

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 unique identifier.

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

(d) 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 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 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 additional CSPs to the veterinarian until the pharmacy has received and evaluate the records for compliance with this provision.

(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 pharmacy.

(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 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 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 a result 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 not be sterilized and depyrogenated, and that will come in direct contact with compounding components must be rinsed with sterile, 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, 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.

(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 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 at least to the genus species, 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 be gram-negative rods, coagulase positive staphylococcus, molds and yeasts.

(c) Whenever growth 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 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 in accordance with all industry standards including the following:

- (1) United States Pharmacopeia (USP) – National Formulary (NF),
- (2) Food Drug and Cosmetic Act (FD&CA) and federal regulations adopted to implement that act,
- (3) Food Drug Administration (FDA) requirements and considering issued Guidance Documents and Alerts, and
- (4) Manufacturers' specifications and requirements.

(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.

1735.12 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.)