

Title 16. Board of Pharmacy

Proposed Language

To Amend § 1735 in Article 4.5 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1735. Compounding in Licensed Pharmacies.

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

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

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

(c) "Compounding" does not include, except in small quantities under limited circumstances as justified by a specific, documented, medical need, preparation of a compounded drug product that is commercially available in the marketplace or that is essentially a copy of a drug ~~product~~ preparation that is commercially available in the marketplace.

(d) The parameters and requirements stated by this Article 4.5 (Section 1735 et seq.) apply to all compounding practices. Additional parameters and requirements applicable solely to sterile ~~injectable~~ compounding are stated by Article 7 (Section 1751 et seq.).

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

To Amend § 1735.1 in Article 4.5 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1735.1. Compounding Definitions.

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

(b) "Batch" means compounding of two or more finished drug preparation units produced during the same continuous cycle of compounding and shall include any multiple dose vials prepared for administration to more than one patient.

(c) "Beyond use date" means the date or date and time after which a compounded drug preparation shall not be stored or transported, or administration begun.

(d) "Buffer area" means an area providing at least an ISO Class 7 or better air quality where the primary engineering control is physically located.

(e) "Cleanroom" (which may also be referred to as a buffer area) means a physically separate room with walls and doors providing at least an ISO Class 7 or better air quality where the primary engineering control is physically located. This room maintains segregation from the adjacent ante-area (ante-room) by means of specific pressure differentials.

(f) "Controlled cold temperature" means 2.2 degrees to 7.7 degrees C (36 degrees to 46 degrees F).

(g) "Controlled freezer temperature" means -25 degrees to -10 degrees C (-13 degrees to 14 degrees F).

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

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

- (j) "First air" means the air exiting the HEPA filter in a unidirectional air stream that is essentially particle free.
- (k) "Gloved fingertip sampling" means a process where, compounding personnel lightly press each fingertip and thumb onto appropriate growth media, that are then incubated at a temperature and for a time period conducive to multiplication of microorganisms, and then examined for growth of microorganisms.
- ~~(b)~~ (l) "Integrity" means that all aspects of quality including sterility, packaging, chemical stability and potency, handling, and transport and storage are maintained throughout the drug preparation process, and retention of potency until the expiration beyond use date noted provided on the label.
- (m) "Media-fill test" means a test that mimics compounding procedures using a growth-based media to demonstrate that aseptic technique of compounding personnel or processes routinely employed do not result in microbial contamination. Media fill tests are conducted on the most challenging and routine compounding procedures performed.
- (n) "Parenteral" means a sterile preparation of drugs for injection or implantation through one or more layers of skin.
- (o) "Personal protective equipment" means clothing or devices that protect the employee from exposure to drug products and minimize the contamination of compounded preparations. These include shoe covers, head and facial hair covers, face masks, gowns, and gloves.
- ~~(e)~~ (p) "Potency" means active ingredient strength within +/- 10% (or the range specified in USP37-NF32, 37th Revision, Effective May 1, 2014) of the labeled amount.
- (q) "Preparation" means a drug or nutrient compounded in a licensed pharmacy; the preparation may or may not contain sterile products.
- (r) "Prescriber's office" or "prescriber office" means an office or suite of offices in which a prescriber regularly sees patients for outpatient diagnosis and treatment.
- (s) "Primary Engineering Control (PEC)" means a device that provides an ISO Class 5 environment or better through the use of unidirectional HEPA filtered first air.
- (t) "Process validation" means demonstrating that when a process is operated within specified limits, the process will consistently produce preparations complying with predetermined

requirements. If any aspect of the process is changed, the process would need to be revalidated.

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

~~(d)~~ (v) "Quality" means the absence of harmful levels of contaminants, including filth, putrid, or decomposed substances, and absence of active and inactive ingredients other than those noted on the label.

(w) "Segregated compounding area" means a designated space where a device that provides unidirectional airflow of ISO Class 5 air quality, including compounding aseptic isolators, is located within either a demarcated area (three to six foot perimeter) or room. Such area shall contain and shall be void of activities and materials that are extraneous to sterile compounding. The segregated compounding area shall not be in a location that has unsealed windows or doors that connect to the outdoors, in a location with high traffic flow, or in a location that is adjacent to construction sites, warehouses, or food preparation, and shall not have a sink located within three to six feet of the ISO Class 5 PEC. This sterile compounding area will be restricted to preparing sterile-to-sterile compounded preparations .

(x) "Smoke test" means an analysis of the airflow in the ISO Class 5 PEC using a smoke generating device.

~~(e)~~ (y) "Strength" means amount of active ingredient per unit of a compounded drug ~~product~~ preparation.

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

To Amend § 1735.2 in Article 4.5 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1735.2. Compounding Limitations and Requirements; Self-Assessment.

(a) Except as specified in (b) and (c), no drug ~~product~~ preparation shall be compounded prior to receipt by a pharmacy of a valid prescription for an individual patient where the prescriber has approved use of a compounded drug ~~product~~ preparation either orally or in writing. Where approval is given orally, that approval shall be noted on the prescription prior to compounding.

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

(c) A “reasonable quantity” furnished to a prescriber for office use by the prescriber as authorized by ~~as used in~~ Business and Professions Code section 4052 subdivision (a)(1) means that amount of compounded drug ~~product~~ preparation that:

(1) is ordered and paid for by the prescriber, using a purchase order or other documentation received by the pharmacy prior to furnishing that lists the number of patients seen or to be seen in the prescriber’s office for whom the drug is needed or anticipated, and the quantity for each patient that is sufficient for either office administration ~~or application to patients in the prescriber’s office, or for distribution of not more than~~ or furnishing of a 72-hour supply ~~to the prescriber’s patients, as estimated by the prescriber;~~ and

(2) is delivered to the prescriber office and signed for by the prescriber; and

(3) is sufficient for administration or application to patients solely in the prescriber's office, or for furnishing of not more than a 72-hour supply solely to the prescriber's own patients seen as part of regular treatment in the prescriber's office, as estimated by the prescriber and documented on the purchase order or other documentation submitted to the pharmacy; and

(4) is reasonable considering the intended use of the compounded medication and the nature of the prescriber’s practice; and

~~(3)~~ (5) for any individual prescriber and for all prescribers taken as a whole, is an amount which the pharmacy is capable of compounding in compliance with pharmaceutical standards for integrity, potency, quality and strength of the compounded drug ~~product~~ preparation; and

(6) does not exceed an amount the pharmacy can reasonably and safely compound.

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

(1) is classified by the FDA as demonstrably difficult to compound;
(2) appears on a FDA list of drugs that have been withdrawn or removed from the market because such drugs or components of such drugs have been found to be unsafe or not effective; or
(3) is a copy or essentially a copy of one or more drug products, unless that drug product appears on an ASHP (American Society of Health-System Pharmacists) or FDA list of drugs that are in short supply at the time of compounding and at the time of dispense. The pharmacy shall retain a copy of the documentation of the shortage in the pharmacy records for three years.

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

- (1) Active ingredients to be used.
- (2) Equipment to be used.
- (3) ~~Expiration dating requirements.~~ The rationale or reference source for determining the maximum allowable beyond use date for this preparation.
- (4) Inactive ingredients to be used.
- (5) ~~Process and/or Specific compounding steps procedure~~ used to prepare the drug.
- (6) Quality reviews required at each step in preparation of the drug.
- (7) Post-compounding process or procedures required, if any.

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

~~(f g)~~ The pharmacist performing or supervising compounding is responsible for the integrity, potency, quality, and labeled strength of a compounded drug ~~product~~ preparation until it is dispensed.

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

(h i) Every compounded drug ~~product preparation~~ shall be given an ~~expiration~~ beyond use date representing the date beyond which, in the professional judgment of the pharmacist performing or supervising the compounding, it should not be used, stored, transported, or administration begun. This “beyond use date” of the compounded drug ~~product preparation~~ shall not exceed 180 days from preparation or the shortest expiration date of any component in the compounded drug ~~product preparation~~, unless a longer date is supported by stability studies of finished drugs or compounded drug ~~products preparations~~ using the same components and packaging. Shorter dating than set forth in this subsection may be used if it is deemed appropriate in the professional judgment of the responsible pharmacist.

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

(j k) Prior to allowing any drug ~~product preparation~~ to be compounded in a pharmacy, the pharmacist-in-charge shall complete a self-assessment for compounding pharmacies developed by the board as required by Section 1715 of Title 16, Division 17, of the California Code of Regulations. ~~(Incorporated by reference is “Community Pharmacy & Hospital Outpatient Pharmacy Compounding Self-Assessment” Form 17M-39 Rev. 02/12.)~~ That form contains a first section applicable to all compounding, and a second section applicable to sterile ~~injectable~~ compounding. The first section must be completed by the pharmacist-in-charge before any compounding is performed in the pharmacy. The second section must be completed by the pharmacist-in-charge before any sterile ~~injectable~~ compounding is performed in the pharmacy. The applicable sections of the self-assessment shall subsequently be completed before July 1 of each odd-numbered year, within 30 days of the start date of a new pharmacist-in-charge or change of location, and within 30 days of the issuance of a new pharmacy license. The primary purpose of the self-assessment is to promote compliance through self-examination and education.

(l) Packages of ingredients that lack a supplier’s expiration date are subject to the following limitations:

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

documented inspection or analytical testing indicates that the ingredient has retained its purity and quality for use in compounded drug preparations, considering the container in which it is packaged and the storage conditions, and
(2) such ingredients cannot be used for any sterile compounded drug preparation more than one (1) year after the date of receipt by the pharmacy, unless either appropriate and documented inspection or analytical testing indicates that the ingredient has retained its purity.

Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code, Sections 1735, 1735.1, 1735.8, and 1751.1-1751.8 of Title 16, Division 17, of the California Code of Regulations.

To Amend § 1735.3 in Article 4.5 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1735.3. ~~Records~~ Recordkeeping of for Compounded Drug ~~Products~~ Preparations.

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

- (1) The master formula record.
- (2) The date the drug ~~product preparation~~ was compounded.
- (3) The identity of ~~the any~~ pharmacy personnel ~~who compounded the~~ engaged in compounding the drug ~~product preparation~~.
- (4) The identity of the pharmacist reviewing the final drug ~~product preparation~~.
- (5) The quantity of each component used in compounding the drug ~~product preparation~~.
- (6) The manufacturer, expiration date and lot number of each component. If the manufacturer name is demonstrably unavailable, the name of the supplier may be substituted. Exempt from the requirements in this paragraph are sterile ~~products preparations~~ compounded on a one-time basis for administration within seventy-two (72) hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code and stored in accordance with standards for “Redispensed CSPs” found in Chapter 797 of the United States Pharmacopeia – National Formulary (USP37-NF32) (~~35~~ 37th Revision, Effective May 1, ~~2012~~

2014), hereby incorporated by reference, ~~to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.~~

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

(8) The ~~expiration beyond use~~ date of the final compounded drug ~~product~~ preparation.

(9) The final quantity or amount of drug ~~product~~ preparation compounded for dispensing.

(10) Storage preparation for the drug preparation.

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

(c) Active pharmaceutical ingredients shall be obtained from a FDA registered supplier. All other ~~C~~chemicals, bulk drug substances, and drug products, ~~and components~~ used to compound drug ~~products~~ preparations shall be obtained, whenever possible, from ~~reliable~~ FDA-registered suppliers. The pharmacy shall acquire and retain ~~any available~~ certificates of purity or analysis for chemicals, and bulk drug substances, ~~drug products, and components~~ used in compounding. ~~Certificates of purity or analysis are not required for drug products that are approved by the Food and Drug Administration. Certificates of purity or analysis are to be matched to the product received.~~

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

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

To Amend § 1735.4 in Article 4.5 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

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

(a) In addition to the labeling information required under Business and Professions Code section 4076, the label of a compounded drug ~~product~~ preparation shall contain the generic name(s) of the principal active ingredient(s).

(b) A statement that the drug has been compounded by the pharmacy shall be included on the container or on the receipt provided to the patient.

(c) Drug ~~products~~ preparations compounded into unit-dose containers that are too small or otherwise impractical for full compliance with subdivisions (a) and (b) shall be labeled with at least the name of the compounding pharmacy and dispensing pharmacy, if different, the name(s) of the active ingredient(s), concentration or strength, volume or weight, pharmacy reference or lot number, and ~~expiration~~ beyond use date.

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

To Amend § 1735.5 in Article 4.5 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1735.5. Compounding Policies and Procedures.

(a) Any pharmacy engaged in compounding shall maintain a written policy and procedure manual for compounding that establishes procurement procedures, methodologies for the formulation and compounding of drugs, facilities and equipment cleaning, maintenance, operation, and other standard operating procedures related to compounding. The pharmacy shall follow its policies and procedures and failure to follow these policies and procedures shall constitute grounds for disciplinary action.

(b) The policy and procedure manual shall be reviewed and such review shall be documented on an annual basis by the pharmacist-in-charge and shall be updated whenever changes in processes are implemented.

(c) The policy and procedure manual shall include the following:

(1) Procedures for notifying staff assigned to compounding duties of any changes in processes or to the policy and procedure manual.

- (2) Evidence that staff have been educated and trained on all policies and procedures.
- ~~(2 3)~~ Documentation of a ~~A written~~ plan for recall of a dispensed compounded drug ~~product preparation~~ where subsequent verification demonstrates the potential for adverse effects with continued use ~~of a compounded drug product~~. All affected doses can be accounted for as part of the recall.
- ~~(3 4)~~ The procedures for maintaining, storing, calibrating, cleaning, and disinfecting equipment used in compounding, and for training on these procedures as part of the staff training and competency evaluation process.
- (5) The procedures for evaluating, maintaining, certifying, cleaning, and disinfecting the facility (physical plant) used for compounding, and for training on these procedures as part of the staff training and competency evaluation process.
- ~~(4 6)~~ Documentation of the methodology appropriate to compounded drug preparations used to ~~test validate~~ integrity, potency, quality, and labeled strength of compounded drug ~~products preparations~~.
- ~~(5 7)~~ Documentation of the methodology used to determine appropriate ~~expiration beyond use~~ dates for compounded drug ~~products preparations~~.
- (8) Dates of annual reviews of the policy and procedure manual by the pharmacist-in-charge, signed and dated by the pharmacist-in-charge.
- (9) Dates of any revisions to the policy and procedure manual approved by the pharmacist-in-charge, signed and dated by the pharmacist-in-charge.
- (10) Policies and procedures for storage of compounded sterile drug preparations in the pharmacy and daily documentation of all room, refrigerator, and freezer temperatures.
- (11) Policies and procedures regarding ensuring appropriate functioning of refrigeration devices, monitoring refrigeration device temperatures, and actions to take regarding any out of range temperature variations.

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

To Amend § 1735.6 in Article 4.5 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1735.6. Compounding Facilities and Equipment.

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

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

(c) Any equipment that weighs, measures, or transfers ingredients used to compound drug ~~products~~ preparations for which calibration or adjustment is appropriate shall be calibrated prior to use, per manufacturer's specifications, to ensure accuracy. Documentation of each such calibration shall be recorded in writing and these records of calibration shall be maintained and retained in the pharmacy.

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

To Amend § 1735.7 in Article 4.5 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1735.7. Training of Compounding Staff.

(a) Any pharmacy engaged in compounding shall maintain written documentation sufficient to demonstrate that pharmacy personnel have the skills and training required to properly and accurately perform their assigned responsibilities relating to compounding.

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

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

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

To Amend § 1735.8 in Article 4.5 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1735.8. Compounding Quality Assurance.

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

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

(c) The quality assurance plan shall include written standards for qualitative and quantitative integrity, potency, quality, and labeled strength analysis of compounded drug ~~products~~ preparations. All qualitative and quantitative analysis reports for compounded drug ~~products~~ preparations shall be retained by the pharmacy and collated with the compounding record and master formula.

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

(e) The quality assurance plan shall include a written procedure for responding to out-of-range temperature variations, including for preparations furnished to patient care areas.

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

To Amend § 1751 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

Article 7. Sterile ~~injectable~~ Compounding

1751. Sterile ~~injectable~~ Compounding; Compounding Area; Self-Assessment.

(a) Any pharmacy engaged in compounding sterile ~~injectable~~ drug ~~products~~ preparations shall conform to the parameters and requirements stated by Article 4.5 (Section 1735 et seq.), applicable to all compounding, and shall also conform to the parameters and requirements stated by this Article 7 (Section 1751 et seq.), applicable solely to sterile ~~injectable~~ compounding.

(b) Any pharmacy compounding sterile ~~injectable~~ drug ~~products~~ preparations shall have a designated compounding area designated for the preparation of sterile ~~injectable~~ drug ~~products~~ preparations that is in a restricted location where traffic has no impact on the performance of the PEC(s). The buffer area, including the walls, ceilings, and floors, shall be constructed in accordance with Section 1250 of Title 24, Part 2, Chapter 12, of the California Code of Regulations. The pharmacy shall be ventilated in a manner in accordance with Section 505.12 of Title 24, Part 4, Chapter 5 of the California Code of Regulations. ~~which shall meet the following standards: The environments within the pharmacy shall meet the following standards:~~

~~(1) Clean Room and Work Station Requirements, shall be in accordance with Section 1250 of Title 24, Part 2, Chapter 12, of the California Code of Regulations.~~

~~(2) Walls, ceilings and floors shall be constructed in accordance with Section 1250 of Title 24, Part 2, Chapter 12, of the California Code of Regulations.~~

~~(3) Be ventilated in a manner in accordance with Section 505.12 of Title 24, Part 4, Chapter 5 of the California Code of Regulations.~~

~~(4) Be Each ISO environment shall be certified annually at least every six months~~ by a qualified technician ~~who is familiar with the methods and procedures for certifying laminar air flow hoods and clean room requirements, in accordance with standards adopted by the United States General Services Administration~~ in accordance with Section 1751.4 of Title 16, Division 17, of the California Code of Regulations. Certification records must be retained for at least 3 years.

~~(5) (2) The pharmacy shall be arranged in accordance with Section 1250 of Title 24, Part 2, Chapter 12, of the California Code of Regulations.~~ Items related to the compounding of sterile injectable drug products preparations within the compounding area shall be stored in such a way as to maintain the integrity of an aseptic environment.

~~(6) (3)~~ A sink shall be included in accordance with Section 1250 of Title 24, Part 2, of the California Code of Regulations. Sinks and drains shall not be present in an ISO Class 7 or better buffer area, nor within three feet of an ISO Class 5 PEC or better located in segregated compounding areas. A sink may be located in an ante-area.

~~(7) (4)~~ There shall be a refrigerator and, ~~or~~ where appropriate, a freezer, of sufficient capacity to meet the storage requirements for all material requiring refrigeration or freezing.

(c) Any pharmacy compounding a sterile injectable drug product preparation from one or more non-sterile ingredients shall comply with Business and Professions Code section 4127.7.

Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, 4127 and 4127.7, Business and Professions Code; Sections 1735, 1735.1,-1735.8., and 1751.1-1751.8. of Title 16, Division 17, of the California Code of Regulations; and Section 18944, Health and Safety Code.

To Amend § 1751.1 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1751.1. Sterile ~~Injectable~~ Compounding Recordkeeping Requirements.

~~(a) Pharmacies compounding sterile injectable products for future use pursuant to section 1735.2 shall, in addition to those records required by section 1735.3, make and keep records indicating the name, lot number, amount, and date on which the products were provided to a prescriber.~~

~~(b)~~ In addition to the records required by section 1735.3 ~~and subdivision (a)~~, for sterile compounded drug products preparation compounded from one or more non-sterile ingredients, the following records must be made and kept by the pharmacy:

(1) The training and competency evaluation of employees in sterile product preparation procedures.

~~(2)~~ Results of hand hygiene and garbing assessment with integrated gloved fingertip testing.

~~(3)~~ Results of assessments of personnel for aseptic techniques including results of media fill tests and gloved fingertip testing performed in association with media fill testing.

~~(4)~~ Results of viable volumetric air and surface sampling.

~~(2)~~ (5) Daily documentation of room, R refrigerator, and freezer temperatures appropriate for drug preparations consistent with the temperatures listed in section 1735.1 for:-

(A) Controlled room temperature.

(B) Controlled cold temperature.

(C) Controlled freezer temperature.

~~(3)~~ (6) Certification(s) of the sterile compounding environment.

~~(7)~~ Daily documentation of air pressure differentials or air velocity between adjoining all ISO rooms or areas and measurement between all ISO rooms or areas, including those associated with compounding aseptic (containment) isolators.

~~(4)~~ (8) Other facility quality control logs specific to the pharmacy's policies and procedures (e.g., cleaning logs for facilities and equipment).

~~(5)~~ (9) Logs or other documentation of inspections for expired or recalled pharmaceutical products or raw ingredients.

~~(6)~~ (10) Preparation records including the master work sheet, the preparation work sheet, and records of end-product evaluation results.

(b) Pharmacies compounding sterile drug preparations for future use pursuant to section 1735.2 shall, in addition to those records required by section 1735.3, make and keep records indicating the name of the compounded drug preparation, lot number, amount, and date on which the preparation was provided to a prescriber.

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

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

To Amend § 1751.2 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1751.2. Sterile ~~Injectable Compounding~~ Labeling Requirements.

In addition to the labeling information required under Business and Professions Code section 4076 and section 1735.4, a pharmacy which compounds sterile ~~injectable drug products preparations~~ shall include the following information on the labels for those ~~products preparations~~:

(a) Telephone number of the pharmacy, except for sterile ~~injectable drug products preparations~~ dispensed ~~for to~~ inpatients ~~of by~~ a hospital pharmacy.

(b) Name and concentrations of ingredients contained in the sterile ~~injectable drug product preparation~~.

(c) Instructions for storage and handling.

(d) All ~~cytotoxic hazardous~~ agents shall bear a special label which states ~~“Chemotherapy– Dispose of Properly” or “Cytotoxic Hazardous – Dispose of Properly” or “Chemotherapy - Dispose of Properly,”~~ if applicable.

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

To Amend § 1751.3 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1751.3. Sterile Injectable Compounding Policies and Procedures.

(a) Any pharmacy engaged in compounding sterile injectable drug products preparations shall maintain a written policy and procedure manual for compounding that includes, in addition to the elements required by section 1735.5, written policies and procedures regarding the following:

- (1) Compounding, filling, and labeling of sterile injectable compounds drug preparations.
- (2) Labeling of the sterile injectable drug product preparations based on the intended route of administration and recommended rate of administration.
- (3) Proper use of Equipment and supplies.
- (4) Training of staff in all aspects of the preparation of sterile injectable drug products preparations including didactic training and knowledge/competency assessments that include at minimum: hand hygiene and garbing; cleaning and disinfection of controlled compounding areas and proper aseptic technique.
- (5) Hand hygiene and garbing.
- (6) Cleaning and maintenance of ISO environments and segregated compounding areas.
- (7) An environmental sampling plan and procedures specific to viable air, surface and gloved fingertip sampling as well as nonviable particle sampling.
- (8) For compounding aseptic isolators and compounding aseptic containment isolators, documentation of the manufacturer's recommended purge time.
- (9) Media fill testing procedure.
- (10) Compounded sterile drug preparation stability and beyond use dating.

(11) Visual inspection and other final quality checks of sterile drug preparations.

~~(5) (12)~~ Procedures for handling, compounding and disposal of cytotoxic hazardous agents.

~~(6) (13)~~ Quality assurance program.

~~(7) (14)~~ Record keeping requirements.

(b) The ingredients and the compounding process for each preparation must be determined in writing before compounding begins and must be reviewed by a pharmacist.

(c) Pharmacies compounding sterile injectable drug products preparations shall have written policies and procedures for the disposal of infectious materials and/or materials containing cytotoxic hazardous residues. The written policies and procedures shall describe the pharmacy protocols for cleanups and spills in conformity with local health jurisdiction standards.

(d) Pharmacies compounding sterile injectable drug products preparations from one or more non-sterile ingredients must have written policies and procedures that comply with the following:

(1) All written policies and procedures shall be immediately available to all personnel involved in these activities and board inspectors.

(2) All personnel involved must read the policies and procedures before compounding sterile injectable drug products preparations, and any additions, revisions, and deletions to the written policies and procedures must be communicated to all personnel involved in sterile compounding.

(3) Policies and procedures must address at least the following:

(A) Orientation, training, and competency evaluation of compounding personnel.

(B) Storage and handling of products and supplies.

(C) Storage and delivery of final products.

(D) Media fill testing and Process validation.

(E) ~~Personnel access and movement of materials into and near the controlled area~~ Conduct of personnel in controlled areas and aseptic technique overview.

(F) Use and maintenance of ~~environmental control devices~~ PECs used to create the critical direct compounding area for ~~manipulation of sterile products~~ compounding of sterile drug

~~preparations (e.g., laminar airflow workstations, biological safety cabinets, class 100 cleanrooms, and barrier isolator workstations).~~

(G) ~~Regular~~ Daily and monthly cleaning and disinfection schedule for the controlled area~~s~~ and any equipment in the controlled area ~~and the alternation of disinfectants as specified in section 1751.4. Pharmacies subject to an institutional infection control policy may follow that policy as it relates to cleaning schedules and the alternation of disinfectants in lieu of complying with this subdivision.~~

(H) ~~Disposal of packaging materials, used syringes, containers, and needles to enhance sanitation and avoid accumulation in the controlled area.~~ Non-viable particle testing.

(I) ~~For sterile batch compounding; written policies and procedures must be established for the use of master formulas and work sheets and for appropriate documentation.~~ Viable air sampling.

(J) ~~Sterilization.~~ Surface sampling.

(K) ~~End-product evaluation and testing.~~ Airflow considerations and pressure differential monitoring.

(L) Temperature and humidity monitoring in compounding and controlled storage areas.

(M) Facility management including certification and prevention maintenance of controlled environments and related equipment.

(N) Gloved fingertip sampling.

(O) Compounded sterile product stability and assignment of beyond use dating

(P) Use of automated compounding devices (if applicable).

(Q) Hazardous drug compounding (if applicable).

(i) Hazardous drug employee training and safety program.

(ii) Hazardous drug handling, storage, labeling and transport.

(iii) Hazardous drug compounding techniques.

(iv) Hazardous drug spill, deactivation and waste management.

(R) Preparing sterile solutions from nonsterile components (if applicable).

(S) Hand hygiene and garbing.

(4) Pharmacies subject to an institutional infection control policy may follow that policy as it relates to cleaning schedules and the alternation of disinfectants in lieu of complying with this subparagraph.

(A) Disposal of packaging materials, used syringes, containers, and needles to enhance sanitation and avoid accumulation in the controlled area.

(B) For sterile batch compounding:

(i) use of master formulas and compounding work sheets;

(ii) appropriate documentation; and

(iii) appropriate sterility and bacterial endotoxin testing.

(C) For non-sterile to sterile compounding:

(i) Sterilization methods

(ii) End-product evaluation and testing.

(D) Action levels for colony-forming units (CFUs) detected during viable surface testing, glove fingertip and volumetric air sampling.

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

To Amend § 1751.4 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1751.4. Facility and Equipment Standards for Sterile ~~injectable~~ Compounding.

(a) No sterile ~~injectable drug product preparation~~ shall be compounded if it is known, or reasonably should be known, that the compounding environment fails to meet criteria specified in the pharmacy's written policies and procedures for the safe compounding of sterile ~~injectable drug products preparations~~.

(b) During the compounding of preparation of sterile ~~injectable drug products preparations~~, access to the areas designated ~~area or cleanroom~~ for compounding must be limited to those individuals who are properly attired.

(c) All equipment used in the areas designated ~~area or cleanroom~~ for compounding must be made of a material that can be easily cleaned and disinfected.

(d) Cleaning and disinfecting surfaces in the ISO Class 5 PEC shall occur frequently, including:

(1) at the beginning of each shift;

(2) before and after each batch;

(3) after each spill; and

(4) when surface contamination is known or suspected.

~~(d) (e) Exterior workbench surfaces and other hard surfaces in the designated area, such as walls, floors, ceilings, shelves, tables, and stools, must be disinfected weekly and after any unanticipated event that could increase the risk of contamination. Counters, cleanable work surfaces and floors shall be cleaned with a germicidal detergent and water and disinfected with a suitable agent (e.g., sterile isopropyl alcohol) daily. Walls, ceilings, storage shelving, tables and stools shall be cleaned with a germicidal detergent and water and disinfected with a suitable agent (e.g., sterile isopropyl alcohol) monthly. Cleaning and disinfecting shall occur after any unanticipated event that could increase the risk of contamination.~~

~~(e) (f) Pharmacies preparing sterile compounded preparations require the use of a PEC that provides ISO Class 5 air or better. Certification and testing of primary and secondary engineering controls shall be performed no less than every six months and whenever the device or area designated for compounding is relocated, altered or a service to the facility is performed that would impact the device or area. Certification must be completed by a qualified technician who is familiar with certification methods and procedures in accordance with CETA Certification Guide for Sterile Compounding Facilities (CAG-003-2006-11, Revised January 31, 2012). Certification records must be retained for at least 3 years. Compounding aseptic isolators or compounding aseptic containment isolators may be used outside of an ISO Class 7 buffer area if the isolator meets the following criteria:~~

~~(1) particle counts sampled approximately 6-12 inches upstream of the critical exposure site shall maintain ISO Class 5 levels during compounding operations.~~

(2) not more than 3520 particles (0.5 um and larger) per cubic meter shall be counted during material transfer, with the particle counter probe located as near to the transfer door as possible without obstructing transfer.

(3) recovery time to achieve ISO Class 5 air quality shall be documented and internal procedures developed to ensure that adequate recovery time is allowed after material transfer before and during compounding operations.

Compounding aseptic isolators or compounding aseptic containment isolators that do not meet the requirements as outlined in this subdivision and are not located within an ISO Class 7 buffer area may only be used to compound preparations that meet the criteria specified in accordance with subdivision (d) of Section 1751.8 of Title 16, Division 17, of the California Code of Regulations.

(g) Pharmacies preparing ~~parenteral sterile cytotoxic hazardous~~ agents shall do so in accordance with Section 505.12.1 of Title 24, Chapter 5, of the California Code of Regulations, requiring a ~~laminar air flow hood~~ negative pressure PEC. The ~~hood~~ negative pressure PEC must be certified ~~annually~~ every six months by a qualified technician who is familiar with ~~the methods and procedures for certifying laminar air flow hoods and cleanroom requirements, in accordance with National Sanitation Foundation Standard 49 for Class II (Laminar Flow) Biohazard Cabinetry, as revised May, 1983 (available from the National Sanitation Foundation, 3475 Plymouth Road, P.O. Box 1468, Ann Arbor, Michigan 48106, phone number (313) 769-8010) or manufacturer's specifications.~~ CETA Certification Guide for Sterile Compounding Facilities (CAG-003-2006-11, Revised January 31, 2012). ~~Certification records must be retained for at least 3 years.~~ Pharmacies that primarily compound hazardous drugs but also routinely compound non-hazardous drugs, even if used with antineoplastic chemotherapy regimens, must install a compounding aseptic isolator in a pharmacy location that is not located within the negative pressure hazardous drug buffer area or install a laminar flow hood on the clean side of the line of demarcation from the ISO Class 7 ante-room, at least six feet from the sink. Any drug preparation that is compounded in a hazardous drug PEC where hazardous drugs are prepared must be labeled as hazardous, regardless of whether the drug ingredients are considered hazardous.

During the hazardous drug compounding that is performed in a compounding aseptic containment isolator, full hand hygiene and garbing must occur, complete with hair cover, facemask, beard cover (if applicable), polypropylene or low shedding gown that closes in the back, shoe covers, and two layers of gloves that have been tested to meet ASTM 6978-05 with the outermost glove that contacts the sterile drug preparation.

(h) If a compounding aseptic isolator is certified by the manufacturer to maintain ISO Class 5 air quality during dynamic operation conditions during compounding as well as during the transfer of ingredients into and out of the compounding aseptic isolator, then it may be placed into a non-ISO classified room. Individuals that use compounding aseptic isolators in this manner must ensure appropriate garbing, which consists of donning sterile gloves over the isolator gloves immediately before non-hazardous compounding. These sterile gloves must be changed by each individual whenever continuous compounding is ceased and before compounding starts again.

(i) Viable surface and volumetric air sampling by impaction shall be done at least monthly for low and medium risk-level compounding and weekly for high-risk compounding by a qualified individual who is familiar with the methods and procedures for surface testing and air sampling. Viable air sampling is to be performed under dynamic conditions that simulate actual production. Surface sampling is to be performed under dynamic conditions of actual compounding. When the environmental monitoring action levels are exceeded, the pharmacy shall identify the CFUs at least to the genus level in addition to conducting an investigation. Remediation shall include an immediate investigation of cleaning and compounding operations and facility management.

(j) The pharmacy shall have a comfortable and well-lighted working environment, which includes a room temperature of 20 degrees Celsius (68 degrees Fahrenheit) or cooler to maintain comfortable conditions for compounding personnel when attired in the required compounding garb. Humidity levels should be consistent ASHRAE Standard 55 (30-65% RH).

Note: Authority Cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052 and 4127, Business and Professions Code; and Section 18944, Health and Safety Code.

To Amend § 1751.5 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1751.5. Sterile ~~Injectable~~ Compounding Attire.

~~(a) When preparing cytotoxic agents, gowns and gloves shall be worn.~~

~~(b) (a)~~ When compounding sterile drug products preparations from one or more non-sterile ingredients the following standards must be met:

(1) ~~Cleanroom garb~~ Personal protective equipment consisting of a ~~low non-~~shedding ~~coverall gown~~, head cover, face mask, facial hair covers (if applicable), and shoe covers must be worn inside the designated area at all times.

(2) ~~Cleanroom garb~~ Personal protective equipment must be donned and removed in an ante-area or outside the designated area immediately outside the segregated compounding area.

(3) Personnel shall don personal protective equipment in an order that proceeds from those activities considered the dirtiest to those considered the cleanest. The following order is to be followed unless the pharmacy has a procedure in place that documents a method equivalent to or superior to the method described here: The donning of shoe covers or dedicated shoes, head and facial hair covers and face masks shall be followed by the washing of hands and forearms up to the elbows for 30 seconds with soap and water, drying hands, and then the donning of a non-shedding gown.

~~(3) (4)~~ Compounding personnel shall not wear Hhand, finger, and or wrist jewelry ~~must be eliminated~~. If jewelry cannot be removed then it must be thoroughly cleaned and covered with a sterile glove.

~~(4) Head and facial hair must be kept out of the critical area or be covered.~~

(5) ~~Gloves made of low-shedding materials are required.~~ Sterile gloves that have been tested for compatibility with disinfection with isopropyl alcohol are required. Hand cleansing with a persistently active alcohol-based product followed by the donning of sterile gloves may occur within the ante or buffer area. Gloves are to be routinely disinfected with sterile 70 percent isopropyl alcohol before entering or re-entering the PEC and after contact with non-sterile objects. Gloves shall also be routinely inspected for holes, punctures, or tears and replaced immediately if such are detected.

(6) Individuals experiencing rashes, sunburn, weeping sores, conjunctivitis, active respiratory infections, or those wearing cosmetics shall be excluded from the compounding areas until their conditions are remedied.

~~(c) The requirements of subdivision (b) do not apply if a barrier isolator is used to compound sterile injectable products from one or more non-sterile ingredients.~~

(b) When preparing hazardous agents, appropriate gowns and personal protective equipment shall be worn regardless of the PECs used (e.g., biological safety cabinet and compounding aseptic containment isolator).

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

To Amend § 1751.6 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1751.6 ~~Training of Sterile Injectable Compounding Staff, Patient, and Caregiver.~~ Sterile Compounding Consultation; Training of Sterile Compounding Staff.

(a) Consultation shall be available to the patient and/or primary caregiver concerning proper use, storage, handling, and disposal of sterile ~~injectable drug products preparations~~ and related supplies furnished by the pharmacy.

(b) The pharmacist-in-charge shall ~~be responsible to~~ ensure that all pharmacy personnel engaging in compounding sterile ~~injectable drug products preparations~~ shall have training and

demonstrated competence in the safe handling and compounding of sterile injectable drug products preparations, including cytotoxic hazardous agents if the pharmacy compounds products with cytotoxic hazardous agents.

(c) Records of training and demonstrated competence shall be available for each individual and shall be retained for three years beyond the period of employment.

(d) The pharmacist-in-charge shall be responsible to ensure the continuing competence of pharmacy personnel engaged in compounding sterile injectable drug products preparations.

(e) Pharmacies that compound sterile products from one or more non-sterile ingredients preparations must comply with the following training requirements:

(1) The pharmacy must establish and follow a written program of training and performance evaluation designed to ensure that each person working in the designated area has the knowledge and skills necessary to perform their assigned tasks properly. This program of training and performance evaluation must address at least the following:

(A) Aseptic technique.

(B) Pharmaceutical calculations and terminology.

(C) Sterile product preparation compounding documentation.

(D) Quality assurance procedures.

(E) Aseptic preparation procedures using media fill tests which are as complicated as the most complex manipulations performed by staff and which contain the same amount of volume transferred during the selected manipulations.

(F) Proper hand hygiene, gowning and gloving technique.

(G) General conduct in the controlled area.

(H) Cleaning, sanitizing, and maintaining of the equipment and used in the controlled area.

(I) Sterilization techniques for compounding sterile drug preparations from one or more non-sterile ingredients.

(J) Container, equipment, and closure system selection.

(2) Each person assigned to the controlled area engaged in sterile compounding must successfully complete practical skills training in aseptic technique and aseptic area practices.

Evaluation must include written testing and a written protocol of periodic routine performance

checks involving adherence to aseptic area policies and procedures. Each person's proficiency and continuing training needs must be reassessed at least every 12 months. Results of these assessments must be documented and retained in the pharmacy for three years.

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

To Amend § 1751.7 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1751.7. Sterile ~~Injectable~~ Compounding Quality Assurance and Process Validation.

(a) Any pharmacy engaged in compounding sterile ~~injectable~~ drug ~~products preparations~~ shall maintain, as part of its written policies and procedures, a written quality assurance plan including, in addition to the elements required by section 1735.8, a documented, ongoing quality assurance program that monitors personnel performance, equipment, and facilities. The end product shall be examined on a periodic sampling basis as determined by the pharmacist-in-charge to assure that it meets required specifications. The ~~Q~~quality ~~A~~assurance ~~P~~program shall include at least the following:

(1) ~~Procedures for C~~leaning and sanitization of the ~~parenteral medication~~ sterile preparation area.

~~(2) The storage of compounded sterile injectable products in the pharmacy and periodic documentation of refrigerator temperature.~~

~~(3)~~ (2) Actions to be taken in the event of a drug recall.

~~(4)~~ (3) ~~Written justification of~~ Documentation justifying the chosen ~~expiration beyond use~~ dates for compounded sterile ~~injectable drug products-preparations~~.

(b) Each individual involved in the preparation of sterile ~~injectable drug products-preparations~~ must first successfully demonstrate competency by successfully performing aspect media fill tests ~~complete a validation process on technique~~ before being allowed to prepare sterile

injectable drug products preparations. The validation process shall be carried out in the same manner as normal production, except that an appropriate microbiological growth medium is used in place of the actual product used during sterile preparation. The validation process shall be representative of all types of manipulations, products and batch sizes the individual is expected to prepare. The media fill testing process shall be as complicated as the most complex manipulations performed by staff and contain the same amount of volume transferred during the compounding process. The same personnel, procedures, equipment, and materials must be involved. Media used must have demonstrated the ability to support and promoted growth. Completed ~~medium~~ media samples must be incubated in a manner consistent with the manufacturer's recommendations. If microbial growth is detected, then the employee's sterile preparation process must be evaluated, corrective action taken and documented, and the validation process media fill testing repeated. Personnel competency must be revalidated at least every twelve months for sterile to sterile compounding and at least every six months for individuals compounding sterile products from non-sterile ingredients, whenever the quality assurance program yields an unacceptable result, when the compounding process changes, equipment used in the compounding of sterile ~~injectable drug products preparations~~ is are repaired or replaced, the facility is modified in a manner that affects airflow or traffic patterns, or whenever improper aseptic techniques are observed. Revalidation must be documented. Three media fill tests per day for three consecutive days must be included in annual revalidation.

(c) All compounding personnel must successfully complete an initial competency evaluation. In addition, immediately following the initial hand hygiene and garbing procedure, all compounding personnel must successfully complete a gloved fingertip sampling procedure (zero colony forming units for both hands) at least three times before initially being allowed to compound sterile drug products-preparations.

(d) Re-evaluation of garbing and gloving competency shall occur at least every 12 months for personnel compounding products made from sterile ingredients and at least every six months for personnel compounding products from non-sterile ingredients.

~~(e)~~ (e) Batch-produced sterile ~~injectable~~ drug ~~products~~ preparations compounded from one or more non-sterile ingredients ~~shall be subject to documented end product testing for sterility that are exposed longer than 12 hours at 2 to 8 degrees and longer than 6 hours at warmer than 8 degrees before they are sterilized shall meet the sterility test in accordance with methodologies and processes found in Chapter 71 of the United States Pharmacopeia – National Formulary (USP37-NF32) (37th Revision, Effective May 1, 2015), and testing for pyrogens in accordance with the methods of Chapters 85 and 151 of the United States Pharmacopeia – National Formulary (USP37-NF32) (37th Revision, Effective May 1, 2014), hereby incorporated by reference,~~ and shall be quarantined until the end product testing confirms sterility and acceptable levels of pyrogens before dispensing. This requirement of end product testing confirming sterility and acceptable levels of pyrogens prior to dispensing shall apply regardless of any sterility or pyrogen testing that may have been conducted on any ingredient or combination of ingredients that were previously non-sterile.

In a circumstance where a batch-produced sterile drug preparation compounded from one or more non-sterile ingredients is necessary for immediate dispensing where failure to dispense could result in loss of life or intense suffering, the drug preparation may be dispensed before receipt of test results so long as the pharmacy complies with a written procedure included in the pharmacy's policies and procedures that includes:

(1) Prior to dispensing:

(A) Notifying the prescriber of the inability to conduct testing;

(B) Suggesting an available alternative product to the prescriber; and

(C) Securing the prescriber's written consent to dispense.

(2) And subsequent to dispensing:

(A) Daily observation of the incubating test specimens; and

(B) Immediate recall of the dispensed compounded sterile preparation's when there is any evidence of microbial or pyrogen growth in the test specimens.

Any such dispensing shall be only in such quantity as is necessary to meet the immediate need and the circumstance causing the immediate need shall be documented in accordance with policies and procedures.

~~(d) Batch-produced sterile to sterile transfers shall be subject to periodic testing through process validation for sterility as determined by the pharmacist in charge and described in the written policies and procedures.~~

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

To Amend § 1751.8 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1751.8. Beyond Use Dating for Sterile Compounded Drug Preparations.

In addition to the requirements and limitations of section 1735.2, subdivision (h), every sterile compounded drug preparation shall be given and labeled with a beyond use date that conforms to the following limitations, except that the beyond use date shall not exceed any expiration date or beyond use date provided by the manufacturer for any component in the preparation.

(a) Where the sterile compounded drug preparation was compounded solely with aseptic manipulations

(1) entirely within an ISO Class 5 PEC located in an ISO Class 7 buffer area with an ante-area, using only sterile ingredients, products, components, and devices; and

(2) the compounding process involves transferring, measuring, and mixing manipulations using not more than three commercially manufactured packages of sterile preparations and not more than two entries into any one sterile container or package of sterile preparations or administration containers/devices to prepare the drug preparation; and

(3) compounding manipulations are limited to aseptically opening ampules, penetrating disinfected stoppers on vials with sterile needles and syringes, and transferring sterile liquids in sterile syringes to sterile administration devices, package containers of other sterile preparations, and containers for storage dispensing

in the absence of passing a sterility test in accordance with standards for sterility testing found in Chapter 797 of the United States Pharmacopeia – National Formulary (USP36-NF31 through 1st Supplement) (36th Revision, Effective August 1, 2013), hereby incorporated by reference, that would justify a more extended beyond use date, the beyond use date shall specify that storage and exposure periods cannot exceed the following: 48 hours at controlled room temperature; 14 days at controlled cold temperature; and 45 days at controlled freezer temperature.

(b) Where the sterile compounded drug preparation was compounded solely with aseptic manipulations

(1) entirely within an ISO Class 5 PEC located in an ISO Class 7 buffer area with an ante-area, using multiple individual or small doses of sterile preparations combined or pooled to prepare a compounded sterile preparation that will be administered either to multiple patients or to one patient on multiple occasions; and

(2) the compounding process involves complex aseptic manipulations other than the single-volume transfer; and

(3) the compounding process requires unusually long duration such as that required to complete dissolution or homogenous mixing

in the absence of passing a sterility test in accordance with standards for sterility testing found in Chapter 797 of the United States Pharmacopeia – National Formulary (USP36-NF31 through 1st Supplement) (36th Revision, Effective August 1, 2013), hereby incorporated by reference, that would justify a more extended beyond use date, the beyond use date shall specify that storage and exposure periods cannot exceed the following: 30 hours at controlled room temperature; 9 days at controlled cold temperature; and 45 days at controlled freezer temperature.

(c) Where the sterile compounded drug preparation was compounded solely with aseptic manipulations entirely within an ISO Class 5 PEC located in an ISO Class 7 buffer area with an ante-area, using non-sterile ingredients, including manufactured preparations not intended for sterile routes of administration, or non-sterile devices, before terminal sterilization, or where the sterile compounded drug preparation lacks effective antimicrobial preservatives, in the

absence of passing a sterility test in accordance with standards for sterility testing found in Chapter 797 of the United States Pharmacopeia – National Formulary (USP36-NF31 through 1st Supplement) (36th Revision, Effective August 1, 2013), hereby incorporated by reference, that would justify a more extended beyond use date, the beyond use date shall specify that storage and exposure periods cannot exceed the following: 24 hours at controlled room temperature; 3 days at controlled cold temperature; and 45 days at controlled freezer temperature.

For the purposes of this paragraph, “non-sterile” includes sterile contents of commercially manufactured preparations, sterile surfaces of devices, and containers for the preparation, transfer, sterilization, and packaging of compounded sterile preparations, that are exposed to worse than ISO Class 5 air quality for more than one hour.

(d) Where the sterile compounded drug preparation was compounded solely with aseptic manipulations

(1) entirely within an ISO Class 5 PEC that is located in a segregated compounding area and restricted to sterile compounding activities, using only sterile ingredients, components, and devices, by personnel properly cleansed and garbed; and

(2) the compounding process involves simple transfer of not more than three commercially manufactured packages of sterile nonhazardous preparations or diagnostic radiopharmaceutical preparations from the manufacturer’s original containers; and

(3) the compounding process involves not more than two entries into any one container or package (e.g., bag, vial) of sterile infusion solution or administration container/device

in the absence of passing a sterility test in accordance with standards for sterility testing found in Chapter 797 of the United States Pharmacopeia – National Formulary (USP36-NF31 through 1st Supplement) (36th Revision, Effective August 1, 2013) hereby incorporated by reference, that would justify a more extended beyond use date, the beyond use date shall specify that storage and exposure periods cannot exceed 12 hours in a laminar air flow workbench or biological safety cabinet.

(e) Where the sterile compounded drug preparation was compounded

(1) using or containing hazardous drugs or components; and

(2) using two tiers of containment (e.g., a closed system transfer device within a biological safety cabinet or a laminar air flow workbench that is located in a non-negative pressure room with at least 12 air changes per hour)

the beyond use date shall specify that storage and exposure periods cannot exceed 12 hours.

(f) Where any sterile compounded drug preparation was compounded either outside of an ISO class 5 PEC or under conditions that do not meet all of the requirements for any of subdivisions (a) through (e), the sterile compounded drug preparation shall be labeled “for immediate use only” and administration shall begin no later than one hour following the start of the compounding process. Unless the “immediate use” preparation is immediately and completely administered by the person who prepared it or immediate and complete administration is witnessed by the preparer, the preparation shall bear a label listing patient identification information, the names and amounts of all ingredients, the name or initials of the person who prepared the compounded sterile preparation, and the exact one-hour beyond use date and time. If administration has not begun within one hour following the start of the compounding process, the compounded sterile preparation shall be promptly, properly, entirely, and safely discarded. This provision does not preclude the use of a PEC to compound an “immediate use” preparation.

Such “immediate use” preparations shall be compounded only in those limited situations where there is a need for immediate administration of a sterile preparation compounded outside of an ISO class 5 environment and where failure to administer could result in loss of life or intense suffering. Any such compounding shall be only in such quantity as is necessary to meet the immediate need and the circumstance causing the immediate need shall be documented in accordance with policies and procedures.

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

To Add § 1751.9 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1751.9 Single-Dose and Multi-Dose Containers; Limitations on Use

(a) Single-dose ampules are for immediate use only, and once opened shall not be stored for any time period.

(b) Unless otherwise specified by the manufacturer, any single-dose container of a compounded sterile drug preparation other than an ampule, such as a bag, bottle, syringe or vial, shall be used in its entirety or its remaining contents discarded within the following time limit, depending on the environment:

(1) When needle-punctured in an environment with air quality worse than ISO Class 5, within one (1) hour;

(2) When needle-punctured in an environment with ISO Class 5 or better air quality, within six (6) hours.

(c) Unless otherwise specified by the manufacturer, a multi-dose container stored according to the manufacturer's specifications shall be used in its entirety or its remaining contents discarded within twenty eight (28) days from initial opening or puncture. Any multi-dose container not stored according to the manufacturer's specifications shall be discarded immediately upon identification of such condition.

Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference:

Sections 4005, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.

To Amend § 1751.10 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1751.8. 1751.10. Sterile ~~Injectable~~ Compounding Reference Materials.

In any pharmacy engaged in compounding sterile drug ~~products~~ preparations, there shall be current and appropriate reference materials regarding the compounding of sterile ~~injectable drug~~ products preparations located in or immediately available to the pharmacy.

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

DRAFT

To Add Article 7.5 of Division 17 of Title 16 of the California Code of Regulations to read as follow

Article 7.5 Furnishing for Home Administration

To Amend § 1751.10 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1751.10, 1752. Furnishing to Parenteral Patient at Home.

Subject to all provisions of this article, a pharmacist may carry and furnish to a patient at home dangerous drugs, other than controlled substances, and devices for parenteral therapy when the dangerous drug or device is one currently prescribed for the patient.

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

To Amend § 1751.11 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

1751.11, 1753. Furnishing to Home Health Agencies and Licensed Hospices.

Subject to the following conditions, a licensed pharmacy may furnish to a home health agency licensed under provisions of Chapter 8 (commencing with section 1725 of Division 2 of the Health and Safety Code) or to a hospice licensed under provisions of Chapter 8.5 (commencing with section 1745 of Division 2 of the Health and Safety Code) dangerous drugs for parenteral therapy other than controlled substances, in a portable container for furnishing to patients at home for emergency treatment or adjustment of parenteral drug therapy by the home health agency or licensed hospice.

(a) The pharmacy, having ownership and responsibility for the portable containers, shall ensure that each portable container is:

- (1) furnished by a registered pharmacist;
- (2) sealed in such a manner that a tamper-proof seal must be broken to gain access to the drugs;
- (3) under the effective control of a registered nurse, pharmacist or delivery person at all times when not in the pharmacy;
- (4) labeled on the outside of the container with a list of the contents;
- (5) maintained at an appropriate temperature according to United States Pharmacopeia Standards (1995, 23rd Revision), and protected at all times from extreme temperatures that could damage the contents.

(b) The portable container may contain up to:

- (1) 1000mL of 0.9% sodium chloride intravenous infusion in containers of a size determined by the pharmacy;
- (2) 1000mL of 5% dextrose in water injection in containers of a size determined by the pharmacy;
- (3) two vials of urokinase 5000 units;
- (4) Each of the following items shall be in sealed, unused containers; the furnishing pharmacy may select any or all of these dangerous drugs in up to five dosage units for inclusion in the sealed, portable container:
 - (A) heparin sodium lock flush 100 units/mL;
 - (B) heparin sodium lock flush 10 units/mL;
 - (C) epinephrine HCl solution 1:1000;
 - (D) epinephrine HCl solution 1:10,000;
 - (E) diphenhydramine HCl 50mg/mL;
 - (F) methylprednisolone 125mg/2mL;
 - (G) normal saline, preserved, up to 30 mL vials;
 - (H) naloxone 1mg/mL 2 mL;
 - (I) droperidol 5mg/2mL;

(J) prochlorperazine 10mg/2mL;

(K) promethazine 25mg/mL;

(L) dextrose 25gms/50mL;

(M) glucagon 1mg/mL;

(N) insulin (human) 100 units/mL;

(O) bumetamide 0.5mg/2mL;

(P) furosemide 10mg/mL;

(Q) EMLA Cream 5 gm tube;

(R) Lidocaine 1 percent 30mL vials.

(5) The pharmacy shall ensure that the specific dangerous drugs and quantities to be included in the portable container are listed in the home health agency's or licensed hospice's policy and procedures.

(c) The pharmacy shall not supply a portable container to a home health agency or licensed hospice which does not:

(1) implement and maintain policies and procedures for:

(A) the storage, temperature stability and transportation of the portable container;

(B) the furnishing of dangerous drugs from the portable container upon the written or oral authorization of a prescriber; and

(C) a specific treatment protocol for the administration of each medication contained in the portable container.

(2) have the policies, procedures and protocols reviewed and revised (as needed) annually by a group of professional personnel including a physician and surgeon, a pharmacist and a registered nurse.

(d) A copy of these policies, procedures and protocols shall be maintained by the furnishing pharmacy from each home health agency or licensed hospice for which the pharmacy furnishes portable containers.

(e) In cases where a drug has been administered to a patient pursuant to the oral order of a licensed prescriber, the pharmacy shall ensure that the oral order is immediately written down by the registered nurse or pharmacist and communicated by copy or fax within 24 hours to the

furnishing pharmacy, with a copy of the prescriber-signed document forwarded to the dispensing pharmacy within 20 days.

(f) The pharmacy shall ensure that within seven days (168 hours) after the seal has been broken on the portable container, the home health agency's director of nursing service or a registered nurse employed by the home health agency or licensed hospice returns the container to the furnishing pharmacy. The furnishing pharmacy shall then perform an inventory of the drugs used from the container, and if the container will be reused, must restock and reseal the container before it is again furnished to the home health agency or licensed hospice.

(g) The furnishing pharmacy shall have written policies and procedures for the contents, packaging, inventory monitoring, labeling and storage instructions of the portable container.

(h) The furnishing pharmacy shall ensure that the home health agency or licensed hospice returns the portable containers to the furnishing pharmacy at least every 60 days for verification of product quality, quantity, integrity and expiration dates, or within seven days (168 hours) after the seal has been broken.

(i) The furnishing pharmacy shall maintain a current inventory and record of all items placed into and furnished from the portable container.

Note: Authority cited: Sections 4005 and ~~and~~ 4057, Business and Professions Code. Reference: Sections 4040, 4057, 4081 and 4332, Business and Professions Code.

To Amend § 1751.12 in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

~~1751.12~~ 1754. Obligations of a Pharmacy Furnishing Portable Containers.

(a) A licensed pharmacy shall not issue portable containers to any home health agency or licensed hospice unless the home health agency or licensed hospice complies with provisions of section 1751.11.

(b) A licensed pharmacy shall cease to furnish portable containers to a home health agency or licensed hospice if the home health agency or licensed hospice does not comply with provisions of section 1751.11.

Note: Authority cited: Sections 4005 and 4057, Business and Professions Code. Reference: Sections 4040, 4057, 4081 and 4332, Business and Professions Code.

DRAFT

To Amend §1250.4 in Chapter 12 of Part 2 of Title 24 of the California Code of Regulations to read as follows:

1250.4 Sterile Compounding Area ~~for Parenteral Solutions~~.

The pharmacy shall have a designated area for the compounding of sterile preparations for dispensing which shall:

1. In accordance with ~~Federal Standard 209(b), Clean Room and Work Station Requirements, Controlled Environment as approved by the Commission, Federal Supply Service, General Services Administration meet standards for class 100~~ ISO 14644-1 Cleanrooms and associated controlled environments – Part 1 Classification of air cleanliness the environment inside the PECs must meet the standards for ISO Class 5 and buffer areas (cleanrooms) must meet ISO Class 7 through HEPA (high efficiency particulate air) filtered air ~~such as laminar airflow hood or clean room~~ resulting in less than 3520 and 352,000 respectively of particles less than 0.5 µm and larger per cubic meter measured under dynamic operating conditions.
2. Have nonporous and cleanable surfaces, ceilings and ceiling tiles, walls, floors and floor coverings.
3. The pharmacy shall be arranged in such a manner that the ~~laminar flow hood is~~ PECs are located in ~~an area~~ s which is exposed to minimal traffic flow, and ~~is~~ separate from any area used for bulk storage of items not related to the compounding of ~~parenteral~~ solutions. There shall be sufficient space, well separated from the ~~laminar flow hood area~~ buffer area (cleanroom) for the storage of bulk materials, equipment and waste materials.
4. A sink with hot and cold running water must be ~~within the parenteral solution compounding area or adjacent to it~~ located adjacent to the sterile compounding area, however not inside the buffer area or immediately adjacent to the PEC located within the segregated compounding area.

5. Any pharmacy that compounds sterile ~~injectable drug products preparations from one or more nonsterile ingredients~~ must compound the medication in one of the following environments:

5.1 An ISO class 5 ~~laminar airflow hood~~ PEC(s) within an ISO class 7 cleanroom. The cleanroom must have a positive air pressure differential of at least 0.02" water column positive relative to each adjacent areas.

5.2 ~~An ISO class 5 cleanroom.~~ The cleanroom must have a positive air pressure differential relative to adjacent areas.

~~5.3 A barrier isolator that provides an ISO class 5 environment for compounding.~~

5.3 A compounding isolator (either compounding aseptic isolator or compounding aseptic containment isolator) that provides an ISO Class 5 environment for compounding within an ISO Class 7 cleanroom unless documentation from the manufacturer of the barrier isolator permits operation of the barrier isolator in an environment that exceeds ISO Class 7.

6. When compounding hazardous drugs, the surrounding environment must provide at least 0.01 water column negative air pressure and 12 air changes per hour.

To Amend §505.5 in Chapter 5 of Part 4 of Title 24 of the California Code of Regulations to read as follows:

505.5 Pharmacies: Primary Engineering Controls for Non-Hazardous Sterile Compounding Area of Parenteral Solutions. [CA – Board of Pharmacy] In all pharmacies preparing non-hazardous sterile drug preparations, all compounding shall be conducted within a certified laminar air flow workbench or compounding aseptic isolator. ~~The pharmacy shall have a designated area for the preparation of sterile products for dispensing which shall be ventilated in a manner not interfering with laminar air flow.~~

To Amend §505.5.1 in Chapter 5 of Part 4 of Title 24 of the California Code of Regulations to read as follows:

505.5.1 Pharmacies: ~~Laminar Flow Biological Safety Cabinet.~~ Primary Engineering Controls for Hazardous Drug Compounding. [CA – Board of Pharmacy]

In all pharmacies preparing ~~parenteral cytotoxic~~ hazardous agents, all compounding shall be conducted within a certified Class II Type A₂ ~~or Class II Type B₂ or compounding aseptic containment isolator.~~ vertical laminar airflow hood with bag in-bag out design. ~~The pharmacy must ensure that contaminated air plenums that are under positive air pressure are leak tight.~~

DRAFT