California State Board of Pharmacy
2720 Gateway Oaks Drive, Suite 100
Sacramento, CA 95833
Phone: (916) 518-3100 Fax: (916) 574-8618
www.pharmacy.ca.gov

Business, Consumer Services and Housing Agency
Department of Consumer Affairs
Gavin Newsom, Governor

Compounding Committee Report
July 11, 2019

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

1. Call to Order and Establishment of Quorum

2. Public Comment for Items Not on the Agenda, Matters for Future Meetings*
   **Note: The committee may not discuss or take action on any matter raised during the public comment section that is not included on this agenda, except to decide to place the matter on the agenda of a future meeting. Government Code Sections 11125 and 11125.7(a)*

3. 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.

   During this meeting

   During this meeting, members will have the opportunity to review proposed regulations 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 committee will have the opportunity to discuss the proposal and, if appropriate, make recommendations for the board's consideration during its July 2019 meeting.

   Attachment 1 includes two documents:
   1. Proposed regulation language to repeal and replace Article 4.5 related to Compounding.

2. Proposed regulation language that also includes a brief description of the necessity for the regulation provisions.

4. Approval of the April 16, 2019, Meeting Minutes

Attachment 2

Provided in **Attachment 2** for the committee's review and approval are the draft minutes from the February committee meeting.

5. Future Committee Meeting Dates

- August 28, 2019 – Staff is working to secure a location in Southern California. Once the location is finalized, the board's website will be updated and a subscriber alert will be sent.
- September 24, 2019
- October 16, 2019

6. Adjournment

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

1735. Compounding in Licensed Pharmacies

(a) "Compounding" as defined by United States Pharmacopeia in Pharmaceutical Compounding -Nonsterile Preparations Chapter 795 (USP Chapter <795>) 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 all requirements shall apply.

(c) Repackaging in accordance with directions which have not been FDA approved are still consider 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-commercial available perpetrations 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 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, or 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 and 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)Weighing, measuring, compounding, and/or preforming 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) Weighing, measuring, compounding, and/or preforming 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.

(e) "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.

(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.

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

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

(j) “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.

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

1735.2 PERSONNEL TRAINING AND, EVALUATION
In addition to the requirements in USP Chapter 795 and referenced chapters.

(a) Training, evaluation, and requalification 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) The 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 CSNP.

(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) Any person assigned to provide training must have documentation to show that they have obtained training and demonstrated competency an 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) Compounding personnel experiencing any of the following: rashes, recent tattoos or oozing

sores, conjunctivitis, active respiratory infection or and other conditions which could contaminate a CNSP or the environment shall not be allowed 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/scrub sink used for compounding and/or hand hygiene 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) If compounding is performed daily, no activity other than compounding shall take place in the compounding area.

(e) 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) Cleaning and sanitizing of the compounding area must be documented each time it occurs. The personnel completing the cleaning and sanitizing shall be identified as well as 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 manufacturers' specifications.

(b) Any weighing, measuring, or other manipulation of a components in powder form shall occur inside a closed system processing device such as a ventilated enclosures (CVEs), or biological safety cabinets (BSCs).

(1) Closed system processing devices shall be certified according to current Controlled Environment Testing Association (CETA) guidelines.

(c) 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 formula (NF),

(2) Food Drug and Cosmetic Act (FD&CA),

(3) Food Drug Administration (FDA), and

(4) Manufacturers' specifications and requirements.

(d) 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 Bulk Pharmaceutical Excipient-certificate of analysis, USP Chapter 1080. All COAs shall be readily retrievable for at least 3 years from last use in CNSP.

(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.

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 formula 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.
(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 formula 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 log 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) 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 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 incompliance with USP Chapter 795 and the following:
(1) label shall also include:
(A) Route of intended administration
(B) Name of compounding pharmacy and dispensing pharmacy (if different)
(2) Labeling shall also include:
(A) Any special handling instructions
(B) Any warning statements that are applicable
(C) Name, address, 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

(b)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 California Code of Regulations, title 16, 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 on that date.

(b) No Beyond Use Date (BUDs) shall be assigned that exceeds:
(1) The limits defined 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)
(4) shortest remaining expiration date or BUD of any of the starting components.

(c) 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 Antimicrobial Effectiveness Testing USP Chapter <51>.
(1) 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 3 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 Quality Assurance in Pharmaceutical Compounding USP Chapter 1163, and
(3) include 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 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 written policies and procedures for compounding. Any material failure to follow the pharmacy's written policies and procedures shall constitute a basis for disciplinary action.

(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 in policies and procedures 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 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 Quality Assurance in Pharmaceutical Compounding USP chapter 1163 and shall include the integrated components and standard operating procedures.

(4) Quality assurance program shall be compliant with section CCR 1711.

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 heat/cold 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) The 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) Recalls shall be carried out 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

1735. Compounding in Licensed Pharmacies

(a) "Compounding" as defined by United States Pharmacopeia in Pharmaceutical Compounding -Nonsterile Preparations Chapter 795 (USP Chapter <795>) 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 all requirements 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) Repackaging in accordance with directions which have not been FDA approved are still consider 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-commercial available perpetrations 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 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, or 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 and 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 o 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)Weighing, measuring, compounding, and/or preforming 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) Weighing, measuring, compounding, and/or preforming 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.

(e) "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.

(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.

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

(h) "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.

(i) "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.

(j) "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.

(j) "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.

1735.2 PERSONNEL TRAINING AND, EVALUATION
In addition to the requirements in USP Chapter 795 and referenced chapters.

(a) Training, evaluation, and requalification 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) The 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 CSNP.

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) Any person assigned to provide training must have documentation to show that they have obtained training and demonstrated competency an 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.

1735.3 PERSONAL HYGIENE AND GARBING
In addition to the requirements in the USP Chapter 795 and referenced chapters

(a) Compounding personnel experiencing any of the following: rashes, recent tattoos or oozing sores, conjunctivitis, active respiratory infection or and other conditions which could contaminate a CNSP or the environment shall not be allowed to enter the compounding area.

Necessity: To eliminate the potential of contamination of CNSPs, such protections are mandatory, not discretionary. 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/scrub sink used for compounding and/or hand hygiene 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) If compounding is performed daily, no activity other than compounding shall take place in the compounding area.

Necessity: To provide clarity to the regulated public on what can and cannot occur in the compounding area.

(e) 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) Cleaning and sanitizing of the compounding area must be documented each time it occurs. The personnel completing the cleaning and sanitizing shall be identified as well as the cleaning and sanitizing agents used.

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

(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 manufacturers' specifications.

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

(b) Any weighing, measuring, or other manipulation of a components in powder form shall occur inside a closed system processing device such as a ventilated enclosures (CVEs), or biological safety cabinets (BSCs).

(1) Closed system processing devices shall be certified according to current Controlled Environment Testing Association (CETA) guidelines.

Necessity: To ensure containment of any powder and avoid possible cross contamination and inadvertent inhalation of powders.

(c) 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 formula (NF),

(2) Food Drug and Cosmetic Act (FD&CA),

(3) Food Drug Administration (FDA), and

(4) Manufacturers' specifications and requirements.

Necessity: To ensure safe and appropriate component selection in CNSPs to avoid patient harm.

(d) 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 Bulk Pharmaceutical Excipient-certificate of analysis, USP Chapter 1080. 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 formula 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.
(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 formula 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 log 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 log, 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) 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 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 incompliance with USP Chapter 795 and the following:
(1) label shall also include:
(A) Route of intended administration
(B) Name of compounding pharmacy and dispensing pharmacy (if different)
(2) Labeling shall also include:
(A) Any special handling instructions
(B) Any warning statements that are applicable
(C) Name, address, 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

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.

(b)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 California Code of Regulations, title 16, 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

(a) Beyond use dates (BUDs) assigned with only a date shall expire at midnight on that date.

Necessity: To provide clarity to the regulated public on the board's expectation regarding

determination of a BUD.

(b) No Beyond Use Date (BUDs) shall be assigned that exceeds:
(1) The limits defined 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)
(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) 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 Antimicrobial Effectiveness Testing USP Chapter <51>.
(1) 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 3 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 Quality Assurance in Pharmaceutical Compounding USP Chapter 1163, and
(3) include 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 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 written policies and procedures for compounding. Any material failure to follow the pharmacy's written policies and procedures shall constitute a basis for disciplinary action.

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 in policies and procedures 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 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 Quality Assurance in Pharmaceutical Compounding USP chapter 1163 and shall include the integrated components and standard operating procedures.

(4) Quality assurance program shall be compliant with section CCR 1711.

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 heat/cold 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) The 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) Recalls shall be carried out 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 editable to ensure proper tracking and compliance. This is needed to ensure the original document is correct and appropriate audit of changes is maintained.

Attachment 2

California State Board of Pharmacy
1625 N. Market Blvd, N219
Sacramento, CA 95834
Phone: (916) 574-7900 Fax: (916) 574-8618
www.pharmacy.ca.gov

Business, Consumer Services and Housing Agency
Department of Consumer Affairs
Gavin Newsom, Governor

DRAFT

COMPOUNDING COMMITTEE MEETING MINUTES

DATE: April 16, 2019

LOCATION: Department of Consumer Affairs
First Floor Hearing Room
1625 N. Market Blvd.
Sacramento, CA 95834

COMMITTEE MEMBERS PRESENT: Maria Serpa, Licensee Member, Chairperson
Stan Weisser, Licensee Member, Vice Chairperson
Victor Law, Licensee Member
Allen Schaad, Licensee Member

COMMITTEE MEMBERS NOT PRESENT: Shirley Kim, Public Member

STAFF MEMBERS PRESENT: Anne Sodergren, Interim Executive Officer
Julia Ansel, Chief of Enforcement
Christine Acosta, Supervising Inspector
Laura Hendricks, Staff Analyst
Laura Freedman, DCA Staff Counsel
Kelsey Pruden, DCA Staff Counsel

1. **Call to Order and Establishment of Quorum and General Announcements**

   Chairperson Serpa called the meeting to order at 10:05 am. Board members present: Allen Schaad, Maria Serpa, Stan Weisser and Victor Law. A quorum was established.

2. **Public Comment on Items not on the Agenda/Agenda Items for Future Meetings**

   There were no comments from the committee or the public.

3. **Presentation on the Proposed USP Chapter 800 – Hazardous Drugs – Handling in Healthcare Settings**

   The committee heard a presentation on the current proposed revisions to USP General Chapter 800 regarding the handling of hazardous drugs by Supervising Inspector Christine Acosta.

Supervising Inspector Acosta provided an overview of the United States Pharmacopeia (USP) 2015-2020 Council of Experts including Healthcare Quality Standards Collaborative Group which includes compounding. USP maintains resolutions to work with stakeholders in the development and maintenance of practice and quality standards in sterile and nonsterile compounding. USP includes General Chapters: <795> – Pharmaceutical Compounding – Nonsterile Products; <797> – Pharmaceutical Compounding – Sterile Preparations; <800> – Hazardous Drugs – Handling in Healthcare Settings; and <825> – Radiopharmaceutical Preparation, Compounding, Dispensing, and Repackaging. Dr. Acosta updated the committee on the status of USP revising Chapter <797> and subsequent revisions. The committee was provided with a summary of the changes made in draft Chapter <797> based on the 18 sections.

Dr. Acosta stated that the National Institute for Occupational Safety and Health (NIOSH) is a division of Center for Disease Control and Prevention (CDC). She explained that NIOSH developed a list of antineoplastic and other hazardous drugs in healthcare settings. Dr. Acosta noted that the list has not been updated in 2018, but an updated list is expected to be released soon (typically it is updated every two years).

Dr. Acosta reviewed the following six characteristics that are used by NIOSH to determine if a drug is hazardous in humans or animals.

- Carcinogenicity
- Teratogenicity or fertility impairment
- Reproductive toxicity
- Organ toxicity
- Genotoxicity
- Structure and toxicity profiles of new drugs that mimic existing drugs determined hazardous

Dr. Acosta explained that NIOSH organizes hazardous drugs into categories which are commonly referred to as "tables." Dr. Acosta summarized the characteristics of each of the tables as provided below.

Table 1. Group 1: Antineoplastic drugs

- One or more of the NIOSH criteria for a hazardous drug.
- Many of these drugs are cytotoxic.
- Represent an occupational hazard to healthcare workers and should ***always*** be handled with use of recommended engineering controls and personal protective equipment (PPE), regardless of their formulation.

Table 2. Group 2: Non-antineoplastic drugs that meet one or more of the NIOSH criteria for a hazardous drug

- Some of these drugs may represent an occupational hazard to males or females who are actively trying to conceive, women who are pregnant or may become pregnant, and women who are breast feeding, because they may be present in breast milk.
- Unopened, intact tablets and capsules may not pose the same degree of occupational exposure risk as injectable drugs, which usually require extensive preparation.

Table 3. Group 3: Non-antineoplastic drugs that primarily have adverse reproductive effects

- NIOSH criteria for reproductive hazards.
- Represent a potential occupational hazard to males or females who are actively trying to conceive, women who are pregnant or may become pregnant, and women who are breast feeding, as they may be present in breast milk.
- Unopened, intact tablets and capsules may not pose the same degree of occupational risk as injectable drugs that usually require extensive preparation.

Table 4

- Contains drugs that were deleted from the 2014 NIOSH hazardous drug list for the 2016 update; however, there are no deletions to report.

Table 5

- Provides general guidance for some of the possible scenarios that may be encountered in healthcare settings where hazardous drugs are handled.

Dr. Acosta explained that NIOSH defines the criteria and identifies hazardous drugs (HD), while USP develops the standards for handling these HDs to minimize the risk to public health. Dr. Acosta stated that the goals of the USP standards are to help increase awareness, provide uniform guidance to reduce the risk of managing HD, and help reduce the risk posed to patients and the healthcare workforce. Dr. Acosta noted that healthcare workers will become patients if they are exposed to these HDs without the proper precautions.

Dr. Acosta stated that there has been a delay in enforceable date for USP 800 due to the number of comments and stakeholders involved; however, it is expected to become enforceable on December 1, 2019.

Dr. Acosta recommended that interested parties visit the frequently asked questions section of USP's website because it contains a wealth of information broken down in an easy to search format.

Dr. Acosta reported that USP 800 is broken down into the following 18 sections. She noted that her presentation would also be broken down into these sections.

1. Introduction and Scope
2. List of Hazardous Drugs
3. Types of Exposure
4. Responsibilities of Personnel Handling Hazardous Drugs
5. Facilities and Engineering Controls
6. Environmental Quality and Control
7. Personal Protective Equipment
8. Hazard Communication Program
9. Personnel Training
10. Receiving
11. Labeling, Packaging, Transport, and Disposal
12. Dispensing Final Dosage Forms
13. Compounding

14. Administering
15. Deactivating, Decontaminating, Cleaning, and Disinfecting
16. Spill Control
17. Documentation and Standard Operating Procedures
18. Medical Surveillance

Section 2. List of Hazardous Drugs

Dr. Acosta explained that NIOSH maintains a list of antineoplastic and other HDs used in healthcare. The entity must maintain a list of HDs, which must include any items on the current NIOSH list that the entity handles. Dr. Acosta added that the list must be reviewed at least every 12 months and whenever a new agent or dosage form is used.

Dr. Acosta explained that section two contains the criteria that can be used by pharmacists to determine if containment requirements in USP 800 must be followed or when an "assessment of risk" can be conducted to determine alternative containment strategies.

Dr. Acosta explained that any HD active pharmaceutical ingredient (API) must follow the requirements in the chapter. She also provided the following definition of API: "any substance or mixture of substances intended to be used in the compounding of a drug 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." Dr. Acosta stated that any antineoplastic requiring HD manipulation must also follow all of the requirements of the chapter.

Dr. Acosta explained that drugs on the NIOSH list that do not have to follow all of the containment requirements of this chapter if an assessment of risk (AOR) is performed and implemented include: final dosage forms of compounded HD preparations and conventionally manufactured HD products, including antineoplastic dosage forms that do not require any further manipulation other than counting or repackaging (unless required by the manufacturer). Dr. Acosta stated that for dosage forms of other HDs on the NIOSH list, the entity may perform an assessment of risk to determine alternative containment strategies and work practices.

Dr. Acosta reported that an AOR must document what alternative containment strategies and/or work practices are being employed for dosage forms to minimize occupational exposure. She added that it must be reviewed at least every 12 months and the review must be documented. Dr. Acosta also stated that the AOR must, at a minimum, consider the following:

- Type of HD (e.g., antineoplastic, non-antineoplastic, reproductive risk only)
- Dosage form
- Risk of exposure
- Packaging
- Manipulation

Dr. Acosta explained that an assessment of risk (AOR) may be performed for dosage forms to determine alternative containment strategies and/or work practices.

Section 3. Types of Exposure

Dr. Acosta highlighted the potential opportunities of exposure based on activity as provided in Section 3. For example, the risk of exposure that can occur while transporting HDs within a healthcare setting. Dr. Acosta provide Table 1 further examples.

Section 4. Responsibility of Personnel Handling Hazardous Drugs

Dr. Acosta explained that each facility must have a designated person who:

- is qualified and trained to be responsible for developing and implementing appropriate procedures;
- oversees compliance with this chapter and other applicable laws, regulations, and standards;
- ensures competency of personnel;
- ensures environmental control of the storage and compounding areas.
- thoroughly understands:
  - rationale for risk-prevention policies,
  - risks to themselves and others,
  - risks of noncompliance that may compromise safety,
  - the responsibility to report potentially hazardous situations to the management team.
- Is responsible for the oversight of monitoring the facility and maintaining reports of testing/sampling performed in facilities and acting on the results.

Section 5. Facilities and Engineering Controls

Dr. Acosta stated that HDs must be handled under conditions that promote patient safety, worker safety, and environmental protection. Signs designating the hazard must be prominently displayed before the entrance to the HD handling areas. She explained that access to areas where HDs are handled must be restricted to authorized personnel to protect persons not involved in HD handling.

Dr. Acosta also reported that HD handling areas must be located away from breakrooms and refreshment areas for personnel, patients, or visitors to reduce risk of exposure. There must be designated areas available for: receipt and unpacking, storage of HDs, nonsterile HD compounding, and sterile HD compounding. Dr. Acosta reviewed the following criterial for the designated areas.

- Designated areas:
  - Receipt and unpacking: (Antineoplastic HDs and all HD APIs)
    - neutral/normal or negative pressure relative to the surrounding areas.
- Storage of HDs:
  - Not on floor
  - Antineoplastic HDs (requiring manipulation) and all HD APIs:
    - stored separately from non-HDs
    - stored in an externally ventilated, negative-pressure room with at least 12 air changes per hour (ACPH).

- Non-antineoplastic, reproductive risk only, and final dosage forms of antineoplastic HDs:
  - may be stored with other inventory if permitted by entity policy.
- Refrigerated antineoplastic HDs must be stored in a dedicated refrigerator in a negative pressure area with at least 12 ACPH.

Dr. Acosta explained that a containment primary engineering control (C-PEC) is a ventilated device to minimize worker and environmental HD exposure and it must operate continuously if it supplies some or all of the negative pressure in the C-SEC or if it is used for sterile compounding.

Dr. Acosta stated that a containment secondary engineering control (C-SEC) is the room in which the C-PEC is placed and must:

- be externally vented,
- be physically separated (a different room from other areas),
- have an appropriate air exchange (ACPH); and
- have a negative pressure **between** 0.01 and 0.03 inches of water column relative to all adjacent areas.

Dr. Acosta reported that supplemental engineering controls (closed-system drug-transfer device (CSTD)) are adjunct controls to offer additional levels of protection.

Dr. Acosta noted that a sink must be available for hand washing and the water source and drain must be located at least one-meter way from the C-PEC.

Dr. Acosta explained that C-PECs must be placed in separate rooms, unless the C-PECs used for nonsterile compounding are sufficiently effective that the room can continuously maintain ISO 7 classification throughout the nonsterile compounding activity. She added that if they are in the same room they must be placed at least one-meter apart and particle-generating activity must not be performed when sterile compounding is in process.

Dr. Acosta stated that nonsterile HD compounding must be performed in a C-PEC within a C-SEC. she added that the C-SEC surfaces of ceilings, walls, floors, fixtures, shelving, counters, and cabinets in the nonsterile compounding area must be smooth, impervious, free from cracks and crevices, and non-shedding.

Dr. Acosta reviewed the following requirements for C-PECs (Class II or III Biological Safety cabinet or compounding aseptic containment isolator):

- must be externally vented
- must provide an ISO Class 5 or better air quality
- must not be used for the preparation of a non-HD unless:
  - non-HD is placed into a protective outer wrapper during removal from the C-PEC and is labeled to require PPE handling precautions.
- must be located in a C-SEC

Dr. Acosta explained that in the HD cleanroom suite the C-SEC (clean/buffer room) must have:

- fixed walls,
- minimum of 30 ACPH of HEPA-filtered supply air,
- air quality of ISO Class 7 or better; and
- negative pressure **between** 0.01 and 0.03 inches of water column relative to all adjacent areas

Dr. Acosta also explained that the C-SEC (Anteroom) must have:

- Fixed walls,
- Minimum of 30 ACPH of HEPA-filtered supply air
- Positive pressure of at **least** 0.02 inches of water column relative to all adjacent unclassified areas
- Air quality of ISO Class 7 or better
- Hand-washing sink **must** be placed in the ante-room at least 1 meter from the entrance to the HD buffer room

Dr. Acosta stated that if the HD buffer room is entered through the positive-pressure non-HD buffer room, the following is also required: (Not a recommended facility design)

- Line of demarcation must be defined within the negative-pressure buffer room for donning and doffing PPE
- Method to transport HDs, HD CSPs, and HD waste into and out of the negative pressure buffer room to minimize the spread of HD contamination.
  - If using a pass-through chamber (buffer area and adjacent space).
    - must be included in the facility's certification (particles and pressure)
    - refrigerator pass-through must not be used.

Dr. Acosta reported that containment segregated compounding areas (C-SCA) must have:

- Fixed walls,
- Negative pressure **between** 0.01 and 0.03 inches of water column relative to all adjacent areas,
- 12 ACPH
- Externally vented
- hand-washing sink must be placed at least 1 meter from C-PEC
  - either inside the C-SCA or directly outside the C-SCA.
- Only low-and medium-risk HD CSPs may be prepared in a C-SCA.

Dr. Acosta explained that a closed-system drug-transfer device (CSTD) may limit the potential of generating aerosols during compounding. She also stated that it must not be used as a substitute for a C-PEC when compounding. Dr. Acosta explained that a CSTD should be used when compounding HDs when the dosage form allows and when administering antineoplastic HDs when the dosage form allows.

Section 6. Environmental Quality and Control

Dr. Acosta stated that environmental wipe sampling for HD surface residue should be performed routinely.

Dr. Acosta explained that surface wipe sampling should include:

- Interior of the C-PEC and equipment contained in it
- Pass-through chambers
- Surfaces in staging or work areas near C-PEC
- Areas adjacent to C-PECs (floors, staging, and dispensing area)
- Areas immediately outside the HD buffer room or the C-SCA
- Patient administration areas

Dr. Acosta stated that if any measurable contamination is found, the designated person **must** identify, document, and contain the cause of contamination.

Section 7. Personal Protective Equipment (PPE)

Dr. Acosta reviewed the types of personal protective equipment must be used by the staff.

- Gloves:
  - Must meet American Society for Testing and Materials (ASTM) standard D6978
  - worn for handling all HDs
  - must be powder-free
  - must be inspected for physical defects before use.
  - for sterile compounding: two pairs required
    - the outer chemotherapy gloves must be sterile
    - changed every 30 minutes
    - must be changed when torn, punctured, or contaminated
- Gowns:
  - must be disposable and shown to resist permeability by HDs
  - must be selected based on the HDs handled
  - must close in the back (i.e., no open front), be long sleeved, and have closed cuffs that are elastic or knit
  - must not have seams or closures
  - must be changed per the manufacturer's information for permeation of the gown. If none every 2–3 hours
  - must not be worn to other areas

- Respiratory Protection:
  - Surgical masks must not be used when respiratory protection is required.
  - For most activities, a fit-tested NIOSH-certified N95 or more is sufficient to protect against airborne particles.
    - no protection against gases and vapors and little protection against direct liquid splashes
  - Appropriate full-facepiece, chemical cartridge-type respirator or powered air-purifying respirator (PAPR) should be worn when there is a risk of respiratory exposure to HDs, including when:
    - Attending to HD spills larger than what can be contained with a spill kit
    - Deactivating, decontaminating, and cleaning underneath the work surface of a C-PEC
    - There is a known or suspected airborne exposure to powders or vapors

- Disposal of Used Personal Protective Equipment:
  - All PPE worn when handling HDs to be contaminated with, at minimum, trace quantities of HDs.
  - All PPE worn be disposed of in the proper waste container before leaving the C-SEC.
  - Chemotherapy gloves and sleeve covers worn during compounding must be carefully removed and discarded immediately into a waste container approved for trace contaminated waste inside the C-PEC or contained in a sealable bag for discarding outside the C-PEC.

Section 8. Hazard Communication Program

Dr. Acosta reviewed the requirements for hazard communication programs as provided below.

- Required to establish P&Ps that ensure worker safety during all aspects of HD handling.
- Must develop SOPs to ensure effective training regarding proper labeling, transport, storage, and disposal of the HDs and use of Safety Data Sheets (SDS), based on the Globally Harmonized System of Classification and Labeling of Chemicals (GHS).
- Elements of the hazard communication program plan must include:
  - Written plan that describes how the standard will be implemented
  - All containers of hazardous chemicals must be labeled, tagged, or marked with the identity of the material and appropriate hazard warnings
  - must have an SDS for each hazardous chemical they use (29 CFR 1910.1200)
  - must ensure that the SDSs for each hazardous chemical used are readily accessible to personnel during each work shift and when they are in their work areas
  - Personnel who may be exposed to hazardous chemicals when working must be provided information and training before the initial assignment to work with a hazardous chemical, and also whenever the hazard changes
  - Personnel of reproductive capability must confirm in writing that they understand the risks of handling HDs

Section 9. Personnel Training

Dr. Acosta informed the committee that all personnel must be trained based on their job functions. She added that the training must occur before the employee handles any HDs and each employee must demonstrate the effectiveness of the training. Dr. Acosta stated that the training must include at least the following:

- Overview of entity's list of HDs and their risks
- Review of the entity's SOPs related to handling of HDs
- Proper use of PPE
- Proper use of equipment and devices (e.g., engineering controls)
- Response to known or suspected HD exposure
- Spill management
- Proper disposal of HDs and trace-contaminated materials

Dr. Acosta explained that all training must be documented and must be reassessed every 12 months.

Section 10. Receiving

Dr. Acosta provided the following requirements for receiving of HD products.

- HD products should be received from the supplier in impervious plastic to segregate them from other drugs.
- HD products must be delivered to the HD storage area immediately after unpacking.
- PPE, including chemotherapy gloves, must be worn when unpacking HDs.
- A spill kit must be accessible in the receiving area.
- The entity must enforce policies that include a tiered approach, starting with visual examination of the shipping container for signs of damage or breakage (e.g., visible stains from leakage, sounds of broken glass).
- Damaged shipping containers: transported to a C-PEC designated for nonsterile compounding.
    - Damaged containers are considered spills and must be reported to the designated person and managed.

Section 11. Labeling, Packaging, Transport and Disposal

Dr. Acosta provided a summary of each section as provided below.

- Labeling
    - HDs identified must be clearly labeled at all times during their transport.
    - Personnel must ensure that the labeling processes for compounded preparations do not introduce contamination into the non-HD handling areas.
- Packaging
    - must select and use packaging containers and materials that will maintain physical integrity, stability, and sterility (if needed) of the HDs during transport.
    - must protect the HD from damage, leakage, contamination, and degradation, while protecting healthcare workers who transport HDs.
    - must have written SOPs to describe appropriate shipping containers and insulating materials.
- Transport
    - must be labeled, stored, and handled in accordance with applicable federal, state, and local regulations.
    - must be in containers that minimize the risk of breakage or leakage.
    - must ensure that labels and accessory labeling for the HDs include storage instructions, disposal instructions, and HD category information in a format that is consistent with the carrier's policies.
- Disposal
    - All personnel performing custodial waste removal and cleaning activities must be trained in appropriate procedures.
    - Disposal of all HD waste, including, but not limited to, unused HDs and trace-contaminated PPE and other materials, must comply with all applicable federal, state, and local regulations.

Section 12. Dispensing Final Dosage Forms

Dr. Acosta explained that HDs that do not require any further manipulation, other than counting or repackaging of final dosage forms, may be prepared for dispensing without any further requirements for containment unless required by the manufacturer or if visual indicators of HD exposure hazards are present (e.g., HD dust or leakage). She added that clean equipment should be dedicated for use with HDs and should be decontaminated after every use. Dr. Acosta also noted that tablet and capsule forms of antineoplastic HDs must not be placed in automated counting or packaging machines.

Section 13. Compounding

Dr. Acosta stated that all compounding must be compliant with the appropriate USP standards for compounding including <795> and <797> and must be done in proper engineering controls.

Dr. Acosta explained that when compounding HD preparations in a C-PEC, a plastic-backed preparation mat should be placed on the work surface of the C-PEC and the back should be changed immediately if a spill occurs and regularly during use and should be discarded at the end of the daily compounding activity.

Dr. Acosta reported that bulk containers of liquid and API HD must be handled carefully to avoid spills. She also explained that APIs or other powdered HDs must be handled in a C-PEC to protect against occupational exposure, especially during particle-generating activities

Section 14. Administering

Dr. Acosta explained that HDs must be administered safely using protective medical devices and techniques and appropriate PPE must be worn. She added that PPE must be removed and disposed of in a waste container approved for trace contaminated HD waste at the site of drug administration.

Dr. Acosta stated that equipment (such as tubing and needles) and packaging materials must be disposed of properly, such as in HD waste containers, after administration.

Dr. Acosta explained that If HD dosage forms do require manipulation such as crushing tablet(s) or opening capsule(s) for a single dose, personnel **must** don appropriate PPE and use a plastic pouch to contain any dust or particles generated.

Section 15. Deactivating, Decontaminating, Cleaning and Disinfecting

Dr. Acosta explained that all areas where HDs are handled and all reusable equipment and devices must be deactivated, decontaminated, and cleaned. She noted that sterile compounding areas and devices must be subsequently disinfected.

Dr. Acosta stated that policies and procedures for cleaning must include procedures, agents used, dilutions (if used), frequency, and documentation requirements.

Dr. Acosta described appropriate PPE as follows:

- resistant to the cleaning agents used,
- two pairs of chemotherapy gloves
- impermeable disposable gowns
- eye protection and face shields must if splashing is likely
- respiratory protection must be used, if warranted

Dr. Acosta explained that agents used for deactivation, decontamination, and cleaning should be applied through the use of wipes wetted with appropriate solution and all disposable materials must be discarded to meet EPA regulations and the entity's policies.

Dr. Acosta also reminded that committee that all cleaning must be performed in areas that are sufficiently ventilated.

Dr. Acosta provided the committee with the following definitions of deactivating, decontaminating, cleaning and disinfecting.

- Deactivation
  - renders a compound inert or inactive.
  - Residue must be removed by decontaminating the surface.
  - There is no one proven method for deactivating all compounds. (EPA-registered oxidizing agents that are appropriate for the intended use
- Decontamination
  - inactivating, neutralizing, or physically removing HD residue and transferring it to absorbent, disposable materials (e.g., wipes, pads, or towels) appropriate to the area being cleaned.
  - The work surface of the C-PEC must be decontaminated between compounding of different HDs.
  - The C-PEC must be decontaminated at least daily, any time a spill occurs, before and after certification, any time voluntary interruption occurs, and if the ventilation tool is moved.
    - areas under the work tray must be deactivated, decontaminated, and cleaned at least monthly
- Cleaning
  - a process that results in the removal of contaminants (e.g., soil, microbial contamination, HD residue) from objects and surfaces using water, detergents, surfactants, solvents, and/or other chemicals.
  - Cleaning agents used on compounding equipment should not introduce microbial contamination.
- Disinfection
  - a process of inhibiting or destroying microorganisms.
  - must be done for areas intended to be sterile, including the sterile compounding areas.

Section 16. Spill Control

Dr. Acosta provided the committee with the following information regarding spill control.

- personnel must receive proper training in spill management and the use of PPE and NIOSH-certified respirators

- Spills must be contained and cleaned immediately by qualified personnel with appropriate PPE.
- Qualified personnel must be available at all times while HDs are being handled.
- Signs must be available for restricting access to the spill area.
- Spill kits must be readily available in all areas where HDs are handled.
- All spill materials must be disposed of as hazardous waste.
- The circumstances and management of spills must be documented.
- Personnel potentially exposed during the spill or spill cleanup or who have direct skin or eye contact with HDs require immediate evaluation.
- Non-employees exposed to an HD spill should follow entity policy, which may include reporting to the designated emergency service for initial evaluation and completion of an incident report or exposure form.
- SOPs must:
    - be developed to prevent spills and to direct the cleanup of HD spills.
    - address the size and scope of the spill and specify who is responsible for spill management and the type of PPE required.
    - address the location of spill kits and clean-up materials as well as the capacity of the spill kit.

Section 17. Documentation and Standard Operating Procedures (SOP)

Dr. Acosta explained that standard operating procedures must be reviewed (and documented) at least every 12 months and should include:

- Hazard communication program
- Occupational safety program
- Designation of HD areas
- Receipt
- Storage
- Compounding
- Use and maintenance of proper engineering controls
- Hand hygiene and use of PPE based on activity
- Deactivation, decontamination, cleaning, and disinfection
- Dispensing
- Transport
- Administering
- Environmental monitoring
- Disposal
- Spill control
- Medical surveillance

Dr. Acosta stated that personnel who transport, compound, or administer HDs must document their training according to OSHA standards (OSHA Standard 1910.120) and other applicable laws and regulations.

Section 18. Medical Surveillance

Dr. Acosta explained that Medical surveillance is part of a comprehensive exposure control program complementing engineering controls, safe work processes, and use of PPE. She added that healthcare workers who handle HDs as a regular part of their job assignment should be enrolled in a medical surveillance program.

The committee thanked Dr. Acosta for her presentation and asked for public comments.

A pharmacist that compounds exclusively for veterinary practices asked if the board would be creating an exception that would allow certain veterinary HD products to be handled in a room that is not USP 800 complaint. Dr. Acosta recommended contacting the CDC as they create the NIOSH list which is used to determine how HD products must be handled.

A member of the public asked if the committee could make Dr. Acosta's slides available in an electronic format or in larger printed sizes. Chairperson Serpa reminded the public that the it is the responsibility of the PIC and designated staff to review the USP standards, the slides are only a high-level review of the standards. Slides will soon be added to website.

A compounding pharmacist asked if a pharmacy what provides patient specific HDs to a hospital is responsible to make sure that the HDs are handled appropriately by hospital staff when it is administered (i.e. wearing proper PPE and proper disposal). Chairperson Serpa responded that in some healthcare systems the pharmacy is responsible to oversee the HDs from compounding to administration; however, an independent pharmacy would have different requirements. DCA legal counsel Laura Freedman stated that this question goes beyond the agenda item and should be placed on a future agenda for future discussion.

Interim Executive Officer Anne Sodergren reminded the committee that there is pending legislation that will set the relevant USP chapters as the floor for the board's compounding regulations. After the floor is set the board will have the opportunity to develop additional regulations if nessecary.

4. Approval of the February 20, 2019 Meeting Minutes

Chairperson Serpa noted that in both the February and March minutes on page 2 the term "<825> – Preparation" should be corrected to read "<825> – Radiopharmaceuticals Preparation."

The committee agreed with the changes to both minutes.

Motion: Approve the February 20, 2019, committee meeting minutes with the correction noted by Chairperson Serpa.

M/S: Weisser/Law

Support: 4 Oppose: 0 Abstain: 0

Board Member	Support	Oppose	Abstain	Not Present
Kim				x
Law	x			
Schaad	x			

Board Member	Support	Oppose	Abstain	Not Present
Serpa	x			
Weisser	x			

5. Approval of the March 13, 2019 Meeting Minutes

Motion: Approve the March 13, 2019, committee meeting minutes with the correction noted by Chairperson Serpa.

M/S: Schaad/Weisser

Support: 4 Oppose: 0 Abstain: 0

Board Member	Support	Oppose	Abstain	Not Present
Kim				x
Law	x			
Schaad	x			
Serpa	x			
Weisser	x			

6. Future Committee Meeting Dates

Chairperson Serpa announced the committee's next meeting is scheduled for June 4, 2019, in Sacramento. She added that the July meeting has been rescheduled to July 11, 2019, in Sacramento. Chairperson Serpa noted that the board's website has been updated to reflect the new meeting date.

7. Adjournment

Chairperson Serpa adjourned the meeting at 11:25 a.m.