to manipulate with lead gloves as part of a qualification to don sterile gloves on top of lead gloves and inquired if Dr. Acosta came across that situation. Dr. Acosta had not seen a lead glove and was not sure how the needle would be manipulated. Dr. Acosta noted it was the balance of protecting the person and the stability of the product. Dr. Acosta was accustomed to seeing people using sterile gloves.

Member Barker inquired about the stages when the frequent application of sterile isopropyl alcohol would be done and if the sterile alcohol was exposed in the hood. Dr. Acosta indicated in her experience it was in the biological safety cabinet or in a cart next to it where hands are sprayed after coming out of the ISO 5 similar to a regular USP 797. Cleaning and disinfecting were to be done on a regular basis but the more isopropyl alcohol can be sprayed the better.

Member Barker was unfamiliar with the dose calibrator and inquired how the crucible calibrator calibrates the dose. Dr. Acosta explained there was a pully system that had the syringe or vial and calculates the radiopharmaceutical activity. The math equation is done for what is needed during the time needed. Dr.

Barker asked if the needle was capped after the dose was drawn. Dr. Acosta believed the needle was removed but wasn't able to verify.

Members of the public were provided the opportunity to comment; however, no comments were made.

VIII. Discussion and Consideration of Proposed Addition to Title 16, California Code of Regulations Section 1738 related to Radiopharmaceuticals

Chairperson Serpa advised the Committee would begin work to review the various USP chapters and review current and proposed regulations that may be necessary to implement, clarify, or make more specific requirements related to those respective chapters. Dr. Serpa believed it was appropriate that any such regulations mirror the structure of the respective chapters. Dr. Serpa noted as the Board is a consumer protection agency and as the Committee considered the development of the regulations, the work must be through the lens of the Board's consumer protection mandate as the law makes clear whenever the protection of the public is inconsistent with other interests sought to be promoted, the protection of the public shall be paramount. Dr. Serpa noted it was a dynamic process and individuals would have opportunities to participate throughout the development and rulemaking process.

Chairperson Serpa intended to discuss each section first as a committee, and then ask the moderator to open the lines for public comment with the refining of the language through the discussion with the understanding that any language we amended at the meeting would be reviewed by counsel. Dr. Serpa added after public comment, Dr. Serpa would summarize comments received for each section and the Committee can determine if additional changes to the proposed language was appropriate. Dr. Serpa requested staff display the language during this portion of the meeting to allow for edits to be made during the meeting where changes were appropriate.

Members were provided an opportunity to comment; however, no comments were made.

Members of the public were provided an opportunity to comment; however, no comments were made.

Chairperson Serpa advised the first proposed change was the proposed repeal of CCR sections 1708.3 through 1708.5 with the new regulations as proposed would be established in a new section 1738. Dr. Serpa believed this was appropriate and would make compliance easier for licensees by having information centralized.

Repeal:

~~1708.3. Radioactive Drugs.~~

~~A radioactive drug is any substance defined as a drug in Section 201(g)(1) of the Federal Food, Drug and Cosmetic Act or a radioactive biological product as defined in 21 CFR 600.3(ee) which exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons and includes any such drug or biological product which is intended to be made radioactive. This definition includes non-radioactive reagent kits and nuclide generators which are intended to be used in the preparation of any such substance but does not include drugs such as carbon-containing compounds, potassium-containing compounds or potassium-containing salts which contain trace quantities of naturally occurring radionuclides.~~

~~Authority cited: Section 4005, Business and Professions Code. Reference: Section 4025, Business and Professions Code.~~

~~1708.4. Pharmacist Handling Radioactive Drugs.~~

~~A pharmacist handling radioactive drugs must be competent in the preparation, handling, storage, receiving, dispensing, disposition and pharmacology of radioactive drugs. He must have completed a nuclear pharmacy course and/or acquired experience in programs approved by the Board. Education and experience in non-approved programs may be granted partial or equivalent credit, if, in the opinion of the Board, such programs provide the level of competence as approved programs or the Nuclear Pharmacy Competency Statement adopted by the Board.~~

~~Authority cited: Section 4005, Business and Professions Code. Reference: Sections 4021, 4022, 4025, 4036 and 4037, Business and Professions Code.~~

~~1708.5. Pharmacy Furnishing Radioactive Drugs.~~

~~A pharmacy furnishing radioactive drugs is any area, place or premises described in a permit issued by the board where radioactive drugs are stored, processed, compounded, repackaged, or dispensed. A pharmacy exclusively furnishing radioactive drugs shall be exempt from the patient consultation area requirements of Title 16 Cal. Code of Regulations Section 1714(a) unless the Board finds that the public health and safety require their application.~~

~~A pharmacist qualified under Section 1708.4 to furnish radioactive drugs shall be in the pharmacy whenever the furnishing of radioactive drugs occurs. All personnel involved in the furnishing of radioactive drugs shall be under the immediate and direct supervision of such a qualified pharmacist.~~

~~Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 4005, 4008 and 4008.2, Business and Professions Code.~~

Members were provided an opportunity to comment; however, no comments were made.

Members of the public were provided an opportunity to comment; however, no comments were made.

Chairperson Serpa advised the first new proposed section was CCR section 1738. Dr. Serpa provided the proposed language incorporates USP Chapter 825 into the regulation, providing clarity to the Board's regulated public that the requirements of the Chapter must be met. Dr. Serpa added the authority for such a requirement was established in several sections of pharmacy law as detailed in the language.

Proposal to Add Article XX as proposed with the following:

Article XX Radiopharmaceutical- Preparation, Compounding, Dispensing, and Repackaging

1738. Radiopharmaceuticals – Preparation, Compounding, Dispensing, and Repackaging

This article applies to radiopharmaceuticals as defined in USP Chapter 825. In addition to the requirements provided in this Article, the processing of radiopharmaceuticals shall comply with the standards established by United States Pharmacopeia General Chapter 825, titled *Radiopharmaceuticals – Preparation, Compounding, Dispensing, and Repackaging* ("USP Chapter 825" for the purposes of this Article).

Necessity: Clarity to the regulated public about the requirements to comply with the Section consistent with authority established in the law and the requirements of the Chapter.

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 4005, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

Members were provided an opportunity to comment; however, no comments were made.

Members of the public were provided an opportunity to comment; however, no comments were made.

Chairperson Serpa provided CCR section 1738.1 as proposed reinforces the applicability of the USP Chapter 825 and the definitions included within the chapter. Dr. Serpa added it further provides additional definitions for terms used in the chapter and proposed regulations that were not otherwise defined. Dr. Serpa noted providing these definitions ensures members of the regulated public have a

clear understanding of the Board's definitions when applying both the provisions of the chapter and the board's regulations.

The proposed definitions include:
- Added substances
- Designated person
- Component
- Diluent
- Processing, processed or processing activity
- As well as requirements for use of technologies, techniques, materials, and procedures not described in USP 825 as well as provisions for processing with human whole blood or human whole blood derivatives.

1738.1 INTRODUCTION SCOPE AND COMPOUNDING DEFINITIONS

In addition to the definitions contained in USP Chapter 825, the following definitions apply to this Article and supplement the standards established in USP Chapter 825 when not otherwise provided in USP Chapter 825.

(a) "Added substances" means ingredients that are necessary to compound a preparation but are not intended or expected to cause a pharmacologic response if administered alone in the amount or concentration contained in a single dose of the compounded preparation. The term is used synonymously with the terms inactive ingredients, excipients, and pharmaceutical ingredients.

(b) "Designated person" means a pharmacist identified as assigned, responsible, and accountable for the performance and operation of the radiopharmaceutical processing facility and for personnel who prepare, compound, dispense, and repackage radiopharmaceuticals.

(b) "Component" means any ingredient used in the compounding of a preparation, including any active ingredient, added substance, or conventionally manufactured product.

(c) "Diluent" means a liquid with no pharmacological activity used in reconstitution, such as sterile water for injection.

(d) "Processing," "processed" or "processing activity" means the preparation, compounding, repackaging, or dispensing of a radiopharmaceutical.

(e) The use of technologies, techniques, material, and procedures not described in USP 825 shall be based upon published peer-reviewed literature or documents meeting FDA approved labeling requirements in accordance with sections 201.56 and 201.57 of title 21, Code of Federal Regulations, showing the

technologies, techniques, material, and procedures to be equivalent or superior to those described in USP Chapter 825.

(f) Processing with human whole blood or human whole blood derivatives shall be done in compliance with Health and Safety Code section 1602.5.

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 4005, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

Chairperson Serpa reviewed the language as proposed and believed it was appropriate. Members were provided an opportunity to comment; however, no comments were made.

Members of the public were provided an opportunity to comment; however, no comments were made.

Chairperson Serpa provided CCR proposed section 1738.2 related to Radiation Safety Considerations relied on the standards established in the Chapter. Dr. Serpa added the language will ensure the appropriate placement of equipment etc. to minimize disruptions of airflow. The language will require that disposable absorbent pads are changed to prevent cross-contamination and requires documentation within the SOP of the necessity of deviations.

1738.2 RADIATION SAFETY CONSIDERATIONS

In addition to the standards in the USP Chapter 825, the processing of radiopharmaceuticals shall meet the following radiation safety requirements of this section.

(a) Radiation detectors and measuring devices, and other necessary equipment may be placed inside an ISO Class 5 PEC but must be placed in a manner that minimizes disruptions of airflow.
Necessity: To provide clarity and ensure the appropriate type and material is used. The language establishes a requirement about what actions must be done versus should be done.

(b) Disposable absorbent pads shall be changed after each type of radiopharmaceutical processing.

Necessity: To provide clarity as the Chapter does not specify that pads must be changed. Changing pads is necessary to avoid cross contamination.

(c) Any deviation made to lower radiation exposure to workers shall be evaluated and documented in an SOP by the designated person prior to the deviation occurring. Exceptions to the environmental controls requirements must be documented in the specific radioactive materials license conditions issued by the California Department of Public Health pursuant to section 30190 of Title 17 of the California Code of Regulations, or a specific radioactive materials license issued by another state or the United States Nuclear Regulatory Commission pursuant to pursuant to section 32.72 of title 10 of the Code of Federal Regulations.

Necessity: Provides clarity to ensure that SOPs document the need for deviations.

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 4005, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

Chairperson Serpa reviewed the language as proposed and believed it was appropriate. Members were provided an opportunity to comment; however, no comments were made.

Members of the public were provided an opportunity to comment; however, no comments were made.

Chairperson Serpa advised CCR proposed Section 1738.3 establishes the standards for the immediate use of sterile radiopharmaceuticals and will ensure licensees have a clear understanding that the records required in the Chapter must be maintained consistent with the provisions of BPC section 4081.

1738.3. IMMEDIATE USE OF STERILE RADIOPHARMACEUTICALS

The processing of radiopharmaceuticals for immediate use may only be done in a patient care setting meeting the applicable requirements in this Article. The patient care facility shall maintain all records required in Section 9 of USP Chapter 825 in accordance with Business and Professions Code section 4081.

Chairperson Serpa reviewed the language as proposed and believed it was appropriate. Members were provided an opportunity to comment; however, no comments were made.

Members of the public were provided an opportunity to comment; however, no comments were made.

Chairperson Serpa advised CCR section 1738.4 was related to personnel qualifications, training, and hygiene. Dr. Serpa advised this section establishes requirements necessary for public protection while providing for professional judgement of the designated person to make site specific and person specific decisions on a case-by-case basis. Dr. Serpa noted the regulation was relying on appropriate SOPs to appropriately define how some processes may occur.

1738.4 PERSONNEL QUALIFICATIONS, TRAINING, AND HYGIENE

In addition to the requirements in the USP Chapter 825, the processing of radiopharmaceuticals shall comply with all of the requirements of this section.

(a) Processing personnel experiencing any of the following: rashes, recent tattoos or oozing sores, conjunctivitis, active respiratory infection or and other conditions which could contaminate a sterile radiopharmaceutical, or the environment shall not be allowed to enter the compounding area unless approved by the designated person.

(b) The pharmacist with direct oversight over personnel performing radiopharmaceutical processing shall demonstrate proficiency in skills necessary to ensure the integrity, potency, quality, and labeled strength of radiopharmaceuticals as defined in the facilities SOPs.

(c) Aseptic qualifications from one premises may be used for another premises if the SOPs, facilities, and equipment are identical.

(d) SOPs must clearly define the acceptable use and cleaning for reusable gowns that prevent possible contamination of the CSP and designated compounding area. However, laundered garb must not be reused beyond one day unless garb is laundered with a validated cycle. The facility's SOPs must describe the process that must be followed should the facility allow for the reuse of garb.

(e) Eyeglasses shall be cleaned as part of hand hygiene and garbing, consistent with the standards specified in the SOPs.

(f) Garb shall be donned and removed in an ante-area or immediately outside the SPRA. Donning and doffing garb shall not occur in the ante-room or the SPRA at the same time unless the SOPs define specific processes which must be followed to prevent contamination.

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 4005, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

Chairperson Serpa reviewed the language as proposed and believed the language strikes the right balance for radiopharmaceuticals and was comfortable with the proposed language as it specifically relates to radiopharmaceuticals in this section. Members were provided the opportunity to comment.

Member Barker inquired about subsection (c) regarding if the SOPs, facilities, and equipment were to be identical and if identical meant the exact same extending to the same brand, manufacturers, etc. Dr. Barker recommended clarification. Dr. Serpa noted in regulations, the Board is clarifying and making known what the California expectations are as USP is a little broader, whereas in California regulations state requirements more specifically. Dr. Acosta deferred to legal regarding the term "identical" as when primary engineering control (PEC) the types of equipment are grouped (e.g., biological horizontal flow, CAI, CACI, etc.) together. Counsel Grace Arupo Rodriguez advised the pure meaning is exact and identical which allows for an opportunity to clarify if desired but was not something that would trigger clarification with the Office of Administrative Law. With regard to enforcement, it would help to provide parameters. Dr. Barker thought identical should apply to SOPs but perhaps facilities and equipment could have elaboration. The Committee discussed different iterations of verbiage. Dr. Acosta advised having SOPs and facility remain identical but equipment was more difficult. The Committee agreed to remove equipment and let USP 825 address equipment.

(c) Aseptic qualifications from one premises may be used for another premises if the SOPs and, facilities are identical~~, and equipment are identical~~.

Members of the public were provided the opportunity to comment.

A representative from CPhA commented in appreciation for discussion striving for clarity.

Chairperson Serpa believed the changes were appropriate and requested if the Committee had additional comments. The Committee reached consensus on the updated language for proposed CCR section 1738.4.

1738.4 PERSONNEL QUALIFICATIONS, TRAINING, AND HYGIENE

In addition to the requirements in the USP Chapter 825, the processing of radiopharmaceuticals shall comply with all of the requirements of this section.

(a) Processing personnel experiencing any of the following: rashes, recent tattoos or oozing sores, conjunctivitis, active respiratory infection or and other conditions which could contaminate a sterile radiopharmaceutical, or the environment shall not be allowed to enter the compounding area unless approved by the designated person.

(b) The pharmacist with direct oversight over personnel performing radiopharmaceutical processing shall demonstrate proficiency in skills necessary to ensure the integrity, potency, quality, and labeled strength of radiopharmaceuticals as defined in the facilities SOPs.

(c) Aseptic qualifications from one premises may be used for another premises if the SOPs and, facilities are identical~~, and equipment are identical~~.

(d) SOPs must clearly define the acceptable use and cleaning for reusable gowns that prevent possible contamination of the CSP and designated compounding area. However, laundered garb must not be reused beyond one day unless garb is laundered with a validated cycle. The facility's SOPs must describe the process that must be followed should the facility allow for the reuse of garb.

(e) Eyeglasses shall be cleaned as part of hand hygiene and garbing, consistent with the standards specified in the SOPs.

(f) Garb shall be donned and removed in an ante-area or immediately outside the SPRA. Donning and doffing garb shall not occur in the ante-room or the SPRA at the same time unless the SOPs define specific processes which must be followed to prevent contamination.

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 4005, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

Chairperson Serpa provided CCR Section 1738.5 establishes the requirements for facilities and engineering control. Dr. Serpa noted in addition to the standards established in the Chapter, among other changes the proposed regulation will require that the sink used for compounding or hand hygiene shall not be part of the restroom or water closet. Dr. Serpa noted some of the regulation language was being included where the chapter was silent to provide clarity. Dr. Serpa provided an example of proposed 1738.5(h) explicitly states that only activities necessary for processing a radiopharmaceutical may be perform in the SRPA.

Chairperson Serpa reviewed the language as proposed and believed it was appropriate.

1738.5. FACILITIES AND ENGINEERING CONTROLS

In addition to the requirements in the USP Chapter 825, the processing of radiopharmaceuticals shall comply with all of the requirements of this section.

(a) A sink used for compounding or hand hygiene shall not be part of a restroom or water closet.

(b) The temperature shall be monitored in SRPAs segregated radiopharmaceutical processing area and classified areas each day that processing is performed, either manually or by a continuous recording device.

(c) Storage and elution of non-direct infusion radionuclide generators shall take place in an ISO Class 8 or better area.

(d) If an SRPA is used:

(1) Except for walls, the SRPA's visible perimeter shall be at least 1 meter from all sides of the PEC or in a separate room.

(2) Surfaces within the SRPA shall be smooth, impervious, free from cracks and crevices, and non-shedding so they can be easily cleaned and disinfected and to minimize spaces in which microorganisms and other contaminants can accumulate.

(3) Compounding shall not take place in the SRPA.

(e)(1) Testing and certification of all classified areas shall be completed by a competent individual. A competent individual is a technician who possesses a current accreditation issued by The Controlled Environment Testing Association (CETA), or under the direct supervision of an individual who possesses a current accreditation issued by CETA Certification shall be completed consistent with the provisions established in the USP Chapter 797, titled "Pharmaceutical Compounding—Sterile Preparations" (USP Chapter 797). The facility shall review and maintain a copy of the accreditation documentation in accordance with requirements in section 1738.9.

(2) CETA standard(s) used to perform certification testing in all classified areas shall be recorded on the certification report as required and specified in USP Chapter 797.

(f) SOPs shall specify steps to be taken if a classified area(s) fails to meet the specified ISO classification including the investigative and corrective actions, allowable activities, and retesting procedures.

(g) All classified spaces and equipment must be recertified when there is any change in the Primary Engineering Control (PEC), or the compounding environment. For purposes of this subsection, a change includeswhen the PEC is moved, repaired or replaced, when the facility is modified in a manner that affects airflow or traffic patterns, or when improper aseptic techniques are observed. Further, SOPs must address the conditions under which recertification must also be completed when relocating a PEC.

(h) Activities and tasks carried out within the SRPA and classified areas shall be limited to only those necessary for processing a radiopharmaceutical.

(i) Food, drinks, and materials exposed in patient care and treatment areas must not enter SRPA or classified areas.

(j) A dynamic airflow smoke pattern test must be performed initially and at least every 6 months for all classified spaces and equipment. All dynamic airflow smoke pattern tests shall be immediately retrievable during inspection. A copy of the test shall be provided to the Board's inspector if requested in accordance with the timeframes set forth in Section 4105 of the Business and Professions Code.

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 4005, 4081, 4105 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

Members were provided the opportunity to comment. The Committee discussed the term "water closet" and determined it was a term of trade used by Department of Health Care Access and Information formerly known as OSHPD and was consistent.

Members of the public were provided the opportunity to comment; however, no comments were made.

Chairperson Serpa provided CCR section 1738.6 incorporates the USP standards related to microbiological air and surface monitoring and as proposed include requirements that are silent in the chapter. Such an approach provided clarity to the regulated and ensures everyone has a clear understanding of the Board's requirements.

1738.6. MICROBIOLOGICAL AIR AND SURFACE MONITORING

In addition to the requirements in the USP Chapter 825, the processing of radiopharmaceuticals shall comply with all of the requirements of this section.

(a) SOPs shall specify steps to be taken for processing radiopharmaceuticals when the microbiological air and surface monitoring action levels are exceeded, including the investigative and corrective actions, allowable activities, and resampling procedures.

(b) At a minimum, to trend for growth of microorganisms, during biannual (every 6 months) recertification, any microorganism recovered (growth) shall be identified at least to the genus species, regardless of the CFU count. Professional judgement shall be used to determine the appropriate action necessary to remedy identified trends regardless on the action level. Investigation of a microorganism growth must be consistent with the deviation identified and must include evaluation of trends.

(c) The designated person shall review the sampling results and identify data trends at least every time sample results are received. The designated person shall evaluate trends to determine if corrective action is needed. The results of the review shall be documented in the facility's SOPs and readily retrievable during inspection in accordance with the requirements in section 1738.9.

(d) Incubators must be calibrated and operated in accordance with the manufacturer's specifications and temperatures must be monitored during incubation, either manually or by a continuous recording device, and the results must be reviewed and documented as described in the facility's SOPs.

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 4005, 4081, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

Chairperson Serpa reviewed the language as proposed and believed it was appropriate. Members were provided the opportunity to comment; however, no comments were made.

Members of the public were provided the opportunity to comment; however, no comments were made.

Chairperson Serpa advised CCR proposed section 1738.7 establishes provisions for cleaning and disinfecting again requiring compliance with the provisions of the Chapter as well as explicitly stating that the agents use must be done so consistent with the manufacturer's specifications. Dr. Serpa added the regulation language as proposed prohibits the storage of reusable cleaning supplies within 1 meter of the PEC. This prohibition was included in Chapter 797 but was not included in 825.

1738.7. CLEANING AND DISINFECTING

In addition to the requirements in the USP Chapter 825, the processing of radiopharmaceuticals shall comply with all of the requirements of this section.

(a) Cleaning, disinfection, and sporicidal agents shall be used in accordance with manufacturers' specifications and shall occur at the minimum frequencies listed in Table 5 of USP Chapter 825. Incubators must be cleaned at least monthly.

(b) Reusable cleaning supplies shall not be stored within 1 meter of the PEC.

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 4005, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

Chairperson Serpa reviewed the language as proposed and believed it was appropriate. Members were provided the opportunity to comment; however, no comments were made.

Members of the public were provided the opportunity to comment; however, no comments were made.

Chairperson Serpa advised CCR proposed section 1738.8 will provide additional requirements for assigning beyond use dates to provide clarity and address issues not specifically included in the Chapter. The Chapter provides the process performed but does account for the expiration date of the ingredients. This was a common violation found in compounding making inclusion appropriate as it provides clarity to the regulated public and not all manufacture package inserts allow for an extension of the use-by time. Dr. Serpa noted the proposed language allows for an extension by establishing minimum provisions that must be satisfied to extend the use-by time.

1738.8. ASSIGNING BUD

In addition to the requirements in the USP Chapter 825, the processing of radiopharmaceuticals shall comply with all of the requirements of this section.

(a)A radiopharmaceutical CSP's beyond-use date (BUD) shall not exceed the shortest BUD of any of its components.

(b) No radiopharmaceutical CSP shall be administered after the labeled BUD. A dose shall not be sent for a scheduled administration that would occur after the labeled BUD.

(c) Extension of a conventionally manufactured kit with a suggested use-by time shall not exceed the BUDs in Table 7 of USP Chapter 825, for the sterility of the preparation or product.
Prior to the extension of a suggested use-by time for a conventionally manufactured kit, the SOPs must document at a minimum the following:
(1) Factors which necessitate its extension, which shall include a full assessment of patient needs for the extension.
(2) Evidence which supports that the extension maintains the appropriate quality and purity (radiochemical purity and radionuclidic purity) as specified in individual monographs, and other applicable parameters as clinically appropriate.

For the purposes of this section, the facility shall have SOPs that cover and are specific to each facility's location and kit.

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code.
Reference: Sections 4005, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

Chairperson Serpa reviewed the language as proposed and believed it was appropriate. Members were provided the opportunity to comment; however, no comments were made.

Members of the public were provided the opportunity to comment; however, no comments were made.

Chairperson Serpa provided CCR section 1738.9 relates to the documentation requirements. As proposed the language will establish a requirement for a compounding record if the facility is deviating from the manufacturers approved labeling and makes clear that records must meet the requirements established in BPC section 4081 and establishes an audit trail for revisions and updates of records.

1738.9. DOCUMENTATION

In addition to the requirements in the USP Chapter 825, the processing of radiopharmaceuticals shall comply with all of the requirements of this section.

(a) A record of a preparation must include a compounding record compliant with section 9.2 of USP Chapter 825.

(b) Records of preparation with minor deviations or compounding shall be a single document. The document shall satisfy the requirements of USP Chapter 825, as well as the following:

(1) The assigned internal identification number shall be unique for each preparation.
(2) The manufacturer, lot number, and expiration date shall be recorded for each component for CSPs. Documenting solely the National Drug Code (NDC) does not meet this requirement.
(3) The total quantity compounded shall include the number of units made and either the volume or the weight of each unit.
(4) The identity of each person performing the compounding and pharmacist verifying the final drug preparation
(5) When applicable, endotoxin level calculations and readings.

(c) Records required by USP Chapter 825 or this Article, shall be maintained in a readily retrievable form, for at least three years from the date the record was created or relied upon. If only recorded and stored electronically, on magnetic media, or in any other computerized form, the records shall be maintained as specified by Business and Professions Code section 4081 and 4105.

(d) Records created shall be created and maintained in a manner to provide an audit trail for revisions and updates of each record document as described in this subsection. Prior versions of each record must be maintained in a readily retrievable format (easily readable or
easily rendered into an electronic or paper format that a person can read) and include the changes to the document, identification of individual who made the change, and the date of each change.

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 4005, 4081, 4105, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

Chairperson Serpa reviewed the language as proposed and believed it was appropriate. Members were provided the opportunity to comment; however, no comments were made.

Members of the public were provided the opportunity to comment; however, no comments were made.

Chairperson Serpa advised CCR section 1738.10 establishes the standards for preparation noting in some instances, the proposed regulation will be requiring something that is permissive in the Chapter. Dr. Serpa added as proposed the language requires documentation when deviations from the manufacturers approved labeling occur in the specified areas. The proposed language also addresses requirements for blood components to avoid cross contamination.

1738.10. PREPARATION

In addition to the requirements in the USP Chapter 825, the processing of radiopharmaceuticals shall comply with all of the requirements of this section.

(a) Processing nonsterile radiopharmaceutical shall:
(1) Follow manufacturer preparation instructions, unless minor deviations are made pursuant to subsection (c).
(2) Only use an area which is suitably cleaned and is uncluttered.
(3) Have documented processes in its SOPs for activities (e.g., cleaning) between the preparation cycles of different nonsterile products.

(b) Processing sterile radiopharmaceutical (including intravascular devices) shall:
(1) Follow manufacturer preparation instructions, unless minor deviations are made pursuant to subsection (c).
(2) Use at least the minimum environmental standards from section 7 of USP Chapter 825.

(c) When preparing radiopharmaceuticals with minor deviations ("preparation with minor deviations" as defined in the USP Chapter 825) an SOP shall at least define the circumstances which necessitated the deviation and all quality control testing requirements and limits. Such circumstances shall, at a minimum, include patient need or facts that support the deviation that maintains the appropriate quality and purity (radiochemical purity and radionuclidic purity) as specified in individual monographs, and other applicable parameters as clinically appropriate in the professional judgment of the pharmacist.

For the purposes of this section, the facility shall have SOPs that cover and are specific to each location and manufacturer. Preparations with minor deviations shall maintain the same ingredients but may differ in their proportions. A deviation from the ingredients or proportions thereof exceeds the provisions allowed under a minor deviation and is not allowed under this Article.

(d) Equipment and supplies initially used for processing of blood components (included Red Blood Cells) shall be solely dedicated for processing of blood components. Equipment and supplies shall be thoroughly cleaned and disinfected, in accordance with section 1738.7, prior to initiation of the next patient's prescription.

(e) When processing blood components all garb must be removed and replaced for each patient.

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 4005, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

Chairperson Serpa reviewed the language as proposed and believed it was appropriate. Members were provided the opportunity to comment; however, no comments were made.

Members of the public were provided the opportunity to comment; however, no comments were made.

Chairperson Serpa provided CCR Section 1738.11 relates to compounding and as proposed adds language to ensure the regulated public understands the need to following requirements for RAM licensure related to specified areas. RAM licensure requirements should be specified per the above by CDPH or other comparable authority, NRC. Dr. Serpa added the proposed language also references federal requirements related to components and documentation requirements related specifically to bacterial endotoxin testing.

1738.11. COMPOUNDING

In addition to the requirements in the USP Chapter 825, the processing of radiopharmaceuticals shall comply with all of the requirements of this section.

(a) All compounding of radiopharmaceuticals shall comply with all radioactive materials licensing requirements for appropriate radiation safety considerations issued by the California Department of Public Health pursuant to section 30190 of Title 17 of the California Code of Regulations, another state licensing agency that issues specific radioactive materials licenses, or the United States Nuclear Regulatory Commission pursuant to pursuant to section 32.72 of title 10 of the Code of Federal Regulations, and utilize applicable environmental controls.

(b) Any active pharmaceutical ingredient (API) or added component used to compound a radiopharmaceutical shall be obtained from an FDA-registered facility and shall be accompanied by a valid certificate of analysis (COA). This COA shall be, at minimum, in English.

(c) Except for sterile radiopharmaceuticals made for inhalation or ophthalmic administration, prior to releasing a sterile radiopharmaceutical made from one or more nonsterile component(s) results of bacterial endotoxin testing shall be reviewed and recorded. Results shall be documented in the compounding record specified in Section 9.2 of the USP Chapter 825.

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 4005, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

Chairperson Serpa reviewed the language as proposed and believed it was appropriate. Members were provided the opportunity to comment; however, no comments were made.

Members of the public were provided the opportunity to comment; however, no comments were made.

Chairperson Serpa provided as proposed CCR section 1738.12 establishes dispensing requirements and provides clarity around labeling requirements but does not appear to be understood for outpatient dispensing.

1738.12. DISPENSING

In addition to the requirements in the USP Chapter 825, the processing of radiopharmaceuticals shall comply with all of the requirements of this section.

(a) All dispensed radiopharmaceutical doses shall be labeled with the information required by Business and Professions Code section 4076 and section 1707.5. Outer shielding labels shall contain the name and contact information of the dispensing pharmacy.

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 4005, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

Chairperson Serpa reviewed the language as proposed and believed it was appropriate. Members were provided the opportunity to comment; however, no comments were made.

Members of the public were provided the opportunity to comment; however, no comments were made.

Chairperson Serpa advised as proposed CCR section 1738.13 proposes requirements for repackaging that will apply making mandatory labeling provisions that are included in the Chapter, but currently not required.

1738.13. REPACKAGING

In addition to the requirements in the USP Chapter 825, the processing of radiopharmaceuticals shall comply with all of the requirements of this section.

(a) The inner container of a repackaged radiopharmaceutical shall be labeled with the following:
(1) Standard radiation symbol
(2) The words "Caution—Radioactive Material"
(3) The radionuclide and chemical form (generic name)
(4) Radioactivity with units at time of calibration and the calibration time

(b)The outer shielding of a repackaged radiopharmaceutical shall be labeled with the following:
(1) Standard radiation symbol
(2) The words "Caution—Radioactive Material"
(3) The radionuclide and chemical form (generic name)
(4) Radioactivity with units at time of calibration and the calibration time
(5) Volume, or number of units (e.g., capsules), as applicable
(6) Product expiration or BUD (consistent with Table 7 of USP Chapter 825), as applicable
(7) Special storage and handling instructions

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 4005, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

Chairperson Serpa reviewed the language as proposed and believed it was appropriate. Members were provided the opportunity to comment; however, no comments were made.

Members of the public were provided the opportunity to comment; however, no comments were made.

Chairperson Serpa provided as proposed CCR section 1738.14 proposes requirements for quality assurance and quality control as cross reference to the Board's quality assurance requirement included in existing regulation as well as the requirement established in USP Chapter 1163 and includes a requirement for scheduled actions, such as recalls. Dr. Serpa added as proposed, the regulation establishes notification requirements for adverse drug events, establishes timeframes for review of specified complaints, and specifies that failure to comply with SOPs shall constitute a basis for action.

1738.14. QUALITY ASSURANCE AND QUALITY CONTROL

In addition to the requirements in the USP Chapter 825, the processing of radiopharmaceuticals shall comply with all of the requirements of this section.

(a) The quality assurance program shall comply with section 1711 and the standards contained in USP Chapter 1163, titled "Quality Assurance in Pharmaceutical Compounding". In addition, the program shall include a written procedure for any scheduled action, such as a recall, in the event that radiopharmaceutical processing is discovered to be outside the expected quality and purity of the radiopharmaceutical.

(b)The Board shall be notified in writing within 72 hours of a complaint or adverse drug event involving a radiopharmaceutical.

(c) All complaints related to a potential quality problem with a radiopharmaceutical and all adverse events shall be reviewed by the pharmacist-in-charge within 72 hours of receipt of the complaint or occurrence of the adverse event. Such review shall be documented and dated as defined in the SOPs.

(d) Failure to follow written SOPs shall constitute a basis for enforcement action.

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 125.9, 4005, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

Chairperson Serpa reviewed the language as proposed and believed it was appropriate. Members were provided the opportunity to comment; however, no comments were made.

Members of the public were provided the opportunity to comment; however, no comments were made.

Chairperson Serpa thanked everyone for their diligence during the review. Dr. Serpa advised at the next meeting, the Committee will follow the same process for USP Chapter 795. Dr. Serpa added after the Committee has completed all of the chapters and proposed regulations, the Committee will consider acting and offer a recommendation to the Board for action.

A summary of the reviewed and updated sections is provided for Board records.

Repeal:

~~**1708.3. Radioactive Drugs.**~~

~~A radioactive drug is any substance defined as a drug in Section 201(g)(1) of the Federal Food, Drug and Cosmetic Act or a radioactive biological product as defined in 21 CFR 600.3(ee) which exhibits spontaneous disintegration of unstable nuclei with the emission of nuclear particles or photons and includes any such drug~~

~~or biological product which is intended to be made radioactive. This definition includes non-radioactive reagent kits and nuclide generators which are intended to be used in the preparation of any such substance but does not include drugs such as carbon-containing compounds, potassium-containing compounds or potassium-containing salts which contain trace quantities of naturally occurring radionuclides.~~
~~Authority cited: Section 4005, Business and Professions Code. Reference: Section 4025, Business and Professions Code.~~

~~1708.4. Pharmacist Handling Radioactive Drugs.~~
~~A pharmacist handling radioactive drugs must be competent in the preparation, handling, storage, receiving, dispensing, disposition and pharmacology of radioactive drugs. He must have completed a nuclear pharmacy course and/or acquired experience in programs approved by the Board. Education and experience in non-approved programs may be granted partial or equivalent credit, if, in the opinion of the Board, such programs provide the level of competence as approved programs or the Nuclear Pharmacy Competency Statement adopted by the Board.~~
~~Authority cited: Section 4005, Business and Professions Code. Reference: Sections 4021, 4022, 4025, 4036 and 4037, Business and Professions Code.~~

~~1708.5. Pharmacy Furnishing Radioactive Drugs.~~
~~A pharmacy furnishing radioactive drugs is any area, place or premises described in a permit issued by the board where radioactive drugs are stored, processed, compounded, repackaged, or dispensed. A pharmacy exclusively furnishing radioactive drugs shall be exempt from the patient consultation area requirements of Title 16 Cal. Code of Regulations Section 1714(a) unless the Board finds that the public health and safety require their application.~~
~~A pharmacist qualified under Section 1708.4 to furnish radioactive drugs shall be in the pharmacy whenever the furnishing of radioactive drugs occurs. All personnel involved in the furnishing of radioactive drugs shall be under the immediate and direct supervision of such a qualified pharmacist.~~
~~Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 4005, 4008 and 4008.2, Business and Professions Code.~~

Proposal to Add Article XX as proposed with the following:

Article XX Radiopharmaceutical- Preparation, Compounding, Dispensing, and Repackaging

1738. Radiopharmaceuticals – Preparation, Compounding, Dispensing, and Repackaging

This article applies to radiopharmaceuticals as defined in USP Chapter 825. In addition to the requirements provided in this Article, the processing of radiopharmaceuticals shall comply with the standards established by United States Pharmacopeia General Chapter 825, titled *Radiopharmaceuticals –Preparation, Compounding, Dispensing, and Repackaging* ("USP Chapter 825" for the purposes of this Article).

Necessity: Clarity to the regulated public about the requirements to comply with the Section consistent with authority established in the law and the requirements of the Chapter.

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 4005, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

1738.1 INTRODUCTION SCOPE AND COMPOUNDING DEFINITIONS

In addition to the definitions contained in USP Chapter 825, the following definitions apply to this Article and supplement the standards established in USP Chapter 825 when not otherwise provided in USP Chapter 825.

(a) "Added substances" means ingredients that are necessary to compound a preparation but are not intended or expected to cause a pharmacologic response if administered alone in the amount or concentration contained in a single dose of the compounded preparation. The term is used synonymously with the terms inactive ingredients, excipients, and pharmaceutical ingredients.

(b) "Designated person" means a pharmacist identified as assigned, responsible, and accountable for the performance and operation of the radiopharmaceutical processing facility and for personnel who prepare, compound, dispense, and repackage radiopharmaceuticals.

(b) "Component" means any ingredient used in the compounding of a preparation, including any active ingredient, added substance, or conventionally manufactured product.

(c) "Diluent" means a liquid with no pharmacological activity used in reconstitution, such as sterile water for injection.

(d) "Processing," "processed" or "processing activity" means the preparation, compounding, repackaging, or dispensing of a radiopharmaceutical.

(e) The use of technologies, techniques, material, and procedures not described in USP 825 shall be based upon published peer-reviewed literature or documents meeting FDA approved labeling requirements in accordance with sections 201.56 and 201.57 of title 21, Code of Federal Regulations, showing the technologies, techniques, material, and procedures to be equivalent or superior to those described in USP Chapter 825.

(f) Processing with human whole blood or human whole blood derivatives shall be done in compliance with Health and Safety Code section 1602.5.

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 4005, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

1738.2 RADIATION SAFETY CONSIDERATIONS

In addition to the standards in the USP Chapter 825, the processing of radiopharmaceuticals shall meet the following radiation safety requirements of this section.

(a) Radiation detectors and measuring devices, and other necessary equipment may be placed inside an ISO Class 5 PEC but must be placed in a manner that minimizes disruptions of airflow.
Necessity: To provide clarity and ensure the appropriate type and material is used. The language establishes a requirement about what actions must be done versus should be done.

(b) Disposable absorbent pads shall be changed after each type of radiopharmaceutical processing.

Necessity: To provide clarity as the Chapter does not specify that pads must be changed. Changing pads is necessary to avoid cross contamination.

(c) Any deviation made to lower radiation exposure to workers shall be evaluated and documented in an SOP by the designated person prior to the deviation occurring. Exceptions to the environmental controls requirements must be documented in the specific radioactive materials license conditions issued by the California Department of Public Health pursuant to section 30190 of Title 17 of the California Code of Regulations, or a specific radioactive materials license issued by another state or the United States Nuclear Regulatory Commission pursuant to pursuant to section 32.72 of title 10 of the Code of Federal Regulations.

Necessity: Provides clarity to ensure that SOPs document the need for deviations.

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 4005, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

1738.3. IMMEDIATE USE OF STERILE RADIOPHARMACEUTICALS

The processing of radiopharmaceuticals for immediate use may only be done in a patient care setting meeting the applicable requirements in this Article. The patient care facility shall maintain all records required in Section 9 of USP Chapter 825 in accordance with Business and Professions Code section 4081.

1738.4 PERSONNEL QUALIFICATIONS, TRAINING, AND HYGIENE

In addition to the requirements in the USP Chapter 825, the processing of radiopharmaceuticals shall comply with all of the requirements of this section.

(a) Processing personnel experiencing any of the following: rashes, recent tattoos or oozing sores, conjunctivitis, active respiratory infection or and other conditions which could contaminate a sterile radiopharmaceutical, or the environment shall not be allowed to enter the compounding area unless approved by the designated person.

(b) The pharmacist with direct oversight over personnel performing radiopharmaceutical processing shall demonstrate proficiency in skills necessary to ensure the integrity, potency, quality, and labeled strength of radiopharmaceuticals as defined in the facilities SOPs.

(c) Aseptic qualifications from one premises may be used for another premises if the SOPs and, facilities are identical ~~, and equipment are identical~~.

(d) SOPs must clearly define the acceptable use and cleaning for reusable gowns that prevent possible contamination of the CSP and designated compounding area. However, laundered garb must not be reused beyond one day unless garb is laundered with a validated cycle. The facility's SOPs must describe the process that must be followed should the facility allow for the reuse of garb.

(e) Eyeglasses shall be cleaned as part of hand hygiene and garbing, consistent with the standards specified in the SOPs.

(f) Garb shall be donned and removed in an ante-area or immediately outside the SPRA. Donning and doffing garb shall not occur in the ante-room or the SPRA at the same time unless the SOPs define specific processes which must be followed to prevent contamination.

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 4005, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

1738.5. FACILITIES AND ENGINEERING CONTROLS

In addition to the requirements in the USP Chapter 825, the processing of radiopharmaceuticals shall comply with all of the requirements of this section.

(a) A sink used for compounding or hand hygiene shall not be part of a restroom or water closet.

(b) The temperature shall be monitored in SRPAs segregated radiopharmaceutical processing area and classified areas each day that processing is performed, either manually or by a continuous recording device.

(c) Storage and elution of non-direct infusion radionuclide generators shall take place in an ISO Class 8 or better area.

(d) If an SRPA is used:

(1) Except for walls, the SRPA's visible perimeter shall be at least 1 meter from all sides of the PEC or in a separate room.

(2) Surfaces within the SRPA shall be smooth, impervious, free from cracks and crevices, and non-shedding so they can be easily cleaned and disinfected and to minimize spaces in which microorganisms and other contaminants can accumulate.

(3) Compounding shall not take place in the SRPA.

(e)(1) Testing and certification of all classified areas shall be completed by a competent individual. A competent individual is a technician who possesses a current accreditation issued by The Controlled Environment Testing Association (CETA), or under the direct supervision of an individual who possesses a current accreditation issued by CETA Certification shall be completed consistent with the provisions established in the USP Chapter 797, titled "Pharmaceutical Compounding—Sterile Preparations" (USP Chapter 797). The facility shall review and maintain a copy of the accreditation documentation in accordance with requirements in section 1738.9.

(2) CETA standard(s) used to perform certification testing in all classified areas shall be recorded on the certification report as required and specified in USP Chapter 797.

(f) SOPs shall specify steps to be taken if a classified area(s) fails to meet the specified ISO classification including the investigative and corrective actions, allowable activities, and retesting procedures.

(g) All classified spaces and equipment must be recertified when there is any change in the Primary Engineering Control (PEC), or the compounding environment. For purposes of this subsection, a change includeswhen the PEC is moved, repaired or replaced, when the facility is modified in a manner that affects airflow or traffic patterns, or when improper aseptic techniques are observed. Further, SOPs must address the conditions under which recertification must also be completed when relocating a PEC.

(h) Activities and tasks carried out within the SRPA and classified areas shall be limited to only those necessary for processing a radiopharmaceutical.

(i) Food, drinks, and materials exposed in patient care and treatment areas must not enter SRPA or classified areas.

(j) A dynamic airflow smoke pattern test must be performed initially and at least every 6 months for all classified spaces and equipment. All dynamic airflow smoke pattern tests shall be immediately retrievable during inspection. A copy of the test shall be provided to the Board's inspector if requested in accordance with the timeframes set forth in Section 4105 of the Business and Professions Code.

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 4005, 4081, 4105 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

1738.6. MICROBIOLOGICAL AIR AND SURFACE MONITORING

In addition to the requirements in the USP Chapter 825, the processing of radiopharmaceuticals shall comply with all of the requirements of this section.

(a) SOPs shall specify steps to be taken for processing radiopharmaceuticals when the microbiological air and surface monitoring action levels are exceeded, including the investigative and corrective actions, allowable activities, and resampling procedures.

(b) At a minimum, to trend for growth of microorganisms, during biannual (every 6 months) recertification, any microorganism recovered (growth) shall be identified at least to the genus species, regardless of the CFU count. Professional judgement shall be used to determine the appropriate action necessary to remedy identified

trends regardless on the action level. Investigation of a microorganism growth must be consistent with the deviation identified and must include evaluation of trends.

(c) The designated person shall review the sampling results and identify data trends at least every time sample results are received. The designated person shall evaluate trends to determine if corrective action is needed. The results of the review shall be documented in the facility's SOPs and readily retrievable during inspection in accordance with the requirements in section 1738.9.

(d) Incubators must be calibrated and operated in accordance with the manufacturer's specifications and temperatures must be monitored during incubation, either manually or by a continuous recording device, and the results must be reviewed and documented as described in the facility's SOPs.

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 4005, 4081, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

1738.7. CLEANING AND DISINFECTING

In addition to the requirements in the USP Chapter 825, the processing of radiopharmaceuticals shall comply with all of the requirements of this section.

(a) Cleaning, disinfection, and sporicidal agents shall be used in accordance with manufacturers' specifications and shall occur at the minimum frequencies listed in Table 5 of USP Chapter 825. Incubators must be cleaned at least monthly.

(b) Reusable cleaning supplies shall not be stored within 1 meter of the PEC.

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 4005, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

1738.8. ASSIGNING BUD

In addition to the requirements in the USP Chapter 825, the processing of radiopharmaceuticals shall comply with all of the requirements of this section.

(a) A radiopharmaceutical CSP's beyond-use date (BUD) shall not exceed the shortest BUD of any of its components.

(b) No radiopharmaceutical CSP shall be administered after the labeled BUD. A dose shall not be sent for a scheduled administration that would occur after the labeled BUD.

(c) Extension of a conventionally manufactured kit with a suggested use-by time shall not exceed the BUDs in Table 7 of USP Chapter 825, for the sterility of the preparation or product.
Prior to the extension of a suggested use-by time for a conventionally manufactured kit, the SOPs must document at a minimum the following:
(1) Factors which necessitate its extension, which shall include a full assessment of patient needs for the extension.
(2) Evidence which supports that the extension maintains the appropriate quality and purity (radiochemical purity and radionuclidic purity) as specified in individual monographs, and other applicable parameters as clinically appropriate.

For the purposes of this section, the facility shall have SOPs that cover and are specific to each facility's location and kit.

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code.
Reference: Sections 4005, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

1738.9. DOCUMENTATION

In addition to the requirements in the USP Chapter 825, the processing of radiopharmaceuticals shall comply with all of the requirements of this section.

(a) A record of a preparation must include a compounding record compliant with section 9.2 of USP Chapter 825.

(b) Records of preparation with minor deviations or compounding shall be a single document. The document shall satisfy the requirements of USP Chapter 825, as well as the following:

(1) The assigned internal identification number shall be unique for each preparation.
(2) The manufacturer, lot number, and expiration date shall be recorded for each component for CSPs. Documenting solely the National Drug Code (NDC) does not meet this requirement.
(3) The total quantity compounded shall include the number of units made and either the volume or the weight of each unit.
(4) The identity of each person performing the compounding and pharmacist verifying the final drug preparation
(5) When applicable, endotoxin level calculations and readings.

(c) Records required by USP Chapter 825 or this Article, shall be maintained in a readily retrievable form, for at least three years from the date the record was created or relied upon. If only recorded and stored electronically, on magnetic

media, or in any other computerized form, the records shall be maintained as specified by Business and Professions Code section 4081 and 4105.

(d) Records created shall be created and maintained in a manner to provide an audit trail for revisions and updates of each record document as described in this subsection. Prior versions of each record must be maintained in a readily retrievable format (easily readable or
easily rendered into an electronic or paper format that a person can read) and include the changes to the document, identification of individual who made the change, and the date of each change.

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 4005, 4081, 4105, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

1738.10. PREPARATION

In addition to the requirements in the USP Chapter 825, the processing of radiopharmaceuticals shall comply with all of the requirements of this section.

(a) Processing nonsterile radiopharmaceutical shall:
(1) Follow manufacturer preparation instructions, unless minor deviations are made pursuant to subsection (c).
(2) Only use an area which is suitably cleaned and is uncluttered.
(3) Have documented processes in its SOPs for activities (e.g., cleaning) between the preparation cycles of different nonsterile products.

(b) Processing sterile radiopharmaceutical (including intravascular devices) shall:
(1) Follow manufacturer preparation instructions, unless minor deviations are made pursuant to subsection (c).
(2) Use at least the minimum environmental standards from section 7 of USP Chapter 825.

(c) When preparing radiopharmaceuticals with minor deviations ("preparation with minor deviations" as defined in the USP Chapter 825) an SOP shall at least define the circumstances which necessitated the deviation and all quality control testing requirements and limits. Such circumstances shall, at a minimum, include patient need or facts that support the deviation that maintains the appropriate quality and purity (radiochemical purity and radionuclidic purity) as specified in individual monographs, and other applicable parameters as clinically appropriate in the professional judgment of the pharmacist.

For the purposes of this section, the facility shall have SOPs that cover and are specific to each location and manufacturer. Preparations with minor deviations shall maintain the same ingredients but may differ in their proportions. A deviation from the ingredients or proportions thereof exceeds the provisions allowed under a minor deviation and is not allowed under this Article.

(d) Equipment and supplies initially used for processing of blood components (included Red Blood Cells) shall be solely dedicated for processing of blood components. Equipment and supplies shall be thoroughly cleaned and disinfected, in accordance with section 1738.7, prior to initiation of the next patient's prescription.

(e) When processing blood components all garb must be removed and replaced for each patient.

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 4005, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

1738.11. COMPOUNDING

In addition to the requirements in the USP Chapter 825, the processing of radiopharmaceuticals shall comply with all of the requirements of this section.

(a) All compounding of radiopharmaceuticals shall comply with all radioactive materials licensing requirements for appropriate radiation safety considerations issued by the California Department of Public Health pursuant to section 30190 of Title 17 of the California Code of Regulations, another state licensing agency that issues specific radioactive materials licenses, or the United States Nuclear Regulatory Commission pursuant to pursuant to section 32.72 of title 10 of the Code of Federal Regulations, and utilize applicable environmental controls.

(b) Any active pharmaceutical ingredient (API) or added component used to compound a radiopharmaceutical shall be obtained from an FDA-registered facility and shall be accompanied by a valid certificate of analysis (COA). This COA shall be, at minimum, in English.

(c) Except for sterile radiopharmaceuticals made for inhalation or ophthalmic administration, prior to releasing a sterile radiopharmaceutical made from one or more nonsterile component(s) results of bacterial endotoxin testing shall be reviewed and recorded. Results shall be documented in the compounding record specified in Section 9.2 of the USP Chapter 825.

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 4005, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

1738.12. DISPENSING

In addition to the requirements in the USP Chapter 825, the processing of radiopharmaceuticals shall comply with all of the requirements of this section.

(a) All dispensed radiopharmaceutical doses shall be labeled with the information required by Business and Professions Code section 4076 and section 1707.5. Outer shielding labels shall contain the name and contact information of the dispensing pharmacy.

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 4005, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

1738.13. REPACKAGING

In addition to the requirements in the USP Chapter 825, the processing of radiopharmaceuticals shall comply with all of the requirements of this section.

(a) The inner container of a repackaged radiopharmaceutical shall be labeled with the following:
(1) Standard radiation symbol
(2) The words "Caution—Radioactive Material"
(3) The radionuclide and chemical form (generic name)
(4) Radioactivity with units at time of calibration and the calibration time

(b)The outer shielding of a repackaged radiopharmaceutical shall be labeled with the following:
(1) Standard radiation symbol
(2) The words "Caution—Radioactive Material"
(3) The radionuclide and chemical form (generic name)
(4) Radioactivity with units at time of calibration and the calibration time
(5) Volume, or number of units (e.g., capsules), as applicable
(6) Product expiration or BUD (consistent with Table 7 of USP Chapter 825), as applicable
(7) Special storage and handling instructions

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 4005, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

1738.14. QUALITY ASSURANCE AND QUALITY CONTROL

In addition to the requirements in the USP Chapter 825, the processing of radiopharmaceuticals shall comply with all of the requirements of this section.

(a) The quality assurance program shall comply with section 1711 and the standards contained in USP Chapter 1163, titled "Quality Assurance in Pharmaceutical Compounding". In addition, the program shall include a written procedure for any scheduled action, such as a recall, in the event that radiopharmaceutical processing is discovered to be outside the expected quality and purity of the radiopharmaceutical.

(b)The Board shall be notified in writing within 72 hours of a complaint or adverse drug event involving a radiopharmaceutical.

(c) All complaints related to a potential quality problem with a radiopharmaceutical and all adverse events shall be reviewed by the pharmacist-in-charge within 72 hours of receipt of the complaint or occurrence of the adverse event. Such review shall be documented and dated as defined in the SOPs.

(d) Failure to follow written SOPs shall constitute a basis for enforcement action.

Authority cited: Sections 4005, 4008 and 4008.2, Business and Professions Code. Reference: Sections 125.9, 4005, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

IX. Review and Discussion of Enforcement Statistics

Chairperson Serpa advised included in the meeting materials were enforcement statistics reflecting enforcement related activities between July 1 and December 31, 2022. Dr. Serpa summarized the Board received 1,839 complaints during this period and closed 1,459 investigations. The Board secured three (3) interim suspensions orders, two (2) automatic suspension orders and has been granted four (4) penal code 23 restriction.

Chairperson Serpa provided as of January 1, 2023, the Board had 1,450 field investigations pending. Dr. Serpa noted the average days for various stages of the investigation process were included in the meeting materials. Dr. Serpa noted there had been a large increase in the supervisor review time and second level review time. Dr. Serpa believed was in part due to a vacancy at the supervising inspector level. Dr. Serpa added the Committee should monitor for improvement in both areas. Dr. Serpa hoped that as the position was filled and onboarding completed, improvement will be seen.

Members were provided the opportunity to comment; however, no comments were made.

Members of the public were provided the opportunity to comment; however, no comments were made.

X. Future Committee Meeting Dates

Chairperson Serpa reminded the next meeting was scheduled for February 15, 2023, noting the meeting will be conducted in person, in Sacramento and members of the public were welcome to attend either in person or via WebEx. Dr. Serpa advised the Board respectfully requested that individuals attending in person follow COVID protocols.

XI. Adjournment

The meeting adjourned at 11:35 a.m.

Attachment 2

<795> FAQs

November 1, 2022

General

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

For FAQs on USP Compounding Standards, please see below:

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

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

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

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

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

Introduction and Scope

4. What is the definition of nonsterile compounding?

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

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

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

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

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

7. What does "official date" mean?

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

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

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

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

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

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

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

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

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

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

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

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

13. Does the chapter address compounded radiopharmaceutical dosage forms?

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

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

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

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

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

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

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

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

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

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

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

19. Please clarify the phrase, "variability from the intended strength of correct ingredients (e.g., ±10% of the labeled strength)".

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

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

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

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

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

Personal Hygiene and Garbing

22. What garb is required for nonsterile compounding?

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

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

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

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

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

Buildings and Facilities

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

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

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

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

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

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

Cleaning and Sanitizing

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

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

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

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

30. What is the difference between cleaning and sanitizing?

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

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

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

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

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

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

Equipment and Components

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

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

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

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

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

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

36. When is the use of distilled water acceptable?

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

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

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

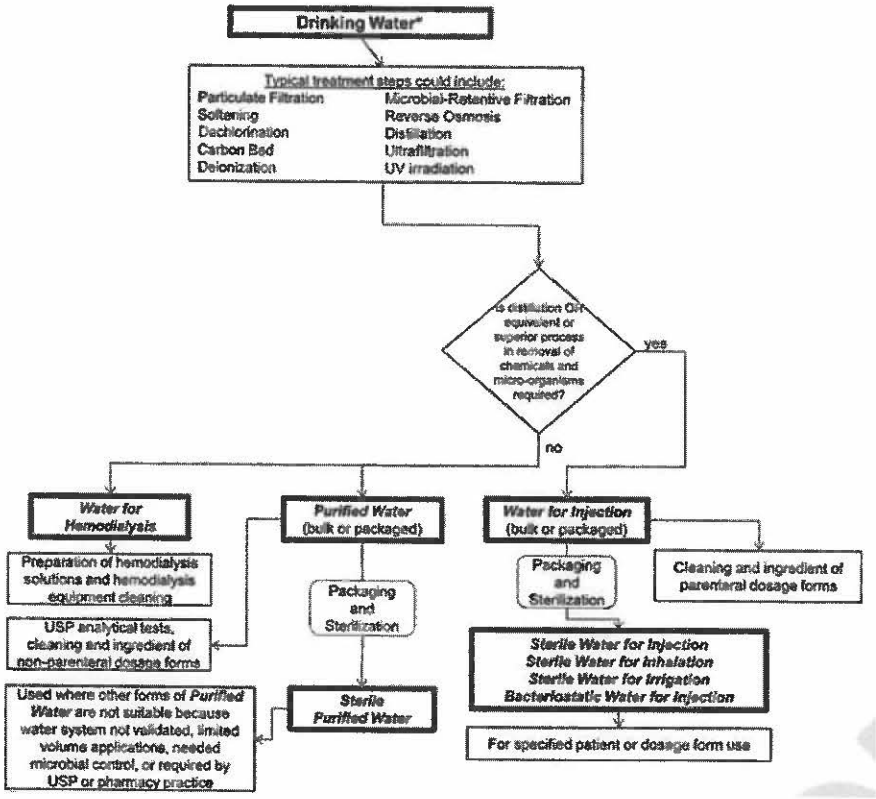
38. Our Board of Pharmacy inspector is questioning our use of *Sterile Water for Irrigation* in place of *Purified Water* in CNSPs. Does USP reference this in other general chapters?

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

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

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

Per <1231>



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

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

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

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

42. What organizations certify BSCs or CVEs?

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

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

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

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

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

Master Formulation and Compounding Records

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

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

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

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

Labeling

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

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

Establishing Beyond-Use Dates

47. What is water activity (a_w)?

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

60. When must <51> testing be performed?

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

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

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

62. Can unpublished antimicrobial effectiveness testing results be used?

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

<795>: Adding Flavor to Conventionally Manufactured Nonsterile Products

November 1, 2022

Disclaimer: This document is intended to be a resource regarding adding flavor to conventionally manufactured nonsterile products. This informational document is intended to supplement *USP* General Chapter <795> *Pharmaceutical Compounding – Nonsterile Preparations*. This supplemental document is not part of the chapter, is not a comprehensive overview of the chapter, and is not intended to be used in place of the chapter. This document is not official *United States Pharmacopeia – National Formulary* (*USP–NF*) text and is not intended to be enforceable by regulatory authorities. Users must refer to the *USP–NF* for official text.

Questions may be sent to CompoundingSL@USP.org.

Background and Introduction

USP General Chapter <795> *Pharmaceutical Compounding — Nonsterile Preparations* provides official standards for compounding quality nonsterile preparations. Nonsterile compounding is defined as combining, admixing, diluting, pooling, reconstituting other than as provided in the manufacturer's labeling, or otherwise altering a drug product or bulk drug substance to create a nonsterile preparation.

Adding components (such as flavors) not stipulated in the labeling to conventionally manufactured products is compounding as defined in <795> and has been within the scope of <795> since the chapter was first published in 2004. Flavors are organic chemicals with reactive functional groups including acids, alcohols, aldehydes, amides, amines, esters, ketones, and lactams. The effect of adding these substances, even in very small quantities or concentrations, to conventionally manufactured products is unpredictable due to the potential for a variety of chemical reactions.

Adoption of USP standards in compounding and ensuring compliance with the requirements of these standards is the responsibility of the applicable regulatory jurisdiction. USP has no role in enforcement.

Assigning Beyond-Use Dates (BUDs)

BUD limits in <795> are based on the ability of a preparation to maintain chemical and physical stability and to suppress microbial growth. In the absence of stability data, BUDs must not exceed any of the following: manufacturers' recommendations, expiration date(s) of component(s), and BUD limits in <795>. In addition to stability data, aqueous preparations require passing antimicrobial effectiveness testing (see *Antimicrobial Effectiveness* Testing <51>) to extend BUDs beyond <795> BUD limits.

Table 1. BUD Limit by Type of Preparation in the Absence of a *USP–NF* Compounded Preparation Monograph or CNSP-Specific Stability Information[a]

Type of Preparation	BUD (days)	Storage Temperature[b]
Aqueous Dosage Forms ($a_w \geq 0.60$)		
Nonpreserved aqueous dosage forms[c]	14	Refrigerator
Preserved aqueous dosage forms[c]	35	Controlled room temperature or refrigerator
Nonaqueous Dosage Forms ($a_w < 0.60$)		
Oral liquids (nonaqueous)[d]	90	Controlled room temperature or refrigerator
Other nonaqueous dosage forms[e]	180	Controlled room temperature or refrigerator

[a] A shorter BUD must be assigned when the physical and chemical stability of the CNSP is less than the BUD limit stated in the table (see *10.4 CNSPs Requiring Shorter BUDs*).
[b] See *Packaging and Storage Requirements* <659>.
[c] An aqueous preparation is one that has an $a_w \geq 0.6$ (e.g., emulsions, gels, creams, solutions, sprays, or suspensions).
[d] A nonaqueous oral liquid is one that has an $a_w < 0.6$.
[e] Other nonaqueous dosage forms that have an $a_w < 0.6$ (e.g., capsules, tablets, granules, powders, nonaqueous topicals, suppositories, and troches or lozenges).

Documentation Requirements

Documentation may be written or electronic and must include:

- **SOPs** on each aspect of the compounding operation, QA and QC programs, and identity of designated person(s)
- **Personnel Training and Competency Assessments** as applicable to assigned tasks
- **Master Formulation Record** for each unique formulation
- **Compounding Record** each time a preparation is compounded
- **Component** receipt
- **Temperature** monitoring of storage area(s)
- **Cleaning and Sanitizing** logs

Summary

Following the requirements in <795> when compounding, including when adding flavor to conventionally manufactured nonsterile products, will help to minimize harm to patients that could result from 1) excessive microbial contamination, 2) variability from the intended strength of correct ingredients (e.g., ±10% of the labeled strength), 3) physical and chemical incompatibilities, 4) chemical and physical contaminants, and/or 5) use of ingredients of substandard quality.

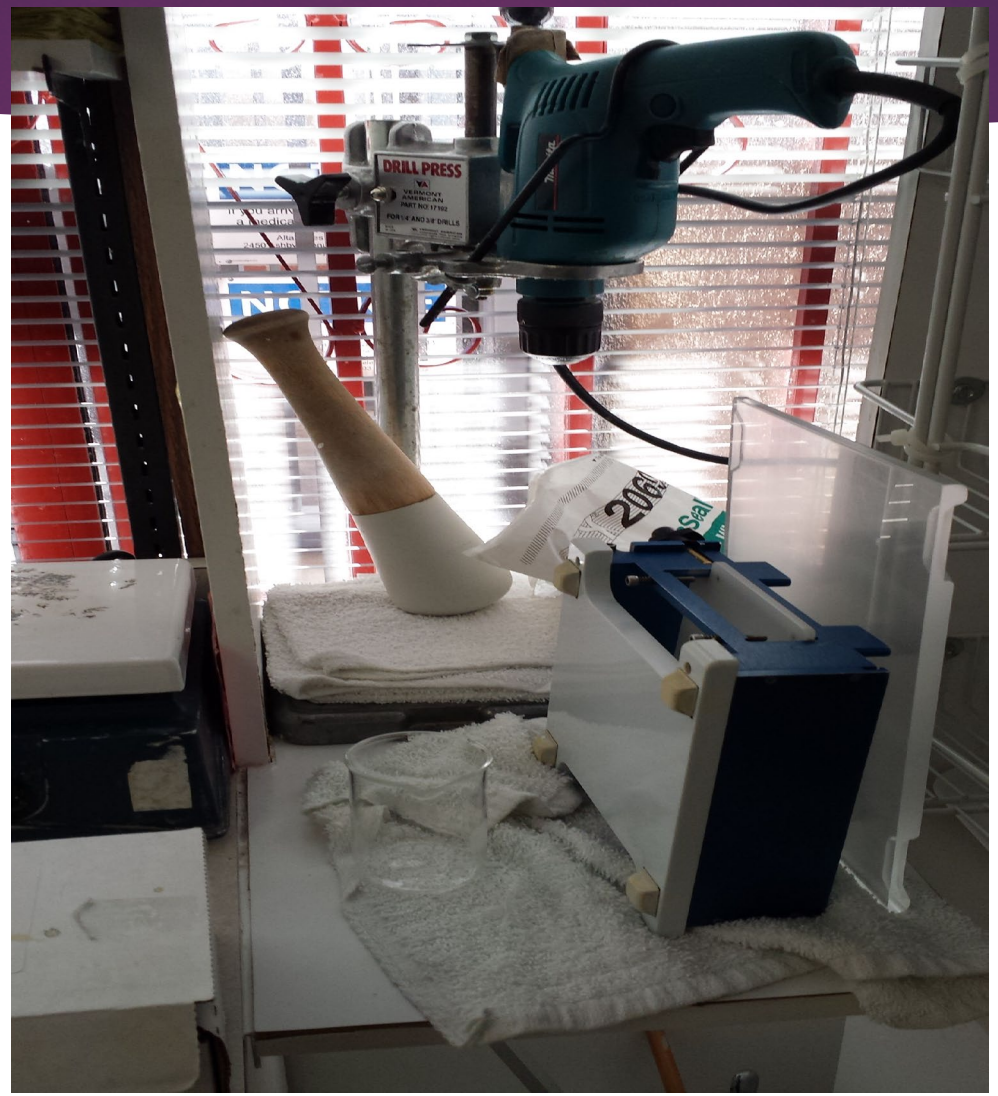
Please refer to <795> *Pharmaceutical Compounding — Nonsterile Preparations* for complete requirements. Questions may be sent to CompoundingSL@USP.org.

November 1, 2022

Inspector Staff Training
FINAL USP <795>

BY: SUPERVISING INSPECTOR PEG PANELLA-SPANGLER FEBRUARY 15, 2023

Why USP Chapter 795 and Regulations



Why USP Chapter 795 and Regulations

Why USP Chapter 795 and Regulations

Overview: Sections

1) INTRODUCTION AND SCOPE
2) PERSONNEL TRAINING AND EVALUATION
3) PERSONAL HYGIENE AND GARBING
4) BUILDINGS AND FACILITIES
5) CLEANING AND SANITIZING
6) EQUIPMENT AND COMPONENTS
7) MASTER FORMULATION AND COMPOUNDING RECORDS
8) RELEASE INSPECTIONS AND TESTING
9) LABELING
10) ESTABLISHING BEYOND-USE DATES (BUD)
11) SOPS
12) QUALITY ASSURANCE AND QUALITY CONTROL
13) CNSP PACKAGING AND TRANSPORTING
14) DOCUMENTATION

Section 1. Introduction And Scope

- Scope Added information on types of Compounded Nonsterile Preparations (CNSP) for humans and animals
- Removed handling of hazardous drugs and added references to General Chapter <800> Hazardous Drugs – Handling in Healthcare Settings.
- Affected Personnel and Settings Added roles and responsibility of the designated person
  - Designated person (DP) = one or more individual responsible and accountable for the performance and operation of the facility and personnel: Must have an SOP describing
  - All places where CNSPS are prepared, not limited to pharmacies

Section 2. Personnel Training and Evaluation

- All personnel who compound or have direct oversight must be trained, demonstrate knowledge and competency prior to performing independently, and must undergo annual refresher training.
- Designated person is responsible for implementing a training program and evaluating competency. This must be documented and retained.
  - Should monitor and observe compounding activities
  - Must take immediate corrective action if deficient practices are observed as described in SOPs
  - The designated person or an assigned trainer may perform training and observation
  - Upon completion of training, the designated person or trainer must document successful completion of training and competency assessments
  - Sole compounders must document training and demonstrate competency

Section 2. Personnel Training and Evaluation

- Proficiency must be demonstrated in at least the following core competencies:
  - Hand hygiene
  - Garbing
  - *Cleaning and sanitizing*
  - *Component selection, handling, and transport*
  - *Performing calculations*
  - *Measuring and mixing*
  - *Proper use of equipment and devices selected to compound CNSPs*
  - *Documentation of the compounding process (e.g., Master Formulation Records and Compounding Records)*

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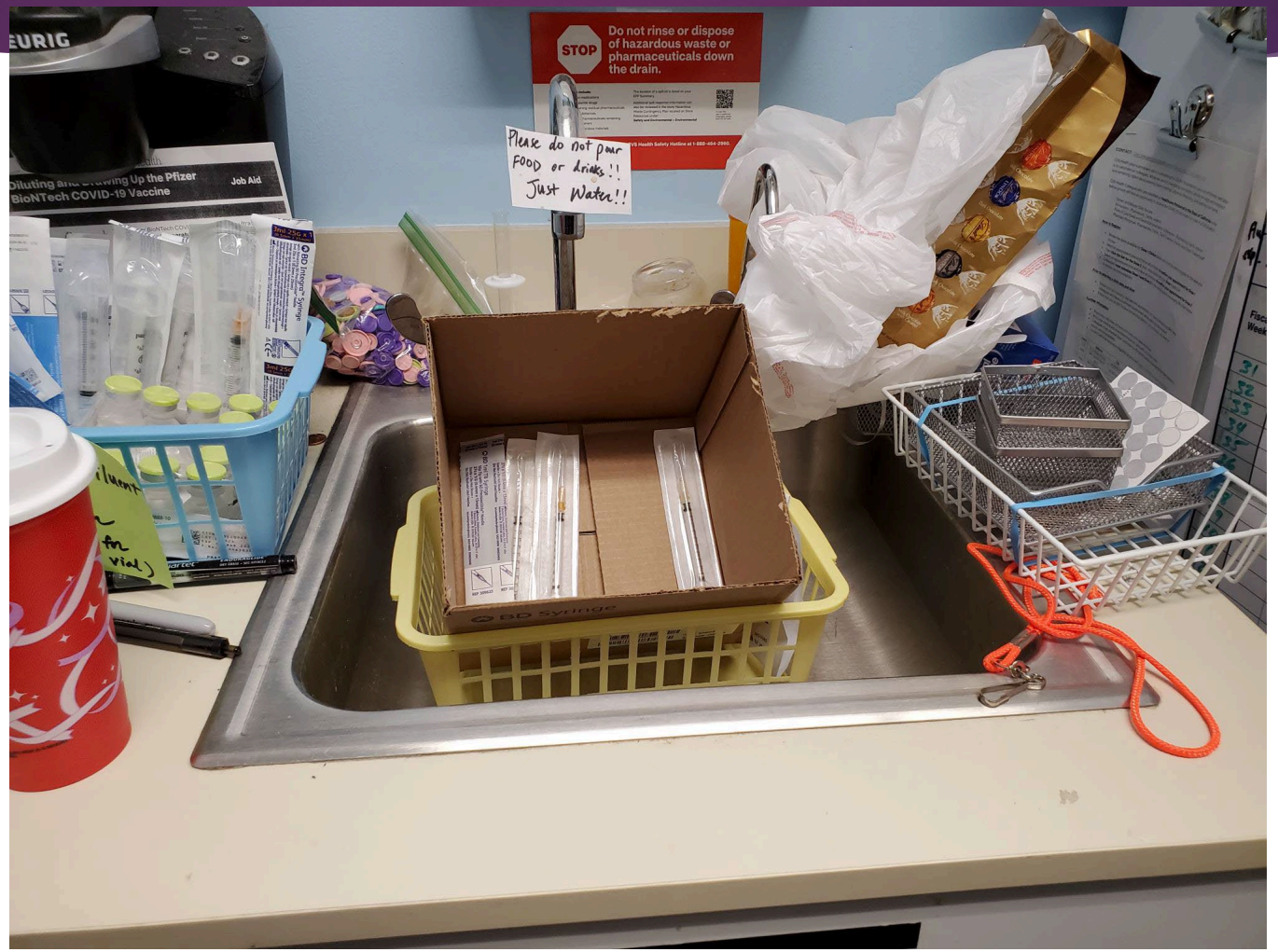

Why USP Chapter 795 and Regulations

Section 3. Personal Hygiene And Garbing

- Compounding personnel must maintain appropriate personal hygiene, evaluate risk of potential contaminating conditions and report to the DP, who will evaluate if the personnel should be excluded from compounding
- Before entering a designated compounding area, compounding staff must remove any items that are not easily cleanable and that might interfere with garbing. At a minimum, personnel must:
  - Remove personal outer garments
  - Remove all hand, wrist, and other exposed jewelry or piercing that can interfere with the effectiveness of the garb or hand hygiene
  - Remove headphones and earphones
  - The designated person may permit accommodations provided the quality of the environment and the CNS will not be affected.

Section 3. Personal Hygiene And Garbing

- Hand Hygiene, the use of alcohol-based hand rub alone is not sufficient
  - Wash hands with soap and water for at least 30 seconds
  - Dry hands with disposable towels or wipers
  - Allow hands and forearms to dry thoroughly before donning gloves
- Gloves must be inspected for punctures tears or holes and replaced
- Gloves should be wiped or replaced before beginning a CNSP with different components

Section 3. Personal Hygiene And Garbing

- Other garb requirements are determined by the facility. It should be worn as needed to protect personnel or prevent contamination
  - Garb must be stored to prevent contamination (e.g., away from sinks to avoid splashing onto garb).
  - Visibly soiled garb or garb with tears or punctures must be changed immediately
  - May reuse gown for one shift if not soiled and retained in the compounding area.
  - Gloves, shoe covers, hair covers, facial hair covers, face masks, or head coverings, may not be reused and must be replaced with new ones
  - Non-disposable garb such as goggles should be cleaned with 70% IPA before re-use

Why USP Chapter 795 and Regulations

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Section 4. Buildings And Facilities

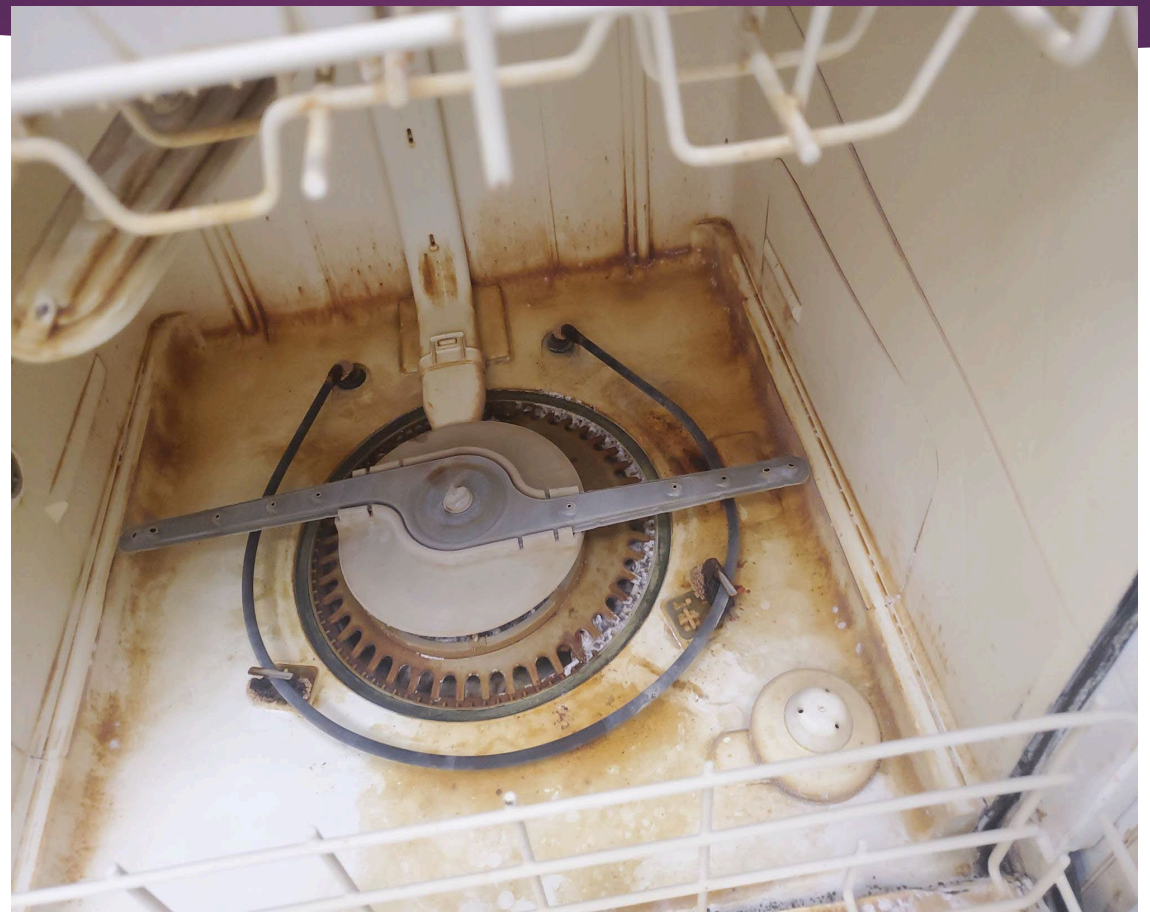
- Designated compounding area is required:
  - Be specifically designated for non-sterile compounding (SOP, LOD).
  - Cannot be used for other activities during nonsterile compounding
  - Areas used to compound hazardous CNSPs must not be used for compounding nonhazardous CNSPs.
  - Have surfaces resistant to damage from cleaners and sanitizing agents and arranged in a way to prevent cross contamination form other areas.
  - Should not be carpeted.
  - Maintained in a clean, orderly, and sanitary condition, and in a good state of repair.

Section 4. Buildings And Facilities

- Facilities:
  - A source of hot and cold water and an easily accessible sink must be available for compounding.
    - The plumbing system must be free of defects.
    - Should use purified water, distilled water or RO water to rinse equipment and utensils
  - All components, equipment, and containers must be stored off the floor and in a manner that will prevent contamination and permit inspection and cleaning of the compounding and storage area.
  - Storage area temperature must be monitored daily when open and results must be store or logged and retrievable.

Why USP Chapter 795 and Regulations

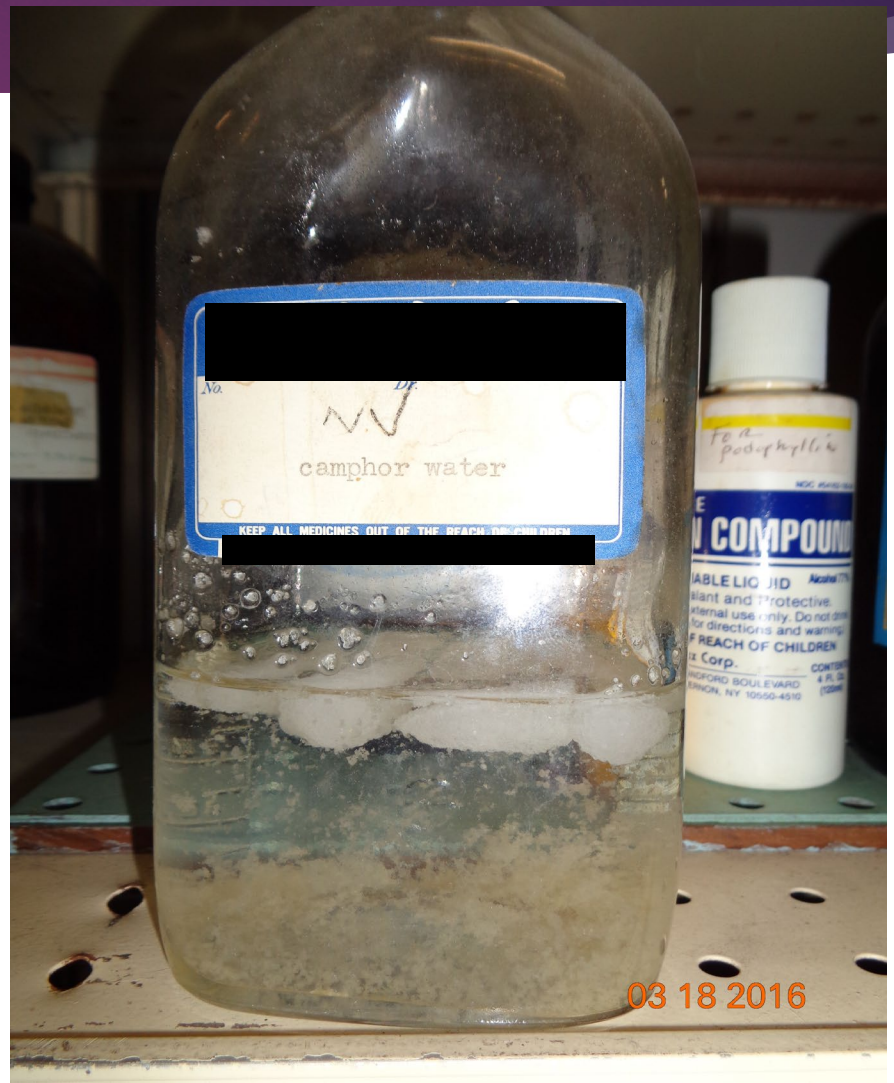
Why USP Chapter 795 and Regulations



Section 5. Cleaning And Sanitizing

- **Cleaning and Sanitizing**
- All surfaces must be cleaned and sanitized:
  - On a regular basis and as specified in the chapter
  - Before compounding if compounding does not occur daily
  - After a spill or if visibly soiled
- When cleaning and sanitizing are separate steps, cleaning comes first
- Effectiveness, compatibility and residue must be considered when selecting agents
- Both cleaning and sanitizing must be documented.

Why USP Chapter 795 and Regulations



Why USP Chapter 795 and Regulations

Why USP Chapter 795 and Regulations

Why USP Chapter 795 and Regulations

Section 6. Equipment, Supplies And Components

- **Equipment and Supplies**
  - Must be suitable for the type of compounding process
  - Must be stored in a manner to minimize the risk of contamination
  - Must be located to facilitate their use, maintenance and cleaning
  - Must be cleaned after compounding
  - Maybe dedicated or disposable
  - Must be inspected prior to use
    - If appropriate verify for accuracy as recommended by the manufacturer or at least every 12 months, whichever is more frequent
- Surfaces that contact components must not
  - Be reactive, additive or sorptive
  - Alter the quality of the CNSP

Section 6. Equipment, Supplies And Components

- If weighing, measuring or manipulating components which may become airborne, you must evaluate if a closed system measuring device is required
- Closed system measuring devices include
  - Biological Safety Cabinets (BSC)
  - Containment ventilated enclosures
- BSCs and CVEs must be
  - Certified every 12 months or/and directed by the manufacturer and all applicable laws and regulations

Section 6. Equipment, Supplies And Components

- **Component Selection**
  - Active Pharmaceutical Ingredients (APIs)
    - Must comply with the USP-NF Monograph if there is one
    - Certificate of Analysis must show compliance with specifications
  - For compounding in the US, must be sourced from an FDA registered facility
  - For compounding outside the US, must be sourced from a facility which complies with local laws and regulations

- **Active pharmaceutical ingredient (API):** Any substance or mixture of substances intended to be used in the compounding of a preparation, thereby becoming the active ingredient in that preparation and furnishing pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease in humans and animals or affecting the structure and function of the body.

Section 6. Equipment, Supplies And Components

- **All components other than the APIs**
  - Should have a COA which verifies it meets the USP-NF monograph and any additional specifications
- Compounding in the US
  - Should be manufactured by an FDA registered facility
  - If it cannot be obtained from an FDA facility, the designated person must select a suitable component for the intended use
- For compounding outside the US, must comply with the local laws and regulations

Section 7. Master Formulation And Compounding Records

- **Master Formulation Records (MFR)**
  - A MFR must be created for each unique formulation of a CNSP
  - Any changes or alterations to the MFR must be approved and documented according to the facilities SOPs
  - CNSPs must be prepared according to the MFR
  - The preparation information is documented on a compounding record (CR)

Section 7. Master Formulation And Compounding Records

- **Master Formulation record include at least the following:**
  - Name, strength or activity, and dosage form of the CNSP
  - Identities and amounts of all components; if applicable, relevant characteristics of components (e.g., particle size, salt form, purity grade, solubility)
  - Container closure system(s)
  - Complete instructions for preparing the CNSP including equipment, supplies, and description of compounding steps
  - Physical description of the final CNSP
  - Beyond-use date (BUD) and storage requirements

Section 7. Master Formulation And Compounding Records

- **Master Formulation record must include at least the following:**
  - Reference source to support the assigned BUD
  - If applicable, calculations to determine and verify quantities and/or concentrations of components and strength or activity of the API(s)
  - Labeling requirements (e.g., shake well)
  - Quality control (QC) procedures (e.g., pH testing, visual inspection) and expected results
  - Other information needed to describe the compounding process and ensure repeatability (e.g., adjusting pH, temperature)

Section 7. Master Formulation And Compounding Records

- **A Compounding Record must:**
  - Be created for all CNSPs
  - Be reviewed for completeness before the CNSP is release
  - Name or other unique identifier of person completing the review and date of the review
  - Permit traceability of all components in case of a recall or quality issue
- A MFR may be used as the basis for a compounding record

Section 7. Master Formulation And Compounding Records

- **A CR must include at least the following:**
  - Name, strength or activity, and dosage form of the CNSP
  - Date—or date and time—of preparation of the CNSP
  - Assigned internal identification number (e.g., prescription, order, or lot number)
  - A method to identify the individuals involved in the compounding process and individuals verifying the final CNSP
  - Name, vendor or manufacturer, lot number, and expiration date of each component

Section 7. Master Formulation And Compounding Records

- **A CR must include at least the following:**
  - Weight or measurement of each component
  - Total quantity of the CNSP compounded
  - Assigned beyond-use date (BUD) and storage requirements
  - If applicable, calculations to determine and verify quantities and/or concentrations of components and strength or activity of the API(s)
  - Physical description of the final CNSP
  - Results of quality control procedures (e.g., pH testing and visual inspection)
  - MFR reference for the CNSP

Section 8. Release Inspections and Testing

- Elements of release inspection must include:
  - Physical appearance is as expected.
    - Checked for certain characteristics (e.g., emulsions must be checked for phase separation
  - CNSP and labeling match compounding records
  - Inspection of container–closure integrity (e.g., checking for leakage, cracks in the container, or improper seals)
- All checks and inspections, and any other tests necessary to ensure the quality of the CNSP (e.g., pH, assays), must be detailed in the facility's SOPs and the MFR and completed before release, and documented as completed.
- Defective CNSPS must be immediately discarded or marked and segregated to prevent release or dispensing

Why USP Chapter 795 and Regulations

Section 9. Labeling

- **Label: A display of written, printed, or graphic matter on the immediate container of any article and must contain.**
  - Assigned internal identification number (e.g., prescription, barcode or lot number)
  - Chemical and/or generic name(s), or active ingredient(s), and amounts or concentrations
  - Dosage form
  - Total amount or volume
  - Storage conditions
  - BUD, the date, or the hour beyond which the preparation cannot be used and must be discarded

Section 9. Labeling

- **Labeling on the CNSP should display:**
  - Route of administration
  - Indication that the preparation is compounded
  - Any special handling instructions
  - Any warning statements that are applicable
  - Name and contact information of the compounding facility if the CNSP is to be sent outside of the facility or healthcare system in which it was compounded

Section 10. Establishing Beyond-Use Dates

- Expiration Date = applies to conventionally manufactured drug products
- Beyond use date (BUD) = the date or time beyond which a CNSP must be discarded (not used). The date or time is determined from the date or time when the preparation was compounded.
- Parameters to consider when establishing a BUD
  - Chemical and physical stability of the API and other added components
  - Compatibility of container-closure system
  - Degradation of container-closure system
  - Potential for microbial proliferation
- If there is a *USP–NF* compounded preparation monograph for the CNSP, the BUD specified in the monograph must be used, unless a shorter BUD is required.

Section 10. Establishing Beyond-Use Dates

- Maximum BUD by Type of Preparation in the **absence** of CNSP-Specific Stability Information.
- Must be in a packaged in tight, light-resistant containers.

Type of Preparation	BUDs	Storage Temperature
Solid dosage forms (Capsules, tablets, granules, powders)	180d	Controlled room temperature
Preserved aqueous dosage forms	35d	Controlled room temperature
Non-preserved aqueous dosage Aw > 0.6 (emulsions, gels, creams, solutions, sprays, or suspensions)	14d	Refrigerator
Nonaqueous dosage forms Aw ≤ 0.6 (suppositories, ointments, fixed oils, or waxes)	90d	Controlled room temperature

Aw= water activity

Section 10. Establishing Beyond-Use Dates

- Extension of the BUD:
  - Max 180 day with a stability study (published or unpublished) using a stability-indicating assay for the specific API, CNSP, and container–closure that will be used
  - Aqueous CNSP must first be tested for antimicrobial effectiveness at the end of the proposed BUD
- CNSPs requiring a shorter BUD:
  - Cannot be extended past the expiration date or BUD of any component in the CNSP
  - APIs or ingredients known to be susceptible to decomposition

Why USP Chapter 795 and Regulations

Section 11: Standard Operating Procedures

- Facilities preparing CNSPs must:
  - Develop SOPs on all aspects of the compounding operation
- All personnel who conduct or oversee compounding
  - Must be trained on the facility's SOPs
  - Are responsible for ensuring that facility SOPs are followed
- One or more persons must be designated to ensure SOPS are fully implemented
- The designated person(s) must ensure follow-up occurs if problems, deviations or errors are identified

Why USP Chapter 795 and Regulations

Section 12. Quality Assurance and Quality Control

- Quality assurance (QA): A system of procedures, activities and oversight which ensures the compounding process consistently meets quality standards
- Quality control (QC): The sampling, testing, and documentation of results that, taken together, ensure that specifications have been met before release of the CNSP.
- Must have a formal, written QA and QC program that establishes a system of adherence to procedures, prevention and detection of errors and other quality problems, and appropriate corrective actions when needed. The SOPs must describe the roles, duties and training of the personnel responsible for each aspect of the QA Program.
- The overall QA and QC program must be reviewed at least once every 12 months by the designated person, results of review must be documented, and action taken as necessary

Section 12. Quality Assurance and Quality Control

Notification About and Recall of Dispensed CNSPs

- Facility must have an SOP and procedures in place to
  - Determine when a recall must be initiated, investigate and document the reason
  - Recall any unused product and quarantine remaining stock
  - Investigate if other lots are affected and recall if necessary
  - Determine the severity of the problem and urgency for implementation
  - Determine the distribution of any affected CNSP
  - Identify patients who have received the CNSP
  - Report the recall to the appropriate regulatory bodies as required

Section 12. Quality Assurance and Quality Control

- **Complaint Handling and Adverse Event Reporting**
  - Facilities must develop and implement SOPs for receiving, acknowledging and handling complaints and adverse event reports
  - Must designate one or more persons to be responsible for handling complaints and adverse event reports
  - Adverse events must be reported in accordance with the facilities SOPs and all laws and regulations. If there is suspected patient harm, the patients and providers potentially affect must be informed.
  - Complaints may include:
    - Concerns or reports on the quality and labeling of a CNSP
    - Possible adverse reactions to a CNSP

Section 12. Quality Assurance and Quality Control

- **Complaint Handling**
- The designated person must ensure that each complaint is reviewed to determine if a complaint indicates a potential quality problem
  - Must initiate and complete a thorough investigation into the cause of a quality problem
  - Must consider whether the quality problem extends to other CNSPs
  - Must implement corrective action, if necessary, for all potentially affected CNSPs
- Consider whether to
  - Initiate a recall of affected/potentially affected CNSPs
  - Cease non-sterile compounding under all underlying problems have been corrected

Section 13: CNSP Packaging and Transporting

Packaging and Transporting of CNSPS:

- Personnel should select and use packaging materials that will maintain the physical and chemical integrity and stability of the CNSPs
- SOPs must describe the packaging of CNSPs
- Packaging materials must simultaneously protect:
  - CNSPS from damage, leakage, contamination and degradation
  - Personnel from exposure
- If transporting CNSPs, the facility must have SOPs that describe:
  - The mode of transportation
  - Any special handling instructions
  - Whether temperature monitoring devices are needed

Section 14. Documentation

- All facilities where CNSPs are prepared must have and maintain written or electronic documentation to demonstrate compliance with this chapter.
- Must include, but is not limited to, the following:
  - Personnel training, competency assessment, and qualification records including corrective actions for any failures
  - Equipment records (e.g., calibration, verification, and maintenance reports)
  - Receipt of components
  - SOPs, Master Formulation Records, and Compounding Records
  - Release testing, including corrective actions for any failures
  - Results of investigations and corrective actions

Section 14. Documentation

- **Documentation required cont'd:**
  - Records of cleaning and sanitizing the designated area
  - Temperature logs
  - Accommodations to personnel compounding CNSPs
  - Information related to complaints and adverse events including corrective actions taken
  - Any required routine review (e.g., yearly review of QA/Q, yearly review of chemical hazard and disposal information)
- Records must be legible and stored in a manner that prevents their deterioration and/or loss
- All required CR for a particular CNSP must be readily retrievable for at least 2 years after preparation or as required by applicable regulatory bodies.

Questions?

Attachment 3

Title 16. Board of Pharmacy
Proposed Regulation

Proposed changes to the current regulation language are shown by ~~strikethrough~~ for deleted language and underline for added language.

Amend title of Article 4.5 and Repeal sections 1735, 1735.1, 1735.3, 1735.4, 1735.5, 1735.6, 1735.7, and 1735.8 of Article 4.5, adopt a new title for and amend section 1735.2, adopt new titles and sections 1735, 1735.1, 1735.3, 1735.4, 1735.5, 1735.6, 1735.7, 1735.8, 1735.9, 1735.10, 1735.11, 1735.12, 1735.13, and 1735.14 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

Article 4.5 Nonsterile Compounding ~~in Pharmacies~~

~~**1735. Compounding in Licensed Pharmacies**~~

~~(a) "Compounding" means any of the following activities occurring in a licensed pharmacy, by or under the supervision of a licensed pharmacist, pursuant to a prescription:~~

~~(1) Altering the dosage form or delivery system of a drug~~
~~(2) Altering the strength of a drug~~
~~(3) Combining components or active ingredients~~
~~(4) Preparing a compounded drug preparation from chemicals or bulk drug substances~~

~~(b) "Compounding" does not include reconstitution of a drug pursuant to a manufacturer's direction(s), nor does it include the sole act of tablet splitting or crushing, capsule opening, or the addition of flavoring agent(s) to enhance palatability.~~

~~(c) The parameters and requirements stated by Article 4.5 (Section 1735 et seq.) apply to all compounding practices. Additional parameters and requirements applicable solely to sterile compounding are stated by Article 7 (Section 1751 et seq.).~~
~~Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.~~

1735. Compounding Definitions.

In addition to the definitions contained in United States Pharmacopeia (USP) General Chapter 795 titled *Pharmaceutical Compounding – Nonsterile Preparations* "USP Chapter 795" for the purposes of this article, the following definitions apply to this article and supplement the definitions provided in USP Chapter 795.

(a) "Approved labeling" means the Food and Drug Administration's (FDA) approved labeling in accordance with sections 201.56 and 201.57 of title 21, Code of Federal Regulations that contains FDA approved information for the diluent, the resultant strength, the container closure system, and storage time.

(b) "Essentially a copy of a commercially available drug product" means all preparations that are comparable in active ingredients to commercially available drug products, except that it does not include any preparations in which there has been a change, made for an identified individual patient, which produces for that patient a clinically significant difference, as determined by a prescribing practitioner, between that compounded preparation and the comparable commercially available drug product.

(c) Designated person(s) means one or more individuals assigned by the pharmacist-in-charge to be responsible and accountable for the performance and operation of the facility and personnel as related to the preparation of the compounded nonsterile preparations ("CNSP" for the purposes of this article). Nothing in this definition allows for the designated person to exceed the scope of their issued license. When the designated person is not the pharmacist, the Pharmacist-in-Charge (PIC) must review all practices related to the operations of the facility that require professional judgement.

(c) "Diluent" means a liquid with no pharmacological activity used in reconstitution, such as water or sterile water for injection.

(d) "Integrity" means retention of strength until the beyond use date provided on the label when the preparation is stored and handled according to the label directions.

(e) "Product" means a commercially or conventionally manufactured product evaluated for safety and efficacy by the FDA in accordance with the Federal Food Drug and Cosmetic Act.

(f) "Quality" means the absence of harmful levels of contaminants, including filth, putrid, or decomposed substances, or the absence of active ingredients other than those listed on the label, or the absence of inactive ingredients other than those listed on the master formulation record as specified in USP Chapter 795.

(g) "Repackaging" means the act of removing a product or preparation from its original primary container and placing it into another primary container, usually of smaller size without further manipulation, when the act is not done pursuant to a prescription.

(i) "Strength" means amount of active ingredient per unit of a compounded drug preparation.

Note: Authority cited: Sections 4001.1, 4005, 4057, 4126.8 of Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, 4057, 4076, 4081, 4126.8 and 4169, 4301 and 4332 of the Business and Profession Code.

~~**1735.1. Compounding Definitions**~~

~~(a) "Ante-area" means an area with ISO Class 8 or better air quality where personnel hand hygiene and garbing procedures, staging of components, and other high particulate-generating activities are performed, that is adjacent to the area designated for sterile compounding. It is a transition area that begins the systematic reduction of particles, prevents large fluctuations in air temperature and pressures in the cleanroom, and maintains air flows from clean to dirty areas. ISO Class 7 or better air quality is required for ante-areas providing air to a negative pressure room.~~

(b) "Beyond use date" means the date, or date and time, after which administration of a compounded drug preparation shall not begin, the preparation shall not be dispensed, and the preparation shall not be stored (other than for quarantine purposes).

(c) "Biological Safety Cabinet (BSC)" means a ventilated cabinet for compounding sterile drug preparations, having an open front with inward airflow for personnel protection, downward HEPA-filtered laminar airflow for product protection, and HEPA-filtered exhausted air for environmental protection. Where hazardous drugs are prepared, the exhaust air from the biological safety cabinet shall be appropriately removed by properly designed external building exhausting. This external exhaust should be dedicated to one BSC or CACI.

d) "Bulk drug substance" means any substance that, when used in the preparation of a compounded drug preparation, processing, or packaging of a drug, is an active ingredient or a finished dosage form of the drug, but the term does not include any intermediate used in the synthesis of such substances.

e) "Cleanroom or clean area or buffer area" means a room or area with HEPA-filtered air that provides ISO Class 7 or better air quality where the primary engineering control (PEC) is physically located.

1) For nonhazardous compounding a positive pressure differential of 0.02 to 0.05 inch water column relative to all adjacent spaces is required.
2) For hazardous compounding at least 30 air changes per hour of HEPA-filtered supply air and a negative pressure of between 0.01 to 0.03 inches of water column relative to all adjacent spaces is required.

(f) "Compounding Aseptic Containment Isolator (CACI)" means a unidirectional HEPA-filtered airflow compounding aseptic isolator (CAI) designed to provide worker protection from exposure to undesirable levels of airborne drug throughout the compounding and material transfer processes and to provide an aseptic environment for compounding sterile preparations. Air exchange with the surrounding environment should not occur unless the air is first passed through a microbial retentive filter (HEPA minimum) system capable of containing airborne concentrations of the physical size and state of the drug being compounded. Where hazardous drugs are prepared, the exhaust air from the isolator shall be appropriately removed by properly designed external building exhaust. This external exhaust should be dedicated to one BSC or CACI. Air within the CACI shall not be recirculated nor turbulent.

(g) "Compounding Aseptic Isolator (CAI)" means a form of isolator specifically designed for nonhazardous compounding of pharmaceutical ingredients or preparations while bathed with unidirectional HEPA-filtered air. It is designed to maintain an aseptic compounding environment within the isolator throughout the compounding and material transfer processes. Air exchange into the isolator from the surrounding environment should not occur unless the air has first passed through a microbial retentive filter (HEPA minimum) system capable of containing airborne concentrations of the physical size and state of the drug being compounded. Air within the CAI shall not be recirculated nor turbulent.

h) "Controlled cold temperature" means 2 degrees to 8 degrees C (35 degrees to 46 degrees F).

(i) "Controlled freezer temperature" means -25 degrees to -10 degrees C (-13 degrees to 14 degrees F) or at a range otherwise specified by the pharmaceutical manufacturer(s) for that product.

(j) "Controlled room temperature" means 20 degrees to 25 degrees C (68 degrees to 77 degrees F).

(k) "Copy or essentially a copy" of a commercially available drug product includes all preparations that are comparable in active ingredients to commercially available drug products, except that it does not include any preparations in which there has been a change, made for an identified individual patient, which produces for that patient a clinically significant difference, as determined by a prescribing practitioner, between that compounded preparation and the comparable commercially available drug product.

(l) "Daily" means occurring every day the pharmacy is operating, except when daily monitoring of refrigerator and freezer temperature are required, then daily means every 24 hours.

m) "Displacement airflow method" means a concept which utilizes a low pressure differential high airflow principle to maintain segregation from the adjacent ante-area by means of specific pressure differentials. This principle of displacement airflow shall require an air velocity of 40 ft per minute or more, from floor to ceiling and wall to wall, from the clean area across the line of demarcation into the ante-area. The displacement concept may not be used to maintain clean area requirements for sterile compounds which originate from any ingredient that was at any time non-sterile, regardless of intervening sterilization of the ingredient, or for hazardous compounds.

(n) "Dosage unit" means a quantity sufficient for one administration to one patient.

(o) "Equipment" means items that must be calibrated, maintained or periodically certified.

p) "First air" means the air exiting the HEPA filter in a unidirectional air stream that is essentially particle free.

(q) "Gloved fingertip sampling" means a process whereby compounding personnel lightly press each fingertip and thumb of each hand onto appropriate growth media, which are then incubated at a temperature and for a time period conducive to multiplication of microorganisms, and then examined for growth of microorganisms.

r) "Hazardous" means all anti-neoplastic agents identified by the National Institute for Occupational Safety and Health (NIOSH) as meeting the criteria for a hazardous drug and any other drugs, compounds, or materials identified as hazardous by the pharmacist-in-charge.

(s) "Integrity" means retention of potency until the beyond-use date provided on the label, so long as the preparation is stored and handled according to the label directions.

(t) "Lot" means one or more compounded drug preparation(s) prepared during one uninterrupted continuous cycle of compounding from one or more common active ingredient(s).

(u) "Media-fill test" means a test used to measure the efficacy of compounding personnel in aseptic techniques whereby compounding procedures are mimicked using a growth-based media and then the resulting preparation is evaluated for sterility. The media-fill test must mimic the most complex compounding procedures performed by the pharmacy.

(v) "Non-sterile-to-sterile batch" means any compounded drug preparation containing two (2) or more dosage units with any ingredient that was at any time non-sterile, regardless of intervening sterilization of that ingredient.

(w) "Parenteral" means a preparation of drugs administered in a manner other than through the digestive tract. It does not (x) "Personal protective equipment" means clothing or devices that protect the employee from exposure to compounding ingredients and/or potential toxins and minimize the contamination of compounded preparations. These include shoe covers, head and facial hair covers, face masks, gowns, and gloves.

y) "Potency" means active ingredient strength within +/- 10% (or the range specified in USP37NF32, 37th Revision, Through 2nd Supplement Effective December 1, 2014) of the labeled amount. Sterile injectable products compounded solely from commercially manufactured sterile pharmaceutical products in a health care facility licensed under section 1250 of the Health and Safety Code are exempt from this definition. For those exempt, the range shall be calculated and defined in the master formula.

(z) "Preparation" means a drug or nutrient compounded in a licensed pharmacy; the preparation may or may not be sterile.

aa) "Prescriber's office" or "prescriber office" means an office or suite of offices in which a prescriber regularly sees patients for outpatient diagnosis and treatment. This definition does not include any hospital, pharmacy, or other facility, whether or not separately licensed, that may be affiliated with, adjacent to, or co-owned by, the prescriber's practice environment.

ab) "Primary Engineering Control (PEC)" means a device that provides an ISO Class 5 or better environment through the use of non-turbulent, unidirectional HEPA-filtered first air for compounding sterile preparations. Examples of PEC devices include, but are not limited to, laminar airflow workbenches, biological safety cabinets, sterile compounding automated robots, compounding aseptic isolators, and compounding aseptic containment isolators.

ac) "Process validation" means demonstrating that when a process is repeated within specified limits, the process will consistently produce preparations complying with predetermined requirements. If any aspect of the process is changed, the process would need to be revalidated.

(ad) "Product" means a commercially manufactured drug or nutrient evaluated for safety and efficacy by the FDA.

~~(ae) "Quality" means the absence of harmful levels of contaminants, including filth, putrid, or decomposed substances, the absence of active ingredients other than those listed on the label, and the absence of inactive ingredients other than those listed on the master formula document.~~

~~(af) "Segregated sterile compounding area" means a designated space for sterile-to-sterile compounding where a PEC is located within either a demarcated area (at least three foot perimeter) or in a separate room. Such area or room shall not contain and shall be void of activities and materials that are extraneous to sterile compounding. The segregated sterile compounding area shall not be in a location that has unsealed windows or doors that connect to the outdoors, in a location with high traffic flow, or in a location that is adjacent to construction sites, warehouses, or food preparation. The segregated sterile compounding area shall not have a sink, other than an emergency eye-washing station, located within three feet of a PEC. The segregated sterile compounding area shall be restricted to preparation of sterile-to-sterile compounded preparations. include topical, sublingual, rectal or buccal routes of administration.~~

~~(1) The BUD of a sterile drug preparation made in a segregated sterile compounding area is limited to 12 hours or less as defined by section 1751.8(d).~~

~~(2) When the PEC in the segregated sterile compounding area is a CAI or a CACI and the documentation provided by the manufacturer shows it meets the requirements listed in section 1751.4(f)(1) (3), the assigned BUD shall comply with section 1751.8(a-b) or (d).~~

~~(ag) "Strength" means amount of active ingredient per unit of a compounded drug preparation~~
~~Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.~~

1735.1. Introduction and Scope - Nonsterile Compounding

In addition to the standards in the USP Chapter 795, the preparation of CNSP shall meet the following requirements of this article.

(a) For the purposes of this article, nonsterile compounding occurs, by or under the supervision of a licensed pharmacist, pursuant to a patient specific prescription.

(b) Repackaging of a conventionally manufactured drug product shall be not considered compounding but must be compliant with USP General Chapter 1178 titled *Good Repackaging Practices*.

(c) Reconstitution of a conventionally manufactured drug product in accordance with directions that have not been Food and Drug Administration (FDA) approved in accordance with 21 U.S.C.A Section 355 is considered compounding and this article applies.

(d) Unless otherwise provided in this article, no CNSP shall be compounded unless the CNSP is compounded for an identified individual patient based on the receipt of a valid prescription order or a notation, approved by the prescriber, on the prescription that a compounded preparation is

necessary for the identified patient and the CSNP otherwise meets the requirements of section 503A of the Federal Food, Drug and Cosmetic Act (21 U.S.C. section 353a), as applicable.

(e) Notwithstanding subdivision (e), a limited quantity of CNSP may be prepared and stored in advance of receipt of a patient specific prescription document where, and solely in such quantity, as is necessary to ensure continuity of care for individual patients of the pharmacy based on a documented history of prescriptions for those individual patients.

(f) In addition to prohibitions and requirements for compounding established in federal law pursuant to 21 U.S.C. section 353a, no CNSP shall be prepared that:

(1) Is essentially a copy of one or more commercially available drug products, unless:

(A) the drug product appears on an ASHP (American Society of Health-System Pharmacists) or FDA Drug Shortages Database that are in short supply at the time of compounding and at the time of dispense, or

(B) the compounding of that CNSP is justified by a specific, documented medical need made known to the pharmacist prior to compounding A copy of the documentation of the shortage or the specific medical need shall be maintained in accordance with Business and Profession Code section 4081 for three years from the date of receipt of the documentation.

(2) Is made with any component not intended for use in a CNSP for the intended patient population.

(~~hg~~) Prior to allowing any CNSP to be compounded, the pharmacist-in-charge shall complete a self-assessment consistent with the requirements established in section 1715.

(~~ih~~) In addition to the provisions provided in Section 1707.2, consultation shall be provided to the patient and/or patient's agent concerning safe handling and disposal of the CNSP and related supplies furnished to the patient and/or patient's agent.

(~~ji~~) CNSPs with human whole blood or human whole blood derivatives shall be prepared in compliance with Health and Safety Code section 1602.5.

(~~kj~~) CNSPs considered to be hazardous drugs as defined in USP Chapter 800 *titled Hazardous Drugs – Handling in Healthcare Settings* shall be handled in compliance with that Chapter and relevant provisions of Pharmacy Law.

Note: Authority cited: Sections 4001.1, 4005, 4057, 4126.8 of Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, 4057, 4076, 4081, 4105, 4126.8 and 4169, 4301, 4306.5 and 4332 of the Business and Profession Code.

~~**1735.2. Compounding Limitations and Requirements; Self-Assessment**~~

~~(a) Except as specified in (b) and (c), no drug preparation shall be compounded prior to receipt by a pharmacy of a valid prescription for an individual patient where the prescriber has approved use of a~~

~~compounded drug preparation either orally or in writing. Where approval is given orally, that approval shall be noted on the prescription prior to compounding.~~

~~(b) A pharmacy may prepare and store a limited quantity of a compounded drug preparation in advance of receipt of a patient-specific prescription where and solely in such quantity as is necessary to ensure continuity of care for an identified population of patients of the pharmacy based on a documented history of prescriptions for that patient population.~~

(c) A "reasonable quantity" that may be furnished to a prescriber for office use by the prescriber as authorized by Business and Professions Code section 4052, subdivision (a)(1), means that amount of compounded drug preparation that:

Commented [SA1]: This portion of the language is not being repealed. However, for ease of the user is being reflected with the remainder of the new text below.

~~(1) Is ordered by the prescriber or the prescriber's agent using a purchase order or other documentation received by the pharmacy prior to furnishing that lists the number of patients seen or to be seen in the prescriber's office for whom the drug is needed or anticipated, and the quantity for each patient that is sufficient for office administration; and~~
~~(2) Is delivered to the prescriber's office and signed for by the prescriber or the prescriber's agent; and~~
(3) Is sufficient for administration or application to patients solely in the prescriber's office, or for furnishing of not more than a 120-hour supply for veterinary medical practices, solely to the prescriber's own veterinary patients seen as part of regular treatment in the prescriber's office, as fairly estimated by the prescriber and documented on the purchase order or other documentation submitted to the pharmacy prior to furnishing; ~~and~~
~~(4) That the pharmacist has a credible basis for concluding it is a reasonable quantity for office use considering the intended use of the compounded medication and the nature of the prescriber's practice; and~~
~~(5) With regard to any individual prescriber to whom the pharmacy furnishes, and with regard to all prescribers to whom the pharmacy furnishes, is an amount which the pharmacy is capable of compounding in compliance with pharmaceutical standards for integrity, potency, quality and strength of the compounded drug preparation; and~~
~~(6) Does not exceed an amount the pharmacy can reasonably and safely compound.~~

Commented [SA2]: This portion of the language is not being repealed. However, for ease of the user is being reflected with the remainder of the new text below.

~~(d) No pharmacy or pharmacist shall compound a drug preparation that:~~

~~(1) Is classified by the FDA as demonstrably difficult to compound;~~
~~(2) Appears on an FDA list of drugs that have been withdrawn or removed from the market because such drugs or components of such drugs have been found to be unsafe or not effective; or~~
~~(3) Is a copy or essentially a copy of one or more commercially available drug products, unless that drug product appears on an ASHP (American Society of Health-System Pharmacists) or FDA list of drugs that are in short supply at the time of compounding and at the time of dispense, and the compounding of that drug preparation is justified by a specific, documented medical need made known to the pharmacist prior to compounding. The pharmacy shall retain a copy of~~

the documentation of the shortage and the specific medical need in the pharmacy records for three years from the date of receipt of the documentation.

(e) A drug preparation shall not be compounded until the pharmacy has first prepared a written master formula document that includes at least the following elements:

(1) Active ingredients to be used.
(2) Equipment to be used.
(3) The maximum allowable beyond use date for the preparation, and the rationale or reference source justifying its determination.
(4) Inactive ingredients to be used.
(5) Specific and essential compounding steps used to prepare the drug.
(6) Quality reviews required at each step in preparation of the drug.
(7) Post-compounding process or procedures required, if any.
(8) Instructions for storage and handling of the compounded drug preparation.

(f) Where a pharmacy does not routinely compound a particular drug preparation, the master formula record for that preparation may be recorded on the prescription document itself.

(g) The pharmacist performing or supervising compounding is responsible for the integrity, potency, quality, and labeled strength of a compounded drug preparation until the beyond use date indicated on the label, so long as label instructions for storage and handling are followed after the preparation is dispensed.

(h) All chemicals, bulk drug substances, drug products, and other components used for drug compounding shall be stored and used according to compendia and other applicable requirements to maintain their integrity, potency, quality, and labeled strength.

(i) Every compounded drug preparation shall be given beyond use date representing the date or date and time beyond which the compounded drug preparation should not be used, stored, transported or administered, and determined based on the professional judgment of the pharmacist performing or supervising the compounding.

(1) For non-sterile compounded drug preparation(s), the beyond use date shall not exceed any of the following:
(A) the shortest expiration date or beyond use date of any ingredient in the compounded drug preparation,
(B) the chemical stability of any one ingredient in the compounded drug preparation;
(C) the chemical stability of the combination of all ingredients in the compounded drug preparation,
(D) for non-aqueous formulations, 180 days or an extended date established by the pharmacist's research, analysis, and documentation,
(E) for water-containing oral formulations, 14 days or an extended date established by the pharmacist's research, analysis, and documentation, and

(F) for water-containing topical/dermal and mucosal liquid and semisolid formulations, 30 days or an extended date established by the pharmacist's research, analysis, and documentation.

(G) A pharmacist, using his or her professional judgment may establish an extended date as provided in (D), (E), and (F), if the pharmacist researches by consulting and applying drug-specific and general stability documentation and literature; analyzes such documentation and literature as well as the other factors set forth in this subdivision, and maintains documentation of the research, analysis and conclusion. The factors the pharmacist must analyze include:

(i) the nature of the drug and its degradation mechanism,

(ii) the dosage form and its components,

(iii) the potential for microbial proliferation in the preparation,

(iv) the container in which it is packaged,

(v) the expected storage conditions, and

(vi) the intended duration of therapy.

Documentation of the pharmacist's research and analysis supporting an extension must be maintained in a readily retrievable format as part of the master formula.

(2) For sterile compounded drug preparations, the beyond use date shall not exceed any of the following:

(A) The shortest expiration date or beyond use date of any ingredient in the sterile compounded drug product preparation,

(B) The chemical stability of any one ingredient in the sterile compounded drug preparation,

(C) The chemical stability of the combination of all ingredients in the sterile compounded drug preparation, and

(D) The beyond use date assigned for sterility in section 1751.8.

(3) For sterile compounded drug preparations, extension of a beyond use date is only allowable when supported by the following:

(A) Method Suitability Test,

(B) Container Closure Integrity Test, and

(C) Stability Studies

(4) In addition to the requirements of paragraph three (3), the drugs or compounded drug preparations tested and studied shall be identical in ingredients, specific and essential compounding steps, quality reviews, and packaging as the finished drug or compounded drug preparation.

(5) Shorter dating than set forth in this subsection may be used if it is deemed appropriate in the professional judgment of the responsible pharmacist.

(j) The pharmacist performing or supervising compounding is responsible for the proper preparation, labeling, storage, and delivery of the compounded drug preparation.

(k) Prior to allowing any drug product preparation to be compounded in a pharmacy, the pharmacist in charge shall complete a self-assessment for compounding pharmacies developed by the board (Incorporated by reference is "Community Pharmacy & Hospital Outpatient Pharmacy Compounding

~~Self-Assessment" Form 17M-39 Rev. 02/12.) as required by Section 1715 of Title 16, Division 17, of the California Code of Regulations. That form contains a first section applicable to all compounding, and a second section applicable to sterile injectable compounding. The first section must be completed by the pharmacist-in-charge before any compounding is performed in the pharmacy. The second section must be completed by the pharmacist-in-charge before any sterile compounding is performed in the pharmacy. The applicable sections of the self-assessment shall subsequently be completed before July 1 of each odd-numbered year, within 30 days of the start date of a new pharmacist-in-charge or change of location, and within 30 days of the issuance of a new pharmacy license. The primary purpose of the self-assessment is to promote compliance through self-examination and education.~~

~~(l) Packages of ingredients, both active and inactive, that lack a supplier's expiration date are subject to the following limitations:~~

~~(1) such ingredients cannot be used for any non-sterile compounded drug preparation more than three (3) years after the date of receipt by the pharmacy.~~

~~(2) such ingredients cannot be used for any sterile compounded drug preparation more than (1) year after the date of receipt by the pharmacy.~~

~~Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.~~

1735.2. Personnel Training and Evaluation

In addition to the standards in the USP Chapter 795, the preparation of CNSP shall meet the following requirements of this article.

(a) In addition to USP Chapter 795's requirements, training, evaluation, and requalification procedures for personnel who compound or who have direct oversight of personnel performing compounding, verifying, and/or handling a CNSP shall also address the following topics:

(1) Quality assurance and quality control procedures,

(2) Container closure and equipment selection, and

(3) Component selection and handling.

(b) A pharmacist responsible for, or directly supervising, the~~,~~ compounding of CNSPs, shall demonstrate proficiency in skills necessary to ensure the integrity, strength, quality, and labeled strength of a CNSP as described in the facilities SOPs as referenced in section 1735.11.

(c) A "reasonable quantity" that may be furnished to a prescriber for office use by the prescriber as authorized by Business and Professions Code section 4052, subdivision (a)(1), means that amount of compounded drug preparation that:

(1) Is sufficient for administration or application to patients solely in the prescriber's office,~~-~~or for furnishing of not more than a 120-hour supply for veterinary medical practices, solely to the prescriber's own veterinary patients seen as part of regular treatment in the prescriber's office,

as fairly estimated by the prescriber and documented on the purchase order or other documentation submitted to the pharmacy prior to furnishing.

(d) Compounding personnel, or personnel with direct oversight over personnel performing compounding, verifying and/or handling a CNSP, who fails any aspect of training or demonstrated competency, shall not be involved in the compounding process until after successfully passing reevaluations in the deficient area(s) detailed in the facility's standard operating procedures ("SOPs) for nonsterile compounding as described in section 1735.11.

(e) Any person assigned to provide the training specified in this section shall obtain training and demonstrated competency in any subject in which the person will provide training or observe and measure competency described in the facilities SOPs as referenced in section 1735.11.

Note: Authority cited: Sections 4001.1, 4005, 4057, 4126.8 of Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, 4057, 4076, 4081, 4126.8 and 4169, 4301, 4306.5 and 4332 of the Business and Profession Code.

~~**1735.3. Recordkeeping of Compounded Drug Preparations**~~

~~(a) For each compounded drug preparation, pharmacy records shall include:~~

~~(1) The master formula document.~~

~~(2) A compounding log consisting of a single document containing all of the following:~~

~~(A) Name and Strength of the compounded drug preparation.~~

~~(B) The date the drug preparation was compounded.~~

~~(C) The identity of any pharmacy personnel engaged in compounding the drug preparation.~~

~~(D) The identity of the pharmacist reviewing the final drug preparation.~~

~~(E) The quantity of each ingredient used in compounding the drug preparation.~~

~~F) The manufacturer, expiration date and lot number of each component. If the manufacturer name is demonstrably unavailable, the name of the supplier may be substituted. If the manufacturer does not supply an expiration date for any component, the records shall include the date of receipt of the component in the pharmacy, and the limitations of section 1735.2, subdivision (l) shall apply.~~

~~(i) Exempt from the requirements in this paragraph (1735.3(a)(2)(F)) are sterile in a single lot for administration within seventy-two (72) hours to a patient in a health care facility licensed under section 1250 of the Health and Safety Code and stored in accordance with standards for "Redispensed CSPs" found in Chapter 797 of the United States Pharmacopeia – National Formulary (USP37-NF32) Through 2nd Supplement (37th Revision, Effective December 1, 2014), hereby incorporated by reference.~~

~~(G) A pharmacy-assigned unique reference or lot number for the compounded drug product preparation.~~

~~H) The beyond use date or beyond use date and time of the final compounded drug, expressed in the compounding document in a standard date and time format.~~

~~I) The final quantity or amount of drug preparation compounded for dispensing.~~
~~(J) Documentation of quality reviews and required post-compounding process and procedures.~~

~~(b) Pharmacies shall maintain records of the proper acquisition, storage, and destruction of chemicals, bulk drug substances, drug products, and components used in compounding.~~

~~(c) Active ingredients shall be obtained from a supplier registered with the Food and Drug Administration (FDA). All other chemicals, bulk drug substances, and drug products used to compound drug preparations shall be obtained, whenever possible, from FDA-registered suppliers. The pharmacy shall acquire and retain certificates of purity or analysis, either written in English or translated into English, for chemicals, bulk drug substances, and drug products used in compounding. Certificates of purity or analysis are not required for drug products that are approved by the FDA. Any certificates of purity or analysis acquired by the pharmacy shall be matched to the corresponding chemical, bulk drug substance, or drug products received.~~

~~(d) Pharmacies shall maintain and retain all records required by this article in the pharmacy in a readily retrievable form for at least three years from the date the record was last in effect. If only recorded and stored electronically, on magnetic media, or in any other computerized form, the records shall be maintained as specified by Business and Professions Code section 4070 subsection (c).~~

~~Authority cited: Sections 4005, 4127, and 4169, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.~~

1735.3. Personnel Hygiene and Garbing

The requirements of this section apply to nonsterile compounding in addition to the standards established by USP Chapter 795.

(a) Prior to admitting any personnel into a compounding area, the supervising pharmacist shall evaluate compounding personnel experiencing any of the following: rashes, recent tattoos or oozing sores, conjunctivitis, active respiratory infection or and other medical conditions to determine if such condition could contaminate a CNSP or the environment ("contaminating conditions"). After such evaluation and determination the supervising pharmacist shall not allow personnel with potentially contaminating conditions to enter the compounding area.

(b) A gown and face mask shall be used whenever a closed system processing device is required.

(c) Disposable garb shall not be shared by staff and shall be discarded after each shift and when soiled. Garb removed during a shift must be maintained in the compounding area.

(d) Gloves shall be wiped or replaced before beginning a CNSP that has different components.

(e) Non-disposable garb shall be cleaned with a germicidal detergent and sanitized with 70% isopropyl alcohol before re-use.

(f) Any garbing accommodations provided by the designated person shall be documented and the record shall include the name of the individual granted the accommodation, date granted and description of the reasons for granting the accommodation. The record shall be retained in accordance with Business and Professions Code section 4081.

Note: Authority cited: Sections 4001.1, 4005, 4057, 4126.8 of Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, 4057, 4076, 4081, 4126.8 and 4169, 4301 and 4332 of the Business and Profession Code.

~~**1735.4. Labeling of Compounded Drug Preparations**~~

~~(a) Each compounded drug preparation shall be affixed with a container label prior to dispensing that contains at least:~~

~~(1) Name of the compounding pharmacy and dispensing pharmacy (if different);~~
~~2) Name (brand or generic) and strength, volume, or weight of each active ingredient. For admixed IV solutions, the intravenous solution utilized shall be included;~~
~~(3) Instructions for storage, handling, and administration. For admixed IV solutions, the rate of infusion shall be included;~~
~~(4) The beyond use date for the drug preparation;~~
~~(5) The date compounded; and~~
~~6) The lot number or pharmacy reference number.~~

~~(b) Any compounded drug preparation dispensed to a patient or readied for dispensing to a patient shall also include on the label the information required under Business and Professions Code section 4076 and California Code of Regulations, title 16, section 1707.5.~~

~~(c) Any compounded drug preparation dispensed to a patient or readied for dispensing to a patient shall also include, on the container label or on a receipt provided to the patient, a statement that the drug has been compounded by the pharmacy.~~

~~(d) Prior to dispensing drug preparations compounded into unit-dose containers that are too small or otherwise impractical for full compliance with subdivisions (a), (b), and (c) shall be labeled with at least the name of the compounding pharmacy and dispensing pharmacy, if different, the name(s) of the active ingredient(s), strength, volume or weight of the preparation, pharmacy reference or lot number, and beyond use date, and shall not be subject to minimum font size requirements. Once dispensed, outer packaging must comply with 1735.4(a) – (c).~~

~~(e) All hazardous agents shall bear a special label which states "Chemotherapy- Dispose of Properly" or "Hazardous – Dispose of Properly."~~

~~Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, 4076 and 4127, Business and Professions Code.~~

1735.4. Building and Facilities

The requirements of this section apply to nonsterile compounding in addition to the standards established by USP Chapter 795.

(a) A sink used for compounding or hand hygiene shall not be part of a restroom or water closet.

(b) Purified water, distilled water, or reverse osmosis water shall be used for rinsing equipment and utensils.

(c) No CNSP shall be compounded if it is known, or reasonably should be known, that the compounding environment fails to meet criteria specified in USP Chapter 795 or the pharmacy's written SOPs referenced in section 1735.11.

Note: Authority cited: Sections 4001.1, 4005, 4057, 4126.8 of Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, 4057, 4076, 4081, 4126.8 and 4169, 4301, 4306.5 and 4332 of the Business and Profession Code.

~~**1735.5. Compounding Policies and Procedures**~~

~~(a) Any pharmacy engaged in compounding shall maintain written policies and procedures for compounding that establishes procurement procedures, methodologies for the formulation and compounding of drugs, facilities and equipment cleaning, maintenance, operation, and other standard operating procedures related to compounding. Any material failure to follow the pharmacy's written policies and procedures shall constitute a basis for disciplinary action.~~

~~(b) The policies and procedures shall be reviewed and such review shall be documented on an annual basis by the pharmacist-in-charge. The policies and procedures shall be updated whenever changes in policies and procedures are implemented.~~

~~(c) The policies and procedures shall include at least the following:~~

~~1) Procedures for notifying staff assigned to compounding duties of any changes in policies .~~

~~2) A written plan for recall of a dispensed compounded drug preparation where subsequent demonstrates the potential for adverse effects with continued use. The plan shall ensure that all affected doses can be accounted for during the recall and shall provide steps to identify which patients received the affected lot or compounded drug preparation(s).~~

~~3) Procedures for maintaining, storing, calibrating, cleaning, and disinfecting equipment used in , and for training on these procedures as part of the staff training and competency evaluation process.~~

~~(4) Procedures for evaluating, maintaining, certifying, cleaning, and disinfecting the facility (physical plant) used for compounding, and for training on these procedures as part of the staff training and competency evaluation process.~~

~~(5) Documentation of the methodology used to validate integrity, potency, quality, and labeled strength of compounded drug preparations. The methodology must be appropriate to compounded drug preparations.~~

~~(6) Documentation of the methodology and rationale or reference source used to determine appropriate beyond use dates for compounded drug preparations.~~

~~(7) Dates and signatures reflecting all annual reviews of the policies and procedures by the pharmacist-in-charge.~~

~~8) Dates and signatures accompanying any revisions to the policies and procedures approved by pharmacist-in-charge.~~

~~9) Policies and procedures for storage of compounded drug preparations in the pharmacy and daily documentation of all room, refrigerator, and freezer temperatures within the pharmacy.~~

~~10) Policies and procedures regarding ensuring appropriate functioning of refrigeration devices, refrigeration device temperatures, and actions to take regarding any out of range temperature variations within the pharmacy.~~

~~(11) Policies and procedures for proper garbing when compounding with hazardous products. shall include when to utilize double shoe covers.~~

~~Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, 4127, and 4301, Business and Professions Code~~

1735.5. Cleaning And Sanitizing

The requirements of this section apply to nonsterile compounding in addition to the standards established by USP Chapter 795.

(a) In addition to the documentation requirements in USP Chapter 795, the facility's documentation of each occurrence of the cleaning and sanitizing of the compounding area shall include a record of the identity of the person completing the cleaning and sanitizing as well as the product name of the cleaning and sanitizing agents used.

(b) Any cleaning or sanitizing agents used by the facility to meet the requirements in this article shall be used in accordance with manufacturers' specifications.

Note: Authority cited: Sections 4001.1, 4005, 4057, 4126.8 of Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, 4057, 4076, 4081, 4126.8 and 4169, 4301 and 4332 of the Business and Profession Code.

~~**1735.6. Compounding Facilities and Equipment**~~

~~(a) Any pharmacy engaged in compounding shall maintain written documentation regarding the facilities and equipment necessary for safe and accurate compounding of compounded drug preparations. This shall include records of maintenance and cleaning of the facilities and equipment. Where applicable, this shall also include records of certification(s) of facilities or equipment.~~

~~(b) Any equipment used to compound drug preparations shall be stored, used, maintained, and cleaned in accordance with manufacturers' specifications.~~

~~c) Any equipment that weighs, measures, or transfers ingredients used to compound drug preparations for which calibration or adjustment is appropriate shall be calibrated prior to use, on a schedule and by a method determined by the manufacturer's specifications, to ensure accuracy. Documentation of each such calibration shall be recorded in a form which is not alterable and these records of calibration shall be maintained and retained in the pharmacy.~~

~~(d) Any pharmacy engaged in any hazardous drug compounding shall maintain written documentation regarding appropriate cleaning of facilities and equipment to prevent cross-contamination with non-hazardous drugs.~~

~~(e) Hazardous drug compounding shall be completed in an externally exhausted physically separate room with the following requirements:~~

~~(1) Minimum of 30 air changes per hour except that 12 air changes per hour are acceptable for segregated compounding areas with a BSC or CACI when products are assigned a BUD of 12 hours or less or when non sterile products are compounded; and~~

~~2) Maintained at a negative pressure of 0.01 to 0.03 inches of water column relative to all adjacent spaces (rooms, above ceiling, and corridors); and~~

~~(3) A) For sterile compounding, each BSC or CACI shall also be externally exhausted. y~~

~~(B) For nonsterile compounding, a BSC, a CACI, or other containment ventilated enclosure shall be used and shall either use a redundant HEPA filter in series or be externally exhausted.; For purposes of this paragraph, a containment ventilated enclosure means a full or partial enclosure that uses ventilation principles to capture, contain, and remove airborne contaminants through high-efficiency particulate air (HEPA) filtration and to prevent their release into the work environment.~~

~~Each PEC in the room shall also be externally vented; and~~

~~4) All surfaces within the room shall be smooth, seamless, impervious, and non-shedding.~~

~~(f) Where compliance with the January 1, 2017 amendments to Article 4.5 or Article 7, requires physical construction or alteration to a facility or physical environment, the board or its designee may grant a waiver of such compliance for a period of time to permit such physical change(s). Application for any waiver shall be made by the licensee in writing, and the request shall identify the provision(s) requiring physical construction or alteration, and the timeline for any such change(s). The board or its designee may grant the waiver when, in its discretion, good cause is demonstrated for such waiver.~~

~~Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052 and 4127, Business and Professions Code.~~

1735.6. Equipment And Components

The requirements of this section apply to nonsterile compounding in addition to the standards established by USP Chapter 795.

(a) Any equipment used to compound a CNSP shall be used in accordance with the manufacturer's specifications.

(b) Any component used to compound a CNSP shall be used and stored in accordance with all federal laws and regulations and industry standards including the manufacturers' specifications and requirements.

Note: Authority cited: Sections 4001.1, 4005, 4057, 4126.8 of Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, 4057, 4076, 4081, 4126.8 and 4169, 4301 and 4332 of the Business and Profession Code.

~~**1735.7. Training of Compounding Staff**~~

~~(a) A pharmacy engaged in compounding shall maintain documentation demonstrating that personnel involved in compounding have the skills and training required to properly and accurately perform their assigned responsibilities and documentation demonstrating that all personnel involved in compounding are trained in all aspects of policies and procedures. This training shall include but is not limited to support personnel (e.g. institutional environmental services, housekeeping), maintenance staff, supervising pharmacist and all others whose jobs are related to the compounding process.~~

~~(b) The pharmacy shall develop and maintain an ongoing competency evaluation process for pharmacy personnel involved in compounding, and shall maintain documentation of any and all training related to compounding undertaken by pharmacy personnel.~~

~~(c) Pharmacy personnel assigned to compounding duties shall demonstrate knowledge about processes and procedures used in compounding prior to compounding any drug preparation.~~

~~Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052 and 4127, Business and Professions Code~~

1735.7. Master Formulation and Compounding Records

The requirements of this section apply to nonsterile compounding in addition to the standards established by USP Chapter 795.

(a) A CNSP shall not be compounded until the pharmacy has first prepared a written master formulation record in compliance with Section 7.1 of USP Chapter 795 and identified in that document the following additional elements:

(1) The referenced source material (e.g., peer reviewed article, published scientific book) used to support the assigned beyond-use date (BUD); each source referenced shall be readily retrievable at the time of compounding and shall be maintained for three years from the date each CNSP is dispensed.

(2) Instructions for storage and handling of the CNSP.

(b) Where a pharmacy does not routinely compound a particular drug preparation, the master formulation record for that preparation may be recorded on the prescription document itself. This record shall comply with USP Chapter 795 standards and this section.

(c) A compounding record shall be a single document. The document shall satisfy the compounding record requirements in Section 7.2 of USP Chapter 795, as well as the following:

(1) The date and time of preparation. The time of preparation is the time when compounding the CNSP started, which also determines when the assigned BUD starts.

(2) The manufacturer, lot number, and expiration date for each component.

(3) The assigned internal identification number shall be unique for each CNSP.

(4) The total quantity compounded shall include the number of units made and the volume or weight of each unit.

(5) The identity of each person performing the compounding, have direct oversight of compounding, and pharmacist verifying the final drug preparation.

Note: Authority cited: Sections 4001.1, 4005, 4057, 4126.8 of Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, 4057, 4076, 4081, 4126.8 and 4169, 4301 and 4332 of the Business and Profession Code.

~~1735.8. Compounding Quality Assurance~~

~~(a) Any pharmacy engaged in compounding shall maintain, as part of its written policies and procedures, a written quality assurance plan designed to monitor and ensure the integrity, potency, quality, and labeled strength of compounded drug preparations.~~

~~(b) The quality assurance plan shall include written procedures for verification, monitoring, and review of the adequacy of the compounding processes and shall also include written documentation of review of those processes by qualified pharmacy personnel.~~

~~(c) The quality assurance plan shall include written standards for qualitative and quantitative analysis of compounded drug preparations to ensure integrity, potency, quality, and labeled strength, including the frequency of testing. All qualitative and quantitative analysis reports for compounded drug preparations shall be retained by the pharmacy and maintained along with the compounding log and master formula document. The quality assurance plan shall include a schedule for routine testing and analysis of specified compounded drug preparations to ensure integrity, potency, quality, and labeled strength, on at least an annual basis.~~

~~(d) The quality assurance plan shall include a written procedure for scheduled action in the event any compounded drug preparation is ever discovered to be outside minimum standards for integrity, potency, quality, or labeled strength.~~

~~(e) The quality assurance plan shall include a written procedure for responding to out-of-range temperature variations within the pharmacy and within patient care areas of a hospital where furnished drug is returned for redispensing.~~

~~Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052 and 4127, Business and Professions Code.~~

1735.8. Release Inspections and Testing

The requirements of this section apply to nonsterile compounding in addition to the standards established by USP Chapter 795.

A pharmacist performing or supervising the nonsterile compounding by other authorized personnel is responsible for the integrity, quality, and labeled strength of a CNSP until the beyond-use date indicated on the label provided the patient or the patient's agent follows the label instructions provided on the CNSP for storage and handling after receiving the CNSP.

Note: Authority cited: Sections 4001.1, 4005, 4057, 4126.8 of Business and Professions Code. Reference: Sections 4005, 4036, 4036.5, 4037, 4051, 4052, 4057, 4076, 4081, 4126.8 and 4169, 4301 and 4332 of the Business and Profession Code.

1735.9. Labeling

The requirements of this section apply to nonsterile compounding in addition to the standards established by USP Chapter 795.

(a) A CNSPs label shall also include the following:

(1) Route of intended administration, and

(2) Name of compounding facility and dispensing facility (if different).

(b) A CNSPs Labeling shall also include:

(1) Any special handling instructions,

(2) Any applicable warning statements, and

(3) Name, address, and phone number of the compounding facility if the CNSP is to be sent outside of the facility or healthcare system in which it was compounded.

(c) Any CNSP dispensed to a patient or readied for dispensing to a patient shall also include on the label the information required by Business and Professions Code section 4076 and section 1707.5.

Note: Authority cited: Sections 4001.1, 4005, 4057, 4126.8 of Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, 4057, 4076, 4081, 4126.8 and 4169, 4301 and 4332 of the Business and Profession Code.

1735.10. Establishing Beyond-Use Dates

The requirements of this section apply to nonsterile compounding in addition to the standards established by USP Chapter 795.

(a) Beyond-use dates (BUDs) assigned with only a date shall expire at 11:59 p.m. on that date.

(b) A CNSP's BUDs shall not exceed:

(1) The chemical and physical stability data of the active pharmaceutical ingredient (API) and any added component in the preparation,

(2) The compatibility and degradation of the container–closure system with the finished preparation (e.g., possible leaching, interactions, and storage conditions),

(3) The shortest remaining expiration date or BUD of any of the starting components, or,

(4) The potential for microbial proliferation in the CNSP.

(c) If a licensee chooses to use antimicrobial effectiveness testing results provided by an current FDA-registered drug establishment or outsourcing facility or published in current peer-reviewed literature sources, the reference (including the raw data and testing method suitability), shall be readily retrievable in accordance with Business and Professions Code section 4081 in its entirety for three years from the last date the CNSP was dispensed.

Note: Authority cited: Sections 4001.1, 4005, 4057, 4126.8 of Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, 4057, 4076, 4081, 4126.8 and 4169, 4301 and 4332 of the Business and Profession Code.

1735.11. Standard Operating Procedures (SOPs)

The requirements of this section apply to nonsterile compounding in addition to the standards established by USP Chapter 795.

(a) The facility's standard operating procedures (SOPs) for nonsterile compounding shall be followed and shall:

(1) Comply with USP Chapter 1163, Quality Assurance in Pharmaceutical Compounding.

(2) In addition to the SOPs required in USP Chapter 1163, Quality Assurance in Pharmaceutical Compounding, SOPs must also be developed to describe the following:

(A) Methods by which the supervising pharmacist will ensure the quality of compounded drug preparations.

(B) Procedures for handling, compounding, and disposal of infectious materials. The written policies and procedures shall describe the pharmacy protocols for cleanups and spills in conformity with local health jurisdictional standards.

(C) The methods a pharmacist will use to determine and approve the ingredients and the compounding process for each preparation before compounding begins.

(D) The method for complying with any other requirements specifically required to be addressed in the facility's SOPS as described in this article.

(b) The SOPs shall be reviewed on an annual basis by the pharmacist-in-charge. Such review shall be documented by the pharmacist-in-charge consistent with the facility's SOPs. The SOPs shall be updated any time changes are made to compounding processes, facility changes or other changes occur that impact the CNSP. Such SOP changes shall be disseminated to the affected staff prior to implementation.

(c) Failure to follow written SOPs shall constitute a basis for enforcement action.

Note: Authority cited: Sections 4001.1, 4005, 4057, 4126.8 of Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, 4057, 4076, 4081, 4126.8 and 4169, 4301 and 4332 of the Business and Profession Code.

1735.12. Quality Assurance And Quality Control

The requirements of this section apply to nonsterile compounding in addition to the standards established by USP Chapter 795.

(a) The quality assurance program shall also comply with section 1711 and the standards contained in USP Chapter 1163, entitled *Quality Assurance in Pharmaceutical Compounding*. In addition to compliance with those standards, the program shall include in its SOPs the following:

(1) A written procedure for scheduled action, such as a recall, in the event any compounded drug preparation is discovered to be outside the expected standards for integrity, quality, or labeled strength.

(2) A written procedure for responding to out-of-range temperature variations within the medication storage areas where a furnished drug may be returned for furnishing to another patient.

(b) The Board shall be notified in writing within 72 hours of the facility's receipt of a complaint or the occurrence of an adverse drug event involving a CNSP.

(c) All complaints related to a potential quality problem with a CNSP and all adverse events shall be reviewed by the pharmacist-in-charge within 72 hours of receipt of the complaint or occurrence of the adverse event. Such review shall be documented and dated as defined in the SOPs.

Note: Authority cited: Sections 4001.1, 4005, 4057, 4126.8 of Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, 4057, 4076, 4081, 4126.8 and 4169, 4301 and 4332 of the Business and Profession Code.

1735.13. Packaging and Transporting

The requirements of this section apply to nonsterile compounding in addition to the standards established by USP Chapter 795.

There shall be written procedures recorded in the facility's SOPs (as described in Section 1735.11) describing validated processes for storage, shipping containers and transportation of temperature sensitive CNPSs to preserve quality standards for integrity, quality and labeled strength.

Note: Authority cited: Sections 4001.1, 4005, 4057, 4126.8 of Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, 4057, 4076, 4081, 4126.8 and 4169, 4301 and 4332 of the Business and Profession Code.

1735.14. Documentation

The requirements of this section apply to nonsterile compounding in addition to the standards established by USP Chapter 795.

(a) Facilities shall maintain each record required by USP Chapter 795 or this article, in a readily retrievable form, for at least three years from the date the record was created or relied upon to meet the requirements of this article.

(b) Records created shall be created and maintained in a manner to provide an "audit trail" to the Board that includes a detailed, chronological record of all revisions and updates made by the facility's personnel of each record document in accordance with this section. To meet the "audit trail" requirement of this section, each record must include the original document created, each subsequent version of that document showing change to the original document, an identification of individual who made the change, and the date of each change.

Note: Authority cited: Sections 4001.1, 4005, 4057, 4126.8 of Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, 4057, 4076, 4081, 4105, 4126.8 and 4169, 4301 and 4332 of the Business and Profession Code.