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

Compounding Committee Report
September 24, 2019

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

   Attachment 1

   Background

   During its September 5, 2019, meeting, members reviewed proposed regulations necessary for patient safety related to pharmaceutical compounding of sterile preparations. These proposed regulations are predicated on the newly revised USP 797 and other relevant state and federal law. The committee reviewed proposed section 1751-1751.11 and requested that members of the public provide specific information in two areas detailed below.

   1. As related to proposed CCR section 1751 (e), provide any products that require sterilization to be performed outside of the licensed pharmacy. Included with the list should be an explanation why the sterilization cannot be performed within the pharmacy. Further, the information should address why the sterilization process is the only process that works for the product, the names of the companies currently performing the sterilization, and any licensure for those companies, if known.
   2. As related to proposed CCR section 1751.9 (e), provide specific examples of preparations that would be impacted.

   These regulations augment the revisions to USP General Chapter 797, Pharmaceutical Compounding – Sterile Preparations.

   The revised USP Chapter is available for download from USP at www.USP.org.

   During this meeting

During this meeting, members will have the opportunity to continue review of the proposed regulations and review responses to the committee's inquiry of two specific proposed regulation sections, 1751(e) 1751.9(e). Comments were also received that are not directly related to the committee's inquiry. These comments are provided as well.

The committee will have the opportunity to continue its discussion of the proposal and, if appropriate, make recommendations for the board's consideration during its November 2019 meeting.

Attachment 1 includes:

1. Proposed regulation language as amended during the September 5, 2019, committee meeting to rename Article 7 Sterile Compounding and Repeal Sections 1751-1751.10 and replace with Article 7 Sterile Compounding in Pharmacies including the addition of Sections 1751-1751.21.
2. Comments received both in response to the committee's requests for additional information as well as to the regulation proposal in general.

4. Approval of the September 5, 2019, Meeting Minutes

Attachment 2

Provided in **Attachment 2** for the committee's review and approval are the draft minutes from the September 5 committee meeting.

5. Future Committee Meeting Dates

- October 16, 2019
- November 14, 2019

6. Adjournment

Attachment 1

Proposal to Rename Article 7 Sterile Compounding and Repeal Sections 1751-1751.10 and Replace as Follows:

Article 7 Sterile Compounding in Pharmacies

1751. Sterile Compounding in Licensed Pharmacies.

This article applies to sterile compounding performed in a pharmacy. A pharmacy performing sterile compounding shall comply with the standards established by United States Pharmacopeia (USP) General Chapter 797 (Chapter 797), titled *Pharmaceutical Compounding – Sterile Preparations*, unless additional or different standards are established by this article.

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

(b) Compounded sterile preparation (CSP) for immediate administration shall only be done in those limited situations where there is a need for immediate administration of a CSP and where failure to administer could result in loss of life or intense suffering. Any such CSP shall be labeled ~~"for immediate use only" and~~ with a beyond use date/time of 4 hours or less. The pharmacy shall maintain records of such CSPs shall at least include CSP made, compounded time, and patient name and patient unique identifier.

(c) Reconstitution in accordance with directions that have not been approved by the FDA, is considered compounding and this article applies.

(d) Except as identified below, ~~No~~ no CSPs shall be compounded prior to receipt by a pharmacy of a valid patient specific prescription document. Where approval is given orally, that approval shall be noted on the prescription document prior to compounding.

(1) ~~Notwithstanding this subdivision, a~~ A pharmacy may prepare and store a limited quantity of a CSP in advance of receipt of a patient specific prescription document.

(2) Notwithstanding this subdivision, a pharmacy may prepare and provide a limited quantity of CSPs to veterinarians for animal patients based on a contract between the pharmacy and veterinarian for office use administration only. The pharmacy and veterinarian practice are jointly responsible for compliance with this section. The contract shall require the veterinarian to provide the pharmacy with the records documenting the dose administered to each patient or destruction record of CSPs. The pharmacy shall be prohibited from providing the same~~additional~~ CSP~~s~~ to the veterinarian until the pharmacy has received and evaluate the records for compliance with this provision.

Commented [SA2]: Clarify additional products or frequency?

(e) No pharmacy or pharmacist shall compound a CSP that:

(1) Is classified by the United States Food and Drug Administration (FDA) as demonstrably difficult to compound;

(2) Appears on an FDA list of drugs which 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) 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 compounding~~ and at the time of dispense, or
(B), the compounding of that CSP 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 CSP for the intended patient population.
(5) Is made with a bulk drugs substance, as defined in Section 503A(b)(1)(A)(i), when there is an FDA approved sterile drug product that is available and appropriate for the intended CSP.
(6) cannot be sterilized within the licensed location~~pharmacy~~.

Commented [SA3]: FAQ

Commented [SA4]: FAQ on examples

(f) Prior to allowing any CSP to be compounded in a pharmacy, the pharmacist-in-charge shall complete a self-assessment, as required by Section 1715.

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

(h) Compounding with blood derived or other biological materials 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 USP Chapter 800, Hazardous Drugs- Handling in Healthcare Settings and any board regulations.

(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 USP Chapter 800, Hazardous Drugs- Handling in Healthcare Settings and any board regulations.

1751.1. Compounding Definitions.

The definitions in in this section supplement the definitions provided in USP Chapter 797.

(a) "Compounding personnel" means any person involved with any procedure, activity or oversight of the compounding process.

(b) "Compounded sterile preparation (CSP)" means a preparation intended to be sterile which is

created by combining, admixing, diluting, pooling, reconstituting other than as provided in the FDA approved manufacturer package insert, repackaging, or otherwise altering a drug product or bulk drug substance.
(c) "Copy or essentially a copy" of a commercially available drug product means all preparations that are comparable in active ingredients to commercially available drug products, except that it does not include any preparations in which there has been a change, made for an identified individual patient, which produces for that patient a clinically significant difference, as determined by a prescribing practitioner, between that compounded preparation and the comparable commercially available drug product.

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

(e) "Designated compounding area or compounding area" means a restricted location with limited access designated for the preparation of CSP, where only activities and items related to compounding are present.

(f) "In process material or in process preparation or stock solution" means any material fabricated, compounded, blended, or derived by chemical reaction that is produced for, and used in, the preparation of the CSP. For purposes of this article, "in process material" shall refer to ~~the~~ all terms used in this subdivision.

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

(h) "Potency" means an active ingredient's strength in a preparation which is within a specified range as determined in the facility's SOP.

(i) "Preparation" means a drug or nutrient compounded in a pharmacy; which may or may not be sterile.

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

(k) "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 formulation document.

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

1751.2 PERSONNEL TRAINING AND, EVALUATION

The requirements of this section apply in addition to the requirements in USP Chapter 797.
(a) Training, evaluation, and requalification procedures for personal preparing, verifying, and/or

handling a CSP shall address the following topics:

(1) Quality assurance and quality control procedures,
(2) Container closure and equipment, selection,
(3) Component selection, and handling, and
(4) Sterilization techniques, when applicable

(b) The pharmacist responsible for or directly supervising, aseptic techniques or practices, shall demonstrate proficiency in the skills necessary to ensure the integrity, potency, quality, and labeled strength of a CSP.

(c) Aseptic manipulation evaluation and requalification documentation shall include the PEC's (Primary Engineering Control) unique identifier used during the evaluation. Aseptic manipulation evaluation and requalification shall be performed using same personnel, procedures, type of equipment, and materials used in compounding drug preparations.

(d) Requalification in hand hygiene, garbing and aseptic manipulation shall occur each time the quality assurance program yields an unacceptable result as defined in the Standard Operating Procedure (SOP)s that may indicate microbial contamination of CSPs. Requalification procedures shall be defined in the pharmacy's SOPs.

(e) Compounding personnel who fail any aspect of training or demonstrated competency, either initially or during requalification, shall not be involved in compounding a CSP until after successfully passing reevaluations in the deficient area(s).

(f) The pharmacy must document that any person assigned to provide training has obtained training and demonstrated competency in any subject in which the person will provide training or observe and measure competency.

1751.3 PERSONAL HYGIENE AND GARBING

The requirements of this section apply in addition to the requirements in USP Chapter 797.

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

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

(c) Personnel protective equipment shall be donned and removed in an ante-area or immediately outside the segregated compounding area (SCA). Donning and doffing garb shall not occur in the ante-room or the SCA at the same time unless the pharmacy's SOP define specific processes that must be followed to prevent contamination.

(d) Eye glasses shall be cleaned as part of hand hygiene and garbing, the standards for which the pharmacy shall specify in its standard operating procedures (SOPs).

(e) RABS and pharmaceutical isolator sleeves and gloves shall be changed according to both the manufacturer's recommendations and the facility's SOP.

(f) Before any hand hygiene or garbing accommodation is granted pursuant to USP 797 Section 3.1, the designated person shall determine that the quality of the environment and any CSPs is not affected. Documentation of the determination shall be done prior to the accommodation being allowed.

1751.4 FACILITIES AND ENGINEERING CONTROLS

The requirements of this section apply in addition to the requirements in USP Chapter 797**.**

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

(b) Reusable equipment and utensils which ~~have~~ cannot ~~not~~ be sterilized and depyrogenated, and that will come in direct contact with compounding components must be rinsed with either sterile water for injection or sterile water for irrigation, ~~, pyrogen free water~~.

(c) If a segregated compounding area (SCA) is used:

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

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

(d) Any room, regardless of its ISO classification, with a PEC used for sterile compounding shall only be used for Category 1 preparation unless it is entered via an ante-room.

(e) (1) Designated compounding area(s) shall typically be maintained at a temperature of 20° Celsius or cooler and shall provide comfortable conditions for compounding personnel attired in the required garb.

(2) The temperature shall be monitored in each room of the designated compounding area each day that compounding is performed, either manually or by a continuous recording device.

(f) Where a pass-through is installed in a secondary engineering control, SOPs must address how both doors will not be opened at the same time. Effective ~~January 1, 2022~~[two years from the effective date of the regulation], all pass-throughs must be interlocking. ~~A pass-through used to access a negative pressure ISO 7 or better space from a non-classified space, must be a HEPA-filtered purge pass-through.~~

Commented [SA5]: Add in definition of PEC

Commented [SA6]: Reference applicable USP Chapters

Commented [SA7]: Develop a small exception for water produced. Will consider COA.

(g) When a RABS is used, an ingress and egress test shall be performed at each certification. If the main chamber of the RABS is opened, the manufacturer's purge time must be met before cleaning takes place. SOPs shall be developed and implemented to ensure compliance.

(h) No CSP shall be compounded if compounding personnel know, or reasonably should have known, that the compounding environment fails to meet criteria specified in USP Chapter 797, this article, and the pharmacy's written SOPs.

1751.5 CERTIFICATION AND RECERTIFICATION

The requirements of this section apply in addition to the requirements in USP Chapter 797.

(a)(1) Testing and certification of all classified areas shall be completed by a qualified technician who is familiar with certification methods and procedures outlined within the Controlled Environment Testing Association (CETA)'s Certification Guide for Sterile Compounding Facilities. Testing shall be performed in accordance with CETA Certification Guide for Sterile Compounding Facilities (CAG-003-2006-13, Revised 2015), which is hereby incorporated by reference. Certification shall demonstrate compliance with all standards in USP 797 and established by this article.

(2) CAG standard(s) used to perform ~~certify~~ certification testing in all classified areas to shall be recorded on certification report.

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

(c) PECs must be recertified whenever the following occurs: 1. Repairs, 2. Alterations to the PEC that could affect airflow or air quality. Further, SOPs must address the conditions under which recertification must also be completed when relocating a PEC.

1751.6 MICROBIOLOGICAL AIR AND SURFACE MONITORING

The requirements of this section apply in addition to the requirements in USP Chapter 797.

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

(b) During biannual recertification, all microorganism recovered (growth) shall be identified by a qualified microbiologist, at least to the genus ~~species~~level, regardless of the cfu count. When identification of an organism of concern, action shall be taken. Organisms of concern shall be identified by the PIC or designated person and shall be documented in a SOP. Some possible

organisms of concern ~~would~~ may, but need not, include~~be~~ gram-negative rods, coagulase positive staphylococcus, and certain molds and yeasts.

(c)Whenever ~~growth is identified~~ cfu action levels are exceeded or an organism of concern is identified as specified in (a) or (b), required action shall include at a minimum, an investigation of (1) cleaning and compounding operations, (2) sampling, (3) personnel training, (4) incubator functionality, (5) facility management, and (6) resampling. Consultation with a competent microbiologist, infection control professional, or industrial hygienist is required when resampling results in growth of an organism of concern or when action levels are exceeded, regardless of count. All actions taken shall be documented.

(d) The designated person shall review the sampling results and identify data trends at least every time sample results are received. The designated person shall evaluate trends to determine if corrective action is needed. The results of the review shall be documented.

(e) Environmental sampling shall be done in compliance with CETA Certification Application Guide USP <797> Viable Environmental Sampling & Gowning Evaluation (CAG-009, current version-20XX-XX, Revised XX), which is hereby incorporated by reference.

1751.7 CLEANING, DISINFECTING, AND APPLYING SPORICIDAL AGENTS IN COMPOUNDING AREAS

The requirements of this section apply in addition to the requirements in USP Chapter 797.

(a) Cleaning, disinfection, and sporicidal agents shall be used in accordance with manufacturers' specifications.

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

1751.8 INTRODUCING ITEMS INTO THE SEC AND PEC

The requirements of this section apply in addition to the requirements in USP Chapter 797**.**

(a) SOPs shall define the process and products to be used on any equipment and other items entering from an unclassified area into the clean side of the ante-room, entering a PEC, and entering the SCA. ~~This~~ These SOPs will define at a minimum, what product is to be used, the dwell time required, and how dwell time will be monitored and documented.

1751.9 EQUIPMENT, SUPPLIES, AND COMPONENTS

The requirements of this section apply in addition to the requirements in USP Chapter 797.

(a) All equipment and supplies used to compound CSP shall be used, in accordance with

manufacturers' specifications and be of suitable composition such that the surfaces which contact components are not reactive or sorptive.

(b) Incubators used by the pharmacy shall be cleaned, maintained, calibrated, and operated in accordance with manufacturers' specifications. For incubators without specific manufacturers' specifications, cleaning shall take place at least monthly and calibration shall take place at least every 12 months. SOPs shall specify the frequency and process cleaning, maintenance, and calibration, including when incubation of samples is taking place such that samples are not compromised. All cleaning, maintenance, and calibration shall be documented.

(c) Any component used to compound a CSP shall be used and stored (1) considering issued Guidance Documents and Alerts (2) in accordance with all industry standards including the following:

(~~1~~A) United States Pharmacopeia (USP) – National Formulary (NF),

(~~2~~B) Food Drug and Cosmetic Act (FD&CA) and federal regulations adopted to implement that act,

(~~3~~C) Food Drug Administration (FDA) requirements and ~~considering issued Guidance Documents and Alerts~~, and

(~~4~~D) Manufacturers' specifications and requirements.

Commented [SA8]: Should this be rephrased.

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

(e) No component shall be used to compound a CSP that meets only the European Pharmacopoeia standards, Japanese Pharmacopoeia standards, dietary supplement standards (such as USP-NF dietary monographs), food ingredient standards (such as Food-Chemical Codex (FCC)), food additive standards (such as General Standard for Food Additive (GSFA)), reagent standard (such as American Chemical Society (ASC)) or is of unspecified quality.

(f) Sterilization and depyrogenation of supplies and/or container–closure systems shall be done in compliance with USP Chapter 1229, Sterilization of Compendial Articles.

1751.10 STERILIZATION AND DEPYROGENATION

The requirements of this section apply in addition to the requirements in USP Chapter 797.

(a) Dry heat depyrogenation shall be done in compliance with USP Chapter 1228.1, Dry Heat Depyrogenation.

(b) Sterilization by filtration shall be done in compliance with USP Chapter 1229.4, Sterilizing Filtration of Liquids.

(c) Sterilizing filters used must be labeled for pharmaceutical use and reflect a sterilizing grade.

(d) Steam sterilization shall be done in compliance with USP Chapter 1229.1, Steam Sterilization by Direct Contact.

(e) Dry heat sterilization shall be done in compliance with USP Chapter 1229.8, Dry Heat Sterilization.

(f) A pharmacy shall not compound a CSP from nonsterile components when the pharmacy cannot sterilize the CSP appropriately with steam sterilization, dry heat sterilization or sterilization by filtration.

1751.11 MASTER FORMULATION AND COMPOUNDING RECORDS

The requirements of this section apply in addition to the requirements in USP Chapter 797.

(a) A CSP shall not be compounded until the pharmacy has first prepared a written master formulation document in compliance with USP Chapter 797 and identified in that document the following additional elements:

(1) Active pharmaceutical ingredient (API) or added substance(s) and their amounts, which shall include, at a minimum, salt form and purity grade, when available,
(2) Container–closure systems to be used, which shall include, container and closure types and volume(s).
(3) The source referenced to assign the BUD; each source referenced shall be readily retrievable at the time of compounding and shall be maintained for three years from the date each CSP is dispensed.
(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 comply with USP Chapter 797 and this section.

(c) A compounding record shall be a single document. The document shall satisfy the requirements of USP Chapter 797, as well as the following:

(1) The date and time of preparation. The time of preparation is the time when compounding the CSP started, which also determines when the assigned BUD starts.
(2) The assigned internal identification number shall be unique for each compounded drug preparation.
(3) The vendor (manufacturer/repackager), lot number, and expiration date shall be recorded for each component for CSPs. Documenting solely the National Drug Code (NDC) does not meet this requirement.
(4) The total quantity compounded shall include the number of units made and either the

volume or the weight of each unit.
(5) The identity of each person performing the compounding and pharmacist verifying the final drug preparation
(6) When applicable, endotoxin level calculations and readings.

~~1735~~1751.12 RELEASE TESTING

The requirements of this section apply in addition to the requirements in USP Chapter 797.

(a) 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, when label instructions for storage and handling are followed after the preparation is dispensed.

(b) Validation of an alternative method for sterility testing shall be done in compliance with USP Chapter 1223, Validation of Alternative Microbiological Methods showing it to be non-inferior to USP Chapter 71, Sterility Tests, and shall demonstrate the method to be suitable for each CSP formulation for which the alternate method is used.

(c) Except for CSPs made for inhalation or ophthalmic administration, prior to releasing a CSP made from one or more nonsterile component(s) the pharmacy shall review and document the results of bacterial endotoxin testing. Results shall be documented in the compounding record.

1751.13 LABELING

The requirements of this section apply in addition to the requirements in USP Chapter 797.

(a) A CSP label shall also include the following:
(1) For admixed CSP, the solution utilized; and
(2) Name and contact information of the compounding pharmacy and, if different, the dispensing pharmacy;
(3) Instructions for administration. For admixed CSP solutions, the rate of infusion, or range of rates in infusion, or the duration when the entire CSP is administered.

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

1751.14 ESTABLISHING BEYOND-USE DATES

The requirements of this section apply in addition to the requirements in USP Chapter 797.

(a) A CSP's beyond use date (BUD) shall not exceed:
(1) The chemical and physical stability data of the API and any added substances in the preparation,
(2) The compatibility of the container–closure system with the finished preparation (e.g., possible leaching, interactions, and storage conditions),
(3) shortest remaining expiration date or BUD of any of the starting components.

(b) A CSP labeled with a BUD with only a date shall expire at midnight at that date.

(c) Prior to the dispensing a CSP that requires sterility and pyrogen testing, the pharmacy shall receive test results and ensure that the results are within acceptable limits. The pharmacy shall retain the results as part of the compounding record.

(d) A CSP shall not be assigned a longer BUD based on an unvalidated alternative microbiological method.

1751.15. USE OF CONVENTIONALLY MANUFACTURED PRODUCTS AS COMPONENTS
The requirements of this section apply in addition to the requirements in USP Chapter 797.

If a single-dose container is entered or punctured outside of an ISO Class 5 area, the product must be discarded immediately.

1751.16. USE OF CSPS AS COMPONENTS

The requirements of this section apply in addition to the requirements in USP Chapter 797.

(a) Where an in process material is nonsterile, it shall be treated as a sterile product for purposes of this article.

1751.17 Standard Operating Procedures (SOPS)

The requirements of this section apply in addition to the requirements in USP Chapter 797.

(a) Standard operating procedures (SOPs) shall:
(1) Comply with USP Chapter 1163, Quality Assurance in Pharmaceutical Compounding,
(2) In addition to the SOP SOPs listed in USP Chapter 1163, Quality Assurance in Pharmaceutical Compounding, include:
(A) Methods by which the supervising pharmacist will the quality of compounded drug preparations.
(B) Procedures for handling, compounding and disposal of infectious materials. The written SOPs shall describe the pharmacy protocols for cleanups and spills in

conformity with local health jurisdictional standards.

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

(b) Any pharmacy engaged in compounding CSPs shall maintain and follow written SOPs for compounding.

(c) The SOPs shall be reviewed on an annual basis by the pharmacist-in-charge. Such review shall be documented by the pharmacist-in-charge. The SOPs shall be updated whenever changes are implemented. Such changes shall be disseminated to the affected staff prior to implementation.

1751.18 QUALITY ASSURANCE AND QUALITY CONTROL

The requirements of this section apply in addition to the requirements in USP Chapter 797.

(a) The quality assurance program shall comply with section 1711 and USP Chapter 1163, Quality Assurance in Pharmaceutical Compounding. In addition, the program shall include:

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

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

(3) A written procedure addressing each of the USP Chapter 1163's integrated components and standard operating procedures.

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

(b) The pharmacy shall process recalls and adverse event reporting in compliance with Business and Professions Code section 4127.8.

(c) 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. Such review shall be documented and dated.

1751.19 CSP HANDLING, PACKAGING, STORAGE, AND TRANSPORT

The requirements of this section apply in addition to the requirements in USP Chapter 797.

(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 CSPs from damage, leakage, contamination, degradation, and adsorption while preventing inadvertent exposure to transportation personnel.

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

1751.20 DOCUMENTATION

The requirements of this section apply in addition to the requirements in USP Chapter 797.

(a) Pharmacies shall maintain each record required by USP Chapter 797 or this article in the pharmacy, in a readily retrievable form, for at least three years from the date the record was last used. 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.

(b) Records created shall be maintained in a manner to allow for all versions of the document to be viewed. When a change to a record must be made, the record's original text must be maintained, and the record must reflect each change, the person who made the change, and the date and time the change was made.

1751.21 COMPOUNDING ALLERGENIC EXTRACTS

The requirements of this section apply in addition to the requirements in USP Chapter 797.

(a) Any allergenic extract compounding shall take place in a dedicated PEC. No other CSP may be made in this PEC.

(b) All required documentation for a Category 1 or Category 2 CSPs are required for allergenic extract compounding. (i.e. Compounding records, labeling, cleaning, temperatures logs, patient specific prescriptions etc.)

From: Jeanette Carpenter
To: Pharmacy, Compounding@DCA
Subject: USP797 BUD Updates
Date: Monday, September 9, 2019 5:38:56 PM

[EXTERNAL]: jeanetteowlrexall@gmail.com

Hello,

I'm asking for clarification on the new sterile compounding regulations. The new USP797 guidelines that are official on 12/1/2019 have drastically changed the beyond-use dating recommendations and I would like clarification on state regulations.

My pharmacy is currently compounding sterile to sterile products in a segregated compounding area (SCA) and using the BUD as per current BOP guidelines (low risk maximum 14 day BUD at fridge temp, etc.). My concern is that starting 12/1/19, I will have to follow USP797 guidelines with a max BUD of 24 hours fridge temperature (Category 1 SCA setup).

My questions are:
1. What date will the changes in the BUD become part of state regulations? Do I need to prepare for a 12/1/19 change or can I continue to compound in my current setup with the BUD that we have been using?
2. Will there be a grace period or an extension application for businesses to continue using the old BUD assignments before switching to Category 1/Category 2 BUD? Extensive remodeling may be needed at my pharmacy to compound Category 2 products.

I would appreciate a call at (626) 962-1061 or a response as soon as possible so that I can make the necessary changes to ensure compliance.

Thank you for your time and attention,

--
Jeanette Carpenter, PharmD
Pharmacy Manager
Owl Rexall Drug
Ph: (626) 962-1061
Fax: (626) 962-1157

From: Jeanette Carpenter
To: Pharmacy, Compounding@DCA
Subject: Clarification on New USP797 guidelines
Date: Tuesday, September 10, 2019 9:37:22 AM

[EXTERNAL]: jeanetteowlrexall@gmail.com

Hello,

I sent an email requesting clarification on the board regulations for sterile compounding and got an automated response about license renewal status. I was NOT inquiring about license renewal.

My question is: my pharmacy has a board-compliant SCA and we are concerned that starting on 12/1/19 we will only be able to use Category 1 BUD assignment (12hr room temp, 24hr fridge temp). **Please clarify if we can continue to use the low, medium, and high risk BUD assignment AFTER 12/1/19 as per current regulations** or if I need to rush renovations to use a BUD >1 day. I already read the compounding committee meeting materials and they were unclear as to the timeline.

Please call me at (626) 962-1061 as soon as possible. Compliance is critical to my practice and we want to ensure no interruptions in patient care on 12/1/19.

Thank you.

--
Jeanette Carpenter, PharmD
Pharmacy Manager
Owl Rexall Drug
Ph: (626) 962-1061
Fax: (626) 962-1157

From:	Pharmacy, Compounding@DCA
To:	Kalantar, Anna@DCA
Cc:	Acosta, Christine@DCA
Subject:	Compounding Regulations Questions
Date:	Friday, September 6, 2019 11:40:24 AM
Attachments:	image001.png image002.png

Hello,

Please see below.

Sterile Compounding, Licensing Unit (AA)
California State Board of Pharmacy
(916) 518-3100 | FAX (916) 518-8617 | www.pharmacy.ca.gov
Be Aware and Take Care: Talk to your Pharmacist!

From: Scarlett Eckert <scarletteckert@gmail.com>
Sent: Friday, September 6, 2019 11:25 AM
To: Pharmacy, Compounding@DCA <Compounding.Pharmacy@dca.ca.gov>
Subject: Fwd: Proposed regulations for 1751

[EXTERNAL]: scarletteckert@gmail.com

Good Day,

September 5th meeting was very well attended and executed. Great job Maria! For the sections we were able to cover during this meeting, I still have a few comments and requests:

1751.7 (b) I would request the committee to please clarify 'reusable cleaning supplies'.

Are you referring to just cleaning solutions? Or are you referring to the reusable cleaning tools (example, F-Mops used with disposable pads to clean ceiling and walls of PEC).

Does the 'reusable supplies' include Sterile IPA? IPA is used to clean gloves and DCA throughout the compounding process, and is usually kept close to the PEC as to not interrupt workflow and create extra movements within the buffer room.

1751.11 (c) (2) as written reads that each individual compounded drug preparation requires an unique identification, this would be a serialization number (which I do believe all products should have as part of their product ID barcode - to allow for tracking of individual products to each patient) BUT I believe, as Christine Acosta indicated in her very last statement of the public comment, this was meant to be an internal lot number for batched non-patient specific CSPs.

Possible rewording: (2) The assigned internal identification number (i.e. internal lot or batch number) shall be unique to each production of compounded drug preparations.

Sections to be discussed at the September 24th meeting:

1751.13 (a) (3) Instructions for administration...
Could this also include 'see eMAR or MAR for infusion rate or instructions'?
Batched production of CSPs available in an ADC, might have different infusion instructions depending on the patient.
CSPs prepared patient specific for titrated administration, could have multiple rate changes during the CSP infusion. The eMAR would have real time administration and infusion rate information

1761.16 I do not understand this statement: non-sterile in process is treated as sterile?

1751.17 (a) (2) (A) I believe is missing a word: Validate, verify, assess?
Methods by which the supervising pharmacist will ____ the quality of compounded drug preparation

1751.17 (C) The SOPs shall be reviewed on an annual basis by the ***Designated Person*** and the PIC. The annual review shall be documented by the PIC. ***All changes to the SOPs must be documented with the date changed and the specific changes noted on the SOP review page by the DP and initialed by PIC.*** All changes shall be disseminated to the affected staff prior to implementation. ***All changes that require staff training, the training shall be completed prior to implementation.***

1751.18 The referenced USP chapters are informational chapters not guidelines. Maybe different wording: should follow or should use as a guideline.

1751.18 (C) would suggest changing PIC to Designated Person and PIC. And would add findings and/or outcome of the review be documented, dated and initialed by the DP and PIC.

Thank you for your time and consideration of my comments and requests.

Warm Regards,

Scarlett

Scarlett Eckert, Pharm. D.,
Pharmacist Consultant

From:	Pharmacy, Compounding@DCA
To:	Kalantar, Anna@DCA
Cc:	Acosta, Christine@DCA
Subject:	Compounding Regulations Questions Wednesday,
Date:	September 11, 2019 8:13:50 AM WCP-
Attachments:	Sterilization_Allen.pdf
	WCP-e-Beam vs Gamma.pdf

Hello,

Please see below.

Sterile Compounding, Licensing Unit (AA)
California State Board of Pharmacy
(916) 518-3100 | FAX (916) 518-8617 | www.pharmacy.ca.gov
Be Aware and Take Care: Talk to your Pharmacist!

-----Original Message-----
From: Mike Pavlovich <mike@westcliffcompounding.com>
Sent: Tuesday, September 10, 2019 5:37 PM
To: Pharmacy, Compounding@DCA <Compounding.Pharmacy@dca.ca.gov>
Subject: E-Beam provider info and 1751 commentary

[EXTERNAL]: mike@westcliffcompounding.com

::
Chairperson Serpa,

Following up on the discussion and request for further

information regarding electron beam sterilization providers

in regards to 1751 (e)(6) and 1751.10 (f).

We use electron beam to sterilize naltrexone pellets, the

only sterile product we currently compound. This drug is in

high demand in the opiate and alcohol addiction and

rehabilitation community. To prohibit us from continuing to

compound it as we have since early 2016 would be a great

loss to patients with problems of dependence and there are

very few providers anywhere. Oral naltrexone has a very poor

track record of compliance for opiate addiction and Vivitrol

is expensive (AWP of nearly $1600/dose), has an erratic

duration of action between 21-28 days, and compliance is

also not great. Having a dosage form that can be administered in a minor surgery, even under local anesthesia, that can last between 3 to 6 months is a significant advantage. I have had a number of occasions where doctors and patients have expressed that the use of our compound has "saved their life".

My eBeam provider is Steri-tek, located in Fremont. I had suggested to former EO Herold that she might want to speak to or visit the facility to increase her understanding of the process. Apparently, her retirement came first.

The website can be found here: https://urldefense.proofpoint.com/v2/url?u=https-3A__steri-2Dtek.com_&d=DwIDaQ&c=LHIwbLRMLqgNuqr1uGLfTA&r=AilKcCriCgDRZ6Z-_U3Vr8T47XVSNe1Oioup2b_tVFM&m=vkZnjBQpWDatcWnzJohwRll1ZtBsYrTC_4-p462ZpU0&s=YDJsPOiR95gyFw8ob68QsNVTuuiyICaSExIsQLlYBDk&e=

Steri-Tek is an ISO 11137 and ISO 13485 certified, FDA registered, DEA registered as well as State of California Medical Device and Drug Manufacturing licensed facility serving the medtech, biotech, pharmaceutical and other industries.

Larry Nichols is CEO and should be prepared for your contact.

As you know, an implantable pellet is an anhydrous formulation, is highly stable, and is not suitable for sterilization by any means available in the pharmacy - wet methods such as steam would degrade the product and not generate sufficient heat (despite the fact Pfizer has sterilized their Testopel product by autoclave for many years) and dry heat methods would destroy these dosage

forms. Irradiation (gamma, electron beam or X-ray) provides distinct advantages. I have excerpted an article I have attached for your review.

– E-beam sterilization is an FDA approved process. It is recognized and accepted by international standards organizations,
– It can penetrate a variety of product packaging materials including foils,
– It can cause no damage to sterile seals on packaging,
– It allows to control of temperature during irradiation process,
– Well-controlled dose range can be achieved,
– The process is cost effective but the construction of the e-beam sterilization institution is expensive, and not suitable for placement inside a pharmacy.
– It is a fast process like a minute in very small lots which effects the efficacy of the procedure and for immediate access to fully sterilized and shippable product, (We are further required to perform a USP <71> sterility test despite this fact)
– It gives dose very rapidly for protecting the properties of the product,
– It has minimal effect on atmosphere. The only effect is the formation of slight amount of ozone,
– For the sterilization procedure, validation guidance documents can be used for the implementation and start up.

As far as why I selected eBeam for terminal sterilization,

after considerable research, the cost, convenience and speed of the process appeared to suit my practice best. A "dry" method that could be used to sterilize the final product in its ultimate container without need for further manipulation, would not degrade the product, and was relatively inexpensive. As you know, USP <797> essentially advocates for the use of terminal sterilization since its potential SAL is 1000 times greater than other methods that can be performed in the pharmacy. The chain of custody for products is well-documented and the facility is licensed by multiple entities, state and federal and tamper-evident measures are applied to all packages. There would be no interest on the facility's part to either contaminate or divert. Aside from testosterone, I know of no other controlled substance that is prepared in a pellet form. Our compounds are not controlled substances but are accounted for similarly.

Without the availability of terminal sterilization, we would not be able to function and patients would suffer. I urge your reconsideration of these two important regulations.

Finally, I would further like to ask what might happen if on December 1st the USP should decide NOT to implement the revised <797> as currently stated. I have heard from some that the BUD guidelines may be reconsidered and if that were the case would we revert to our current standards? As it is, the guidelines appear arbitrary. I would point out that

under <795> , the BUD guidelines for "tablets, capsules, and powders" allows for 180 days BUD. Since our terminal sterilization method does not degrade either the product or the packaging, it stands to reason that an anhydrous product, such as an implantable pellet, could be proven stable and sterile for 180 days. This is not just my opinion. Both Loyd Allen and Bill Mixon have both served USP on committees that addressed BUD and have agreed with this position.

Respectfully submitted,

--

Mike Pavlovich, PharmD, FAPhA

Westcliff Compounding Pharmacy

1901 Westcliff Dr #3

Newport Beach, CA 92660

(949) 272-0775

(888) 391-3206 FAX

https://urldefense.proofpoint.com/v2/url?u=http-3A__www.westcliffcompounding.com&d=DwIDaQ&c=LHIwbLRMLqgNuqr1uGLfTA&r=AilKcCriCgDRZ6Z-_U3Vr8T47XVSNe1Oioup2b_tVFM&m=vkZnjBQpWDatcWnzJohwRll1ZtBsYrTC_4-p462ZpU0&s=o-cgnK9A3cx9AkbOghdBcPrdMuB2nwPtavOGszGDvuU&e=

A copy of the documents attached to the email above will be made available for public inspection at the meeting and are available upon request. Requests may be emailed to debbie.damoth@dca.ca.gov

From: Shauna Lopes
To: Pharmacy, Compounding@DCA
Cc: Rachel Taggs; Patrick Wade
Subject: RE: Sterile Component List Regarding Proposed Regulation 1751.9(e)
Date: Friday, September 13, 2019 1:32:20 PM

[EXTERNAL]: slopes@precisionpharmacy.com

After attending the California Board of Pharmacy Compounding Committee Meeting on 9/5/19, we were asked by the Board to submit information in regards to proposed regulation 1751.9(e). We have attached a list of APIs and inactive ingredients which do not have a USP monograph or would be considered a dietary supplement and are currently used in our veterinary sterile compounds. As stated in the meeting, requiring components to have a USP monograph or not allowing the use of dietary supplements in sterile compounds would greatly affect patient access to medications. The 18 components listed are used in 25 of our sterile compounds which account for 54% of the sterile prescriptions dispensed by our pharmacy to veterinary patients. The limitation of sterile components will not only significantly impact our pharmacy practice but all pharmacies serving California veterinary patients, particularly equine patients. We understand the importance of patient safety but this requirement is so restrictive that patient access to these necessary medications would be impossible for California veterinary patients.

Below is a list of affected components used in veterinary sterile compounds by our practice:

Altrenogest
Ammonium Sulfate
Arginine HCl
Atipamezole HCl
Calcium Chloride
Carbazochrome
Deslorelin Acetate
Detomidine HCl
Ferric Cloride
Histrelin Acetate
Hyaluronic Acid Sodium
Iron Sucrose
Medetomidine HCl
Pentosan Polysulfate Sodium
Romifidine HCl
Sodium Bisulfite
Sodium Cacodylate
Tryptophan

Thank you for your consideration.

Shauna (Lopes) Doherty, PharmD
Pharmacist-in-Charge
Precision Pharmacy

5301 Young St.
Bakersfield, California 93311
(877) 734-3338

CAPITOL OFFICE
STATE CAPITOL
ROOM 4082
SACRAMENTO, CA 95814
TEL (916) 651-4028
FAX (916) 651-4928

DISTRICT OFFICES
45-125 SMURR STREET
SUITE B
INDIO, CA 92201
TEL (760) 398-6442
FAX (760) 398-6470

25186 HANCOCK AVENUE
SUITE 320
MURRIETA, CA 92562
TEL (951) 894-3530
FAX (951) 894-3536

California State Senate

SENATOR
JEFF STONE, PHARM.D.
TWENTY-EIGHTH SENATE DISTRICT

VICE CHAIR
HEALTH
VICE CHAIR
HUMAN SERVICES
MEMBER
BUDGET & FISCAL REVIEW
ENERGY, UTILITIES
AND COMMUNICATIONS
ENVIRONMENTAL
QUALITY
TRANSPORTATION

September 11, 2019

Mr. Gregory Lippe, Acting President
c/o Ms. Anne Sodergren, Interim Executive Officer
California State Board of Pharmacy
2720 Gateway Oaks Drive, Suite 100
Sacramento, CA 95833

Dear Mr. Lippe and Ms. Sodergren:

I would like to take this opportunity to take into consideration several comments and questions that have raised with me as they relate to a proposal to significantly and substantially amend Section 1751 of the Sterile Compounding regulations (pages 1-13).

In full disclosure, you may be aware that I am a practicing compounding pharmacist, but I am writing to you only raise policy considerations that have been shared with me by members of the pharmacy industry. My hope is that you can inform me of the thought process behind the proposal and perhaps we can discuss the rationale used by the State Board of Pharmacy in making these decisions.

As for specific questions regarding the proposed repeal of Section 1751, I have several:

(1) The proposal regarding the administration of a sterile product (1751 b; page 1) being immediately used within 4 hours or less needs some clarification for emergency CSPs that are not a regular part of a pharmacy's normal preparations for a physician that may have a need for the product in an emergency situation. Can you explain how this proposed regulation would work in a practical setting?

(2) With respect to Section 1751.4(b), the proposal calls for rinsing beakers and spatulas with sterile pyrogen free water or sterile alcohol. I would like to know the reasoning behind this recommendation as it seems that rinsing with sterile water is appropriate for a beaker, but sterile alcohol has traditionally been acceptable to rinse a spatula.

(3) It seems curious to many that the State Board of Pharmacy is proposing in Section 1751.4 (e) why the regulation greatly exceeds USP standards. USP clearly states a range between 68 and 77 degrees are quite reasonable. Maintaining temperatures 68 degrees or less appears to be excessive, and I was curious as to the scientific basis for this recommendation.

(4) Regarding the proposed change to Section 1751.9, the proposal calls for a prohibition of using a component to compound a CSP unless it is USP grade. The challenge with this proposal is that it fails to consider the availability of USP. It has been suggested to me that the FDA should be pushed to require all manufacturers of components (USP grade or not) to include endotoxin testing on powders as a part of the Certificate of Analysis (COA). It was further suggested that pharmacies should be allowed to use EU or USP-NF and other components when USP is not available as long as they perform an endotoxin test prior to releasing the CSP. I have been informed this would eliminate situations like the recent Glutathione issue and still allow patient access to these types of medications.

(5) Another proposal involving USP (found on page 10 of 1735.12 (c)) also exceeds USP. While combining one or more nonsterile components prior to releasing CSP's endotoxin testing seems reasonable, there is a concern about what happens if the Beyond Use Date is beyond the USP guidelines. USP has established 4 days nonsterile to sterile and 10 days sterile to sterile on CSP'S with no testing and with no caveats. I have heard many arguments that suggest the proposed regulation should only apply if the BUD chosen is beyond existing USP guidelines. The existing USP standards are scientifically based and going beyond these guidelines restricts patient access and drives up the price of their medications by at least $100 per CSP. In this case, it seems to be more appropriate to encourage the FDA to require manufactures to include endotoxin testing as part of the COA. If that is not deemed appropriate, a bare minimum reasonable comprise appears to be to allow pharmacies to test each lot number of API one time instead of each CSP.

Additionally, with respect to BUD policies, I have been informed that many pharmacies have spent thousands of dollars on required BUD studies from third party laboratories. With respect to 1751 a (1) and (2); it seems appropriate to accept the results of the studies and those results should not be over-looked. If that is agreed to, it would make sense to have the studies supersede proposed 1751.14 (a) (1) and (2). The proposal to simply use 4 days nonsterile to sterile and 10 days sterile to sterile on CSPs with no testing and no caveats seems reasonable and appropriate. Doing otherwise, I am told could be costly and also deny patient access to medications based on arbitrary and unscientific test criteria.

(6) When it comes to labeling instructions for administration for admixed CSP solutions (Section 1751.13 on page 10), many have suggested that the instructions to include rates of infusion are not practical. As you certainly know, these preparations are custom-made for specific patients and administered in a surgical setting. Since the physician often manipulates the rate of infusion at the time its given, it seems reasonable that the rate of infusion be determined by the physician and should not be placed on the label of the solution of the CSP.

(7) Finally, I have been asked about what new proposed Standard Operating Procedures may involve. As it was explained to me, many licensed pharmacists view strict procedures not based on science or accepted best practices could be considered as an attempt to unnecessarily become involved in inconsequential minutia when it comes to day-to-day operations of a pharmacy.

Thank you very much for allowing me the opportunity to share this information with you and for your willingness to seriously consider providing me a thoughtful response to these questions and comments. I truly appreciate all of the hard work your Board does and appreciate the difficult job you face in ensuring Californians are kept safe. If you have any questions, please do not hesitate to call me at (916) 651-4028.

Sincerely,

Jeff Stone, Pharm. D.

Jeff Stone
State Senator, 28th District

From: Jag Rai
To: Acosta, Christine@DCA
Subject: Sterile Compounding Committee Meeting 9/5
Date: Thursday, September 5, 2019 5:40:11 PM

[EXTERNAL]: Jagwant.Rai@sharp.com

::
Hi Christine,

Thank you for the informative Compounding Committee meeting today in Irvine. It was good to see you and hear the many comments regarding the regulations.

It was extremely well attended and really showcased the significance of the new USP 797 chapter and the impact it will have on the compounding of sterile compounded preparations.

I am sorry that I did not get the opportunity to talk to you considering the full house attendance, however I am seeking information and guidance specifically related to USP 71 testing.

I am considering performing in house USP 71 sterility testing for our Category 2 CSPs and wondered if you know of any facilities that are performing this type of testing and/or have any guidance for a facility planning to perform this type of in house sterility testing.

The meeting ended today prior to reviewing section 1751.12 (Release Testing) and since I am not able to attend the next meeting on September 24th, I am respectfully requesting this information.

The second question I have concerns release testing-

When a category 2 CSP batch is tested for sterility, what is the guidance on the release of the batch prior to the results of the sterility testing being known?

Respectfully,

Jag

Jag Rai
Lead Pharmacist
Sharp Centralized Hospital Pharmacy
3558 Ruffin Road, Suite 100
San Diego, CA 92123
Tel: 858-627-5630
Fax: 858-627-5635

Attachment 2

California State Board of Pharmacy
2720 Gateway Oaks Drive, Suite 100
Sacramento, CA 95833
Phone: (916) 515-3100 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: September 5, 2019

LOCATION: University of Southern California
Orange County Center
2300 Michelson Drive
Irvine, CA 92612

COMMITTEE MEMBERS PRESENT: Maria Serpa, Licensee Member, Chairperson
Allen Schaad, Licensee Member, Vice Chairperson
Greg Lippe, Public Member, Acting President

STAFF MEMBERS PRESENT: Anne Sodergren, Interim Executive Officer
Christine Acosta, Supervising Inspector
Anna Kalantar, Supervising Inspector
Laura Freedman, DCA Staff Counsel
MaryJo Tobola, Senior Enforcement Manager
Debbie Damoth, Administration Manager

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

Chairperson Serpa called the meeting to order and provided background on the committee's actions during the previous meetings. The committee determined and the full board agreed that regulations mirror the structure of the USP chapters, including separate requirements for the various types of compounding preparations. Rather than completing one rule making package that encompasses regulations for each USP Chapters, the Board will initiate the formal rulemaking process as regulations for each respective chapter are finalized. This will allow for more immediate transition to the new Chapters and regulations.

Dr. Serpa provided in July 2019, the committee discussed proposed regulations relating to nonsterile preparations, that may be necessary to implement, clarify or make more specific requirements related to USP Chapter 795 as well as to ensure safe compounding processes consistent with the board's consumer protection mandate. The committee's recommendation was considered by the board during the July 2019 board meeting. The board voted to initiate the rulemaking process, which is the first step in the promulgating the regulation. Dr. Serpa advised the rulemaking package was recently submitted to DCA counsel to complete pre-notice review. Upon completion of the pre-notice review by various control agencies, the board will release a notice and advise all interested parties about the proposed

changes and provide a 45-day comment period. Dr. Serpa suggested that anyone interested engage in the regulatory process during the comment period.

Dr. Serpa provided the focus of the meeting will be on proposed regulations for the compounding of sterile preparations to consider regulations that may be necessary to implement, clarify or make more specific requirements related to USP 797. Any such regulation should be consistent with the board's consumer protection mandate. Dr. Serpa noted if the committee is unable to complete the review at this meeting, a subsequent meeting will be convened on September 24th to continue the review. After completing this review on sterile compounding, the committee will move on to subsequent USP chapters 800 and 825 to consider additional regulations.

Chairperson Serpa called the meeting to order at 9:10 am. Board members present at the meeting were: Allen Schaad, Greg Lippe and Maria Serpa. 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. Discussion and Consideration of Proposed Regulations Related to Pharmaceutical Compounding of Sterile Preparations

Chairperson Serpa provided the committee will discuss each section one at a time with time for member and public discussion. Dr. Serpa advised the public if a delayed implementation is necessary for enhanced language in proposed California regulations to please include this in your comments. She noted, the proposed language will be projected so that live edits can be made with the consensus of the members. Dr. Serpa suggested that the committee consider a single motion to make a recommendation to the full board after completing its review of the proposal in its entirety. She advised the committee members and public that included in the meeting materials were draft proposed amendments to regulations that would rename Article 7 and repeal and replace Sections 1751-1751.10 with Sections 1751-1751.21. The second document included the same regulation language, but also included a brief explanation of the rationale and necessity for the proposed regulation.

Section 1751 Sterile Compounding in Licensed Pharmacies

The committee heard public comment on the proposed draft section 1751 (a) – (j).

Section 1751 (a)
The committee heard no comments on section 1751 (a).

Section 1751 (b)
The committee heard comments requesting allowing immediate use beyond the proposed limited situations where failure to administered could result in the loss of life or intense suffering. The committee and board staff explained the intent was to allow immediate use as an exception but in many hospitals, the exception became the practice. The commenter requested removing the labeling requirement of "for immediate use only" as this was redundant and represented additional

programming costs for labeling for each change to the label. The committee agreed and struck ‘ “for immediate use only” and’ from the second sentence of 1751 (b).

The committee heard comments requesting clarification if section 1751 (b) applied to all pharmacy personnel or personnel within the facility. Dr. Serpa clarified the board regulations are specific to the practice of pharmacy.

The committee heard comments about the unique identifier requesting clarification of the requirement during a code and if the unique identifier was specific to the CSP or patient. The committee clarified information on the code log would be sufficient documentation. The committee clarified the unique identifier was specific for the patient. The committee added “patient” before unique identifier in the last sentence of section 1751 (b).

The committee entertained a request to remove the compounded time from the requirements and specify records can be hard copy or electronic. The committee explained the compounded time is the documentation required to verify the product was used correctly.

The committee agreed to the following edits as a result of public comments:

> (b) Compounded sterile preparation (CSP) for immediate administration shall only be done in those limited situations where there is a need for immediate administration of a CSP and where failure to administer could result in loss of life or intense suffering. Any such CSP shall be labeled ~~“for immediate use only” and~~ with a beyond use date/time of 4 hours or less. The pharmacy shall maintain records of such CSPs shall at least include CSP made, compounded time, and patient name and <u>patient</u> unique identifier.

<u>Section 1751 (c)</u>
The committee heard no comments on section 1751 (c).

<u>Section 1751 (d)</u>
A member of the public expressed concern that section 1751 (d) required documentation from the physician. The committee and board staff advised the language is the same for sections 1735 pertaining to non-sterile compounding. Dr. Serpa directed board staff to confirm this information.

The committee heard public comments requesting section 1751 (d) be phrased in a more positive language so as not to be confusing. The commenter also requested the term “limited” to be defined and practice to be added to veterinarian for clarity. Board staff explained “limited” is current law and included in FDA guidance. Board staff indicated this could be included as an FAQ. The committee agreed to add “Except as identified below,” to the beginning of section 1751 (d) and remove “Notwithstanding this subdivision,” from section 1751 (d)(1). The committee agreed to add “practice” after veterinarian in section 1751 (d)(2).

The committee heard comments from pharmacists from large animal pharmacies. The pharmacists requested clarification if section 1751 (d)(2) referred to a single CSP or all CSPs. The committee clarified the requirement was for the specific CSP. To clarify the language, the committee agreed to change the last sentence of section 1751 (d)(2) to replace “additional CSPs” to “the same CSP” and will clarify additional products and frequency.

The committee heard a public comment requesting to have veterinary office dispensing added back into the section. The committee explained USP and current federal law does not allow for veterinary office dispensing. The committee attempted to find a balance to allow for continuance of care when needed without allowing for long-term dispensing from a veterinarian office.

The committee agreed to the following edits as a result of public comments:

> (d) Except as identified below, ~~No~~ no CSPs shall be compounded prior to receipt by a pharmacy of a valid patient specific prescription document. Where approval is given orally, that approval shall be noted on the prescription document prior to compounding.
>
> (1) ~~Notwithstanding this subdivision, a~~ A pharmacy may prepare and store a limited quantity of a CSP in advance of receipt of a patient specific prescription document.
>
> (2) Notwithstanding this subdivision, a pharmacy may prepare and provide a limited quantity of CSPs to veterinarians for animal patients based on a contract between the pharmacy and veterinarian for office use administration only. The pharmacy and veterinarian practice are jointly responsible for compliance with this section. The contract shall require the veterinarian to provide the pharmacy with the records documenting the dose administered to each patient or destruction record of CSPs. The pharmacy shall be prohibited from providing the same ~~additional~~ CSP~~s~~ to the veterinarian until the pharmacy has received and evaluate the records for compliance with this provision.

Section 1751 (e)

The committee heard comments that the language for section 1751 (e) should not refer to the compounding pharmacy. Chairperson Serpa clarified both the pharmacy license and pharmacist-in-charge are held responsible and accountable for the compounding done at the pharmacy.

The committee heard public comment requesting the time of dispensing be removed from section 1751 (e) (3) (A) as this shifted the burden of compounding to the pharmacy should the CSP be removed from the list during the compounding process. While the committee sympathized with the business decision, the committee must focus on the board's mandate of public protection.

Members of the public requested the committee specify human drugs in sections 1751 (e) (2) and (3) (A) and eliminate the duplicative wording in section 1751 (e) (3) (A). The committee removed "and at the time of compounding" in section 1751 (e) (3) (A).

The committee heard comments requesting clarification on section 1751 (e) (3) (A) and (B) which can be addressed in FAQs.

A member of the public requested clarification on section 1751 (e) (4). Board staff clarified raw materials should only be used for approved intended purposes. For example, raw materials for animal use should not be used for human use.

The committee received a request to allow for single exceptions to the requirements of section 1751 (e) (5).

The committee heard comment regarding 1751 (e)(6) requesting clarification if sterilization of product must be done in the pharmacy and cannot be completed outside of the pharmacy. Board staff confirmed the all steps to compounding including sterilization must be completed in the licensed compounding pharmacy.

The committee heard public comment regarding concern about limiting outsourced types of sterilization including gamma radiation, E-Beam and Ethylene Oxid (EtO) gas. The committee expressed concern about components of the compounding procedure leaving the licensed facility to an unlicensed facility and to an entity that should not be possessing dangerous drugs. The committee heard testimony that within the process is terminal sterilization. Once the product leaves the compounding licensed facility, the product is in a sealed vial/container. If tampered with, the product would not be used.

The committee heard testimony that USP 797 advocates for terminal sterilization. Public comment indicated gamma radiation and E-Beam sterilization is safer than autoclaving sterilization. Additional public comment indicated gamma radiation sterilization works better for some products. One commenter urged section 1751 (e)(6) be removed.

The committee understood the benefit of the terminal sterilization but acknowledged a change in statute is required.

The committee entertained a question about the authority to ship products via common carriers such as Fed Ex. Chairperson Serpa explained that is considered distribution to the end user and acceptable.

The committee heard public comment from an analytical lab representative who testified the company tests many compounds and sterile pellets with never having one fail. The representative testified the technique is viable and E-Beam sterilization is the most frequently used sterilization for medical devices. The commenter attested to the chain of custody used throughout the process.

Chairperson Serpa inquired about the opportunities to regulate vendors that are not licensed with the board. Interim Executive Officer Anne Sodergren advised a statutory change would be required.

The committee heard a comment concerning a hospital setting where autoclaving is part of central services. The commenter was concerned this wouldn't be allowed in the proposed draft language and requested the use of the term premise. Board staff advised the committee the definition includes within the licensed location and includes the entire hospital address.

The committee agreed to the following edits as a result of public comments:

(e) No pharmacy or pharmacist shall compound a CSP that:

(1) Is classified by the United States Food and Drug Administration (FDA) as demonstrably difficult to compound;

(2) Appears on an FDA list of drugs which 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) 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 compounding~~ and at the time of dispense, or (B), the compounding of that CSP 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 CSP for the intended patient population.

(5) Is made with a bulk drugs substance, as defined in Section 503A(b)(1)(A)(i), when there is an FDA approved sterile drug product that is available and appropriate for the intended CSP.

(6) cannot be sterilized within the licensed location ~~pharmacy~~.

Section 1751 (f)

The committee heard comment requesting clarification on when a self-assessment was required. The committee referred to section 1715 for clarification of self-assessment requirements.

Section 1751 (g)

The committee heard no comments on section 1751 (g).

Section 1751 (h)

A member of the public requested clarification on the definitions included in section 1751 (h). The committee agreed to the following edits as a result of public comments:

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

Sections 1751 (i) and (j)

The committee received a request for the changes made to section 1751 (i) and (j). Board staff advised "and any board regulations" was added.

The committee took a break at approximately 11:03 am and returned at 11:21 am.

Chairperson Serpa advised to the audience that a decision had not yet been made about using a contracted sterilization company outside the licensed compounding facility. Dr. Serpa asked members of the public to email the board at and notify the board of any products that required being sterilized at a contracted sterilization company outside the licensed compounding facility. Dr. Serpa asked that the product requiring contracted sterilization be identified with an explanation why the contracted sterilization process is the only process that works for that product. Dr. Serpa advised the board will conduct further research on this issue. The email address compounding.pharmacy@dca.ca.gov was provided to the attendees. Supervising Inspector Christine Acosta requested names of outsourcing sterilization companies so the type of licensure can be identified for the companies.

Section 1751.1 Compounding Definitions

The committee heard public comment on the proposed draft section 1751.1 (a) – (l).

Section 1751.1 (a)
The committee heard comments requesting clarification and further definition of compounding personnel. Specifically, the committee was asked if environmental services, printing labels, washing equipment, and messengers to floors were included as part of compounding personnel. Board staff provided this section was intended to include all personnel involved in the compounding process. A member of the public requested this be addressed with FAQs. Dr. Serpa added this will be addressed in 1751.2.

Section 1751.1 (b)

The committee received comments on section 1751.1 (b) requesting clarification if IV admixture is no longer considered a CSP if made by manufacturer instructions. Dr. Serpa and Dr. Acosta clarified the board's proposed regulations further clarify USP 797 in specifying FDA approved labeling by product manufacturer. Dr. Serpa further clarified reconstituting must be done according to the manufacturer's insert. If reconstituting deviates from the manufacturer's insert, that is considered compounding.

A member of the public stated they appreciated "FDA approved" was clarified in this section and requested reconstituting and mixing be clarified as being exempt from compounding provided the approved labeling is being followed. Dr. Acosta stated it is included in USP 797 and this is part the preparation and not the process. Dr. Serpa clarified the board's proposed regulations are to clarify items that are not clear in USP 797.

Section 1751.1 (c) – (e)
The committee heard no comments on section 1751.1 (c) - (e).

Section 1751.1 (f)
The committee heard comments requesting clarification of "in process material" and the meaning of this term. DCA Counsel Freedman provided this was an effort to clarify a confusing definition but the board will continue to refine the language.

The committee heard comments requesting removal of "the" or "all" in the last sentence of Section 1751.1 (f). The committee agreed to the following edits as a result of public comments:

> (f) "In process material or in process preparation or stock solution" means any material fabricated, compounded, blended, or derived by chemical reaction that is produced for, and used in, the preparation of the CSP. For purposes of this article, "in process material" shall refer to ~~the~~ all terms used in this subdivision.

Section 1751.1 (g) – (l)
The committee heard no comments on section 1751.1 (g) - (l).

Section 1751.2 Personnel Training and Evaluation

The committee heard public comment on the proposed draft section 1751.2(a) – (f).

Section 1751.2 (a)
The committee heard no comments on section 1751.2 (a).

Section 1751.2 (b)
The committee heard comments indicating there was confusion if required semiannual or annually and requested adding "at least annually." Dr. Acosta advised the frequency is included in USP 797.

Section 1751.2 (c)
The committee heard comments requesting definitions for primary engineering controls. The committee agreed to the following edits as a result of public comments:

> (c) Aseptic manipulation evaluation and requalification documentation shall include the PEC's (Primary Engineering Control) unique identifier used during the evaluation. Aseptic manipulation evaluation and requalification shall be performed using same personnel, procedures, type of equipment, and materials used in compounding drug preparations.

Section 1751.2 (d)
The committee received comments requesting reference to the action levels in USP and clarification on what levels require action. The committee expressed concern on limiting action to only the tables referenced in USP and explained USP action tables are the minimum requirements. Some standard operating procedures identify any contamination requiring action. The committee expressed concern for limiting those who want to exceed USP standards. The committee heard comments requesting definitions for standard operating procedures. The committee agreed to the following edits as a result of public comments:

> (d) Requalification in hand hygiene, garbing and aseptic manipulation shall occur each time the quality assurance program yields an unacceptable result as defined in the Standard Operating Procedure (SOP)s that may indicate microbial contamination of CSPs. Requalification procedures shall be defined in the pharmacy's SOPs.

Section 1751.2 (e)
The committee heard no comments on section 1751.2 (e).

Section 1751.2 (f)
The committee received comments requesting clarification on what training is required for people working on the floors. Chairperson Serpa advised all personnel involved in compounding would have to have a measure or competency that would prove they are following hospital standard operating procedures. Dr. Acosta advised USP 797 in 1.5 specifies they are subject to the following not listed in categories 1 and 2 such as training, competency testing and personal hygiene for personnel are applicable to all compounding personnel.

Section 1751.3 Personnel Hygiene and Garbing

The committee heard public comment on the proposed draft section 1751.3 (a) – (f).

Section 1751.3 (a)
The committee heard public comment that USP doesn't specify rashes or sores not exposed are restrictive to go into the IV room and how would a pharmacist know without a search. The committee advised this is included under the accommodation section, CCR 1751.3(f). Dr. Acosta provided the discretion from the designated person has been removed in the board's proposed regulations.

Section 1751.3 (b)
The committee heard no comments on section 1751.3 (b).

Section 1751.3 (c)
The committee received a comment requesting clarification if this is referring to hazardous. Chairperson Serpa indicated this would be addressed in the next section at a different meeting.

The committee heard comments requesting to revert to USPs suggestion that donning and doffing do not occur in the ante room rather than making it compulsory. Dr. Serpa advised the intent was to imply in most situations, this should not be done but added the process is required if done.

DCA Counsel Freedman clarified that discussions occurred between Dr. Serpa and staff but not Dr. Serpa and other committee members. Dr. Serpa clarified she worked with staff to provide input and kept up to date on proposed drafts.

Section 1751.3 (d) – (f)
The committee heard no comments on Section 1751.3 (d) – (f).

Section 1751.4 Facilities and Engineering Controls

Committee Member Lippe indicated this would be a good section to define PEC as primary engineering control.

The committee heard public comment on the proposed draft section 1751.4 (a) – (h).

Section 1751.4 (a)
The committee did not hear comments on section 1751.4 (a).

Section 1751.4 (b)
The committee heard a comment requesting reusable equipment and utensils that cannot be sterilized be required to be rinsed with sterile water for injection or sterile water for irrigation as USP does not define pyrogen free water. Dr. Acosta added sterile water for injection or sterile water for irrigation are pyrogen free. The committee agreed to reference applicable USP chapters and agreed to the following edits as a result of public comments:

> (b) Reusable equipment and utensils which ~~have~~ cannot ~~not~~ be sterilized and depyrogenated, and that will come in direct contact with compounding components must be rinsed with either sterile water for injection or sterile water for irrigation, ~~, pyrogen free water~~.

Section 1751.4 (c)

The committee did not hear comments on section 1751.4 (c).

Section 1751.4 (d)

A commenter asked why USP 797 was restated in this section. Dr. Acosta provided this language is to eliminate a plan with an ante room and cleanroom but later the site determines higher volume is needed so a PEC is put in the ante room where the cleanroom is no longer the cleanroom. Dr Acosta continued if the anteroom is used as a SEC then the cleanroom that follows this anteroom is no longer a cleanroom, but is now a SCA.

Section 1751.4 (e)

The committee heard a comment requested removal of section 1751.4 (e)(1) and (e)(2) as it is included in USP and redundant. Dr. Serpa provided temperatures are regulated differently by different regulators. She stated it was the committee's intent with the proposed language to find the best language for the comfort and safety of personnel. The language of "should" from USP was not enforceable which is why the language was changed to "shall" with the allowance of adding "typically." The SCA is added to the language. This will also be added to the FAQs. Dr. Serpa encouraged the public to use ask.inspector@dca.ca.gov for questions about specific sites. The committee also heard comment that this language should be stricter and should be "shall."

The committee heard a comment requesting any deviation to be documented. Dr. Acosta provided that requirement for documentation was already included in USP.

The committee heard a comment requesting the allowance for using non-sterile components in the sterile preparation process provided the process is validated. The commenter requested water for injection produced at the facility to be allowed. Dr. Acosta expressed concern writing law for one business practice and was not aware of other sites that created their own water.

Section 1751.4 (f)

The committee heard a comment that new CA building codes effective 1/1/20 will not allow for a pass through between the hazardous drug buffer room and any unclassified area and won't be allowed in a hospital. The committee also heard a comment requesting the effective date of this requirement to be two years from the effective date of the regulation. The committee agreed to reference applicable USP chapters and agreed to the following edits as a result of public comments:

> (f) Where a pass-through is installed in a secondary engineering control, SOPs must address how both doors will not be opened at the same time. Effective ~~January 1, 2020,~~ [two years from the effective date of the regulation], all pass-throughs must be interlocking. ~~A pass-through used to access a negative-pressure ISO 7 or better space from a non-classified space, must be a HEPA-filtered purge pass-through.~~

Section 1751.4 (g) – (h)

The committee did not hear comments on section 1751.4 (g) and (h).

The committee took a break for lunch at 12:36 pm and returned from lunch at 1:22 pm.

Section 1751.5 Certification and Recertification

The committee heard public comment on the proposed draft section 1751.5 (a) – (c).

Section 1751.5 (a)

The committee heard concerns about referencing CETA guidelines with a specific reference to a version of the guidelines when the guidelines are expected to change in the future. DCA Counsel Freedman provided the Office of Administrative Law will require a version to be specified. Ms. Freedman provided if new guidelines come out during the regulation process, the proposed regulation text can be amended.

The committee heard comment requesting to change "certify" to "certification" in section 1751.5 (a)(2). Based on public comment, the committee agreed to the following change in section 1751.5 (a)(2):

> (2) CAG standard(s) used to perform ~~certify~~ certification testing in all classified areas to shall be recorded on certification report.

Section 1751.5 (b) – (c)
The committee did not hear comments on section 1751.5 (b)-(c).

Section 1751.6 Microbiological Air and Surface Monitoring

The committee heard public comment on the proposed draft section 1751.6 (a) – (e).

Section 1751.6 (a)
The committee heard no comment on section 1751.6 (a).

Section 1751.6 (b)
The committee heard comments concerning the term organism of concern. Dr. Serpa clarified this section is referring to air and surface monitoring. Dr. Kalantar advised the purpose is to have the pharmacies identify the organisms of higher concern and pointed pharmacies to consult a microbiologist to help create the list.

The committee heard comments requesting (b) and (c) reference SOPs and action levels associated with USP 797. Dr. Serpa provided the intent of this requirement is to require the pharmacy to at least biannually know what is growing in the environment even if the levels are below the action levels required by USP.

The board heard comment agreeing with the organism of concern and requesting the board post information on the board's website. The committee advised this is to be handled by the pharmacy and included in the SOPs which will also address geographic differences. The commenter requested removing the organism of concern from the regulation and added to the self-assessment. Board staff and DCA Counsel indicated it needs to be in regulation to clarify in law for the regulated public.

The committee heard a comment requesting removing "species" and replacing with "level" and requesting the change shall be identified "by a qualified microbiologist" to provide reassurance of the biannual testing and the level of species to see if it is an organism of concern.

The committee heard comments requesting specification to the genus level for cfu counts below ISO classification action levels and within the facility's historical trend as being questionable to patient safety and representing increased cost for the patients. The commenter requested reconsideration of moving away from organisms of concern.

The committee heard comment requesting the removal of the last sentence and requested adding to the SOPs identification of organisms of concern. Any time there is growth in the hospital setting, administrators want to know the law. As written now, organisms of concerns include molds or yeast. Dr. Serpa recommended using an adjective or qualifier for molds or yeast.

The committee heard comment that section 1751.6 (b) was beyond the scope of practice for a pharmacist who is not a microbiologist specialist. Dr. Serpa appreciated that it may be above the pharmacist-in-charge, but the pharmacist-in-charge needs to have the general idea and microbiologists are available for consultation.

Based on public comment received, the committee agreed to the following changes in section 1751.6 (b):

> (b) During biannual recertification, all microorganism recovered (growth) shall be identified by a qualified microbiologist, at least to the genus ~~species~~ level, regardless of the cfu count. When identification of an organism of concern, action shall be taken. Organisms of concern shall be identified by the PIC or designated person and shall be documented in a SOP. Some possible organisms of concern ~~would~~ may, but need not, include ~~be~~ gram-negative rods, coagulase positive staphylococcus, and certain molds and yeasts.

Section 1751.6 (c)

The committee heard comments that whenever growth is identified in (a) or (b), resampling has to be redone. The committee indicated the intent was not to require continuous resampling for (b). The intent is only when action levels are exceeded or during biannual testing. The committee made edits to remove "growth is identified" and replace with "cfu action levels are exceeded or an organism of concern is identified."

Based on public comment received, the committee agreed to the following changes in section 1751.6 (c):

> (c)Whenever ~~growth is identified~~ cfu action levels are exceeded or an organism of concern is identified as specified in (a) or (b), required action shall include at a minimum, an investigation of (1) cleaning and compounding operations, (2) sampling, (3) personnel training, (4) incubator functionality, (5) facility management, and (6) resampling. Consultation with a competent microbiologist, infection control professional, or industrial hygienist is required when resampling results in growth of an organism of concern or when action levels are exceeded, regardless of count. All actions taken shall be documented.

Section 1751.6 (d) – (e)

The committee did not hear comments on section 1751.6 (d) or (e).

Section 1751.7 Cleaning, Disinfecting, and Applying Sporicidal Agents in Compounding Areas

The committee heard public comment on the proposed draft section 1751.7 (a) – (b).

Section 1751.7 (a)
The committee heard comment that this was duplication of USP. Dr. Acosta clarified it has to be written in the SOPs for clarity.

The committee received a comment requesting clarification if the disinfectant has to be sterile. Dr. Acosta clarified USP does not specify.

Section 1751.7 (b)
The committee did not hear comment on section 1751.7 (b).

Section 1751.8 Introducing Items into the SEC and PEC

The committee heard public comment on the proposed draft section 1751.8 (a).

Section 1751.8 (a)
The committee heard a comment requesting to change "this" to "these." Based on the comment from the public, the committee agreed to the following change:

> The requirements of this section apply in addition to the requirements in USP Chapter 797**.**
>
> (a) SOPs shall define the process and products to be used on any equipment and other items entering from an unclassified area into the clean side of the ante-room, entering a PEC, and entering the SCA. ~~This~~ These SOPs will define at a minimum, what product is to be used, the dwell time required, and how dwell time will be monitored and documented.

Section 1751.9 Equipment, Supplies, and Components

The committee heard public comment on the proposed draft section 1751.9 (a) – (f).

Section 1751.9 (a) – (b)
The committee did not hear comment on section 1751.9 (a) – (b).

Section 1751.9 (c)
The committee heard comments requesting if the board was moving to making FDA guidance documents a regulatory requirement. Dr. Serpa clarified they should be considered. The commenter requested it be added as a separate item. Dr. Serpa requested Section 1735 be considered.

After hearing public comment, the committee agreed to the following changes with the possible rephrasing:

(c) Any component used to compound a CSP shall be used and stored <u>(1) considering issued Guidance Documents and Alerts (2)</u> in accordance with all industry standards including the following:

(~~1~~ <u>A</u>) United States Pharmacopeia (USP) – National Formulary (NF),

(~~2~~ <u>B</u>) Food Drug and Cosmetic Act (FD&CA) and federal regulations adopted to implement that act,

(~~3~~ <u>C</u>) Food Drug Administration (FDA) requirements and ~~considering issued Guidance Documents and Alerts~~, and

(~~4~~ <u>D</u>) Manufacturers' specifications and requirements.

<u>Section 1751.9 (d)</u>

The committee heard comments expressing concern enforcing USP chapters over 1000 as the chapters are meant to be informational purposes only. The recommendation was made to reference any USP chapter over 1000 rather than requiring it. DCA Counsel Freedman confirmed as proposed in the draft, the requirement is established for USP 1080.

<u>Section 1751.9 (e)</u>

The committee heard comment regarding concern about dietary supplement standards as written would negatively impact patient access. Dr. Serpa provided it is not the board's purpose to get in the way of patient treatment where it is safe for patients, but this was included because there are unsafe practices occurring. Dr. Acosta provided the intent of the language is to prevent people from taking inappropriately graded raw materials and preparing to make injectables and use materials that are graded for injectables. Dr. Serpa indicated human consumption grade need to be considered when selecting raw materials for injections.

Dr. Serpa encouraged the public to provide information via the email address for specific examples that are known that would be impacted by this language.

The committee heard comments that guidance is needed for what is acceptable and standard for injections. Dr. Acosta provided a USP monograph is not required. A USP monograph is one of the acceptable methods but there are other acceptable methods.

The committee heard a comment from a veterinary pharmacist that there several APIs that do not have USP monographs but have the COA. If there are no guidelines, they use what the manufacturer usually tests. They also use vendors that set their own standards. Dr. Serpa requested a list indicated as veterinary use.

The committee heard a comment inquiring about investigational drugs. Dr. Acosta provided investigational drugs are regulated by CDPH and FDA. The FDA makes allowance for FDA-approved products.

<u>Section 1751.9 (f)</u>

The committee heard a comment requesting clarification if section 1751.9 (f) prohibits use of pre-sterilized or pre-pyrogenized components. Dr. Acosta provided it speaks to what is done in the pharmacy.

Section 1751.10 Sterilization and Depyrogenation

The committee heard public comment on the proposed draft section 1751.10 (a) – (f).

Section 1751.10 (a) – (f)
The committee heard public comment that the inclusion of gamma radiation and x-ray should be included in section 1751.9 (f). Dr. Serpa provided as the committee looks to radiation in the previous section, the committee will include corresponding changes to this section. The public is invited to submit comments.

Section 1751.11 Master Formulation and Compounding Records

The committee heard public comment on the proposed draft section 1751.11 (a) – (c).

Section 1751.11 (a)
The committee heard a comment to remove "at least volume" from section 1751.11 (a)(2). Dr. Acosta advised it was removed from nonsterile but kept for sterile.

Section 1751.11 (b)
The committee received a comment requesting clarification of the definition for "routinely" and there is no provision in USP 797 to put the master formula on the prescription itself. There is a provision to put the record of compounding on the prescription. Dr. Acosta clarified it was left in the proposed draft to allow for one offs to not have to change practice. The requirements are the same as USP but need to be on one document.

Section 1751.11 (c)
The committee received an inquiry why section 1751.11 (c)(2) has removed the internal ID number for lots or orders and now it is only for these compounded drug preparations. Dr. Serpa provided this is current process. Dr. Acosta clarified USP does not require unique number and the proposed draft regulations specify the unique number.

The committee received an inquiry why section 1751.11 (c)(3) requirements are for only CSP for more than one patient and from CSP from nonsterile ingredients. Dr. Serpa and Dr. Acosta provided this is current practice.

The committee heard a comment requesting clarification if there was an exemption for lot compounding. Dr. Acosta confirmed the exemption which allows for a loophole that prevented processing of recalls and unable to determine if the product used was expired at the time of the use. It has been an exemption for inpatient practices but is not beneficial to the consumers.

The committee was asked why the number of units is required to be documented if assigned a unique identification number in section 1751.11 (c)(4). The committee explained the board needs to know how many products share in the batch made.

Dr. Serpa thanked the public for the participation and great discussion through section 1751.11. Dr. Serpa advised the continued review of section 1751 will recommence at the next committee meeting on September 24, 2019.

4. Approval of the June 4, 2019, Meeting Minutes

Motion: Approve the June 4, 2019, committee meeting minutes with the following edits:

- On page 4 of 5 of the meeting minutes in the last paragraph, amend the first sentence to remove "in licensed pharmacies" to read "Chairperson Serpa inquired what is the role of the board for regulating the use of radiopharmaceuticals where non-pharmacy personnel are doing activities in the licensed care environment."
- On page 4 of 5 of the meeting minutes in the last paragraph, delete the third sentence.
- On page 4 and 5 of 5 of the meeting minutes in the last paragraph on page 4, amend the last sentence of the last paragraph to add "in these organizations and" after pharmacy leadership to read "Chairperson Serpa added even if it is not under the purview or scope of the board, it is still under the purview of pharmacy leadership in these organizations and other regulators (e.g., Joint Commission, CDPH) to hold the pharmacy accountable for all compounding including radiopharmaceuticals."

M/S: Schaad/Serpa

Support: 2 Oppose: 0 Abstain: 1

Board Member	Support	Oppose	Abstain	Not Present
Schaad	x			
Serpa	x			
Lippe			x	

5. Approval of the July 11, 2019, Meeting Minutes

Motion: Approve the July 11, 2019, committee meeting minutes with the following edits:

- On page 3 of 11 of the meeting minutes in the third paragraph, amend the last sentence to add "and she will contact USP for further clarification" to read "Inspector Christine Acosta stated the USP 795 committee intended for the inclusion of a flavoring agent to be considered compounding and she will contact USP for further clarification."

M/S: Lippe/Schaad

Support: 3 Oppose: 0 Abstain: 0

Board Member	Support	Oppose	Abstain	Not Present
Schaad	x			
Serpa	x			
Lippe	x			

6. Future Committee Meeting Dates

Chairperson Serpa announced the committee's next meeting is scheduled for September 24, 2019, in Sacramento.

7. Adjournment

Chairperson Serpa adjourned the meeting at 2:50 pm.