



## **Compounding Committee Chair Report**

Maria Serpa, Licensee Member, Chair  
Allen Schaad, Licensee Member, Vice Chair  
Greg Lippe, Public Member

### **a. Summary of Presentation on Proposed USP Chapter 825, Radiopharmaceuticals – Preparation, Compounding, Dispensing, and Repackaging.**

June 4, 2019, the committee convened its fourth meeting. The focus of the meeting was education on new USP Chapter 825, Radiopharmaceuticals – Preparation, Compounding, Dispensing, and Repackaging. Paul Mahan, a member of the expert panel for the development of the USP Chapter, provided the presentation. The committee was provided with a general timeline for the development of the new chapter including publication the proposed chapter in July 2017 and comment period that closed in November 2018. The new chapter was published June 1, 2019 and becomes effective December 1, 2019.

The committee was presented with a summary of the minimum standards for each section within the chapter related to radiopharmaceuticals including:

- Introduction
- Radiation Safety Considerations
- Personnel Qualifications, Training, and Hygiene
- Facilities and Engineering Controls
- Microbiological Air and Surface Monitoring
- Cleaning and Disinfecting
- Assigning BUD
- Documentation
- Preparation
- Compounding
- Dispensing
- Repackaging
- Quality Assurance and Quality Control

A copy of the presentation is provided in **Attachment 1**.

**b. Discussion and Consideration of Proposed Amendments to Regulations Related to Pharmaceutical Compounding of Nonsterile Preparation**

**Attachment 1**

Background

During its February 20, 2019, meeting, members received a presentation on the proposed revisions to USP General Chapter 795, Pharmaceutical Compounding – Nonsterile Preparations. As part of that presentation, members were advised of USP’s intended publication date of June 1, 2019, for the final chapter. Further, members were advised that December 1, 2019, is the intended official date for the revised chapter.

USP has since released its final chapter, which is available for download from USP at [www.USP.org](http://www.USP.org).

During its July 11, 2019, members and the public reviewed meeting materials provided in advance of the meeting including proposed regulation language along with a second version that included both the language and a brief statement on the necessity for the provision. To ensure sufficient time for public review in advance of the meeting, the meeting materials were released to the public June 28, 2019, in advance of the meeting.

Further, as the committee conducted its work, the committee accepted public comments on each section of the regulation. Only after the committee had reached consensus on a section did it proceed. To ensure an opportunity for everyone to participate, the language was also projected on screens and live edits made to the document and comments were received and approved by the committee.

During the Meeting

During this meeting, members will have the opportunity to review the proposed regulations being recommended by the committee for promulgation. The proposed regulations are intended to allow for the full implementation of USP 795 and provide clarity to members of the board’s regulated public on the requirements that must be satisfied to prepare such products.

The proposal incorporates the changes made by the committee as well as nonsubstantive changes offered by counsel subsequent to the committee meeting.

**Committee Recommendation:** Recommend to the board approval of committee’s proposal to repeal and replace Article 4.5 Related to Compounding with the proposed new Article 4.5 Related to Nonsterile Preparations, including sections 1735 – 1735.15 as reviewed and edited during the meeting.

### Recent Update

Subsequent to the meeting staff continued reflection on comments made during the meeting. Based on further research and review, board staff request consideration of the below additional changes.

#### **CCR 1735.1**

...

(j) "Potency" means an active ingredient strength typically within +/- 10% (or the range specified in USP) of the labeled amount.

#### **CCR 1735.2**

...

(a) Training, evaluation, and requalification of personnel involved in the preparation, verification, and/or handling of CNSP preparations shall also contain at least the following:

- (1) Quality assurance and quality control procedures,
- (2) Container closure and equipment selection and
- (3) Component selection and handling

#### **CCR 1735.6**

...

(b) Any component used to compound a CNSP shall be used, stored, and dispensed, in accordance with all the following:

- (1) United States Pharmacopeia (USP)- National Formulary (NF),
- (2) Food Drug and Cosmetic Act (FD&CA),
- (3) Food Drug Administration (FDA) issued Guidance Documents and Alerts, and
- (4) Manufacturers' specifications and requirements.

#### **CCR 1735.7**

...

(a) A CNSP shall not be compounded until the pharmacy has first prepared a written master formulation document in compliance with USP Chapter 795 and the following:

- (1) Active pharmaceutical ingredient (API) or added substances identities and amounts shall include at least salt form and purity grade, if available.
- (2) Container-closure systems ~~shall include at least volume~~, and type for each container and closure to be used.
- (3) The reference source of the BUD assignment; each reference shall be fully available at the time of compounding and 3 years from each dispense.
- (4) Instructions for storage and handling of the compounded drug preparation.

### **1735.11 SOPs**

**In addition to the requirements in the USP Chapter 795 and referenced chapters**

(a) Standard operating procedures (SOPs) shall:

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

(2) Include at least the SOPs listed in USP Chapter 1163, Quality Assurance in Pharmaceutical Compounding, and

(3)

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

(B) Include 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) Include the provisions used by a pharmacist to make the determination and approval, ~~by a pharmacist,~~ of the ingredients and the compounding process for each preparation before compounding begins

Should the board agree with the above changes detailed under the Recent Update portion, it may be appropriate to make a subsequent motion to capture these additional changes for inclusion into the board's proposal.

**Attachment 1** includes two documents:

1. Proposed regulation language to repeal and replace Article 4.5 related to Compounding as approved by the committee and nonsubstantive changes offered by counsel.
2. Proposed regulation language that also includes a brief description of the necessity for the regulation provisions.

**c. Future Committee Meeting Dates**

- August 28, 2019 – Irvine, Ca
- September 24, 2019 – Sacramento, Ca
- October 16, 2019 - TBD

# **Attachment 1**

## **Proposal to Repeal Article 4.5 Compounding including Sections 1735-1735.8.**

### **Proposal to Add Article 4.5 as proposed with the following:**

#### **Article 4.5 Nonsterile Compounding in Pharmacies**

##### **1735. Nonsterile Compounding in Licensed Pharmacies**

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

(b) Repackaging of a compounded nonsterile preparation (CNSP) shall be considered compounding and this article shall apply.

(c) Reconstitution in accordance with directions which have not been FDA approved are considered compounding and all requirements shall apply.

(d) No compounded non-sterile preparations (CNSPs) shall be compounded prior to receipt by a pharmacy of a valid patient specific prescription document 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 document prior to compounding. A signed and dated document between a prescriber and a pharmacy may serve as an understanding that all non-commercially available preparations will be compounded the identified patient.

(1) Except that a pharmacy may prepare and store a limited quantity of a CNSP 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 an identified population of patients of the pharmacy based on a documented history of prescriptions for that patient population.

(e) No pharmacy or pharmacist shall compound a CNSP 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 drug preparations 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 (A) the 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, or (B) the compounding of that CNSP 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 or the specific medical need in the pharmacy records for three years from the date of receipt of the documentation.

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

(f) 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. XX/XX.) as required by Section 1715 of Title 16, Division 17, of the California Code of Regulations.

(g) In addition to CCR 1707.2, consultation shall be available to the patient and/or primary caregiver concerning proper use, storage, handling, and disposal of a CNSP and related supplies furnished by the pharmacy.

(h) Compounding with blood or blood components shall be done in compliance with Health and Safety Code section 1602.5.

(i) Storing, weighing, measuring, compounding, and/or performing other manipulation of an active pharmaceutical ingredient (API) or added substance deemed hazardous by Occupational Safety and Health (NIOSH) shall be done in compliance with CCR XXX and USP Chapter 800.

(j) Storing, weighing, measuring, compounding, and/or performing other manipulation of an antineoplastic under Occupational Safety and Health (NIOSH) shall be done in compliance with CCR XXX and USP chapter 800.

#### **1735.1. INTRODUCTION AND SCOPE AND COMPOUNDING DEFINITIONS.**

##### **In addition to the definitions in the USP Chapter 795 and referenced chapters**

(a) “Approved labeling” means the Food and Drug Administration’s (FDA) approved labeling which contains FDA approved information for the diluent, the resultant strength, the container closure system, and storage time.

(b) “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.

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

(d) “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.

(e) "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, that is not pursuant to a prescription

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

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

(h) "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.

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

(j) "Potency" -means an active ingredient strength within +/- 10% (or the range specified in USP) of the labeled amount.

## **1735.2 PERSONNEL TRAINING AND EVALUATION**

**In addition to the requirements in USP Chapter 795 and referenced chapters.**

(a) Training, evaluation, and requalification of personnel involved in the preparation and/or handling of CNSP preparations shall also contain at least the following:

- (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 and controlling compounding of CNSPs, shall demonstrate proficiency in skills necessary to ensure the integrity, potency, quality, and labeled strength of CNSP.

(c) Personnel 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) as detailed in the SOPs.

(d) The pharmacist-in-charge shall be responsible for all activities and decisions made or approved by the designated person(s).

(e) The pharmacy must document that any person assigned to provide training has obtained training and demonstrated competency in any area they will be providing training or observational review.



### **1735.3 PERSONAL HYGIENE AND GARBING**

#### **In addition to the requirements in the USP Chapter 795 and referenced chapters**

- (a) 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 conditions to determine if such condition could contaminate a CNSP or the environment. The supervising pharmacist shall not allow personnel with potentially contaminating conditions to enter the compounding area.
- (b) Prior to entry into the compounding area all hand, wrist, and other exposed jewelry or piercing shall be removed.
- (c) A gown and face mask shall be used whenever a closed system processing device is required.
- (d) 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.
- (e) Non-disposable garb shall be cleaned with a germicidal detergent and sanitized with 70% isopropyl alcohol before re-use.
- (f) Eye glasses shall be cleaned as part of hand hygiene and garbing per a facility standard operating procedures (SOPs).
- (g) Any gowning or garbing accommodation made by the designated person shall be documented and a full assessment of the risk to the CNSPs and environment shall be included. Documentation and assessment shall be done prior to accommodation taking place.

### **1735.4 BUILDING AND FACILITIES**

#### **In addition to the requirements in the USP Chapter 795 and referenced chapters**

- (a) The handwashing stations and scrub sinks used for compounding, hand hygiene, or both, shall not be part of a restroom or water closet.
- (b) Compounding personnel must monitor temperatures in storage area(s) and compounding areas either manually at least once daily on days that the facility is open or by a continuous temperature recording device to determine whether the temperature remains within the appropriate range for the CNSPs or components. This shall be documented.
- (c) Purified water, distilled water, or reverse osmosis water shall be used for rinsing equipment and utensils.
- (d) No CNSP shall be compounded if it is known, or reasonably should be known, that the compounding environment fails to meet criteria specified in the pharmacy's written policies and

procedures or those required in USP chapter 795.

### **1735.5 CLEANING AND SANITIZING**

**In addition to the requirements in the USP Chapter 795 and reference chapters**

- (a) Documentation of the cleaning and sanitizing of the compounding area include the personnel completing the cleaning and sanitizing and the cleaning and sanitizing agents used.
- (b) Decontamination, cleaning, disinfecting and sporicidal agents shall be used in accordance with manufacturers' specifications.

### **1735.6 EQUIPMENT AND COMPONENTS**

**In addition to the requirements in the USP Chapter 795 and referenced chapters**

- (a) Any equipment used to compound CNSP shall be used in accordance with the manufacturer's specifications.
- (b) Any component used to compound a CNSP shall be used, stored, and dispensed, in accordance with all the following:
  - (1) United States Pharmacopeia (USP)- National Formulary (NF),
  - (2) Food Drug and Cosmetic Act (FD&CA),
  - (3) Food Drug Administration (FDA), and
  - (4) Manufacturers' specifications and requirements.
- (c) Any API or added substance used to compound a CNSP shall be obtained from an FDA-registered supplier and shall be accompanied by a valid certificate of analysis (COA). This COA shall be in English and should all the requirements of USP Chapter 1080, Bulk Pharmaceutical Excipient- Certificate of Analysis. All COAs shall be readily retrievable for at least 3 years from last use in CNSP.

### **1735.7. MASTER FORMULATION AND COMPOUNDING RECORDS**

**In addition to the requirements in the USP Chapter 795 and referenced chapters.**

- (a) A CNSP shall not be compounded until the pharmacy has first prepared a written master formulation document in compliance with USP Chapter 795 and the following:
  - (1) Active pharmaceutical ingredient (API) or added substances identities and amounts shall include at least salt form and purity grade, if available.
  - (2) Container-closure systems shall include at least volume, and type for each container and closure to be used.
  - (3) The reference source of the BUD assignment; each reference shall be fully available at the time of compounding and 3 years from each dispense.

(4) Instructions for storage and handling of the compounded drug preparation.

(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 be in compliance with USP 795 and 1735.7(a).

(c) A compounding record shall be a single document and shall include the requirements of USP chapters 795, and 800 as applicable, and the following:

(1) The date and time of preparation shall be the time when compounding started and when the assigned BUD starts.

(2) the assigned internal identification number shall be unique for each compounded drug preparation.

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

(4) The identity of the compounder and pharmacist verifying the final drug preparation.

### **1735.8 RELEASE INSPECTIONS**

#### **In addition to the requirements in the USP Chapter 795 and referenced chapters**

A 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 once the preparation is dispensed.

### **1735.9 LABELING**

#### **In addition to the requirements in the USP Chapter 795 and referenced chapters**

(a) A CNSP shall be labeled in compliance with USP Chapter 795 and shall include the following:

(1) Route of intended administration

(2) Name of compounding pharmacy and dispensing pharmacy (if different)

(b) Labeling shall also include:

(1) Any special handling instructions

(2) Any warning statements that are applicable

(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 under Business and Professions Code section 4076 and Section 1707.5.

### **1735.10 ESTABLISHING BEYOND-USE DATES**

#### **In addition to the requirements in the USP Chapter 795 and referenced chapters**

(a) Beyond use dates (BUDs) assigned with only a date shall expire at midnight at the end of date.

(b) No BUDs shall be assigned that exceed:

- (1) The limits specified in USP Chapter 795,
- (2) The chemical and physical properties of the drug and/or its formulation,
- (3) The compatibility of the container–closure system with the finished preparation (e.g., leachables, interactions, and storage conditions), or
- (4) Shortest remaining expiration date or BUD of any of the starting components.

(c)(1) If the BUD of the CNSP is extended beyond the BUDs in USP Chapter 795, an aqueous CNSP, as defined by USP Chapter 795, shall be tested for antimicrobial effectiveness, in compliance with USP Chapter 51, Antimicrobial Effectiveness Testing.

(2) If a pharmacy chooses to use antimicrobial effectiveness testing results provided by an FDA-registered facility or published in peer-reviewed literature sources the full reference, including the raw data and testing method suitability, and shall be fully available at the time of compounding and three years from each dispense.

### **1735.11 SOPs**

#### **In addition to the requirements in the USP Chapter 795 and referenced chapters**

(a) Standard operating procedures (SOPs) shall:

- (1) Comply with Quality Assurance in Pharmaceutical Compounding USP Chapter 1163,
- (2) Include at least the SOPs listed in USP Chapter 1163, Quality Assurance in Pharmaceutical Compounding, and
- (3)

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

(B) Include 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) Include the determination and approval, by a pharmacist, of the ingredients and the compounding process for each preparation before compounding begins

(b) Any pharmacy engaged in compounding non-sterile drug preparations shall maintain and follow written policies and procedures for compounding.

(c) 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 are implemented. Such changes shall be documented and disseminated to the appropriate staff prior to implementation.

### **1735.12 QUALITY ASSURANCE AND QUALITY CONTROL**

**In addition to the requirements in the USP Chapter 795 and referenced chapters**

(a) The quality assurance program shall comply with Section 1711 and also include 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, potency, quality, or labeled strength.

(2) A written procedure for responding to out-of-range temperature variations within the medication storage areas where furnished drug is returned for redispensing.

(3) Compliance with USP Chapter 1163, Quality Assurance in Pharmaceutical Compounding and shall include the integrated components and standard operating procedures.

### **1735.13 PACKAGING AND TRANSPORTING**

**In addition to the requirements in the USP Chapter 795 and referenced chapters**

(a) There shall be a defined process and documented procedure to ensure temperature sensitive products will arrive at their desired destinations after transporting within the expected quality standards for integrity, potency, quality and labeled strength.

(b) Packaging materials shall protect CNSPs from damage, leakage, contamination, degradation, and adsorption while preventing inadvertent exposure to transport personnel.

(c) A pharmacist supervising compounding is responsible for the proper preparation, labeling, storage, and delivery of the compounded drug preparation.

### **1735. 14 COMPLAINT HANDLING AND ADVERSE EVENT REPORTING**

**In addition to the requirements in the USP Chapter 795 and referenced chapters**

(a) The pharmacy shall process recalls in compliance with Business and Professions Code section 4126.9.

(b) All complaints related to a potential quality problem with a compounded drug preparation and all adverse events shall be reviewed by the pharmacist-in-charge, this review shall be documented and dated. All complaints shall be handled in compliance with Business and Professions Code section 4126.9.

### **1735.15 DOCUMENTATION**

**In addition to the requirements in the USP Chapter 795 and referenced chapters**

(a) Pharmacies shall maintain and retain all records required by this article and requirements in

the USP chapters 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).

(b) Records created shall be in an un-editable form. If edits are needed it must be tracked and the person making the edits along with date and time shall be documented. As used in the subdivision: Tracked is means the original documentation is readable and notes any changes made.

## **Proposal to Repeal Article 4.5 Compounding including Sections 1735-1735.8.**

### **Proposal to Add Article 4.5 as proposed with the following:**

#### **Article 4.5 Nonsterile Compounding in Pharmacies**

##### **1735. Nonsterile Compounding in Licensed Pharmacies**

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

**Necessity:** Defines the locations for USP applicability to the board's regulated public.

(b) Repackaging of a compounded nonsterile preparation (CNSP) shall be considered compounding and this article shall apply.

**Necessity:** Provides clarity to the regulated public as the provisions USP related repackaging provisions speak only to conventionally manufactured products. Absent this provision, the board's regulated public would be unclear if the repackaging of a compounded nonsterile preparations was allowed and if so, under what conditions.

(c) Reconstitution in accordance with directions which have not been FDA approved are considered compounding and all requirements shall apply.

**Necessity:** This provide clarity because USP does not provide direction on what type of practice repackaging of a preparation is.

(d) No compounded non-sterile preparations (CNSPs) shall be compounded prior to receipt by a pharmacy of a valid patient specific prescription document 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 document prior to compounding. A signed and dated document between a prescriber and a pharmacy may serve as an understanding that all non-commercially available preparations will be compounded the identified patient.

(1) Except that a pharmacy may prepare and store a limited quantity of a CNSP 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 an identified population of patients of the pharmacy based on a documented history of prescriptions for that patient population.

**Necessity:** Ensures consistency with 503A provisions.

- (e) No pharmacy or pharmacist shall compound a CNSP 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 drug preparations 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 (A) the 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, or (B) the compounding of that CNSP 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 or the specific medical need in the pharmacy records for three years from the date of receipt of the documentation.
  - (4) Is made with any component not intended for use in a CNSP for the intended patient population.

**Necessity:** To ensure consistency with general provisions of federal law including 503A provisions SEC 503a (353a (b)(3)(A), SEC 503a (353a (b)(1) (C), CFR 216.24 and SEC 503a (353a (b)(1) (D), as well as to allow use of the specified ASHP list as necessary for patient care. Duplication with federal law provides for ease of use with the board's regulated public. Further proposed sections (e)(1) – (3) are consistent with current regulations. Further, (e)(4) ensures only appropriately graded (based on intended use, patient, etc.). Would prohibit inappropriate graded products from use in compounded products.

(f) 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. XX/XX.) as required by Section 1715 of Title 16, Division 17, of the California Code of Regulations.

**Necessity:** This is consistent with current regulation and provides for consumer protection through self-education and assessment by licensee.

(g) In addition to CCR 1707.2, consultation shall be available to the patient and/or primary caregiver concerning proper use, storage, handling, and disposal of a CNSP and related supplies furnished by the pharmacy.

**Necessity:** This is consistent with current requirements.

(h) Compounding with blood or blood components shall be done in compliance with Health and Safety Code section 1602.5.



**Necessity:** Provides clarity to the regulated public about the supplemental requirements established the HSC.

(i) Storing, weighing, measuring, compounding, and/or performing other manipulation of an active pharmaceutical ingredient (API) or added substance deemed hazardous by Occupational Safety and Health (NIOSH) shall be done in compliance with CCR XXX and USP Chapter 800.

**Necessity:** Provides clarity to the regulated public about the supplemental requirements that must be followed in USP 800.

(j) Storing, weighing, measuring, compounding, and/or performing other manipulation of an antineoplastic under Occupational Safety and Health (NIOSH) shall be done in compliance with CCR XXX and USP chapter 800.

**Necessity:** Provides clarity to the regulated public about the supplemental requirements that must be followed in USP 800.

#### **1735.1. INTRODUCTION AND SCOPE AND COMPOUNDING DEFINITIONS.**

##### **In addition to the definitions in the USP Chapter 795 and referenced chapters**

(a) “Approved labeling” means the Food and Drug Administration’s (FDA) approved labeling which contains FDA approved information for the diluent, the resultant strength, the container closure system, and storage time.

**Necessity:** Provides clarity to the regulated public as to what is meant by Approved labeling in USP.

(b) “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.

**Necessity:** Ensures consistency with the provisions of 503A with the increase of the word “clinically’ to eliminate abuse. Reference: SEC 503a (353a (b)(1) (D)(2)).

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

**Necessity:** Provides clarity to the board’s regulated public about what a diluent is for purposes of compounding and its implications for FDA labeling. USP does not provide a definition.

(d) “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.

**Necessity:** Term is broadly used throughout the Chapter, but is not defined. Further, the definition is consistent with current legal definition.

(e) “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, that is not pursuant to a prescription.

**Necessity:** Term is broadly used throughout the Chapter but is not defined. This definition is drawn from USP 797.

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

**Necessity:** This provision is consistent with the board’s current regulation. Further, the definition is necessary to ensure that the regulated public understands that a preparation refers to an item that is compounded versus a commercially available product. The term is broadly used throughout the Chapter but is not defined.

(g) “Product” means a commercially or conventionally manufactured drug or nutrient evaluated for safety and efficacy by the FDA.

**Necessity:** The term is broadly used throughout the Chapter but is not defined

(h) “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.

**Necessity:** Term is broadly used throughout the Chapter but is not defined. Further, the language is consistent with current legal definition in regulation.

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

**Necessity:** Term is broadly used throughout the Chapter but is not defined. Consistent with current legal definition in regulation.

(j) “Potency” means an active ingredient strength within +/- 10% (or the range specified in USP) of the labeled amount.

**Necessity:** Term is broadly used throughout the Chapter but is not defined. Consistent with

current legal definition in regulation.

## **1735.2 PERSONNEL TRAINING AND EVALUATION**

**In addition to the requirements in USP Chapter 795 and referenced chapters.**

(a) Training, evaluation, and requalification of personnel involved in the preparation and handling of CNSP preparations shall also contain at least the following:

- (1) Quality assurance and quality control procedures,
- (2) Container closure and equipment selection and
- (3) Component selection and handling

**Necessity:** Comprehensive training is essential to ensure the safety of California consumers dispensed or administered a CNSP.

(b) A pharmacist responsible for or directly supervising and controlling compounding of CNSPs, shall demonstrate proficiency in skills necessary to ensure the integrity, potency, quality, and labeled strength of CNSP.

**Necessity:** Because USP requires a facility to designate one or more individuals, a designated person, this needs to be clarified to ensure that the requirement applies to a pharmacist, who under pharmacy law, must be supervising or performing the compounding.

(c) Personnel 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) as detailed in the SOPs.

**Necessity:** Allowing an individual to compound inappropriately will compromise consumer protection, as such immediate remediation is necessary.

(d) The pharmacist-in-charge shall be responsible for all activities and decisions made or approved by the designated person(s).

**Necessity:** Remove any doubt about the role of the PIC in pharmacy law and his or her ultimate responsibility for compliance.

(e) The pharmacy must document that any person assigned to provide training has obtained training and demonstrated competency in any area they will be providing training or observational review.

**Necessity:** Provides clarity to the regulated public that any person who has proper training may provide training to others, as long as the person can demonstrate appropriate competency to do so. Also, provides clarity that other staff besides the PIC can, if properly trained, may provide training or observational review.

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### **1735.3 PERSONAL HYGIENE AND GARBING**

#### **In addition to the requirements in the USP Chapter 795 and referenced chapters**

(a) 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 conditions to determine if such condition could contaminate a CNSP or the environment. The supervising pharmacist shall not allow personnel with potentially contaminating conditions to enter the compounding area.

**Necessity:** To eliminate the potential of contamination of CNSPs, ensures a supervising pharmacist appropriately evaluates any such conditions and prevents potential contamination from such conditions. The list of conditions was developed based on the USP 795 requirements.

(b) Prior to entry into the compounding area all hand, wrist, and other exposed jewelry or piercing shall be removed.

**Necessity:** Provides clarity to the regulated public that such items must be removed for patient care. Further, proper fit of garb should not be subjective.

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

**Necessity:** To prevent the cross contamination and inadvertent inhalation of components when the component is a powder.

(d) 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.

**Necessity:** To prevent contamination of the garb used in compounding.

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

**Necessity:** Although this is only a recommendation on the USP chapter, to prevent contamination, the cleaning of such garb must be mandatory. Failure to do so, can lead to product contamination.

(f) Eye glasses shall be cleaned as part of hand hygiene and garbing per a facility standard operating procedures (SOPs).

**Necessity:** To prevent product contamination, some level of cleaning must be performed.

(g) Any gowning or garbing accommodation made by the designated person shall be

documented and a full assessment of the risk to the CNSPs and environment shall be included. Documentation and assessment shall be done prior to accommodation taking place.

**Necessity:** To provide accommodation and flexibility to staff after full assessment of the risk has been considered and determination has been made that preparation is not compromised.

#### **1735.4 BUILDING AND FACILITIES**

**In addition to the requirements in the USP Chapter 795 and referenced chapters**

(a) The handwashing stations and scrub sinks used for compounding, hand hygiene, or both, shall not be part of a restroom or water closet.

**Necessity:** USP is silent on the location of a sink. Restroom sinks are a significant source of contamination and as such are not an appropriate location for such function to occur. This is also consistent with current board regulation.

(b) Compounding personnel must monitor temperatures in storage area(s) and compounding areas either manually at least once daily on days that the facility is open or by a continuous temperature recording device to determine whether the temperature remains within the appropriate range for the CNSPs or components. This shall be documented.

**Necessity:** To ensure the appropriate temperature range of both the components and compounding areas, monitoring must be performed and documented.

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

**Necessity:** To ensure no product contamination results from the use of poor quality (tap water) water being used to wash the equipment used in compounding.

(d) No CNSP shall be compounded if it is known, or reasonably should be known, that the compounding environment fails to meet criteria specified in the pharmacy's written policies and procedures or those required in USP chapter 795.

**Necessity:** Requires the cessation of compounding in an environment found to be noncompliant to prevent the risk of contamination.

#### **1735.5 CLEANING AND SANITIZING**

**In addition to the requirements in the USP Chapter 795 and reference chapters**

(a) Documentation of the cleaning and sanitizing of the compounding area include the personnel completing the cleaning and sanitizing and the cleaning and sanitizing agents used.

**Necessity:** To ensure proper cleaning occurs and appropriate information documented to confirm compliance.

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(b) Decontamination, cleaning, disinfecting and sporicidal agents shall be used in accordance with manufacturers' specifications.

**Necessity:** Only products used consistent with the manufacturers specification can be used to perform decontamination, cleaning, disinfecting and sporicidal agent to ensure appropriate decontamination, cleaning and disinfecting is achieved.

### **1735.6 EQUIPMENT AND COMPONENTS**

**In addition to the requirements in the USP Chapter 795 and referenced chapters**

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

**Necessity:** Failure to use equipment according to manufacturer's specification can impact the safety and efficacy of the preparation.

(b) Any component used to compound a CNSP shall be used, stored, and dispensed, in accordance with all the following:

- (1) United States Pharmacopeia (USP)- National Formulary (NF),
- (2) Food Drug and Cosmetic Act (FD&CA),
- (3) Food Drug Administration (FDA) and
- (4) Manufacturers' specifications and requirements.

**Necessity:** USP requires compliance with all federal and state laws. The provided list is intended to expand to provide more guidance to the board's regulated public on all that is encompassed in that.

(c) Any API or added substance used to compound a CNSP shall be obtained from an FDA-registered supplier and shall be accompanied by a valid certificate of analysis (COA). This COA shall be in English and should all the requirements of USP Chapter 1080, Bulk Pharmaceutical Excipient- Certificate of Analysis. All COAs shall be readily retrievable for at least 3 years from last use in CNSP.

**Necessity:** The FD&C establishes that only APIs from a registered facility can be used. To ensure only proper added substances are used, the same threshold as required for APIs must be applied related to purchasing and COA requirements to avoid patient harm.

(e) Once removed from the original container, components not used in compounding (e.g., excess after weighing) shall be discarded and not returned to the original container to minimize the risk of contaminating the original container.

**Necessity:** To prevent contamination of components by reintroducing already removed product which may have been compromised.

### **1735.7. MASTER FORMULATION AND COMPOUNDING RECORDS**

**In addition to the requirements in the USP Chapter 795 and referenced chapters.**

(a) A CNSP shall not be compounded until the pharmacy has first prepared a written master formulation document in compliance with USP Chapter 795 and the following:

- (1) Active pharmaceutical ingredient (API) or added substances identities and amounts shall include at least salt form and purity grade, if available.
- (2) Container–closure systems shall include at least volume, and type for each container and closure to be used.
- (3) The reference source of the BUD assignment; each reference shall be fully available at the time of compounding and 3 years from each dispense.
- (4) Instructions for storage and handling of the compounded drug preparation.

**Necessity:** Provides clarification regarding the expectation for documentation to ensure complete records. Note: this does not expand upon USP requirements regarding master formulas.

(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 be in compliance with USP 795 and 1735.7(a).

**Necessity:** This will allow the current practice for such documentation to continue for those products not routinely compounded.

(c) A compounding record shall be a single document and shall include the requirements of USP chapters 795, and 800 as applicable, and the following:

- (1) The date and time of preparation shall be the time when compounding started and when the assigned BUD starts.
- (2) the assigned internal identification number shall be unique for each compounded drug preparation.
- (3) the total quantity compounded shall include the number of units made and volume or weight of each unit.
- (4) The identity of the compounder and pharmacist verifying the final drug preparation.

**Necessity:** Provides clarification as what is expected in the documentation to ensure complete records and establishes a requirement to document the staff involved in the compounding on the record, including the pharmacist performing verification of the final drug preparation. Such documentation ensures a complete record and allows for identification and remediation of staff if necessary.

## **1735.8 RELEASE INSPECTIONS**

### **In addition to the requirements in the USP Chapter 795 and referenced chapters**

A 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 once the preparation is dispensed.

**Necessity:** This is current law. USP does not establish the responsibility of the pharmacist involvement in compounding as the USP Chapter applies to all settings where compounding occurs. Clarification is necessary to ensure the board's regulated public has a clear understanding of his or her responsibility.

## **1735.9 LABELING**

### **In addition to the requirements in the USP Chapter 795 and referenced chapters**

(a) A CNSP shall be labeled in compliance with USP Chapter 795 and shall include the following:

- (1) Route of intended administration
- (2) Name of compounding pharmacy and dispensing pharmacy (if different)
- (b) Labeling shall also include:
  - (1) Any special handling instructions
  - (2) Any warning statements that are applicable
  - (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

**Necessity:** It is imperative that any CNSP leaving a facility shall be properly labeled for patient safety and to avoid patient harm, USP provisions make these items recommendations only. Patients must have a clear understanding of how to take their medications as well as how to contact the compounding pharmacy.

(c) Any CNSP 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 Section 1707.5.

**Necessity:** This is current law and requires patient specific labeling on a compounded product.

## **1735.10 ESTABLISHING BEYOND-USE DATES**

### **In addition to the requirements in the USP Chapter 795 and referenced chapters**

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(a) Beyond use dates (BUDs) assigned with only a date shall expire at midnight at the end of date.

**Necessity:** To provide clarity to the regulated public on the board's expectation regarding determination of a BUD.

(b) No BUDs shall be assigned that exceed:

- (1) The limits specified in USP Chapter 795,
- (2) The chemical and physical properties of the drug and/or its formulation,
- (3) The compatibility of the container–closure system with the finished preparation (e.g., leachables, interactions, and storage conditions), or
- (4) Shortest remaining expiration date or BUD of any of the starting components.

**Necessity:** To avoid patient harm the above parameters shall be used to assign the BUD. Under USP section 10 the above items may be optional in establishment of a BUD. To ensure the integrity, potency, quality and labeled strength of a preparation the above parameters shall be used to limit the BUD.

(c)(1) If the BUD of the CNSP is extended beyond the BUDs in USP Chapter 795, an aqueous CNSP, as defined by USP Chapter 795, shall be tested for antimicrobial effectiveness, in compliance with USP Chapter 51, Antimicrobial Effectiveness Testing.

- (2) If a pharmacy chooses to use antimicrobial effectiveness testing results provided by an FDA-registered facility or published in peer-reviewed literature sources the full reference, including the raw data and testing method suitability, and shall be fully available at the time of compounding and three years from each dispense.

**Necessity:** Ensures compliance with relevant USP Chapters and establishes the timeframe for documentation. Further, this provides clarity to the board's regulated public on the board's expectations.

### **1735.11 SOPs**

#### **In addition to the requirements in the USP Chapter 795 and referenced chapters**

(a) Standard operating procedures (SOPs) shall:

- (1) Comply with Quality Assurance in Pharmaceutical Compounding USP Chapter 1163,
- (2) Include at least the SOPs listed in USP Chapter 1163, Quality Assurance in Pharmaceutical Compounding, and
- (3)
  - (A) Include methods by which the supervising pharmacist will ensure the quality of compounded drug preparations.
  - (B) Include 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) Include the determination and approval, by a pharmacist, of the ingredients and the compounding process for each preparation before compounding begins

**Necessity:** Ensures compliance with relevant USP Chapters and provides clarity to the board's regulated public on the board's expectation.

(b) Any pharmacy engaged in compounding non-sterile drug preparations shall maintain and follow written policies and procedures for compounding.

**Necessity:** The above language is in current law in the under CCR 1735.3(a) and 1735.5(a) and provides clarity to the regulated public on the board's expectations and enforceability.

(c) 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 are implemented. Such changes shall be documented and disseminated to the appropriate staff prior to implementation.

**Necessity:** The above language is in current law and clarifies the need to document any changes in the policy prior to implementation. CCR 1735.5(b).

## **1735.12 QUALITY ASSURANCE AND QUALITY CONTROL**

### **In addition to the requirements in the USP Chapter 795 and referenced chapters**

(a) The quality assurance program shall comply with Section 1711 and also include 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, potency, quality, or labeled strength.

(2) A written procedure for responding to out-of-range temperature variations within the medication storage areas where furnished drug is returned for redispensing.

(3) Compliance with USP Chapter 1163, Quality Assurance in Pharmaceutical Compounding and shall include the integrated components and standard operating procedures.

**Necessity:** A robust QA program is essential for consumer protection. The proposed language is consistent with current legal requirements in board regulation (e.g. 1735.8(d) and CCR 1735.8(e). USP established separate sections for Quality Assurance and Quality Control (Section 12) and Complaint Handling and Adverse Event Reporting (Section 14.) Further, a comprehensive QA program must include the process to follow in the event of a recall and procedures to follow in

the event of a temperature excursion. This section also provides cross reference to relevant USP chapters to assist with full compliance with USP and to ensure consistency within the practice.

### **1735.13 PACKAGING AND TRANSPORTING**

#### **In addition to the requirements in the USP Chapter 795 and referenced chapters**

(a) There shall be a defined process and documented procedure to ensure temperature sensitive products will arrive at their desired destinations after transporting within the expected quality standards for integrity, potency, quality and labeled strength.

**Necessity:** A process and procedure is necessary to ensure the product arrives with the same integrity, potency, quality and labeled strength as labeled. USP provides general requirements but lacks sufficient specificity on the minimum requirements.

(b) Packaging materials shall protect CNSPs from damage, leakage, contamination, degradation, and adsorption while preventing inadvertent exposure to transport personnel.

**Necessity:** USP provides this as a recommendation only, however to ensure proper packaging of a CNSP to ensure patient safety it must be a requirement.

(c) A pharmacist supervising compounding is responsible for the proper preparation, labeling, storage, and delivery of the compounded drug preparation.

**Necessity:** This provision is consistent with current board regulation. Further, because USP is applicable in all settings where compounding can occur, clarification to board licensees on the board's requirements and board jurisdiction is necessary.

### **1735. 14 COMPLAINT HANDLING AND ADVERSE EVENT REPORTING**

#### **In addition to the requirements in the USP Chapter 795 and referenced chapters**

(a) The pharmacy shall process recalls in compliance with Business and Professions Code section 4126.9.

**Necessity:** Establishes a cross-reference to the underlying statute regarding recall provisions for nonsterile compounded drug products.

(b) All complaints related to a potential quality problem with a compounded drug preparation and all adverse events shall be reviewed by the pharmacist-in-charge, this review shall be documented and dated. All complaints shall be handled in compliance with Business and Professions Code section 4126.9.

**Necessity:** As USP requirements apply to all settings where compounding can occur, clarification on the board's expectation regarding the responsibility of the PIC is necessary to

ensure a common understanding of the applicability of the requirement for board licensees.

### **1735.15 DOCUMENTATION**

#### **In addition to the requirements in the USP Chapter 795 and referenced chapters**

(a) Pharmacies shall maintain and retain all records required by this article and requirements in the USP chapters 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).

**Necessity:** The above language is in current law (CCR 1735.3(b) and clarifies the board's expectation for compliance.

(b) Records created shall be in an un-editable form. If edits are needed it must be tracked and the person making the edits along with date and time shall be documented. As used in the subdivision: Tracked is means the original documentation is readable and notes any changes made.

**Necessity:** Records should not be editable to ensure proper tracking and compliance. This is needed to ensure the original document is correct and appropriate audit of changes is maintained.