



XII. Discussion and Possible Action to Make Changes in Response to Comments or to Adopt or Amend Proposed Text at Title 16 California Code of Regulations Sections 1735 e seq. and 1751 et seq. Relating to Pharmacy Compounding

At the July 2014 Board Meeting, the board moved to initial notice of proposed changes in the California's compounding regulations (located in 16 California Code of Regulations Sections 1735 et seq. and 1751 et seq). The 45 day comment period ran from September 5, 2014 – October 20, 2014. A regulation hearing was held on November 4, 2014 to provide the public with an opportunity to provide comments in another forum.

At the January 2015 Board Meeting, the board adopted the revised language incorporating many of the comments submitted during the 45 day comment period, and voted to notice the revised language for a 15 day comment period. The 15 day comment period ran from February 6, 2015 – February 20, 2015.

At the March 2015 Board Meeting, the board adopted the revised language incorporating many of the comments submitted during the 15 day comment period, and voted to notice the revised language for a second 15 day comment period. The second 15 day comment period ran from March 11, 2015 – March 25, 2015.

At the April 2015 Board Meeting, the board the board made a motion not to proceed with the existing rulemaking and notice a new rulemaking to allow for an additional 45-day comment period. The 45 day comment period ran from May 8, 2015 – June 22, 2015. A regulation hearing was held on June 25, 2015 to provide the public with an opportunity to provide comments in another forum.

Attachment 1 is the current regulation language as noticed on May 8, 2015.

A compilation document of the written comments received during the 45 day comment period, as well as modified language will be available at the Board meeting.

At this Meeting

The board will have the opportunity to discuss the regulation, the comments received and determine what course of action it wishes to pursue. Among its options:

1. Adopt the regulation as approved at the March 2015 Board meeting
2. Amend the regulation in some way(s) to address concerns expressed in the 45 day comment period and notice the modified text for a 15 day comment period.

Attachment 1

Title 16. Board of Pharmacy
Proposed Text

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 that is commercially available in the marketplace~~

~~(d)~~ (c) 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” means an ISO Class 8 or better air quality 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 or cleanroom, and maintains air flows from clean to dirty areas.

~~(e)~~(b) “Beyond use date” means the date, or date and time, after which administration of a compounded drug preparation shall not be begun, the preparation shall not be dispensed, and the preparation shall not be stored (other than for quarantine purposes).

(c) “Biological Safety Cabinet (BSC)” means a ventilated cabinet for compounded sterile drug preparations, having an open front with inward airflow for personnel protection, downward HEPA-filtered laminar airflow for product protection, and HEPA-filtered exhausted air for environmental protection.

(d) “Buffer area” means an area which maintains segregation from the adjacent ante-area by means of specific pressure differentials. The principle of displacement airflow shall be employed. This concept utilizes a low pressure differential, high airflow principle. Using displacement airflow typically requires an air velocity of 40 ft per minute or more from the buffer area across the line of demarcation into the ante-area. The displacement concept may not be used to maintain buffer area requirements for sterile compounds which originate from any ingredient that was at any time non-sterile, regardless of intervening sterilization of the ingredient, for hazardous compounds, or for chemotherapy compounds.

(e) “Bulk drug substance” means any substance that, when used in the preparation of a compounded drug preparation, processing, or packaging of a drug, becomes an active ingredient or a finished dosage form of the drug, but the term does not include any intermediate used in the synthesis of such substances.

(f) "Cleanroom" means a physically separate room with walls and doors that provides at least an ISO Class 7 or better air quality where the primary engineering control (PEC) is physically located. A minimum differential positive pressure of 0.02- to 0.05-inch water column is required.

(g) "Compounding Aseptic Isolator (CAI)" means a form of isolator specifically designed for compounding pharmaceutical ingredients or preparations. It is designed to maintain an aseptic compounding environment within the isolator throughout the compounding and material transfer processes. Air exchange into the isolator from the surrounding environment should not occur unless the air has first passed through a microbial retentive filter (HEPA minimum) system capable of containing airborne concentrations of the physical size and state of the drug being compounded.

(h) "Compounding Aseptic Containment Isolator (CACI)" means a compounding aseptic isolator (CAI) designed to provide worker protection from exposure to undesirable levels of airborne drug throughout the compounding and material transfer processes and to provide an aseptic environment for compounding sterile preparations. Air exchange with the surrounding environment should not occur unless the air is first passed through a microbial retentive filter (HEPA minimum) system capable of containing airborne concentrations of the physical size and state of the drug being compounded. Where volatile hazardous drugs are prepared, the exhaust air from the isolator should be appropriately removed by properly designed building ventilation.

(i) "Controlled cold temperature" means 2 degrees to 8 degrees C (35.6 degrees to 46.4 degrees F).

(j) "Controlled freezer temperature" means -25 degrees to -10 degrees C (-13 degrees to 14 degrees F) or at a range otherwise specified by the pharmaceutical manufacturer.

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

(l) "Copy or essentially a copy" of a commercially available drug product includes all preparations that are comparable in active ingredients to commercially available drug products, except that it does not include any preparations in which there has been a change,

made for an identified individual patient, which produces for that patient a significant difference, as determined by a prescribing practitioner, between that compounded preparation and the comparable commercially available drug product.

(m) "Daily" means occurring every day that a pharmacy is operating.

(n) "Dosage unit" means a quantity sufficient for one administration to one patient, except that for self-administered ophthalmic drops, a quantity sufficient for 30 days or less shall be considered one dosage unit.

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

(p) "First air" means the air exiting the HEPA filter in a unidirectional air stream that is essentially particle free.

(q) "Gloved fingertip sampling" means a process whereby compounding personnel lightly press each fingertip and thumb onto appropriate growth media, which are then incubated at a temperature and for a time period conducive to multiplication of microorganisms, and then examined for growth of microorganisms.

(r) "Hazardous" means all anti-neoplastic agents identified by the National Institute for Occupational Safety and Health (NIOSH) as meeting the criteria for a hazardous drug and any other drugs, compounds, or materials identified as hazardous by the pharmacist-in-charge.

~~(b)~~(s) "Integrity" means retention of potency until the expiration-beyond use date noted provided on the label, so long as the preparation is stored and handled according to the label directions after it is dispensed.

(t) "Lot" means one or more compounded drug preparation(s) prepared during one uninterrupted continuous cycle of compounding from one or more common active ingredient(s).

(u) "Media-fill test" means a test that mimics compounding procedures using a growth-based media to demonstrate that aseptic techniques of compounding personnel or processes routinely employed do not result in microbial contamination. To be valid, media-fill tests must be conducted on both the most routine and the most challenging compounding procedures performed.

(v) "Non-sterile-to-sterile batch" means any compounded drug preparation containing two (2)

or more dosage units with any ingredient that was at any time non-sterile, regardless of intervening sterilization of that ingredient.

(w) "Parenteral" means a preparation of drugs administered in a manner other than through the digestive tract. This includes, but is not limited to, injection through one or more layers of skin, administration into the eye, and by inhalation.

(x) "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)~~(y) "Potency" means active ingredient strength within +/- 10% (or the range specified in USP37-NF32, 37th Revision, Through 2nd Supplement Effective December 1, 2014) of the labeled amount.

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

(aa) "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. This definition does not include any hospital, pharmacy, or other facility, whether or not separately licensed, that may be affiliated with, adjacent to, or co-owned by, the prescriber's practice environment.

(ab) "Primary Engineering Control (PEC)" means a device that provides an ISO Class 5 or better environment through the use of unidirectional HEPA-filtered first air for the exposure of critical sites when compounding sterile preparations. Examples of PEC devices include, but are not limited to, laminar airflow workbenches, biological safety cabinets, compounding aseptic isolators, and compounding aseptic containment isolators.

(ac) "Process validation" means demonstrating that when a process is repeated 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.

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

~~(d)~~(ae) "Quality" means the absence of harmful levels of contaminants, including filth, putrid,

or decomposed substances, ~~and~~ the absence of active ingredients other than those listed on the label, and the absence of inactive ingredients other than those listed on the master formula record.

(af) "Segregated sterile compounding area" means a designated space for sterile-to-sterile compounding where a PEC is located within either a demarcated area (at least three foot perimeter) or in a separate room. Such area or room shall not contain and shall be void of activities and materials that are extraneous to sterile compounding. The segregated sterile 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. The segregated sterile compounding area shall not have a sink, other than an emergency eye-washing station, located within three feet of a PEC. The segregated sterile compounding area shall be restricted to preparing non-hazardous sterile-to-sterile compounded preparations.

~~(e)~~(ag) "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~~ preparation 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” ~~as used in~~ that may be furnished to a prescriber for office use by the prescriber as authorized by Business and Professions Code section 4052, subdivision (a)(1), means that amount of compounded drug ~~product~~ preparation that:

- (1) ~~is~~ ordered by the prescriber or the prescriber’s agent and paid for by the prescriber at a price that fairly reflects the fair market value of each drug preparation, 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’s office and signed for by the prescriber or the prescriber’s agent; 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 for human medical practices, or a 120-hour supply for veterinary medical practices, solely to the prescriber's own patients seen as part of regular treatment in the prescriber's office, as fairly estimated by the prescriber and documented on the purchase order or other documentation submitted to the pharmacy prior to furnishing; and
- ~~(2)~~(4) That the pharmacist has a credible basis for concluding is reasonable considering the intended use of the compounded medication and the nature of the prescriber’s practice; and
- ~~(3)~~ (5) for With regard to any individual prescriber to whom the pharmacy furnishes, and with regard to for all prescribers to whom the pharmacy furnishes, 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 an 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 commercially available drug products, unless that drug product appears on an ASHP (American Society of Health-System Pharmacists) or FDA list of drugs that are in short supply at the time of compounding and at the time of dispense, and the compounding of that drug preparation is justified by a specific, documented medical need made known to the pharmacist prior to compounding. The pharmacy shall retain a copy of the documentation of the shortage and the specific medical need in the pharmacy records for three years from the date of receipt of the documentation.

~~(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 maximum allowable beyond use date for the preparation, and the rationale or reference source justifying its determination.

(4) Inactive ingredients to be used.

~~(5) Process and/or procedure~~ Specific compounding steps 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.

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

~~(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~~ the beyond use date indicated on the label, so long as label instructions for storage and handling are followed after the preparation 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 compendial 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, nor shall it exceed 180 days from preparation unless a ~~longer~~ later date is supported by stability studies of finished drugs or compounded drug products preparations using ~~the same~~ identical 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)~~ Prior to allowing any drug product preparation to be compounded in a pharmacy, the pharmacist in charge shall complete a self-assessment for compounding pharmacies developed by the board (Incorporated by reference is “Community Pharmacy & Hospital Outpatient Pharmacy Compounding Self-Assessment” Form 17M-39 Rev. 02/12.) as required by Section 1715 of Title 16, Division 17, of the California Code of Regulations. 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.

(k) Packages of ingredients, both active and inactive, 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 and 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 and quality for use in compounded drug preparations, considering the container in which it is packaged and the storage conditions.

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. If the manufacturer does not supply an expiration date for any component, the records shall include the date of receipt of the component in the pharmacy, and the limitations of section 1735.2, subdivision (k) shall apply. Exempt from the requirements in this paragraph are sterile ~~products~~ preparations compounded ~~on a one-time basis in a single lot~~ 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) Through 2nd Supplement (35 37th Revision, Effective ~~May~~ December 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 or beyond use date and time of the final compounded drug ~~product~~ preparation, expressed in the compounding record in a standard date and time format.

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

(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 ingredients shall be obtained from a supplier registered with the Food and Drug Administration (FDA). 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, either written in English or translated into English, for chemicals, bulk drug substances, and drug products, and components used in compounding. Certificates of purity or analysis are not required for drug products that are approved by the FDA. Any certificates of purity or analysis acquired by the pharmacy shall be matched to the corresponding 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 or brand 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. Exempt from the requirements of this paragraph are those sterile drug preparations compounded within a health care facility solely for administration, by a licensed health care professional, to patient of the facility. To be treated as such, the "health care facility" must be licensed under Health and Safety Code section 1250.

(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 of the preparation, 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 policyies and procedures 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. Any failure to follow the pharmacy's written policies and procedures shall constitute a basis for disciplinary action.

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

(c) The policyies and procedures manual shall include at least the following:

(1) Procedures for notifying staff assigned to compounding duties of any changes in ~~processes~~ or to the policyies or procedures manual.

(2) ~~Documentation of a~~ A written plan for recall of a dispensed compounded drug ~~product~~ preparation where subsequent ~~verification~~ information demonstrates the potential for adverse effects with continued use ~~of a compounded drug product~~. The plan shall ensure that all affected doses can be accounted for during the recall.

(3) 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.

(4) 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) Documentation of the methodology used to ~~test~~ validate integrity, potency, quality, and labeled strength of compounded drug ~~products~~ preparations. The methodology must be appropriate to compounded drug preparations.

(5) Documentation of the methodology and rationale or reference source used to determine appropriate ~~expiration~~ beyond use dates for compounded drug ~~products~~ preparations.

(7) Dates and signatures reflecting all annual reviews of the policies and procedures manual by the pharmacist-in-charge.

(8) Dates and signatures accompanying any revisions to the policies and procedures manual approved by the pharmacist-in-charge.

(9) Policies and procedures for storage of compounded drug preparations in the pharmacy and daily documentation of all room, refrigerator, and freezer temperatures within the pharmacy.

(10) 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 within the pharmacy.

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. This shall include records of maintenance and cleaning of the facilities and equipment. Where applicable, this shall also include records of certification(s) of facilities or equipment.

(b) Any equipment used to compound drug ~~products~~ preparations shall be stored, used, ~~and~~ maintained, and cleaned 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, on a schedule and by a method determined by the manufacturer's specifications, to ensure accuracy. Documentation of each such calibration shall be recorded ~~in writing~~ in a form which is not alterable and these records of calibration shall be maintained and retained in the pharmacy.

(d) Any pharmacy engaged in any hazardous drug compounding shall maintain written documentation regarding appropriate cleaning of facilities and equipment to prevent cross-contamination with non-hazardous drugs.

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. Additionally, documentation demonstrating that staff have been trained on all policies and procedures shall be maintained.

(b) The pharmacy shall develop and maintain an ongoing 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 analysis of compounded drug preparations to ensure integrity, potency, quality, and labeled strength, including the frequency of testing, ~~analysis of compounded drug products preparations~~ preparations. All qualitative and quantitative analysis reports for compounded drug ~~products preparations~~ preparations shall be retained by the pharmacy and ~~collected~~ maintained along with the compounding record and master formula. The quality assurance plan shall include a schedule for routine testing and analysis of compounded drug preparations to ensure integrity, potency, quality, and labeled strength, on at least an annual basis.

(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 within the pharmacy or within patient care areas of a hospital where furnished drug is returned for redispensing.

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 or cleanroom, including the walls, ceilings, and floors, shall be constructed in accordance with Section 1250.4 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 505.5 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, 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. Certification records must be retained for at least 3 years in the pharmacy.~~

~~(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 1250.4 of Title 24, Part 2, Chapter 12, of the California Code of Regulations. Sinks and drains shall not be present in any ISO Class 7 or better buffer area or cleanroom, nor in a segregated sterile compounding area within three feet of an ISO Class 5 or better PEC. 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, and a backup plan to ensure continuity of available compounded drug preparations in the event of a power outage.~~

~~(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, and 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), any pharmacy engaged in any compounding of for sterile drug products preparations compounded from one or more non-sterile ingredients, shall make and keep the following records must be made and kept by within the pharmacy:~~

~~(1) The Documents evidencing training and competency evaluations of employees in sterile product drug preparation policies and procedures.~~

~~(2) Results of hand hygiene and garbing assessments 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 tests.~~

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

~~(2)-(5) Documents indicating daily recordation of room, R refrigerator, and freezer temperatures appropriate for sterile compounded 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(s).~~

~~(7) Documents indicating daily recordation of air pressure differentials or air velocity measurements between all adjoining ISO rooms or areas, including those associated with compounding aseptic (containment) isolators, and air pressure differentials or air velocity measurements between all rooms or spaces with an immediate entry or opening to ISO~~

rooms or areas.

~~(4)-(8)~~ Other facility quality control ~~logs~~ records 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, chemicals, bulk drug substances, drug products, or other 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, lot number, and amount of any drug preparation compounded for future use, the date on which any preparation was provided to a prescriber, and the name, address, and license number of the 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 California Code of Regulations section 1735.4, a pharmacy ~~which that~~ compounds sterile ~~injectable drug products~~ preparations shall include the following information on the

labels for ~~each such these products~~ preparation:

- (a) ~~The T~~Telephone number of the pharmacy. ~~, except~~ The telephone number is not required on the label for sterile injectable drug products preparations dispensed for to inpatients of a within the hospital pharmacy.
- (b) Name and ~~concentration~~ strength, volume, or weight of each 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."

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~~ ies and procedures 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 product~~ compounded drug preparations based on the intended route of administration and recommended rate of administration.
- (3) Proper use of E equipment and supplies.
- (4) ~~Training of staff in the preparation of sterile injectable drug products~~ Hand hygiene and garbing.
- (5) ~~Procedures for handling cytotoxic agents~~ Media-fill testing procedure.
- (6) Quality assurance program.
- (7) Record keeping requirements.

- (8) Compounded sterile drug preparation stability and beyond use dating.
- (9) Visual inspection and other final quality checks of sterile drug preparations.
- (10) Use of automated compounding devices (if applicable).
- (11) Preparing sterile compounded drug preparations from non-sterile components (if applicable).
- (12) Orientation, training, and competency evaluation of staff in all aspects of the preparation of sterile drug preparations including didactic training and knowledge/competency assessments that include at minimum: hand hygiene and garbing; decontamination (where applicable); cleaning and disinfection of controlled compounding areas; and proper aseptic technique.
- (13) Airflow considerations and pressure differential monitoring.
- (14) Cleaning and maintenance of ISO environments and segregated compounding areas.
- (15) An environmental sampling plan and procedures specific to viable air, surface and gloved fingertip sampling as well as nonviable particle sampling.
- (16) For compounding aseptic isolators and compounding aseptic containment isolators, documentation of the manufacturer's recommended purge time.
- (17) Temperature monitoring in compounding and controlled storage areas.
- (18) Facility management including certification and maintenance of controlled environments and related equipment.
- (19) Action levels for colony-forming units (CFUs) detected during viable surface testing, glove fingertip and volumetric air sampling.
- ~~(b)~~ (20) The determination and approval by a pharmacist of 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)~~ (21) 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. Procedures for handling, compounding and disposal of hazardous agents. The written policies and procedures shall describe the pharmacy protocols for cleanups and spills in conformity with local health jurisdiction standards.

(22) Procedures for handling, compounding and disposal of infectious materials. The written policies and procedures shall describe the pharmacy protocols for cleanups and spills in conformity with local health jurisdiction standards.

(23) Daily and monthly cleaning and disinfection schedule for the controlled areas and any equipment in the controlled area as specified in section 1751.4.

(b) For lot compounding, the pharmacy shall maintain a written policies and procedures manual that includes, in addition to the elements required by section 1735.5 and 1751.3(a), written policies and procedures regarding the following:

(1) Use of master formulas and compounding work sheets.

(2) Appropriate documentation.

(3) Appropriate sterility and potency testing.

(c) For non-sterile-to-sterile batch compounding, the pharmacy shall maintain a written policies and procedures manual for compounding that includes, in addition to the elements required by section 1735.5 and 1751.3(a), written policies and procedures regarding the following:

(1) Sterilization methods.

(2) End-product evaluation and testing.

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

~~(d)(2)~~(e) All personnel involved must read the policies and procedures before compounding sterile ~~injectable products~~ drug preparations, and any additions, revisions, and deletions to the written policies and procedures must be communicated to all personnel involved in sterile compounding. This review must be documented by a signature and date.

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

~~(A) Competency evaluation.~~

~~(B) Storage and handling of products and supplies.~~

~~(C) Storage and delivery of final products.~~

~~(D) Process validation.~~

~~(E) Personnel access and movement of materials into and near the controlled area.~~

~~(F) Use and maintenance of environmental control devices used to create the critical direct compounding area for manipulation of sterile products (e.g., laminar airflow workstations, biological safety cabinets, class 100 cleanrooms, and barrier isolator workstations).~~

~~(G) Regular cleaning schedule for the controlled areas and any equipment in the controlled area and the alternation of disinfectants. 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.~~

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 lot;

(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 daily. Walls, ceilings, storage shelving, tables and stools shall be cleaned with a germicidal detergent and water and disinfected with a suitable agent 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 air quality. 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 or *cleanroom* 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 or 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 cytotoxic sterile hazardous agents shall do so in accordance with Section 505.125.1 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 CETA Certification Guide for Sterile Compounding Facilities (CAG-003-2006-11, Revised January 31, 2012). ~~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. Certification records must be retained for at least 3 years.~~ Any drug preparation that is compounded in a 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 with the outermost glove tested to meet ASTM 6978-05. Where the documentation provided by CACI manufacturer does not require garbing, only the two glove requirement shall apply.

(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 sampling shall be done at least quarterly for all sterile-to-sterile compounding and monthly for all non-sterile-to-sterile compounding. Volumetric air sampling by impaction shall be done at least once every six months. Viable surface and volumetric air sampling shall be performed 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.

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, unless the compounding aseptic isolator or compounding aseptic containment isolator manufacturer can provide written documentation, based on validated environmental testing, that any component of the personal protective equipment or personnel cleansing is not required.

~~(2) Cleanroom garb~~ Personal protective equipment must be donned and removed outside the designated area in an ante-area or 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 H₁ hand, 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 or cleanroom. 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 ISO Class 5 and ISO Class 7 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 ~~drug 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 or greater 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 ~~Quality Assurance~~ Program shall include at least the following:

(1) Procedures for cleaning 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 aseptic 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 or greater 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 promote 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. Aseptic work practice assessments via media fill tests must be revalidated, as appropriate to the circumstance or personnel found to be deficient, 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 ~~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.

(c) All sterile 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 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.

~~(c)~~ (e) Batch-produced sterile injectable drug products compounded from one or more non-sterile ingredients. Non-sterile-to-sterile batch drug preparations shall be subject to documented end product testing for sterility and pyrogens and shall be quarantined until the end product testing confirms sterility and acceptable levels of pyrogens, per USP chapter 85 limits, 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.

~~(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 conformity with and 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 does not exceed the expiration date or beyond use date provided by the manufacturer for any component in the preparation, and that, 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 (USP37-NF32) Through 2nd Supplement (37th Revision, Effective December 1, 2014), hereby incorporated by reference, that would justify a more extended beyond use date, conforms to the following limitations:

(a) The beyond use date shall specify that storage and exposure periods cannot exceed 48 hours at controlled room temperature, 14 days at controlled cold temperature, and 45 days at controlled freezer temperature, where the sterile compounded drug preparation is compounded solely with aseptic manipulations and all of the following apply:

(1) The preparation is compounded entirely within an ISO Class 5 PEC located in an ISO Class 7 buffer area or cleanroom 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.

(b) The beyond use date shall specify that storage and exposure periods cannot exceed 30 hours at controlled room temperature, 9 days at controlled cold temperature, and 45 days at controlled freezer temperature, where the sterile compounded drug preparation is compounded solely with aseptic manipulations and all of the following apply:

(1) The preparation is compounded entirely within an ISO Class 5 PEC located in an ISO Class 7 buffer area or cleanroom 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.

(c) The beyond use date shall specify that storage and exposure periods cannot exceed 24 hours at controlled room temperature, 3 days at controlled cold temperature, and 45 days at controlled freezer temperature, where the sterile compounded drug preparation is compounded solely with aseptic manipulations 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.

For the purposes of this subdivision, "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) The beyond use date shall specify that storage and exposure periods cannot exceed 12 hours where the sterile compounded drug preparation is compounded solely with

aseptic manipulations and all of the following apply:

(1) The preparation was compounded entirely within an ISO Class 5 PEC that is located in a segregated sterile 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.

(e) 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. A PEC used solely to compound 'immediate use' preparations need not be placed within an ISO Class 7 buffer area or cleanroom, with an ante-area.

(1) 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 storage circumstance.

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 ~~injectable 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.

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 policies 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.