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XIV. Proposed Regulations to Amend Title 16 California Code of Regulations (CCR) sections 1735 et seq., and 1751 et seq., Relating to 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.

At the July 2015 Board Meeting, 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 July 31, 2015 – August 15, 2015.

Attachment 1 is the current regulation language as noticed on July 31, 2015.
Attachment 2 is a compilation document of the comments received during the 45 day comment period and the regulation hearing.
Attachment 3 is a compilation document of the comments received during the 15 day comment period
Attachment 4 is the regulation text modified based on feedback received from staff and stakeholders.

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 July 2015 Board meeting
2. Amend the regulation to address concerns expressed by staff and stakeholders and notice the modified text for a second 15 day comment period.

Attachment 1

Title 16. Board of Pharmacy

Modified Text

Changes made to the originally proposed language are shown by ~~double strike-through~~ for deleted language and <u>double underline</u> for added 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 <u>compounded</u> drug ~~product~~ <u>preparation</u> 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<u>,</u> topical, or injectable administration, nor does it include <u>the sole act of</u> tablet splitting <u>or crushing, capsule opening,</u> 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.

(b) "Beyond use date" means the date, or date and time, after which administration of a compounded drug preparation shall not ~~be begun~~ begin, 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. Where hazardous drugs are prepared, the exhaust air from the biological safety cabinet should be appropriately removed by properly designed external building ventilation.

~~(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)~~(d) "Bulk drug substance" means any substance that, when used in the preparation of a compounded drug preparation, processing, or packaging of a drug, ~~becomes~~ is 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)~~(e) "Cleanroom or clean area or buffer area" means a ~~physically separate~~ room or area ~~with walls and doors~~ with HEPA-filtered air that provides ~~at least an~~ ISO Class 7 or better air quality where the primary engineering control (PEC) is physically located.

(1) For nonhazardous compounding a~~A~~ minimum ~~differential~~ positive pressure differential of 0.02- to 0.05-inch water column relative to all adjacent spaces is required.

(2) For hazardous compounding at least 30 air changes per hour of HEPA-filtered supply air and a negative pressure of at least 0.01 inches of water column relative to all adjacent spaces is required.

~~(h)~~(f) "Compounding Aseptic Containment Isolator (CACI)" means a unidirectional 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 external building ventilation.

(g) "Compounding Aseptic Isolator (CAI)" means a form of isolator specifically designed for non-hazardous compounding pharmaceutical ingredients or preparations while bathed with unidirectional air. 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.

(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(s) for that product.

(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 clinically 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, except when daily monitoring of refrigerator and freezer temperature are required, then daily means every 24 hours.

(n) Displacement airflow method: a concept which utilizes a low pressure differential, high airflow principle to maintain segregation from the adjacent ante-area by means of specific pressure differentials. This principle of displacement airflow shall require an air velocity of 40 ft per minute or more from the clean area across the line of demarcation into the ante area. The displacement concept may not be used to maintain clean area requirements for sterile compounds which originate from any ingredient that was at any time non-sterile, regardless of intervening sterilization of the ingredient, or for hazardous compounds.

~~(n)~~(o) “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)~~~~(c)~~(p)“Equipment” means items that must be calibrated, maintained or periodically certified.

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

~~(q)~~(r) “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)~~(s) "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)~~(t) "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)~~(u) "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)~~(v) "Media-fill test" means a test that mimics compounding procedures using a growth-based media to demonstrate the competency of compounding personnel in aseptic techniques. The media fill test must mimic the most complex compounding procedures performed by the pharmacy ~~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)~~(w) "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)~~(x) "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. It does not include topical, sublingual, rectal or buccal routes of administration.

~~(x)~~(y) "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.

~~(c)~~~~(y)~~(z)"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. Sterile injectable products compounded solely from commercially manufactured sterile pharmaceutical products in a health care facility licensed under section 1250 of the Health and Safety Code are exempt from this definition. For those exempt, the range may be calculated and defined in the master formula.

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

~~(aa)~~(ab) "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)~~(ac) "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, sterile compounding automated robots, compounding aseptic isolators, and compounding aseptic containment isolators.

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

~~(d)~~~~(ae)~~(af) "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~~ document.

~~(af)~~(ag) "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.

(1) The BUD of a sterile drug preparation made in a segregated sterile compounding area is limited to 12 hours or less as defined by section 1751.8(d).

(2) When the PEC in the segregated sterile compounding area is a CAI or a CACI and the documentation provided by the manufacturer shows it meeting the requirements listed in section 1751.4(f)(1)-(3), the assigned BUD shall comply with section 1751.8(a)-(b).

~~(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) ~~i~~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 veterinary 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 the quantity provided for office use 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~~ document 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 and essential 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 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 a~~n expiration~~ beyond use date representing the date beyond which the compounded drug preparation should not be used, stored, transported or administered; and determined based on the professional judgment of the pharmacist performing or supervising the compounding.~~, 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~~ ingredient in the compounded drug ~~product~~ preparation, nor shall it exceed 180 days for non-aqueous formulations, 14 days for water-containing oral formulations, and 30 days for water-containing topical/dermal and mucosal liquid and semisolid formuations, ~~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~~ ingredient, specific and essential compounding steps, quality reviews, 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~~ document.

(2) The compounding document shall include the following:

~~(2)~~(A) The date the drug ~~product~~ preparation was compounded.

~~(3)~~(B) The identity of ~~the~~ any pharmacy personnel ~~who compounded the~~ engaged in compounding the drug ~~product~~ preparation.

~~(4)~~(C) The identity of the pharmacist reviewing the final drug ~~product~~ preparation.

~~(5)~~(D) The quantity of each ~~component~~ ingredient used in compounding the drug ~~product~~ preparation.

~~(6)~~(E) 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.

(i) Exempt from the requirements in this paragraph (1735.3(a)(2)(E)) are sterile ~~products~~ preparations compounded ~~on a one- time basis~~ in a single lot for administration within seventy-two (72) hours to a~~n in~~patient 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)~~(F) A pharmacy-assigned reference or lot number for the compounded drug ~~product~~ preparation.

~~(8)~~(G) The ~~expiration~~ beyond use date or beyond use date and time of the final compounded

drug ~~product~~ preparation, expressed in the compounding ~~record~~ document in a standard date and time format.

~~(9)~~(H) 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 and under California Code of Regulations section 1707.5, the label of a compounded drug ~~product~~ preparation shall contain the generic or brand name(s) of ~~the principal~~ all 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 a 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 and shall not be subject to minimum font size requirements.

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~~y~~ies 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 material failure to follow the pharmacy's written policies and procedures shall constitute a basis for disciplinary action.

(b) The policy~~y~~ies 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 policy~~y~~ies 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~~ policy~~y~~ies 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~~5) 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~~6) 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 compounding of ~~ed~~ 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.

(e) Hazardous drug compounding shall be completed in a physically separate room with the following requirements:

(1) Minimum of 12 air changes per hour; and

(2) Maintained at a negative pressure of at least 0.01 inches of water column relative to all adjacent spaces (rooms, above ceiling, and corridors); and

(3) All surfaces with the room shall be smooth, seamless, impervious, and non-shedding.

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) A pharmacy engaged in compounding shall maintain documentation that demonstrates personnel involved in compounding have the skills and training required to properly and accurately perform their assigned responsibilities and documentation that personnel involved in compounding was trained in all aspects of policies and procedures. This training shall include but is not limited to support personnel (e.g. institutional environmental services, housekeeping), maintenance staff, supervising pharmacist and all others whose jobs are related to the sterile compounding process. ~~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. All qualitative and quantitative analysis reports for compounded drug ~~products~~ preparations shall be retained by the pharmacy and ~~collated~~ maintained along with the

compounding ~~record~~ document and master formula document. 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~~ and 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, with the exception of emergency eye-rinsing stations. A sink may be located in an ante-area.

(A) When the PEC in the segregated sterile compounding area is a CAI or CACI and the documentation provided by the manufacturer shows it meets the requirements listed in 1751.4(f)(1)-(3) they are exempt from the room requirement listed in 1751(b)(3)

~~(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~~ maintain the following records ~~must be made and kept by~~ readily retrievable 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~~ documentation 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 documentation ~~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 ~~l~~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 formula document ~~work sheet~~, the preparation compounding document~~work sheet~~, and records of end-product evaluation testing and 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 sections 1707.5 and 1735.4, a pharmacy ~~which~~ that compounds sterile ~~injectable~~ drug ~~products~~ preparations shall include the following information on the label~~s~~ for each such ~~those 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 ~~in~~patients ~~of a~~ within the hospital ~~pharmacy~~.

(b) Name (brand or generic) and ~~concentration~~ strength, volume, or weight of each active ingredient~~s~~ 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 drug preparations shall maintain a written policies and procedures manual for compounding. Any material failure to follow the pharmacy's written policies and procedures shall constitute a basis for disciplinary action. In addition to the elements required by section 1735.5, written policies and procedures regarding the following:

(1) Action levels for colony-forming units (CFUs) detected during viable surface sampling, glove

fingertip, and viable air sampling.

(2) Airflow considerations and pressure differential monitoring.

(3) An environmental sampling plan and procedures specific to viable air, surface and gloved fingertip sampling as well as nonviable particle sampling.

(4) Cleaning and maintenance of ISO environments and segregated compounding areas.

(5) Compounded sterile drug preparation stability and beyond use dating.

(6) Compounding, filling, and labeling of sterile drug preparations.

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

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

(9) For compounding aseptic isolators and compounding aseptic containment isolators, documentation of the manufacturer's recommended purge time.

(10) Hand hygiene and garbing.

(11) Labeling of the sterile compounded drug preparations based on the intended route of administration and recommended rate of administration.

(12) Media-fill testing procedure.

(13) 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.

(14) Preparing sterile compounded drug preparations from non-sterile components (if applicable). This shall include sterilization method suitability testing for each master formula document.

(15) 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.

(16) 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.

(17) Proper use of equipment and supplies.

(18) Quality assurance program.

(19) Record keeping requirements.

(20) Temperature monitoring in compounding and controlled storage areas.

(21) The determination and approval by a pharmacist of ingredients and the compounding process for each preparation before compounding begins.

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

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

~~(a) Any pharmacy engaged in compounding sterile injectable drug products preparations shall maintain a written policyies and procedures manual for compounding. Any material failure to follow the pharmacy's written policies and procedures shall constitute a basis for disciplinary action. that includes, i~~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). This shall include sterilization method suitability testing for each master formula.~~

~~document.~~

~~(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, sampling, glove fingertip, and volumetric viable 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 formula~~s~~ documents and compounding documents ~~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 and shall include sterilization method suitability testing for each master formula document.

(2) End-product evaluation, quantitative, and qualitative 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:~~ Cleaning shall be done using a germicidal detergent and sterile water. The use of a sporicidal agent is required to be used at least monthly.

(1) All ISO Class 5 surfaces, work table surfaces, carts, counters, and the cleanroom floor shall be cleaned at least daily. After each cleaning, disinfection using a suitable sterile agent shall occur

on all ISO Class 5 surfaces, work table surfaces, carts, and counters.

(2) Walls, ceilings, storage shelving, tables, stools, and all other items in the ISO Class 7 or ISO Class 8 environment shall be cleaned at least monthly.

(3) Cleaning shall also occur after any unanticipated event that could increase the risk of contamination.

(4) All cleaning materials, such as wipers, sponges, and mops, shall be non-shedding and dedicated to use in the cleanroom, or ante-area, and segregated sterile compounding areas and shall not be removed from these areas except for disposal.

(e) Disinfection, using a suitable sterile agent, shall also occur on all surfaces in the ISO Class 5 PEC frequently (at least every 30 minutes), 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) (c) 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. Unidirectional ~~C~~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~~ cleanroom 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.~~12~~5.1 of Title 24, Chapter 5, of the California Code of Regulations, requiring a ~~laminar air flow hood~~ negative pressure PEC. Additionally, each PEC used to compound hazardous agents shall be externally vented.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.

(1) During the hazardous drug compounding that is performed in a compounding aseptic containment isolator, full hand hygiene and garbing must occur~~, complete with~~. Garbing shall include 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 D6978-05 standard. ~~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) Compounding aseptic isolator and compounding aseptic containment isolator used in the compounding of sterile drug preparations shall use unidirectional air flow patterns.

~~(i)~~(j) Viable surface sampling shall be done at least ~~quarterly~~ every six months for all sterile-to-sterile compounding and ~~monthly~~ quarterly for all non-sterile-to-sterile compounding. ~~Volumetric~~ Viable air sampling shall be done by ~~impaction~~ volumetric air sampling procedures which test a sufficient volume of air (400 to 1,000 liters) at each location and shall be done at least once every six months. Viable surface and ~~volumetric~~ viable 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)~~(k) The sterile compounding area is the pharmacy shall have a comfortable and well-lighted working environment, which includes a room temperature of 20-22 degrees Celsius (68-75 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 any wrist, ~~H~~hand, finger, ~~and~~ or ~~wrist~~ other visible jewelry or piercing ~~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 exposed rashes, sunburn, weeping sores, conjunctivitis, active respiratory infections, or those wearing cosmetics, nail polish, or artificial nails 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). Exceptions are as listed in 1751.4(g).

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 ~~Q~~quality ~~A~~assurance ~~P~~program shall include at least the following:

(1) Procedures for ~~C~~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)(1) Batch-produced sterile injectable drug preparation compounded from one or more non-sterile ingredients except as provided in paragraph (2), 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. Exempt from pyrogen testing are non-injectable ophthalmic and inhalation preparation.

(1) The following non-sterile-to-sterile batch drug preparations do not require end product testing for sterility and pyrogens:

(A) Preparations for self-administered ophthalmic drops in a quantity sufficient for administration to a single patient for 30 days or less.

(B) Preparations for self-administered inhalation in a quantity sufficient for administration to a single patient for 5 days or less.

~~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~~ an 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~~ in solid frozen state, 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 or compounded entirely within a CAI or CACI which meets the requirements in 1751.4(f)(1)-(3), 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~~ in solid frozen state, 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 or compounded entirely within a CAI or CACI which meets the requirements in 1751.4(f)(1)-(3), 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~~ in solid frozen state, where the sterile compounded drug preparation is compounded solely with aseptic manipulations using non-sterile ingredients, regardless of intervening sterilization of that ingredient and the following applies: ~~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.~~

(1) The preparation is compounded entirely within an ISO Class 5 PEC located in an ISO Class 7 cleanroom with an ante-area or compounded entirely within a CAI or CACI which meets the requirements in 1751.4(f)(1)-(3).

(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 shall be labeled with a BUD and 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 shall be labeled with a BUD and 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 policy ies 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.

Attachment 2

Code Section	Commenter	Comment
1735(b)	**John Cronin** Institute for Community Pharmacy	(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. In a general sense, this definition is consistent with the definition of “compounding” found in 21 USC 353a, which is the section of the federal law that deals with compounding in pharmacies. However, the language dealing with activities that are excluded from compounding is slightly different. 21 USC 353a(e) reads: "As used in this section, the term ‘‘compounding’’ does not include mixing, reconstituting, or other such acts that are performed in accordance with directions contained in approved labeling provided by the product’s manufacturer and other manufacturer directions consistent with that labeling." This federal definition is somewhat broader than the language at the beginning of the proposed §1735(b), which appears to be limited to “reconstitution,” which is not further defined in the proposed regulation. Without further clarification, this could cause confusion regarding the preparation of certain commercially available products, such as Benzamycin® or Phospholine Iodide® (two products from my earlier days as a practicing pharmacist) which involve preparation prior to dispensing that may not meet all definitions of “reconstitution.” To illustrate the possible confusion that can occur, I’ve included excerpts from the labeling for Benzamycin® and Phospholine Iodide® which show the manufacturer’s directions for preparation for these products, as well as two common, but inconsistent, definitions of “reconstitution. **Continued on next Row.**
1735(b)	**John Cronin** Institute for Community Pharmacy	**Continued from previous Row.** The first question then, is whether preparation of commercially available products consistent with manufacturer directions is, or should, be excluded from the definition of “compounding” even if those directions call for more than simple “reconstitution.” A further question is whether the exemption should be limited to “oral, rectal, topical or injectable administration” as included in the proposed §1735(b) or whether it should extend to products intended for use in the eye or ear, which is consistent with the federal law. Should the Board feel that preparation of any product that is consistent with manufacturer labeling should be excluded from the definition of compounding, we suggest the following amendment of §1735(b) to make it consistent with the federal language found at 21 USC 353a(e): "(b) ‘Compounding’’ does not include mixing, reconstituting, or other such acts that are performed in accordance with directions contained in approved labeling provided by the product’s manufacturer and other manufacturer directions consistent with that labeling 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." Should the Board decide to leave the language as proposed, some clarification of the intent of the language and the intended definition of “reconstitution” should be provided as a reference for pharmacists and the board’s inspectors. If the Board believes these products should be included within the definition of “compounding,” the Board should provide a clear indication of whether the manufacturer’s directions and labeling are adequate to comply with the compounding documentation included elsewhere in these proposed regulations.

Code Section	Commenter	Comment
1735(b)	**Doug O'Brien** Kaiser Permanente	The proposed language is missing some very common and important categories of products that the standards of practice do not call for extra specified conditions, such as Phospholine Iodide eye drops. Relying on the term “topical” to include such categories is unrealistic and adding some specific terms will reduce confusion. Recommendation: Add wording to indicate that the examples are not all inclusive and specifically the categories of “ophthalmic” and “otic” to the list of products where “Compounding” does not include “reconstitution”. Use the following language :“(b) “Compounding” does not include reconstitution of a drug pursuant to a manufacturer’s direction(s), such as for ophthalmic otic, 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. Rationale: Several of the most popular products are ophthalmic products that only have to be reconstituted following manufacturer’s instructions
1735.1	**Judith Brosz and Robert Stein**	Adding the new definitions would make references in other regulations more specific and clear. The proposed additional definitions (indicated by dashes here) would be plugged into the appropriate subsection of 1735.1, and the lettering would be rearranged accordingly. (-) “Controlled area” or “designated area” for sterile processing means any area where the environment is specifically controlled to prevent contamination of sterile compounds. Areas such as the cleanroom, CAI, or CACI would be included in this definition, as would an ante room requiring special preparation to enter. (-) “Sterile compounding personnel” refers to personnel who are actively preparing sterile compounds in the controlled area, or directly supervising such a person in the controlled area. On January 27, 2015, a sterile compounding inspection took place at El Camino Hospital in Mountain View, CA. Certain statements in the inspection report implied that all pharmacists in the department, regardless of whether or not they actually worked in the sterile processing environment, had to pass the rigorous practical test involving long standing times and repeated manipulation of needles. The interpretation that this is a universal requirement makes it difficult or impossible for those with disabilities to work in any capacity in a hospital pharmacy. We do not believe the intent of the regulation is to preclude employers from providing reasonable accommodations to disabled personnel. To correct this situation, for Dr. Brosz and other disabled pharmacists similarly situated, we are recommending some changes in Title 16 that would make clear that the hands-on aseptic testing requirements are limited to those actually working or supervising inside the controlled sterile processing environment, rather than a universal requirement that would exclude disabled people from working in a hospital pharmacy at all.
1735.1	**BJ Bartleson** California Hospital Association	Insert new section after (p), titled “Fully automated IV Robotics”- means a system where the actual compounding is done in an enclosed ISO 5 area by a machine with programming that allows the product to be compounded without human touch in the compounding space” IV robotics requires a definition in order to have instructions for issues such as cleaning.

Code Section	Commenter	Comment
1735.1	**Lynn Paulsen**	CACI/CAI refers to ventilation building requirements. Requesting a delay until USP 800 to finalized. It is unclear why the ventilation requirements apply to the CACI/CAI and not the biological safety cabinets. Additionally, a definition needs to be added for "Automation or Robotics." Language provided by CHA
1735.1(a)	**Judith Brosz and Robert Stein**	(a) “Ante-area” means an ISO Class 8 or better air quality where ~~personnel~~ Sterile Compounding Personnel hand hygiene and garbing procedures, staging of components, and other high-particulate-generating activities are performed … To more clearly differentiate the duties and requirements for those involved in sterile compounding, we have added definitions of “sterile compounding personnel” and “controlled area,” and refer to these terms throughout the regulations that apply exclusively to sterile compounding.
1735.1(c)	**Judith Brosz and Robert Stein**	(c) “Biological Safety Cabinet (BSC)” means a ventilated cabinet for compounded sterile drug preparations, having an open front with inward airflow for ~~personnel~~ Sterile Compounding Personnel protection, downward HEPA-filtered laminar airflow for product protection, and HEPA-filtered exhausted air for environmental protection.
1735.1(d)	**Doug O'Brien** Kaiser Permanente	Recommendation: Adopt the USP Chapter 797 definition for buffer area, “An area where the primary engineering control is located. Activities that occur in this area include the preparation and staging of components and supplies used when compounding CSPs.” Rationale: The proposed definition is not in alignment with USP Chapter 797, which allows for the compounding of hazardous drugs in a buffer area that utilizes the airflow displacement method. The result of this definition (taken in context with the definitions of cleanroom and segregated compounding area) is that neither a CACI nor a BSC can be used to prepare chemotherapy in a cleanroom configuration that utilizes the airflow displacement method. This definition imposes significant and very expensive new requirements as cleanrooms utilizing the airflow displacement method will need to be remodeled to separate the buffer area from the ante-area with walls/doors. This change in definition would necessitate remodeling and construction costs exceeding $60 million for our organization.
1735.1(d)	**Douglas Barcon** Barcon & Associates	Change “The principle of displacement airflow shall be employed” to “Instead of physical separation from the ante-area, the principle of displacement airflow shall be employed.” Without such a change, the regulation states that a buffer area could only use displacement airflow, which is incorrect. Alternate change to above: After “The principle of displacement airflow shall be employed” add to the sentence “where there is no physical separation from the ante-areas by walls or doors. To improve the definition of a “buffer area”, change the first sentence to: “ “Buffer area” means an area where the primary engineering control (PEC) is located which provides at least an ISO Class 7 or better air quality and maintains segregation from the adjacent ante-area by means of specific pressure differentials.” Inclusion of the ISO Class 7 or better air quality is a necessary requirement of a buffer area for sterile compounding in USP 797 and is the location of the PEC, even though it is duplicated in the definition of a cleanroom. Also, remove “physically” because “located” alone confers the same meaning.

Code Section	Commenter	Comment
1735.1(d)	**Rheta Sandoval** Kaweah Delta Health Care	Concerned about the language “for hazardous compounds, or for chemotherapy compounds”. To not permit the displacement concept to maintain clean room area requirements will have significant impact for some facilities in terms of remodeling and construction costs. Outside of the costs and time necessary to complete facility modifications to meet this requirement, there could be negative impacts if a pharmacy could not continue to provide the potentially life-saving “hazardous” medications needed as a facility works towards gaining compliance with the requirement. Some geographic areas of the State may not have a nearby health facility to provide this type of service or the ability to handle the order volume currently managed by the Pharmacy. Understanding a key element of proposed USP <800> is to require that hazardous drugs be stored in a negative or normal/pressure, and compounding must be completed in certified biological safety cabinets or compounding aseptic containment isolators in a separate room with negative pressure, attempts to harmonize State with Federal Standards may be indicated. However, if the BOP adopts the modified text as proposed and there are not reasonable timelines and expectations for compliance established, it could severely limit patient access to needed care or place tremendous burdens on patients and those supporting their care to travel to a facility that is compliant with the regulation. Please consider the following clarifying information: the verbiage in USP 797 specific to “displacement concept” reads, “The displacement concept shall not be used for high-risk compounding.” The reference cited “ISO 14644-4:2001 Cleanrooms and associated controlled environments-Design, construction, and start-up” includes section A.5.2 which describes the displacement concept. The displacement concept is described in this reference as a means to effectively separate clean and less clean adjacent zones without any mention of hazardous compounds or chemotherapy. As such, the term “high-risk” should be taken to mean high risk of microbial contamination as described in USP <797>. Our facility currently meets the “low volume” exemption described in USP <797>, hazardous CSP prepared in an ISO 5 CACI using closed-system transfer devices. The PEC (CACI) is located in the ISO 7 buffer area (located in a non-negative pressure clean room). The buffer area is not physically separated from the ante-area, the principle of displacement airflow is employed. Please delete the language “for hazardous compounds, or for chemotherapy compounds” and consider reintroducing at a later time after fully assessing impacts to Pharmacies holding Sterile Compounding Licenses in this state and establishing reasonable timelines for gaining compliance.
1735.1(d)	**Katherine Palmer** **Rita Shane** Cedars-Sinai Medical Center	"Buffer area" means an area which maintains segregation from the adjacent ante-area by means of specific pressure differentials **(A minimum differential positive pressure of 0.02- to 0.05- inch water column is required.). If physical separation (walls/doors) does not exist between the buffer and ante area, t**he 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 40ft per minute or more from the buffer area across the line of demarcation into the ante-a rea. 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~~. In the absence of a physically separated buffer and ante area for medication preparation, USP 797 allows the use of displacement airflow. Application of this to hazardous drug areas is essential for organizations that don't have a separate room to allow for hazardous medication preparation for cancer patients. In the board response to comments, the terms high-risk and hazardous are used interchangeably (Attachment 2- third response to comment on 1735.l(f). ***(FYI: Attachment 2 was not provided.)***

Code Section	Commenter	Comment
1735.1(d)	**University Compounding Pharmacy** Joe Grasela	Definition for "Buffer area" and "Clean room" In USP 797 are used interchangeably (pg 12 of USP 797). It would be best to clarify that a "Buffer area" is a designated area with no separated doors or walls with a line of demarcation from the Ante room while a "Clean room" is a physical room with walls and/or door separation from the Ante room that allows for compounding of Hazardous and High risk preparations. We associate our "clean room/buffer room" with walls and the door as our line of demarcation that allows us to compound "Hazardous" or "High risk" compounds. With this clarification, we would then term our sterile compounding room as a "clean room" as opposed to a "buffer area". When USP 800 is released, your current definition of “clean room” doesn't address the negative pressure room requirements (ie: 0.01-0.03 inches of water column, externally vented, 30 ACPH). (d) “Buffer area” means an area which maintains segregation from the adjacent ante area by means of specific pressure differentials. The principle displacement airflow shall be employed. This concept utilizes a low pressure differential, high airflow principle...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.
1735.1(e)	**Brian Warren** California Pharmacist Association	(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~~ is 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. An inactive ingredient does not become active.
1735.1(f)	**Doug O'Brien** Kaiser Permanente	This definition is misleading and inaccurate, because it states that a cleanroom must provide ISO Class 7 or better air quality. There are other acceptable configurations of cleanrooms. For example, a cleanroom could also be a physically separate room that contains a buffer area, in which the air quality is ISO Class 7 or better; and an ante area, in which the air quality is ISO Class 8 or better. Displacement airflow concept described in 1735.1 (d) could be used. Recommendation: Adopt the USP Chapter 797 definition for cleanroom: “A room in which the concentration of airborne particles is controlled to meet a specified airborne particulate cleanliness class. Microorganisms in the environment are monitored so that a microbial level for air, surface, and personnel gear are not exceeded for a specified cleanliness class.” This definition accommodates all acceptable cleanroom configurations Remodeling and construction costs exceeding $10 million to convert existing cleanrooms to provide ISO Class 7 air quality.

Code Section	Commenter	Comment
1735.1(f)	**University Compounding Pharmacy** Joe Grasela	Definition for "Buffer area" and "Clean room" In USP 797 are used interchangeably (pg 12 of USP 797). It would be best to clarify that a "Buffer area" is a designated area with no separated doors or walls with a line of demarcation from the Ante room while a "Clean room" is a physical room with walls and/or door separation from the Ante room that allows for compounding of Hazardous and High risk preparations. We associate our "clean room/buffer room" with walls and the door as our line of demarcation that allows us to compound "Hazardous" or "High risk" compounds. With this clarification, we would then term our sterile compounding room as a "clean room" as opposed to a "buffer area". When USP 800 is released, your current definition of “clean room” doesn't address the negative pressure room requirements (ie: 0.01-0.03 inches of water column, externally vented, 30 ACPH). (f) “Clean room” 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. Minimum differential positive pressure of 0.02-0.05 inch water column is required.
1735.1(f)	**Douglas Barcon** Barcon & Associates	Change to “A minimum differential positive pressure of 0.02-to 0.05-inch water column is required” to “A minimum differential positive pressure of 0.02-to 0.05-inch water column is required to segregate the room from the surrounding unclassified spaces to reduce the risk of contaminants being blown, dragged, or otherwise introduced into the filtered unidirectional airflow environment.”
1735.1(g)	**Douglas Barcon** Barcon & Associates	Change to “Compounding Aseptic Isolator (CAI)” means a form of isolator specifically designed for compounding non-hazardous pharmaceutical ingredients or preparations.” A negative pressure CACI should be used to compound hazardous pharmaceutical ingredients or preparations. A CAI should not be used to compound antineoplastic hazardous drugs per draft USP 800 revision Fall 2014 (C151881).
1735.1(h)	**Douglas Barcon** Barcon & Associates	After volatile, add “, particle-generating, aerosol-producing, or sterile” This is a composite of board of pharmacy text and USP 800 revision Fall 2014 (C151881) sections 5.3.1 and 5.3.2.
1735.1(j)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: In the May 2015 Compilation version, what was omitted was “or a range otherwise specified by the pharmaceutical manufacturer.” We believe that this is verbiage that should be kept to encapsulate all of the scenarios where it is warranted to store certain medications outside of the “-25 C to -10 C” range. Solution: Reinsert the verbiage “or a range otherwise specified by the pharmaceutical manufacturer” to better encapsulate all possible scenarios.

Code Section	Commenter	Comment
1735.1(j)	**Douglas Barcon** Barcon & Associates	Cannot have two definitions for “controlled freezer temperature.” Use of “or” creates two definitions. Note that there is no definition of “controlled freezer temperature” in USP General Chapter 659 Packaging and Storage Requirements, USP 797, or the general notices in USP-37 NF-32. Should delete the word “controlled” from definition and leave remainder of text intact to be consistent with USP 797. Delete “manufacturer” and replace with “manufacturer(s) of the respective products.” There is some concern that products which specify a temperature range colder than -25 degrees C on the lower end of the range, such as a vaccine at -40 degrees C, could be comingled at the colder temperature in the same freezer with products that specify -20 degrees C at the low end of the range, and this could jeopardize stability of the product or container with the storage limitation of -20 degrees C if stored colder than -20 degrees C. A separate freezer may be necessary to accommodate products with -40 degree C storage conditions to avoid comingling.
1735.1(l)	**Douglas Barcon** Barcon & Associates	This definition precludes a pharmacy from compounding a sterile preparation, such as premixed large volume intravenous solutions and for example, a 1 gram cefazolin or ceftriaxone antibiotic IVPB, if a manufacturer provides these as frozen IVPB products or inactivated IVPB form. Proprietary bag-vial systems such as ADD-Vantage, Mini-Bag Plus, and others require physical attachment to the infusion bag and should not be considered a commercially available compounded product in the regulation, or many compounded antibiotic IVPBs would be considered a copy. Also need to comply with the Drug Quality and Security Act regarding sterile preparations demonstrably difficult to compound. Suggest changing to: “Copy or essentially a copy” of a commercially available drug product includes all preparations that are comparable in active ingredients and dosage form to commercially available drug products, except premixed large volume intravenous solutions that are not demonstrably difficult to compound; premixed, inactivated, or frozen small volume parenteral products; or proprietary bag-vial systems such as ADD-Vantage, AddEASE, Mini-Bag Plus, and others; and 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.
1735.1(m)	**Lynn Paulsen**	Should occur "every" day and not just when the pharmacy is open.
1735.1(m)	**BJ Bartleson** California Hospital Association	“Daily “means occurring every day. Pharmacies must be responsible to check refrigerated temperatures every day- the term operating may be interpreted as either open that day or operating as a licensed pharmacy and therefore should be removed.
1735.1(n)	**Brian Warren** California Pharmacist Association	(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~~. Suggested modification to conform with modifications suggested to Section 1751.7(e) (see below). Further, substantive provisions (i.e., requirements and exceptions) should be placed in the substantive provisions of the regulations, not the definitions (see Martineau R. and Salerno M., Legal, Legislative, and Rule Drafting in Plain English, Thomson West, 2005). By placing the exception for self-administered ophthalmic drops in the definitions section, pharmacists may not understand its impact.
1735.1(q)	**Judith Brosz and Robert Stein**	(q) “Gloved fingertip sampling” means a process whereby compounding ~~personnel~~ Sterile Compounding Personnel lightly press each fingertip and thumb onto appropriate growth media …

Code Section	Commenter	Comment
1735.1(r)	**Douglas Barcon** Barcon & Associates	In order to bring in line with the NIOSH List of Anti-Neoplastic and Other Hazardous Drugs document and reinforce and clarify the regulation, suggest changing definition to include hazardous drugs portion too: “Hazardous” means all anti-neoplastic agents and other hazardous drugs as 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. This change also provides guidance to the PIC in regard to hazardous drugs that are not anti-neoplastic agents.
1735.1(s)	**Lynn Paulsen**	It is unclear why both integrity and potency (y) are defined separately.
1735.1(t)	**Doug O'Brien** Kaiser Permanente	The wording of this definition is confusing and requires clarification. We believe “lot” could be interpreted two different ways. 1. It could be interpreted to include different types of preparations that are prepared during one uninterrupted continuous cycle of compounding. A typical example of this interpretation in a hospital pharmacy: compounding four doses of azithromycin 500 mg/250mL dextrose 5% for four different patients, and two doses of famotidine 40 mg in 250mL dextrose 5% 250mL for one patient, and five doses of furosemide 100mg/100mL dextrose 5% for five different patients. All of these would be prepared in an uninterrupted continuous cycle of compounding. Recommendation: If the above example is the intended interpretation, then we recommend this language: “Lot” means one or more different compounded drug preparation(s) prepared during one uninterrupted continuous cycle of compounding from one or more common active ingredient(s).” 2. It could be interpreted to mean a single type of drug preparation compounded during one uninterrupted continuous cycle of compounding from one or more common active ingredient(s). Using the example above, four doses of azithromycin 500 mg/250mL dextrose 5% for four different patients would be considered one lot. Recommendation: If interpretation #2 is correct, then we recommend this language: “Lot” means a single type of drug preparation(s) prepared during one uninterrupted continuous cycle of compounding from one or more common active ingredient(s).”
1735.1(t)	**BJ Bartleson** California Hospital Association	“Lot” designation should be limited to the products made in anticipation of an order and cannot be tracked any other way. For example, a lot should be differentiated from six 1.5 gram Vancomycin doses made for six specific patients in a hospital pharmacy or six doses made for a patient at home.
1735.1(t)	**William Stuart** Hartley Medical	Recommend: “Lot” means ~~one~~ two or more compounded drug preparation(s) prepared during one uninterrupted continuous cycle of compounding from one or more common active ingredient(s). Rationale: Lot being “one or more” would encompass every patient-specific prescription or unit of one. This would require each prescription to undergo testing. This clause seems to be directed towards covering all batches but is unknowingly infringing onto patient-specific prescriptions. Testing patient-specific prescriptions would increase the volume needed to prepare, which would increase the amount of drug needed. The testing and the increase in the amount of drug would needlessly raise the price and delay of the therapy. The above recommendation will also align with the use of “two or more” in the definition of “Non-sterile-to-sterile batch” in 1735.1(v).

Code Section	Commenter	Comment
1735.1(t)	**Katherine Palmer** **Rita Shane** Cedars-Sinai Medical Center	"Lot" means ~~one or more~~ **"non-sterile to sterile batch" which means any compounded drug preparation containing two or more dosage units with any ingredient that was at any time non-sterile, regardless of intervening sterilization of that ingredien**t. ~~compounded drug preparation(s) during one uniterrupted continuous cycle of compounding from one or more common active ingredient(s).~~ OR Alternatively, recommend changing definition of "lot" to "greater than one dose" in order to ensure timely preparation of compounded drugs to treat emergency patients' conditions where immediate administration of medications is essential. When medications are prepared as single doses, time is of the essence and documentation requirements for a lot would delay patient treatment. "Lot" means ~~one or more~~ "**greater than one dose of compounded drug preparation prepard in anticipation of immediate patients needs**. ~~compounded drug preparation(s) during one uniterrupted continuous cycle of compounding from one or more common active ingredient(s).~~
1735.1(u)	**Judith Brosz and Robert Stein**	(u) "Media-fill test" means a test that mimics compounding procedures using a growth-based media to demonstrate that aseptic techniques of compounding ~~personnel~~ Sterile Compounding Personnel or processes routinely employed do not result in microbial contamination. …
1735.1(u)	**William Stuart** Hartley Medical	Recommend: "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. Rationale: The "most routine procedure" is not referenced beyond this definition nor in USP <797>. We recommend removing the most routine procedure to remain consistent with the following uses of media-fill tests in the proposed text and USP: 1751.6(e)(1)(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 volume transferred during the selected manipulations." 1751.7(b) "Each individual involved in the preparation of sterile drug preparations must first successfully demonstrate competency by successfully performing aseptic media-fill tests before being allowed to prepare sterile drug preparations. 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…" **Media-Fill Test Procedure**—This test or an equivalent test is performed at least annually under conditions that closely simulate **the most challenging or stressful conditions encountered during compounding.**
1735.1(w)	**Lynn Paulsen**	Does it include topical. Defintion needs to be further defined. Okay with Irrigation, Opthalmic, Inhalation, Through the skin.
1735.1(y)	**Lynn Paulsen**	Potency USP 797 requirements of +/- 10% is not addressing the dilution of commercial product. They are addressing making a product from chemical ingredents. Need to define dilutions separately because of titrations. Commerical products are already +/-10% and then are diluted the resulting diluted product will exceed +/-10%. USP standard is for USP products and is different than diluting products.
1735.1(y)	**Jeannette Hanni**	Exempt when final product is the result of dilutions. Example: 1gram in 250cc bag. The bag is already is +/- 10% (USP Standard). Adding the 1gram will change the potency further.

Code Section	Commenter	Comment
1735.1(y)	**Doug O'Brien** Kaiser Permanente	Recommendation: ""Potency" means active ingredient strength within +/- 10% of the labeled amount for sterile commercial products. Rationale: Sterile commercial products are already at +/- 10% so unable to meet this requirement for sterile compounded preparations in which multiple commercial products are utilized to compound the final preparation.
1735.1(y)	**BJ Bartleson** California Hospital Association	With the definition as stated, the potency definition will be impossible to meet. For example: a typically compounded product is Vancomycin 1 gram injected into a 250 ml bag of normal saline. The 250 ml bag is a commercially available product purchased from manufacturers who may add as much as 25 ml's of overfill to their bags, which would result in a volume of 275 ml's. The 1 gram Vancomycin vial from the manufacturer is reconstituted with 20 ml's of sterile water and added to the 275 bag of saline, equaling a final volume of 295 ml's resulting in a final concentration of 3.39 mg/ml (1000mg/295ml), the labeled potency of the 1g/250ml piggyback would result in a discrepancy of 15%- well above the +/-10% allowance. These are simple compounds from standard manufacturer ingredients and will result in a continuous state of ono-compliance with the potency range as defined in the proposed regulations.
1735.1(y)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: USP 797 only describes potency in terms of ensuring potency by monitoring controlled storage areas. In addition, considering the many drugs that could be compounded (biosimilars, immune mediators, blood derivatives, etc) it may be too arbitrary to put such a hard limit on this definition. Solution: Remove section that defines "potency" altogether.
1735.1(ab)	**Amy Gutierrez**	At today's sterile compounding training, we discussed the use of sterile compounding robots, which have become popular in California. As we don't have reference to robots in our regs, I am proposing a modification to 1735.1 (ab) to the following (changes in bold): (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, **sterile compounding automated robots**, compounding aseptic isolators, and compounding aseptic containment isolators.
1735.1(ae)	**Marie Cottman** Pacific Compounding Pharmacy	Comments: "…the absence of inactive ingredients other than those listed on the master formula record." There are times when the compounding record inactive ingredients will slightly deviate from the master formula record. For instance, if the sweetener stevia is outdated, we may use (one time only) acesulfame as the sweetener. Or we may use Ora Plus sugar free in place of Ora Plus, if there is a backorder from our wholesaler for the Ora Plus listed in the master formula record. When these rare changes take place, compounders SHOULD MAKE NOTE ON THE COMPOUNDING RECORD, but should not be required to modify the master formula record. Please note: these are rare exceptions. Recommendation: Change "master formula record" to "compounding record."

Code Section	Commenter	Comment
1735.1(af)	**Doug O'Brien** Kaiser Permanente	Recommendation: Allow compounding of hazardous drugs in a segregated compounding area within a CACI by removing the language "non-hazardous". The applicable sentence would read, "The segregated sterile compounding area shall be restricted to preparing non-hazardous sterile to sterile compounded preparations." Rationale: The USP 797 definition of a Segregated compounding area is "a designated space, either a demarcated area or room, that is restricted to preparing low-risk level CSPs with 12 hour or less BUD". USP 797 section Placement of Primary Engineering Controls allows placement of a CACI (used for hazardous drug compounding) in less clean than ISO Class 7 areas if the following conditions are met: -The isolator shall provide isolation from the room and maintain ISO Class 5 during the dynamic operating conditions, including transferring ingredients, components, and devices into and out of the isolator and during preparation of CSPs -Particle counts sampled approximately 6 to 12 inches upstream of the critical exposure site shall maintain ISO Class 5 levels during compounding operations -Not more than 3520 particles per m3 shall be counted during material transfer, with the particle count probe located as near to the transfer door as possible without obstructing the transfer.
1735.1(af)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: Many hospitals have established pharmacy satellites nearby patient care areas to serve our most vulnerable patients (e.g. Intensive Care Units). The central pharmacy is too far from these patient care areas and the pharmacy satellites provide a venue to provide patient care that is closer to the patients. These pharmacy satellites are one room that provides a place for the pharmacy to perform order verification, drug storage, and drug preparation. Many of the pharmacy satellites have very limited room, thus the pharmacy will place compounding aseptic containment isolators (CACIs) which are enclosed to the surrounding environment and should have evidence from the manufacturer that they meet USP chapter 797 and Controlled Environment Testing Association (CETA) requirements. If one were to believe that this is an unverified study then one would have to question most of the conclusions derived from USP 797 as many of the conclusions taken from there are not based on "randomized controlled trials". We believe that we can remove the 3 foot no sink/drain requirement when CACIs are used to support pharmacy satellites. The alternative would be to close these pharmacy satellites that do not have the room to abide by the 3 foot no sink/drain rule which is not consistent with a patient centered care model. Solution: Make an exception that if the ISO Class 5 PEC is a CACI, that the three foot sink/drain rule does not apply while maintaining that sinks and drains should not be placed in a buffer area or in ISO class 7 or better.
1735.1(af)	**Anonymous**	Recommendation/ Comments: While some PEG may gain benefit by having the 3 foot perimeter, other PEG's such as barrier isolators does not have such requirement, yet for other poorly designed PEGs, the 3 foot may still not be enough. Therefore, the size of the demarcated area should be according to PEG's mfg recommendation/specification, rather than a fixed 3 foot for all. I checked with my barrier isolator mfg, and there is a list of location requirements and specifications, but mfg does not require a 3 foot clearance. Having such clearance provides no additional safety margin. Barrier isolator is already a self-contained "clean room" and "ante room". To require anther 3 foot clearance around it is like saying there needs to be 3 foot clearance outside the clean room. The fiscal impact of this regulation is much more than anticipated, and in some cases, there is no safety margin gained. Many smaller hospitals and satellite pharmacies have recently undergone renovations to be in compliance with the current regulation. Most isolators are 4 to 5 foot wide. Requiring another 3 foot perimeter means the room has to be at least 10 foot. Smaller hospital pharmacies and satellite pharmacies simply do not have the space. Passing this regulation would mean more renovations and construction, which may interrupt patient care and reduce safety margin.
1735.2	**Lynn Paulsen**	Some Hospitals have not changed from expiration date to BUDs and the change cannot be done overnight due to the training of thousands of nurses and staff. An implementation schedule over the next year or two would be necessary.

Code Section	Commenter	Comment
1735.2(c)(1)	**Doug O'Brien** Kaiser Permanente	This proposed regulatory language is vague and does not reflect either California statutory authority nor federal case law. The term "fair market value" cannot practically apply to pharmacy-compounded items because there are no published prices that compounding pharmacies can use to determine that fair market value, unlike resources that are available for products approved for distribution in interstate commerce by the FDA. Compounding pharmacies are prohibited by anti-trust law from contacting other compounding pharmacies to discuss established prices. Further, there is no reference material available to even determine which competing pharmacies are compounding and distributing the exact same compounded products. Each compounding pharmacy has to determine its own pricing based on its costs, risk calculations, and marketing strategy. Generally speaking the costs per unit compounded by a pharmacy will be substantially higher than the market value of FDA approved similar products because of a lack of "economy of scale" vs manufacturing facilities. Further, Calif. Business and Professions Code Section 4380 establishes in California statutory law recognition of two federal court cases that allow non-profit institutions to acquire products at prices generally unavailable to for-profit organizations and use of those products for the treatment of specified patients related to the not-for-profit institutions, e.g. certain hospitals and health plans. Such products are often supplied to physicians in medical office environments at no charge for treatment of such patients. This includes pharmacy-compounded products supplied to prescribers for prescriber office use under Business and Professions Code Section 4052(a)(1).
1735.2(c)(1)	**Brian Warren** California Pharmacist Association (Also commented on at hearing by Tony Park)	(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 The proposed requirement that physician office use compounded preparations be sold "at a price that fairly reflects the fair market value of each drug preparation" is arbitrary, difficult to enforce, and beyond the scope of the Board's mandate of protection of the public health and safety. In no other statute or regulation does the Board attempt to regulate the prices or pricing of prescription drugs dispensed by pharmacists. The Board's Initial Statement of Reasons states that the changes to Section 1735.2 are intended to ensure that compounding regulations reflect current statutory provisions and are in alignment with USP 37 <797>. does not specify the purpose for this change.
1735.2(d)(3)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: Many medications that are in short supply in "real time" may not be on the ASHP or FDA drug shortage list in a timely manner (e.g. most recent example IV Protonix January 2015). ASHP and FDA recognize that this may happen as they have to rely on clear communications to them for their source of information. Solution: Add "Manufacturer, Wholesaler, and/or Distributor acknowledge and provide documentation that the drug is in short supply."

Code Section	Commenter	Comment
1735.2(d)(3)	**Michael Tou** Providence Health	(d) No pharmacy or pharmacist shall compound a sterile drug preparation that: (3) is a copy or essentially a copy of one or more commercially available compendial drug products… The current wording of 1735.2(d)(3) prohibits pharmacies from diluting their own vancomycin 1 gram as in the example above because it is "essentially a copy" of a commercially-available drug product. The implications of this restriction would be far-reaching: - Costs to pharmacies and costs to treat patients would be exponentially more expensive if pharmacies cannot compound their own sterile IVPBs even when a commercial premix product is available. - Manufacturers who produce premixed products would corner the market and profit from this regulation. Generic drug manufacturers that produce FDA approved drug vials and solutions to be used for sterile compounding will suffer. - Drug shortages will worsen since premix sterile dilution products are the only ones that could be used in the state. It will drive the demand for these premix IVPB products and the lone manufacturers would not be able to meet the needs of pharmacies. - In the event of a drug recall of a premix commercially-available product, pharmacies may not be able to perform compounding unless the drug appears on the ASHP or FDA drug shortage list. If the rest of the country is not restricting pharmacies from compounding copies or essential copies of commercially-available drug products, no shortage will be listed. Even TPN (total parenteral nutrition) is available commercially as premixed bags. TPN contents are usually customized to meet the nutrition, caloric, and electrolyte needs for the patient. Some of the TPN formulas are available as premixed bags from the manufacturers. The language in this section would prohibit the pharmacy from preparing a TPN formula that matches those available as TPN products. It would not be feasible for pharmacies to stock every commercially available TPN bag in order to provide the TPN needs for every patient. Being able to compound the TPN using sterile products is a necessity. **Continued on Next Row:**
1735.2(d)(3)	**Michael Tou** Providence Health	**Continued from Previous Row:** We agree that preparation of sterile drug products that are copies or essentially copies of commercially-available drug products should be prohibited when those processes involve utilizing non-sterile ingredients to prepare sterile drug products unless there is a documented current drug shortage and appropriate safety measures and procedures are followed. For example, preparation of calcium chloride sterile solution for injection utilizing non-sterile calcium powder. Non-sterile compounding of commercially-available drugs should be permitted for non-parenteral administration. For example, caffeine citrate oral solution is commercially available in a ready-to-administer solution but is also safely compounded utilizing caffeine powder, citric acid powder, and water to prepare essentially the same drug product with the strength/concentration and formulation. Stability studies have been done on the extemporaneous compounded formulation from these powders and have been shown to be safe and effective for treating patients.
1735.2(e)(5)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: The language may be too broad. We understand it would be hard to place exactly what is required considering all of the entities that will be using these regulations, but perhaps we can narrow the language by inserting phrases such as "essential compounding steps". This will help facilitate pharmacies to receive approval during the policy approving process who are based in institutions with multidisciplinary committees by leaving out unwanted minutia of the compounding process in policies and procedures. Solution: Reword section to state "Specific and essential compounding steps used to prepare the drug"

Code Section	Commenter	Comment
1735.3(a)(1)	**Marie Cottman** Pacific Compounding Pharmacy	Comment: The description of this section warrants naming the document that will contain all of this information (a)(1) through (a)(9). In practice it is referred to as a compounding log or formula log. Recommendation: Clarify the reference term for the document that is described in section 1735.3(a)1 as a "compounding formula record" or "compounding record" or "compounding work sheets" as referenced in 1751.3 (b)(1). Question: Can the master formula record be contained in electronic format? Though the master formula record is critical to consistency from batch to batch (or lot to lot) of the same compounded preparation, it does not contain any information that would not be included on the compounding record (which is much more specific to what and how a preparation was made). Recommendation: Clarify that the master formula record must be available but does not have to be maintained WITH the compounding record.
1735.3(a)(5)	**Marie Cottman** Pacific Compounding Pharmacy	Comments: The term "component" is inconsistent with language in section 1735.2 e1 and 1735.2 e4 which reference active ingredients and inactive ingredients respectively. Recommendation: Change the term "component" to "ingredient."
1735.3(a)(6)	**Marie Cottman** Pacific Compounding Pharmacy	Comments: The term "component" is inconsistent with language in section 1735.2 e1 and 1735.2 e4 which reference active ingredients and inactive ingredients respectively. Recommendation: Change the term "component" to "ingredient."
1735.3(a)(6)	**Doug O'Brien** Kaiser Permanente	Recommendation: Include ambulatory oncology clinic pharmacies in the seventy-two (72) hour exception language, in a manner similar to inpatient pharmacies. Rationale: Ambulatory oncology clinic pharmacies compound preparations in a similar manner to inpatient pharmacies
1735.4(c)	**Brian Warren** California Pharmacist Association	(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 and shall not be subject to minimum font size requirements. The Board is proposing to add the name of the compounding pharmacy and dispensing pharmacy to the text of what must be included on unit-dose containers that are too small or otherwise impractical for full compliance with all labelling requirements. Adding this additional text to unit-dose labels may place space limitations on those labels, thereby necessitating that labels be printed in a smaller font size. This modification is within the scope of these proposed regulations because the Board is adding additional text to be included on the label.
1735.5(a)	**Brian Warren** California Pharmacist Association (Also commented on at hearing by Tony Park)	(a) Any pharmacy engaged in compounding shall maintain a written policy~~y~~ies 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 ***material*** failure to follow the pharmacy's written policies and procedures ***may*** ~~**shall**~~ constitute a basis for disciplinary action. Regulations should give the Board the authority to take disciplinary action, they should not require that the board take disciplinary action. Additionally, disciplinary action should be taken for material failure to follow policies and procedures, not for any deviations irrelevant to the compounding of drugs.

Code Section	Commenter	Comment
1735.6(d)	**Brian Warren** California Pharmacist Association (Also commented on at hearing by Tony Park)	(d) ***(1)*** 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. ***(2) Any pharmacy engaged in any hazardous drug compounding shall perform such compounding with the use of a powder containment hood.*** All pharmacies compounding hazardous drugs should use powder containments hoods to ensure pharmacist and pharmacy technician safety.
1735.8(c)	**Doug O'Brien** Kaiser Permanente	Recommendation: "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, of compounded drug preparations. The criteria by which preparations would be tested for potency, quantitative analysis, and labeled strength analysis shall be described in the quality assurance plan. All qualitative and quantitative analysis reports for compounded drug preparations shall be retained by the pharmacy and maintained along with the compounding record and master formula. Rationale: This language could be interpreted to require that quantitative and qualitative analysis be performed on all compounded products regardless of cost, availability of the actual assay, or scientific validity. It has been our experience that some Board of Pharmacy inspectors have interpreted this language to require end product potency testing of all pharmacy-compounded products. KP. Many pharmacy professionals disagree with those requirements as they are inconsistent with the intent and provisions of the regulation 1735, et. seq. Pharmacies are compliant with 1735.8(c) if they have a PLAN that includes the elements mentioned above. Quantitative and qualitative laboratory type testing is not required unless specified for each product in our policies and procedures generally or by category - or in the Master Formula for a particular product. Test records of tests only have to be retained if such test was done either as a matter of policy or pursuant to an investigation after the raising of a quality concern for particular compounded preparation or a batch of a compounded preparation. Please see the detailed testimony from KP regarding this issue which was presented to the BOP Enforcement and Compounding Committee on September 16, 2014. The Board's proposed regulation language perpetuates substantial confusion and inhibits compliance and enforcement. As proposed the regulation would add major costs to hospital and other pharmacy-compounding thus adversely affecting the cost and affordability for therapeutic availability, the effectiveness and safety of patient care with scientific justification.
1735.8(e)	**Douglas Barcon** Barcon & Associates	Change "or" to "and", so the QA plan includes responding to out-of-range temperatures in the pharmacy and patient care areas versus one or the other.
1751(b)(3)	**Brian Warren** California Pharmacist Association	~~(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, with the exception of emergency eye rinsing stations. A sink may be located in an ante-area. This comment was submitted during the last rulemaking and had been accepted, though was not incorporated into this rulemaking. Additionally, the definition of a segregated sterile compounding area in Section 1735.1(af) includes the exception for emergency eye-rinsing stations. The emergency eye-rinsing station should be included here for consistency.

Code Section	Commenter	Comment
1751(b)(3)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: Many hospitals have established pharmacy satellites nearby patient care areas to serve our most vulnerable patients (e.g. Intensive Care Units). The central pharmacy is too far from these patient care areas and the pharmacy satellites provide a venue to provide patient care that is closer to the patients. These pharmacy satellites are one room that provides a place for the pharmacy to perform order verification, drug storage, and drug preparation. Many of the pharmacy satellites have very limited room, thus the pharmacy will place compounding aseptic containment isolators (CACIs) which are enclosed to the surrounding environment and should have evidence from the manufacturer that they meet USP chapter 797 and Controlled Environment Testing Association (CETA) requirements. If one were to believe that this is an unverified study then one would have to question most of the conclusions derived from USP 797 as many of the conclusions taken from there are not based on "randomized controlled trials". We believe that we can remove the 3 foot no sink/drain requirement when CACIs are used to support pharmacy satellites. The alternative would be to close these pharmacy satellites that do not have the room to abide by the 3 foot no sink/drain rule which is not consistent with a patient centered care model. Solution: Make an exception that if the ISO Class 5 PEC is a CACI, that the three foot sink/drain rule does not apply while maintaining that sinks and drains should not be placed in a buffer area or in ISO class 7 or better.
1751(b)(3)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: In the March 2015 BOP Draft (5th Draft) there was verbiage that stated "with the exception of emergency eye-rinsing stations". We believe that this exception is the safest for the employees preparing sterile products and complies with NIOSH Guidelines. Solution: Reinsert the exception to include emergency eye-rinsing stations in these areas in addition to the above solution (Number 2) to allow CACI's be an exception also.
1751.1	**Judith Brosz and Robert Stein**	(a) In addition to the records required by section 1735.3 , any pharmacy engaged in any compounding of sterile drug preparations, shall make and keep the following records within the pharmacy: (1) Documents evidencing training and competency evaluations of ~~employees~~ Sterile Compounding Personnel in sterile drug preparation policies and procedures. (2) Results of hand hygiene and garbing assessments of Sterile Compounding Personnel with integrated gloved fingertip testing. (3) Results of assessments of ~~personnel~~ Sterile Compounding Personnel for aseptic techniques including results of media-fill tests and gloved fingertip testing performed in association with media-fill tests. References to personnel made more specific to indicate those actually engaged in sterile compounding in the controlled environment.

Code Section	Commenter	Comment
1751.1	**Michael Tou** Providence Health	Add to Section 1751.1 definition: Compendial drugs are drug products or preparations for which there is a monograph provided in an official compendia (e.g. United States Pharmacopeia, National Formulary, or Homeopathic Pharmacopeia) recognized by the Food, Drug, and Cosmetic Act. The compendium sets forth standards for the strength, quality and purity of the drug product. -OR- Add: (4) Compounding (reconstitution and/or dilution) of FDA approved drug products is excluded from this restriction. If the intent of the board was to prevent what would essentially be the manufacturing of copies of compendial drug products by pharmacies, the language needs to be modified to clearly indicate this. Dilution/reconstitution and compounding of drug products using FDA-approved drug products should be exempted. Providence recommends changing the language to allow compounding (reconstitution and/or dilution) using FDA-approved drug products. The proposed language seen in the center column can be interpreted to prohibit dilution of FDA-approved drug products per FDA instructions, if there is a pre-diluted (premix) drug product commercially available. As defined in 1735.1(l) “copy or essentially a copy” of a commercially-available drug product would include all diluted intravenous infusion bags, including IV piggy backs or IVPBs that are available as premix bags from the manufacturer. Some brand name manufacturers have FDA-approved “premixed” IV bags that are ready-to-administer and are virtually the same preparation as other FDA-approved drug vials that are diluted prior to administration per the FDA-approved package insert instructions. Premix IV bags would fall into the definition since they are commercially-available drug products. **Continued in Next Row:**
1751.1	**Michael Tou** Providence Health	**Continued from Previous Row:** For example: Vancomycin is available as a frozen premix IVPB bag in different strengths that are the most commonly prescribed (e.g., 1 gram). The frozen premix bag is thawed and administered to the patient without further dilution. Vancomycin is more commonly available as a sterile powder vial that requires further dilution (per FDA-approved package insert instructions and labeling) into an IV solution bag prior to administration. Vancomycin premix IVPB is 1 gram of vancomycin in D5W 200ml. Pharmacies can typically prepare that same IVPB bag of 1 gram of vancomycin in D5W 200ml using a vancomycin sterile powder vial, reconstituting it as directed with sterile water and further diluting the 1 gram amount into an IVPB bag of D5W solution. The resulting preparations are the same: same active and inactive drug and diluent, same dose, same volume. The cost of utilizing the sterile powder vial of vancomycin and the plain D5W IV solution bag is less expensive than purchasing the vancomycin bag that is already diluted and ready-to-administer.
1751.1(a)(5)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: In the March 2015 BOP Draft (5th Draft) there was verbiage that stated the recordation was for “sterile compounded drug preparations”. The new verbiage removed the word “sterile” implying that all compounded drug preparations required this documentation which in not the focus of the intended section. Solution: Reinsert the verbiage “sterile” in the compounded drug preparation requirement to maintain consistent with the section.
1751.1(a)(5)(c)	**Douglas Barcon** Barcon & Associates	There is no definition of “controlled freezer temperature” in USP general chapter 659 Packaging and Storage Requirements, USP 797, or the general notices in USP-37 NF-32. Suggest deletion of the word “controlled” as in 1735.1 (j) comment.

Code Section	Commenter	Comment
1751.1(a)(7)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: USP 797 allows for at least daily documentation or by using a continuous recording device. We would like to continue to allow the use of a continuous recording device as an alternative which would also give the facility better “real time” data. Solution: Reword the section to state “Documents indicating daily recordation or by continuous recording device of air pressure differentials…”
1751.1(a)(10)	**Marie Cottman** Pacific Compounding Pharmacy	Comments: The terms “preparation work sheet” and “master work sheet” are inconsistent with compounding record and master formula record. Recommendation: Be consistent in the terms for a master formula record (well prescribed in section 1735.3) and the compounding record (see comments regarding 1735.3 (a)(1).
1751.2(b)	**Marie Cottman** Pacific Compounding Pharmacy	Comments: This can become a very long list depending on the formulation. Why do we need to include the inactive ingredients as well as the active ingredients when this is not done for non-sterile compounding? Do you want us to list on the label how much hydrochloric acid or sodium hydroxide we added to get to the right pH? How would this be indicated correctly? For instance, we start with a 1% HCl solution and add 3 drops to a final volume of 15 ml…. the math to determine the final strength is doable (0.01%), but may vary from batch to batch and will have no relevance to the end user. Recommendation: Please provide clarification on implementation specific to inactive ingredients.
1751.2(b)	**Michael Tou** Providence Health	Name and strength, volume or weight of each <u>active</u> ingredient contained in the sterile drug preparation. Request clarification or guidance on this requirement for “each ingredient:” - Are inactive ingredients required on the label? - If inactive ingredients are required on the label, please exclude inactive agents used to reconstitute a powder vial (e.g., sterile water) that will be further diluted in solution for the sterile compounded drug preparation. If sterile water appears on the label of the compounded sterile drug preparation, it would be confusing for those reading the label since the sterile water for reconstitution is not part of the prescription or drug order and of no clinical significance to the patient. - Providence recommends that each active ingredient be required on the label and the only inactive ingredient(s) required should be the final diluent solution used to dilute the sterile compounded preparation’s active ingredient. This would be consistent with the modified language proposed in 1735.1(ae). 1735.1(ae) implies that only active ingredients are listed on the label and inactive ingredients do not have to be listed on the label because they are in the compounding log: (d)(w)(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 noted on the compounding log label. - 1735.4(c) requires the name(s) of the active ingredient(s) only. It does not require the inactive ingredients as well. - Sterile compounded drug preparations are prepared in single-dose containers or unit-dose containers and each ingredient would not fit on the label if inactive ingredients were also required. **Continued on next Row:**

Code Section	Commenter	Comment
1751.2(b)	**Michael Tou** Providence Health	**Continue from Previous Row:** Providence also recommends changing the requirement of the concentration on the label to include the strength, volume or weight of the ingredient(s). - This would be consistent with labeling requirements from 1735.4(c) that require the name of the active ingredient(s), strength, volume or weight of the preparation. - B&PC 4076 requires only the strength of the drug. - If the active ingredient dose or strength is on the label and the final volume of the diluent is also on the label, then the concentration should not be required. Most drugs that are sterile compounded preparations are prescribed, ordered and prepared as the drug dose only (not the concentration). For example, prescribers order Vancomycin 1 gram IV once. The current labels typically will state the drug name, dose, and volume and name of the appropriate diluent: "Vancomycin 1 gram in 200ml of Normal Saline." This is much more clear and accurate than if the label were to state vancomycin 5mg/ml which is the concentration.
1751.3	**Judith Brosz and Robert Stein**	(a) Any pharmacy engaged in compounding sterile drug preparations shall maintain a written policies and procedures manual for compounding that includes, in addition to the elements required by section 1735.5, written policies and procedures regarding the following: … (12) Orientation, training, and competency evaluation of ~~staff~~ Sterile Compounding Personnel 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. The original word "staff" may be subject to misinterpretation and lead to a universal practical testing requirement in a pharmacy. Additionally, in various sections of the proposed regulations, staff are referred to as "personnel," "staff," and "employees." We believe these terms are intended to refer to the same individuals and recommend using consistent terminology.
1751.3	**Lynn Paulsen**	USP 797 requires indentifying CFUs to genesis level to trigger action. This is because individual bacteria of a specific type may trigger action; while others may not require immediate action until 10 or more CFUs are identified.
1751.3(a)	**Marie Cottman** Pacific Compounding Pharmacy	Comments: The items in this list are fine, but the order of this list is awkward and feels like someone just threw a bunch of ideas down during a brainstorming session. Recommendation: Sort this list by importance, sequence of events (Garbing and Gloving procedure should occur before fingertip testing), or alphabetically as done for definitions.
1751.3(b)(1)	**Marie Cottman** Pacific Compounding Pharmacy	Comments: The term "compounding work sheets" is inconsistent with language in several other sections. Recommendation: Change "compounding work sheets" to "compounding formula record."

Code Section	Commenter	Comment
1751.4(d)	**Doug O'Brien** Kaiser Permanente	Consider a typical scenario in a clean room in a hospital pharmacy. During a 15-minute period of compounding operations, pharmacy personnel could compound four doses of azithromycin 500 mg/250mL dextrose 5% for four different patients, two doses of famotidine 40 mg in 250mL dextrose 5% 250mL for one patient, and five doses of furosemide 100mg/100mL dextrose 5% for five different patients. Under the definition of "lot", pharmacy personnel would be required to clean and disinfect the ISO Class 5 PEC before and after each lot – four times in 15 minutes. If one considers the number of lots that would be compounded in four hours, the PECs would need to be cleaned and disinfected 50 to 60 times. We therefore recommend that 1751.4(d)(2) be deleted. Subsections 1751.4(d)(1) , 1751.4(d)(3) , and 1751.4(d)(4) are sufficient. Proposed language adds confusion and inhibits compliance and enforcement Unnecessary cleaning delays product provision and increases costs that will adversely affect patient access to care.
1751.4(d)	**William Stuart** Hartley Medical	Recommend: (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~~ batch; (3) Not longer than 30 minutes following the previous surface disinfection when ongoing compounding activities are occurring; ~~(3)~~(4) After ~~each~~ spills; and (5) When surface contamination is known or suspected. Rationale: We recommend remaining consistent with USP <797> guidelines. Site: ISO Class 5 Primary Engineering Control Minimum Frequency: "At the beginning of each shift, before each batch, not longer than 30 minutes following the previous surface disinfection when ongoing compounding activities are occurring, after spills, and when surface contamination is known or suspected" (Source: Chapter <797>, Table 3. Minimum Frequency of Cleaning and Disinfecting Compounding Areas, USP 38-NF 33, February 2015)
1751.4(d)	**BJ Bartleson** California Hospital Association	No change in wording proposed- Simple recommendation to changing the numbering from 1751.4 (d) to 1754.4 (d)(1) for entire section so the below can be added.
1751.4(d)(2)	**BJ Bartleson** California Hospital Association	Insert new language, "alternate cleaning schedules may be submitted to the Board, as in the case of fully automated IV robots" A contained robotic compounder is possible contaminated by the cleaning process. An alternative schedule such as mini clean daily, full clean weekly, etc., should be appended to the self-assessment form with documentation for the first submission.
1751.4(d) & (e)	**Lynn Paulsen**	Add language for self cleaning robot. A self-contained robot is not cleaned after every prep. Contamination comes from hands and arms. Mini-clean once a day, full clean once a week. Manufacturer instructions. Board can review alternative methods for approval. The cleaning requirements as is would eliminate the ability to use robotics in California.

Code Section	Commenter	Comment
1751.4(d)(2)	**Rheta Sandoval** Kaweah Delta Health Care	Cleaning AND disinfecting surfaces of the ISO Class 5 PEC before and after each lot (per the proposed definition in 1735(t)) may not be feasible depending on the scale of operations. There could be interference with timely medication preparation and dispensing in the hospital setting and significant operational impacts. For hospital pharmacies that are preparing upwards of 60,000 dosage units annually, 5 minutes or more spent cleaning surfaces followed by disinfecting surfaces in the ISO 5 PEC before and after compounding each "lot" would have a definite impact on operations and costs. USP and ASHP Guidelines on Compounding Sterile Preparations requires cleaning and disinfecting before each batch, with a "batch" defined differently than the BOPs proposed definition of "lot". Adopting USP 797s minimum frequency of cleaning and disinfecting the PEC with the term "batch" interchanged with "lot" could result in a regulation that would be difficult if not impossible for some facilities to comply with depending on compounding volume. The USP intent of the cleaning the PEC with a germicidal detergent is that it only needs to be done once a day (end of the compounding day or the beginning) (Personal Communication. Eric S. Kastango, MBA, RPh, FASHP. 3/25/15). The work areas need to be disinfected with sterile IPA or another suitable agent before each batch (Personal Communication. Eric S. Kastango, MBA, RPh, FASHP. 3/25/15). In the "Cleaning and Disinfecting the Compounding Area" section of USP <797>, it states "When the surface to be disinfected has heavy soiling, a cleaning step is recommended prior to the application of the disinfectant". In light of these points and keeping the general principle of cleaning in mind, that "all surfaces need to be visibly wetted, but not dripping, and the agent must be allowed to air dry" (K. Douglas, ES. Kastango. Requirements and Best Practices for Sanitizing Engineering Controls, pppmag, September 2013), the proposed regulation 1751.4(d)(2) is not feasible across all pharmacy sterile compounding settings. Please consider the following modification: 1. Revise 1751.4(d)(2) to read: before and after each lot (at minimum, disinfection);
1751.4(d)(2)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: The most recent USP 797 regulations state that cleaning of the ISO 5 PEC should occur at the beginning of each work shift, before each batch (USP 797 only uses the word batch in referencing high-risk compounding) preparation is started, every 30 minutes during continuous compounding periods of individual CSPs, when there are spills, and when surface contamination is known or suspected from procedural breaches. With the new proposed definition of "lot," interruption of workflow of hospital compounding in order to clean before and after each lot may impact the timeliness of medication delivery to patient and could introduce potential for medication errors. Solution: Remove "before and after each lot" and replace with "every 30 minutes during continuous compounding."
1751.4(d)(4)	**Marie Cottman** Pacific Compounding Pharmacy	Comments: We do not access our cleanroom on a daily basis, but use it approximately one or two times per week. As "daily" is defined in section 1735.1(m) as every day a pharmacy is operating, this regulation would require that my staff enter and clean the counters, work surfaces and floors even on days that the facility is not used! This, in my opinion, would increase the risk of contamination by excessive entry that is not necessary. Recommendation: Clarify the regulation by changing "daily" to "on each day of use."
1751.4(e)	**BJ Bartleson** California Hospital Association	"Outside the PEC, counters, cleanable work and table surfaces and floors shall be cleaned with germicidal detergent and rinsed with water daily. Walls, ceilings, storage shelving, and stools shall be cleaned with a germicidal detergent and rinsed with water monthly " CHA has concerns that the definitions of disinfectants and germicidal detergent overlap significantly. Disinfection of walls, ceilings, stools and floors as separate and distinct from the germicidal detergent is not supported by evidence.

Code Section	Commenter	Comment
1751.4(e)	**Michael Tou** Providence Health	Counters, and cleanable work surfaces ~~and floors~~ shall be cleaned with a germicidal detergent and water and disinfected with a suitable agent daily. Floors in the buffer or clean area, ante-area, and segregated compounding area are cleaned by mopping with a cleaning and disinfecting agent once daily at a time when no aseptic operations are in progress. Providence recommends adding USP 797 wording for floor cleaning requirements. The current proposed wording of this section requires a three-step cleaning for floors which USP 797 does not require (a germicidal detergent and water and a disinfecting agent). If a single cleaning agent both cleans and disinfects it can be used alone according to USP 797. Water is not required separately for floor cleaning and a separate disinfecting agent is not required.
1751.4(e)	**Lynn Paulsen**	Stated 1754.4 @ hearing; however, that section does not exist. Germicidal cleaner – Need to identify the difference between germicidal cleaner and disinfectant. Germicidal clearner is a disinfectant with detergent. USP 797 germicidal cleaner followed by water. Hood would be cleaned with germicidial cleaner and alcohol. Change language for floors, ceailing, walls, shelves – clean with germicidal cleaner and water and nothing after that.
1751.4(f)	**Douglas Barcon** Barcon & Associates	Within the same section of USP 797 that includes numbers (1), (2), and (3) criteria, it also states: “It is incumbent on the compounding personnel to obtain documentation from the manufacturer that the CAI/CACI will meet this standard when located in environments where the background particle counts exceed ISO Class 8 (see Table 1) for 0.5-um and larger particles.” While criteria (1), (2), (3) include “shall” as in the source text of USP 797 in the section on placement of primary engineering controls, the intent in USP 797 is to also include manufacturer documentation that the CAI or CACI will meet criteria (1), (2), (3) in conditions worse than an ISO Class 8 ante-area, i.e., uncontrolled air quality or non-ISO classified room. Note that USP 797 makes no reference to placement of a CAI or CACI in an ISO Class 8 compliant area. It must be inferred that CAI or CACI placement in such area would fall under the same category as air quality worse than ISO Class 8 because it exceeds ISO Class 7. Suggest add (4): (4) manufacturer documentation/certification states that the CAI or CACI is compliant with (1), (2), and (3) of this section when located in located in environments where the background particle counts exceed ISO Class 8 for 0.5-um and larger particles or is a non-ISO classified area. The addition of “or is a non-ISO classified area” was made because CAI/CACI manufacturers also test their units for compliance in regular room air, which is not tested for ISO compliance but generally is worse than ISO Class 8. Section 1751.4 (h) addresses placement of a CAI in a non-ISO classified room but seems out of sync with the criteria in section 1751.4 (f) and conflicts with it if not changed.
1751.4(g)	**Brian Warren** California Pharmacist Association	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. The proposed regulations require use of a hair cover, beard cover, full gown, and shoe covers. Given the complete isolating nature of compounding within aseptic containment isolators, it is unclear why these garbing requirements are necessary.

Code Section	Commenter	Comment
1751.4(g)	**BJ Bartleson** California Hospital Association	Remove the last sentence that states, “where the documentation provided by CACI manufacturer does not require garbing, only the two glove requirement shall apply” CHA believes that a CACI manufacturer should not eliminate the requirement for protective garb and feels this has been confused with CAI requirements.
1751.4(g)	**University Compounding Pharmacy** Joe Grasela	Gloves tested to meet ASTM 6978-05 are standard practice for assessment of resistance of medical gloves to permeation by chemotherapy drugs. Why is it necessary to double glove? USP 800 doesn't require or propose a double glove when working with hazardous compounds. During the hazardous drug compounding that is performed in a compounding aseptic containing aseptic containment isolator, full hand hygiene and garbing must occur, complete with hair cover,...and two layers of gloves with the outermost glove tested to meet ASTM 6978-05.
1751.4(i)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: The most recent USP 797 regulations state that viable surface sampling be done periodically. Many hospitals conduct surface sampling every six months to coincide with the requirements for PEC and cleanroom certification. Pharmacies may also not have access to qualified individuals every quarter for surface sampling, but would have access to these qualified individuals every six months for the PEC and cleanroom certifications. Solution: Reduce the viable surface sampling requirement to every six months to coincide with other sampling that will be performed by qualified outside vendors.
1751.4(j)	**Brian Warren** California Pharmacist Association	(j) The pharmacy shall have a comfortable and well-lighted working environment, which includes a***n appropriate*** 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. The structure of the working environment standards in Section 1751.4(j) do not contemplate compounding pharmacies using exclusively compounding aseptic isolators and/or compounding aseptic containment isolators. Some of these PECs do not require full garbing. If a compounding pharmacist is not wearing full garbing, the proposed temperature of 20 degrees Celsius may be uncomfortably cold for that pharmacist. We recommend requiring that comfortable conditions be maintained without mandating a specific temperature.
1751.4(j)	**Judith Brosz and Robert Stein**	(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~~ Sterile Compounding Personnel when attired in the required compounding garb.
1751.4(j)	**Anonymous**	Since this proposed regulation is intended to address comfort, then it should be a range to accommodate everyone. What is a comfortable temperature is very subjective. Some Californians will find 68 degrees too cold, especially during winter. There is already a regulation defining controlled room temperature. Do we really need another state law to tell us what is comfortable for us? Please let me decide what is comfortable for me.
1751.4(j)	**Lynn Paulsen**	Some Hospitals do not have air conditioners or may keep an area cool, but not at or below 68 degrees. Recommendation is to eliminate temperature or change the wording. The cost to add air conditioning to hospitals would be substantial and would not be offset by patient safety.
1751.4(j)	**BJ Bartleson** California Hospital Association	Remove temperature requirement so section will read: “The pharmacy shall have a comfortable and well lighted working environment that maintains comfortable conditions for compounding personnel when attired in the required compounding garb.” Some hospital pharmacies are challenged with precision temperature control, however can continue to maintain a comfortable temperature for employees. The exact temperature stated in this section cannot be supported by evidence and is not required by Cal/OSHA. Therefore, CHA recommends removal of the exact temperature of 68 degrees.

Code Section	Commenter	Comment
1751.4(j)	**Douglas Barcon** Barcon & Associates	The temperature in this section should pertain to the sterile compounding area only per USP. It should not pertain to the whole pharmacy. Cooling the entire pharmacy to 68 degrees Fahrenheit will generally cause staff not garbed for compounding to feel cold and will cause excessive HVAC energy consumption. This may be good to increase profits for PG&E, Southern California Edison, and Sempra Energy, but is not an efficient use of energy.
1751.5(a)(4)	**Judith Brosz and Robert Stein**	(a)(4) ~~Compounding personnel~~ Sterile Compounding Personnel shall not wear hand, finger, or wrist jewelry. If jewelry cannot be removed then it must be thoroughly cleaned and covered with a sterile glove.
1751.5(a)(6)	**Doug O'Brien** Kaiser Permanente	Recommendation: Change the wording to indicate that only persons with "exposed" rashes, sunburn, weeping sores, etc. and "exposed" cosmetics" be excluded from the designated areas. "Individuals experiencing with exposed rashes, sunburn, weeping sores, conjunctivitis, active respiratory infections, or those wearing exposed cosmetics shall be excluded from the ISO Class 5 and ISO Class 7 compounding areas until their conditions are remedied." Rationale: The is no risk to patients unless the specified conditions are exposed. Proposed language adds confusion and inhibits compliance and enforcement. The is only a safety risk if the conditions specified are exposed. The rest of section 1751.5 specifies that 100% or nearly 100% of a person's body is covered with "Personal protective equipment", from head to toe. The proposed unnecessary provision would cause patient care delays and increase costs that will adversely affect patient access to care. If a NON-exposed condition is discovered after compounding, this proposed regulation provision would cause confusion about what subsequent procedure should be followed. Should the product be recalled despite no risk from a NON-exposed condition? Further, there are serious employee privacy concerns. Should management require a "strip search inspection" before each compounding session to assure that products will not have to be recalled?
1751.5(a)(6)	**Dennis Lau**	Many hospital pharmacy departments are staffed with very few staff members thereby necessitating all staff members, including administrators to be called into action for compounding sterile products. 1. Could the Board specify the cosmetic types or formulations not allowed (shedding of flakes and particles) in ISO Class 5 and ISO Class 7 compounding areas similar to the FDA cosmetic product categories outlined below? FDA Product category code = 03 [Eye Makeup Preparations] a. Eyebrow Pencil b. Eyeliner c. Eye Shadow d. Eye Lotion e. Eye Makeup Remover f. Mascara g. Other Eye Makeup Preparations FDA Product category code = 07 [Makeup Preparations (not eye)] a. Blushers (all types) b. Face Powders c. Foundations d. Leg and Body Paints e. Lipstick f. Makeup Bases g. Rouges h. Makeup Fixatives i. Other Makeup Preparations 2. Would the Board allow use of face shields as is used in surgery by operating room nurses for persons wearing cosmetics? 3. Would the Board allow use of cosmetic "sealers" used by professional makeup artists?

Code Section	Commenter	Comment
1751.5(a)(6)	**BJ Bartleson** California Hospital Association	"Individuals experiencing active infections, visible rashes or other breaks in exposed skin integrity shall be excluded from the ISO Class 5 and ISO Class 7 compounding areas. Cosmetics, gel nails or nail polish are not allowed. Eyelash extensions are not prohibited." CHA suggests new wording in this section to improve specificity and compliance with the regulation.
1751.6	**Judith Brosz and Robert Stein**	1751.6. Sterile Compounding Consultation; Training of Sterile Compounding ~~Staff~~ Personnel (b) The pharmacist-in-charge shall ensure that all ~~pharmacy personnel engaging in compounding sterile drug preparations~~ Sterile Compounding Personnel have training and demonstrated competence in the safe handling and compounding of sterile drug preparations, including hazardous agents if the pharmacy compounds products with hazardous agents. (d) The pharmacist-in-charge shall be responsible to ensure the continuing competence of ~~pharmacy personnel engaged~~ Sterile Compounding Personnel in compounding sterile drug preparations. (e) Pharmacies that compound sterile drug 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~~ Sterile Compounding Personnel ~~has~~ have the knowledge and skills necessary to perform their assigned tasks properly. … (E) Aseptic preparation procedures using media-fill tests which are as complicated as the most complex manipulations performed by ~~staff~~ Sterile Compounding Personnel and which contain the same amount or greater of volume transferred during the selected manipulations. (2) ~~Each person engaged in sterile compounding~~ Sterile Compounding Personnel must each successfully complete practical skills training in aseptic technique and aseptic area practices.
1751.7(b)	**Judith Brosz and Robert Stein**	(b) ~~Each individual involved in the preparation of sterile drug preparations~~ Sterile Compounding Personnel must each first successfully demonstrate competency by successfully performing aseptic media-fill tests before being allowed to prepare sterile drug preparations. The media fill testing process shall be as complicated as the most complex manipulations performed by ~~staff~~ Sterile Compounding Personnel and contain the same amount or greater of volume transferred during the compounding process. … If microbial growth is detected, then the ~~employee's~~ Sterile Compounding Personnel's sterile preparation process must be evaluated, corrective action taken and documented, and the media-fill testing repeated. ~~Personnel~~ Sterile Compounding 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~~ Sterile Compounding 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 drug preparations is 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.
1751.7(b)	**Judith Brosz and Robert Stein**	(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~~ Sterile 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.

Code Section	Commenter	Comment
1751.7(e)	**Katherine Palmer** **Rita Shane** Cedars-Sinai Medical Center	1751.7 (e) Sterile Compounding Quality Assurance and Process Validation In a circumstance where a 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, (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 **and patient's** written consent to dispense. (2) And subsequent to dispensing: **(A)Send random sample for sterility and pyrogen testing as part of process validation** **(B) Notify physician if results demonstrate microbial growth or pyrogens** **(C) Have protocol approved by the Pharmacy & Therapeutics Committee** Would recommend including this section back into the regulation revision to avoid patient loss of life or intense suffering due to the inability to provide emergency medications to patients. In rare circumstances medications such as Alum and Formalin are needed to treat hemorrhagic cystitis that can be life- threatening. Evidence supports that these drugs are needed when other measures fail. The patient could bleed to death without this provision.
1751.7(e)	**Marie Cottman** Pacific Compounding Pharmacy	Comments: With regards to pyrogen testing, this regulation is in conflict with USP <797>, <85> and <771> recommendations for testing ALL sterile products. USP <797> specifically exempts ophthalmic drops and inhalations from testing for pyrogens. Additionally, USP <85> only provides guidance and limits for pyrogens found in injectable products. **There is no defined limit** of a pyrogen for a sterile ophthalmic drop or for an inhalation. Without a defined industry standard, it is inappropriate to expect that compounders can comply with this regulation as proposed. Recommendation: Clarify that pyrogen testing is for sterile INJECTABLE drugs only. Consider rewording 1751.7 (e): All ~~N~~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. Additionally, non-sterile-to-sterile batch injectable drug preparations shall be subject to documented end product testing for pyrogens and shall be quarantined until the end product testing confirms both sterility and acceptable levels of pyrogens, per USP chapter 85 limits, before dispensing. This requirement of end product testing confirming sterility and/or 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. References: USP <797> High Risk Sterile Compounds Sterility Testing and Bacterial Endotoxin (Pyrogen) Testing. USP <85> Bacterial Endotoxins Testing USP <771> Ophthalmic Preparations- Quality Tests. This document is consistent with <797> and <85> in that on page 8, Sterility is a quality test required for ALL ophthalmic dosage forms, but Bacterial Endotoxins is required **only** for injected ophthalmic drug products.

Code Section	Commenter	Comment
1751.7(e)	**Brian Warren** California Pharmacist Association (Also commented on at hearing by Tony Park)	~~(c)~~ (e) ***(1)*** ~~Batch-produced sterile injectable drug products compounded from one or more non-sterile ingredients~~ ***Except as provided in paragraph (2),*** ~~**N**~~ ***n*** on-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. ***(2) The following non-sterile-to-sterile batch drug preparations do not require end product testing for sterility and pyrogens:*** ***(A) Preparations for self-administered ophthalmic drops in a quantity sufficient for administration to a single patient for 30 days or less.*** ***(B) Preparations for self-administered inhalation in a quantity sufficient for administration to a single patient for 30 days or less.*** ***(C) Preparations compounded in a batch of 25 or fewer doses for a single patient that are terminally sterilized by autoclave or dry heat sterilization.*** ***(D) Preparations needed for emergency administration to prevent the loss of life or intense suffering, when compounded for administration to a single patient and only in a quantity sufficient for the emergency course of therapy.*** ***(E) Preparations compounded for a single patient with a chemical stability of 14 days or less.*** As stated in the Board's Initial Statement of Reasons, the justification for changes to this section is to address "the problem of ensuring that board regulations are aligned with compounding standards in USP 37 <797> and reducing such discrepancy for the compounding profession who are compounding drug products in California and shipping into California so as to ensure the safety of all consumers receiving compounded drugs in California." As currently drafted, the Board's proposed regulation is not in alignment with USP <797>, and could negatively impact patients due to delays in availability of non-sterile-to-sterile preparations and increases in the cost of non-sterile-to-sterile preparations. **Continued on the next ROW**
1751.7(e)	**Brian Warren** California Pharmacist Association	**Continued from previous ROW** We also acknowledge the Board's mandate to protect patient safety above all other considerations and understand the intent of adopting standards that are more strict that USP <797>. As such, we recommend establishing a limited number of narrow exceptions to the Board's end-product testing requirements. The recommended exceptions are consistent with USP <797>. These narrow exceptions include non-sterile-to-sterile compounds for single-patient, short term ophthalmic products (which is already included by the Board) and inhalation products. Additionally, we propose an exception for small batches compounded for a single patient that are terminally sterilized. Always requiring end-product testing for these preparations will unnecessarily increase costs and harm patient access to these important medications (by about $150 per batch tested). We also recommend an exception for emergency use. This is particularly important when hospitals experience drug shortages. Absent this exception, it is likely that these preparations will be compounded by non-pharmacists in the hospital setting who have no sterile compounding qualifications. For example, consider the use of LETS (lidocaine, epinephrine, tetracaine, and sodium metabisulfite) solution, commonly used for sterile irrigation and topical anesthesia for lacerations in children. LETS solution should be treated as a non-sterile-to-sterile preparation with terminal sterilization using microfiltration. However, LETS "kits" are also sold in convenient packaging containing all pre-weighed ingredients in their raw, nonsterile forms, which are then compounded in a non-sterile environment using sterile water with or without terminal sterilization. Practices such as this will likely become more common if facilities and providers experience delays in accessing non-sterile-to-sterile preparations from sterile compounding phacompounding pharmacies. Use of these kits by healthcare personnel other than pharmacists trained in sterile compounding presents a threat to the public health and safety. Lastly, we recommend an exception for preparations with short-term chemical stability. These preparations will experience chemical degradation prior to completion of end-product testing, which takes 14 days.

Code Section	Commenter	Comment
1751.7(f) - Add	**Judith Brosz and Robert Stein**	(f) Personnel that are not directly engaged in sterile compounding, but are involved in other compounding activities such as remote checking of compounded products outside the controlled area, do not need to perform practical aseptic preparation tests, but shall otherwise complete all written competency examinations on the process. Added (f) to clarify that remote checking should not have identical training requirements to actual production of sterile drug preparations in the controlled environment. While written competency tests are appropriate, demonstrations of cleaning and needle handling are not necessary for those personnel not entering the controlled area.
1751.8	**Lauren Berton** CVS Health	It is recommended that the members of the Board review the possibility of removing all language in the 1751.8 a-e and only refer to USP chapter 797 as suggested below. This recommendation is based on reviews and changes to USP chapters on Beyond Use Dating, which would require rewriting of the current rules with every change. 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, be labeled with a beyond use date that conforms to ~~the following limitations~~ the storage and beyond use dating guidelines in Chapter 797 of the United States Pharmacopeia – National Formulary (USP37-NF32).
1751.8	**Douglas Barcon** Barcon & Associates	Delete “a more” and replace with “an”
1751.8	**Doug O'Brien** Kaiser Permanente	Recommendation: Add specific language stating that the BUDs defined in sections (a) through (d) may be utilized for preparations compounded in CAIs or CACIs that meet the requirements delineated in 1751.4(f)
1751.8(a)	**Douglas Barcon** Barcon & Associates	There is no definition for “controlled freezer temperature” in USP 659, USP 797, or general notices in USP-37 NF-32. USP 797 states: “and for 45 days in solid frozen state between -25 degrees and -10 degrees C.” Inconsistent freezer temperatures throughout the freezer can result in some sterile compounded drug preparations or products (premixed piggybacks) being in semi-solid state even though the reported temperature is within range. The key is solid frozen state to qualify for 45-days BUD. Suggest incorporate USP 797 definition including solid frozen state.

Code Section	Commenter	Comment
1751.8(a)	**University Compounding Pharmacy** Joe Grasela	...in the absence of passing a sterility test ... (a) The beyond use date shall specify that the 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...(1) The preparation is compounded entirely within an ISP Class 5 PEC located in an ISO Class 7 buffer area or cleanroom...using only sterile ingredients, products, components, and devices,...(2) ...using not more than 3 commercially manufactured packages of sterile preparations and not more than two entries into any one sterile container... (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, there 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….a compounded sterile preparation that will be administered either to multiple patients or to one patient on multiple occasions...(2) The compounding process involves complex manipulations other than the single-volume transfer... Section (b) is clearly defines the end user and applicable to multiple patients or to one patient using a multi-use container however section (a) does not define it's end user. Is section (a) also applicable to multiple patients or multi-use container as well? Section (b) is only applicable if using more than 3 commercially manufactured packages. Is that the only difference? Therefore why wouldn't section (a) be applicable for multiple users or multi-use container?
1751.8(a)(1)	**Michael Tou** Providence Health	(1) The preparation is compounded entirely within an ISO Class 5 PEC ~~in an ISO Class 7 buffer area or cleanroom with an ante-area~~, or better air quality… The proposed language restricts sterile compounding with USP 797 defined beyond-use dating to only within an ISO 7 buffer area with an ante-area. USP 797 guidelines allow for sterile compounding within a CAI or CACI that meets all of the operational criteria as defined in Section 1751.4(f) and use of beyond-use dating specified. A buffer area and ante-area should not be required. Providence recommends adopting the wording used in USP 797.
1751.8(b)	**Douglas Barcon** Barcon & Associates	There is no definition for “controlled freezer temperature” in USP 659, USP 797, or general notices in USP-37 NF-32. USP 797 states: “and for 45 days in solid frozen state between -25 degrees and -10 degrees C.” Inconsistent freezer temperatures throughout the freezer can result in some sterile compounded drug preparations or products (premixed piggybacks) being in semi-solid state even though the reported temperature is within range. The key is solid frozen state to qualify for 45-days BUD. Suggest incorporate USP 797 definition including solid frozen state.
1751.8(b)(1)	**Michael Tou** Providence Health	(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~~, or better air quality… The proposed language restricts sterile compounding with USP 797 defined beyond-use dating to only within an ISO 7 buffer area with an ante-area. USP 797 guidelines allow for sterile compounding within a CAI or CACI that meets all of the operational criteria as defined in Section 1751.4(f) and use of beyond-use dating specified. A buffer area and ante-area should not be required. Providence recommends adopting the wording used in USP 797.
1751.8(c)	**Douglas Barcon** Barcon & Associates	There is no definition for “controlled freezer temperature” in USP 659, USP 797, or general notices in USP-37 NF-32. USP 797 states: “and for 45 days in solid frozen state between -25 degrees and -10 degrees C.” Inconsistent freezer temperatures throughout the freezer can result in some sterile compounded drug preparations or products (premixed piggybacks) being in semi-solid state even though the reported temperature is within range. The key is solid frozen state to qualify for 45-days BUD. Suggest incorporate USP 797 definition including solid frozen state.

Code Section	Commenter	Comment
1751.8(c)	**William Stuart** Hartley Medical	Recommend: 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. Rationale: **The clause, "or where the sterile compounded drug preparation lacks effective antimicrobial preservatives" is not referenced in USP <797>.** Numerous CSP's prepared do not contain antimicrobial preservatives, such as: Total Parenteral Nutrition, Large and Small Volume Parenterals, Antibiotics, and Morphine Infusions utilized in home care setting that are currently categorized as Low and Medium Risk preparations. Antimicrobial preservatives are contra-indicated in epidural / intrathecal infusions. Therefore, Morphine (Infumorph) and bupivacaine (Marcaine), which are currently categorized as Low Risk with a 14-day BUD, would change to 72 hours under proposed regulations. Certain compounded preparations have inherent antimicrobial properties. The active pharmaceutical ingredient, osmotic forces, base vehicle, and pH can contribute to decreased microbial survivability. (Source: Rosenberg H and Renkonen O: Antimicrobial Activity of Bupivacaine and Morphine. Anesthesiology 62: 178-179, 1985.)
1751.8(e)(1)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: Many large health care facilities already employ the use of an "immediate use only" label for reasons other than a 1 hour BUD (e.g. criticality of the drug, cost of the drug, etc.) In addition, other regulatory agencies (i.e. The Joint Commission) have stipulations in existence for labeling "immediate use" sterile products (i.e. medication name, strength, quantity, diluent and volume, expiration date when not used within 24 hours, and expiration time when expiration occurs in less than 24 hours). To avoid confusion, it would be beneficial to specifically remove the requirement of labeling the product for "immediate use only" and impose the existing regulation of the expiration time when expiration occurs in less than 24 hours. Solution: Replace the requirement of labeling for "immediate use only" with the exact one hour beyond use date and time. Reason for Concern: This section does not stipulate as to whether this applies to all healthcare professionals who are qualified to engage in immediate use sterile compounding drug preparation outside the profession of pharmacy. Solution: Please clarify and insert verbiage to make clear of whether or not this stipulation applies to all professions outside of pharmacy who are qualified to engage in immediate use sterile compounding (e.g. RN).
1751.8(e)(2)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: Other regulatory agencies (i.e. The Joint Commission) have stipulations in existence for one to compound immediate use sterile products which include: "…a delay could harm the patient …or the products stability is short. To mitigate risk of confusion we recommend adopting similar language that would accomplish the intent of this section. Solution: Reword section to use "a delay could harm the patient" or "the products stability is short".

Code Section	Commenter	Comment
1751.9(a), (b), (c)	**Doug O'Brien** Kaiser Permanente	Recommendation: Include above language from USP 797 allowing the use of proven technologies with quality assurance procedures (for example, Closed System Transfer Devices) allowing for extension of BUD for single-dose vials. Rationale: One of the hallmarks of USP and Current Good Manufacturing Practices (cGMP) is the ability of entities under the guidelines to be innovative and advance practice with validated processes that differ from the current standards. The advancement of knowledge, technology, and validation processes in a very fluid environment must be allowed to flourish; thus the ability to design programs that meet or exceed current outcomes is essential. The key statement allowing this within the USP 797 is as follows: “The use of technologies, techniques, materials, and procedures other than those described in this chapter is not prohibited so long as they have been proven to be equivalent or superior with statistical significance to those described herein.” The regulation as proposed is confusing to industry professionals and the Board of Pharmacy’s intent. The recommendation aids in concordance with USP Chapter 797 National Standards and aids in reduction in drug wastage, increases opportunities to save drug during manufacturer shortages and may result in significant health care cost savings.
1751.9(b)	**Katherine Palmer** **Rita Shane** Cedars-Sinai Medical Center	~~(c)~~ **(3)** 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. **(4) The use of technologies, techniques, materials, and procedures other than those described in this sterile compounding section is not prohibited so long as they have been proven to be equivalent or superior with statistical significance to those described herein" (USP 797 page 1).** Additionally, as a result, counterfeit chemotherapy is an area of national concern, until such time as E-Pedigree is available. Closed system transfer devices (CTSD) protect the vial from entry of external bacteria after initial puncture beyond the USP 797 approved 6 hour time limit. It has been shown that one of these systems maintains sterility of the vials to which it is attached for up to 168 hours (7 days). Recommendation: Allowance to use CTSDs with supporting literature to extend the beyond use date of single dose vials of chemotherapy to 24 hours or use through the end of the shift, whichever is shorter. This recommendation is more conservative than the timeframe of 7 days listed in the CTSD study and would assist institutions in conserving scarce chemotherapy medications.
General Comment	**University Compounding Pharmacy** Joe Grasela	Just a suggestion. If we go with USP 797 and 795 and 71 and 800 I think all the work is done for you. its reviewed by the usp and sent out to all states BOP’S and people involved for review. Also our inspection for a sterile license would satisfy other states that require 797 compliance.
General Comment	**Michael Tou** Providence Health	We urge the board to clarify the intent of the rule language in section 1735.2(d)(3) and 1751.2(b). The board committed to preparing guidance rather than amend the language for these two sections in response to our comments during previous rulemaking.

Code Section	Commenter	Comment
General Comment	**Katherine Palmer** **Rita Shane** Cedars-Sinai Medical Center	1) Ability to provide emergency therapy to patients to avoid patient loss of life or intense suffering when other hemorrhagic cystitis treatments have failed. 2) Ability to provide chemotherapy to patients in the setting of continued drug shortages of cancer medications by using equivalent or superior technologies for preserving medication vials.

Attachment 3

Code Section	Commenter	Comment
1735(b)	**Doug O'Brien** Kaiser Permanente	Recommendation: Add wording to indicate that the examples are not all inclusive and specifically the categories of “ophthalmic” and “otic” to the list of products where “Compounding” does not include “reconstitution”. Use the following language :“(b) “Compounding” does not include reconstitution of a drug pursuant to a manufacturer’s direction(s), such as for ophthalmic otic, 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. Rationale: Several of the most popular products are ophthalmic products that only have to be reconstituted following manufacturer’s instructions. The proposed language is missing some very common and important categories of products that the standards of practice do not call for extra specified conditions, such as Phospholine Iodide eye drops. Relying on the term “topical” to include such categories is unrealistic and adding some specific terms will reduce confusion.
1735.1(a)	**Doug O'Brien** Kaiser Permanente	Recommendation: “Ante-area” means and ISO Class 8 or better air quality for a positive pressure buffer area or ISO Class 7 or better air quality for a negative pressure buffer area…….” Rationale: To be in alignment with USP Chapter 797, the Ante-area for a negative pressure buffer area must be ISO Class 7 or better air quality. The Ante-area for a positive pressure buffer area may be ISO Class 8 or better air quality. An ISO Class 8 Ante-area is inappropriate for a negative pressure buffer area.
1735.1(c)	**Jeffrey Nehira** Dignity Health	Recommend removing added text, "Where hazardous drugs are prepared, the exhaust air from the biological safety cabinet should be appropriately removed by properly designed external building ventilation." This is currently not a requirement of USP<797> or current hazardous compounding regulation and does not have foundation in evidenced base practice.
1735.1(c)	**Michael Tou** Providence Health	Proposed Text: Where hazardous drugs are prepared, the exhaust air from the biological safety cabinet should be appropriately removed by properly designed external building ventilation. Providence requests the board issue exemptions to hospital pharmacies which are unable to immediately comply with the requirements of section 1735.1(c).
1735.1(d)	**Jeffrey Nehira** Dignity Health	Recommend using USP<797> definition of buffer area, "Buffer Area-An area where the primary engineering control (PEC) is physically located. Activities that occur in this area include the preparation and staging of components and supplies used when compounding CSPs.
1735.1(d)	**Jeffrey Nehira** Dignity Health	Recommend using USP<797> definition, "A container of a sterile preparation for parenteral use that contains many single doses."
1735.1(e)	**Katherine Palmer** **Rita Shane** Cedars-Sinai Medical Center	For hazardous compounding at least ~~30~~ 12 air changes per hour of HEPA- Filtered supply air and a negative pressure of at least 0.01inches of water column relative to all adjacent spaces is required. To remain consistent with 1735.6,e,1(p. 17) and USP 797, recommend changing number of air changes per hour required for hazardous drug preparation areas from 30 to 12.
1735.1(e)	**Jeffrey Nehira** Dignity Health	Recommend removing the requirement for HEPA-filtered air. This is not in USP<797> and is not required. If an IV room has lower particulate matter of IS0-7 or better, this in itself decreases the risk for contamination. IS0-5 areas where compounding occurs should have HEPA filtered air, as those are the locations of actual manipulation. HEPA filtration of the room will not necessarily reduce any incidence of contamination and is a costly upgrade for any compounding facility; especially hospitals which typically have low risk due to the short turn around times from the preparation of a medication to administration.

1735.1(e)	**Doug O'Brien** Kaiser Permanente	Recommendations: 1. Adopt the USP Chapter 797 definition for buffer area, “An area where the primary engineering control is located. Activities that occur in this area include the preparation and staging of components and supplies used when compounding CSPs.” 2. Adopt the USP Chapter 797 definition for cleanroom: “A room in which the concentration of airborne particles is controlled to meet a specified airborne particulate cleanliness class. Microorganisms in the environment are monitored so that a microbial level for air, surface, and personnel gear are not exceeded for a specified cleanliness class.” This definition accommodates all acceptable cleanroom configurations including cleanrooms with the displacement airflow method design. 3. Allow the use of the displacement airflow method design for positive pressure buffer areas (1735.1(n)). This design utilizes a high airflow principle rather than a door and pressure differentials between the Buffer Area and the Ante Area. 4. Delay implementation of the requirement for a negative pressure buffer area for compounding hazardous drugs until USP Chapter 800 is finalized. **Continued in Next Row**
1735.1(e)	**Doug O'Brien** Kaiser Permanente	**Continued from Previous Row** 5. If a negative pressure room requirement will be included in the Regulations, allow an adequate period for the phase-in of this design. For some facilities, this redesign process could take several years due to numerous factors including physical constraints within the facility, cost of the redesign, and time to obtain the appropriate permits from regulatory agencies such as OSHPD. Rationale: Combining the definition of cleanroom and buffer area is non-standard, confusing, and inaccurate as the most common “cleanroom” designs include both a Buffer Area and an Ante-Area. For example, a cleanroom could also be a physically separate room that contains a buffer area, in which the air quality is ISO Class 7 or better; and an ante area, in which the air quality is ISO Class 8 or better. Displacement airflow concept described in 1735.1 (n) could be used. USP Chapter 797 allows for the compounding of low volumes of hazardous drugs in a positive pressure buffer area with appropriate primary engineering controls. Remodeling and construction costs exceeding $75 million to convert existing cleanrooms in KFH hospitals and Ambulatory Oncology Infusion Centers to provide separate positive pressure and negative pressure buffer areas and eliminate all cleanrooms with the displacement airflow method of design
1735.1(e)(1)	**Jeffrey Nehira** Dignity Health	Pt1. This statement is confusing with regard to the addition of "buffer area" to the clean room definition. If a room has both a buffer area and a designated ante area the pressure differential would be between the ante area and the adjacent space. Pt.2 The recommendation of the differential positive pressure of 0.02 to 0.05 inch is not standard practice. Recommend following USP<797> 2014 pg13, "The pressure between the ISO Class 7 (see Table1) and the general pharmacy area shall not be less than 5 Pa (0.02 inch water column). In facilities where low- and medium-risk level CSPs are prepared, differential airflow shall maintain a minimum velocity of 0.2 meters per second (40 feet per minute) between buffer area and ante-area.

1735.1(e)(1-2)	**Rachel Taggs** **Shauna Doherty** Precision Pharmacies	(e) (1) References a minimum range of pressure. Implying anything outside of this range is not allowed. We recommend the following: (1) For nonhazardous sterile compounding a minimum positive pressure differential of 0.02 inch water column relative to all adjacent spaces is required. (e) (1) and (2) Nothing in these sections references "sterile preparations" we recommend the following: (e) "Cleanroom or clean area or buffer area" means a room or area with HEPA-filtered air that provides ISO Class 7 or better air quality where the primary engineering control (PEC) is physically located, typically utilized for sterile compounding. (1) For nonhazardous sterile compounding a minimum positive pressure differential of 0.02 inch water column relative to all adjacent spaces is required. (2) For hazardous sterile compounding at least 30 air changes per hour of HEPA-filtered supply air and a negative pressure of at least 0.01 inches of water column relative to all adjacent spaces is required.
1735.1(e)(2)	**Jeffrey Nehira** Dignity Health	This statement does not correspond with current CETA engineering requirements compared with USP<797>. The amount of Air Changes Per Hour (ACPH) required should be dependent upon the volume of hazardous compounding done as well as risk category (low, medium, versus high). Room pressure differentials should also be dependent on both compounding volume and risk category. Recommend reclassifying this requirement according to CETA flowchart of Engineering Control Requirements for Hazardous Drugs revised May 2009 (see attached document).
1735.1(e)(2)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: USP 797 makes the stipulation of 12 air changes per hour as the air displacement requirement when compounding hazardous drugs. In addition, this is a contradiction to the same proposed BOP regulations in 1735.6 (e) (1) where it states that for hazardous drug compounding, 12 air changes per hour are sufficient. Solution: Replace the 30 ACPH with 12 ACPH in this section in accordance with USP 797 and in accordance with these same proposed BOP regulations in 1735.6 (e) (1).
1735.1(e)(2)	**Rheta Sandoval** Kaweah Delta Health Care	In the proposed USP Chapter <800>, alternate ACPH requirements are being offered that are fewer air changes than what is being proposed in this modified text depending upon the type of hazardous drug being compounded (nonsterile or sterile) and the facility configuration. Please consider adding alternate ACPH requirements that are consistent with the proposed USP Chapter <800>. If the BOP adopts the modified text as proposed, please consider establishing reasonable timelines and expectations for compliance so as not to severely limit patient access to needed care or place tremendous burdens on patients and those supporting their care to travel to a facility that is compliant with the regulation. Outside of the costs and time necessary to complete facility modifications to meet this requirement, there could be negative impacts if a pharmacy could not continue to provide the potentially life-saving "hazardous" medications needed as a facility works towards gaining compliance with the requirement. Some geographic areas of the State may not have a nearby health facility to provide this type of service or the ability to handle the order volume currently managed by the Pharmacy.
1735.1(f)	**Jeffrey Nehira** Dignity Health	This statement does not correspond with current CETA engineering requirements compared with USP<797>. Recommend reclassifying this requirement according to CETA flowchart of Engineering Control Requirements for Hazardous Drugs revised May 2009 (see attached document).

1735.1(f)	**Douglas Barcon** Barcon & Associates	Between “unidirectional” and “compounding” insert: unidirectional HEPA-filtered airflow. Consider strengthening (change should to must) and rewriting for clarity (not physical location of duct): “Where volatile hazardous drugs are prepared, the exhaust air from the isolator ~~should~~ must be vented externally by properly designed building ventilation.”
1735.1(g)	**Douglas Barcon** Barcon & Associates	Between “unidirectional” and “air” insert: HEPA-filtered
1735.1(i)	**Jeffrey Nehira** Dignity Health	Calculation of C to F does not take into account significant figures. Suggest 2-8 degrees C(35 to 46 degrees F) as this is typically the temperature range posted for refrigeration. This is consistent with the calculation of Controlled Freezer temperature and Controlled Room temperature following this definition in the regulation.
17351(l)	**University Compounding Pharmacy** Joe Grasela	Definition should be changed to keep it consistent with the Federal law section 503A which is what most typical compounding pharmacies are and follow. “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 individual patient, which produces for that patient a significant difference, as determined by the prescribing practitioner, between the compounded drug and the comparable commercially available drug product. 503A regarding “essentially a copy”. (D) Does not compound regularly or in inordinate amounts (as defined by the Secretary) any drug products that are essentially copies of a commercially available drug product.” Definition: For purposes of paragraph (1)(D), the term 'essentially a copy of a commercially available drug product' does not include a drug product in which there is a change, made for an identified individual patient, which produces for that patient a significant difference, as determined by the prescribing practitioner, between the compounded drug and the comparable commercially available drug product.' **Continued in Next Row**
17351(l)	**University Compounding Pharmacy** Joe Grasela	**Continued from Previous Row** Reasons for change: The Federal definition state “significant difference” only vs the proposed language of “clinically significant difference” (1) Most pharmacies do not have access to patient charts therefore to include “clinically significant difference, as determined by a prescribing practitioner” implies that for every compounded prescription the pharmacist is supposed to followup with the practitioner and document the clinical significance which will impose more issues. Issues include: (1) Contacting the physician for every single prescription. (2 &3)Which will delay the prescription from being compounded therefore delaying therapy to the patient. (4) Contacting physicians frequently for followup/notation of “clinically significant difference” will over burden the MD office (5)Was this cleared by the AMA or medical board to impose on a physician to notate/determine the clinical significance when using a compound that is “essentially of copy”? Is this included in medicine law? (6) Are we now interfering with the practice of medicine? (7) Overall, including that statement “clinically significant difference” will cause unnecessary burden on the physician, patient, and pharmacy. (8) The law is unenforceable for out of state pharmacies because they follow their state laws. BOP does not inspect out of state pharmacies for non-sterile compounded preparations which is the majority of the compounding business.
1735.1(m)	**Jeffrey Nehira** Dignity Health	Defining daily as every 24 hours is not correct and will provide future problems with definitions which conflict with national standards. Daily is defined within the 24 hours of a calendar day. 24 hours extremely restricts the use of the term daily and is confusing when defining standards of practice. If requirements are to be defined within 24 hours, they should state that in the regulation.

1735.1(m)	**P. Kim Peterson** University of California, Davis Medical Center	Recommendation/ Comments: remove “daily means every 24 hours” as this would imply within the hour of exact same time for measurement to be recorded each day. In the hospital setting, critical patient care issues may interrupt normal routines delaying the recording of the temperature if continuous or electronic monitoring not in place. Twice yearly time changes would also impact.
1735.1(n)	**Rheta Sandoval** Kaweah Delta Health Care	The verbiage in USP 797 specific to “displacement concept” reads, “The displacement concept shall not be used for high-risk compounding.” The reference cited “ISO 14644-4:2001 Cleanrooms and associated controlled environments-Design, construction, and start-up” includes section A.5.2 which describes the displacement concept. The displacement concept is described in this reference as a means to effectively separate clean and less clean adjacent zones without any mention of hazardous compounds or chemotherapy. As such, the term “high-risk” should be taken to mean high risk of microbial contamination as described in USP <797> and should not be taken to mean hazardous compounds. Some facilities are currently meeting the “low volume” exemption described in USP <797>, hazardous CSP prepared in an ISO 5 CACI using closed-system transfer devices. The PEC (CACI) is located in the ISO 7 buffer area (located in a positive pressure room where the buffer area is not physically separated from the ante-area and the principle of displacement airflow is employed. Adopting the language as proposed will put some facilities in this state out of compliance limiting patient access to needed cancer care or placing tremendous burdens on patients and those supporting their care to travel to a facility that is compliant with the regulation. Please consider the following remedies: 1. If the modified text is adopted as proposed, please establish reasonable timelines and expectations for compliance and a process for waiver application that would allow facilities to continue to provide services out of their existing sterile compounding pharmacies as they work to gain regulatory compliance. 2. Please delete the language “or for hazardous compounds” and consider reintroducing at a later time after fully assessing impacts to Pharmacies holding compounding licenses in this state and establishing reasonable timelines for gaining compliance. 3. Please consider deleting 1735.1(n) in its’ entirety. The term “displacement airflow method” is not used in 16 CCR Articles 4.5, 7 or 7.5 except in the proposed definition.
1735.1(n)	**Doug O'Brien** Kaiser Permanente	Recommendation: “Displacement airflow method: For buffer areas not physically separated from the ante-areas, this concept utilizes a low pressure differential, high airflow principle. The principle of displacement airflow shall require an airflow velocity of 40 ft per minute or more from the buffer across the line of demarcation into the ante-area.” Rationale: USP Chapter 797 allows the compounding of low volumes of hazardous drugs within a positive pressure buffer area with the displacement airflow method of design, with appropriate primary engineering controls. Remodeling and construction costs exceeding $75 million to convert existing cleanrooms in KFH hospitals and Ambulatory Oncology Infusion Centers to provide separate positive pressure and negative pressure buffer areas and eliminate all cleanrooms with the displacement airflow displacement method of design.
1735.1(s)	**Douglas Barcon** Barcon & Associates	Should include NIOSH hazardous drugs that are not anti-neoplastic to provide additional guidance for the pharmacist-in-charge and to help ensure that staff does not inadvertently handle a hazardous drug as non-hazardous because the PIC overlooked it. Suggest adding “or NIOSH” at end after “pharmacist-in-charge.”

1735.1(u)	**Doug O'Brien** Kaiser Permanente	The wording of this definition is confusing and requires clarification. We believe “lot” could be interpreted two different ways. 1. It could be interpreted to include different types of preparations that are prepared during one uninterrupted continuous cycle of compounding. A typical example of this interpretation in a hospital pharmacy: compounding four doses of azithromycin 500 mg/250mL dextrose 5% for four different patients, and two doses of famotidine 40 mg in 250mL dextrose 5% 250mL for one patient, and five doses of furosemide 100mg/100mL dextrose 5% for five different patients. All of these would be prepared in an uninterrupted continuous cycle of compounding. Recommendation: If the above example is the intended interpretation, then we recommend this language: “Lot” means one or more different compounded drug preparation(s) prepared during one uninterrupted continuous cycle of compounding from one or more common active ingredient(s).” 2. It could be interpreted to mean a single type of drug preparation compounded during one uninterrupted continuous cycle of compounding from one or more common active ingredient(s). Using the example above, four doses of azithromycin 500 mg/250mL dextrose 5% for four different patients would be considered one lot. Recommendation: If interpretation #2 is correct, then we recommend this language: “Lot” means a single type of drug preparation(s) prepared during one uninterrupted continuous cycle of compounding from one or more common active ingredient(s).”
1735.1(u)	**Katherine Palmer** **Rita Shane** Cedars-Sinai Medical Center	"Lot" means ~~one or more~~ **"non-sterile to sterile batch" which means any compounded drug preparation containing two or more dosage units with any ingredient that was at any time non-sterile, regardless of intervening sterilization of that ingredien**t. ~~compounded drug preparation(s) during one uniterrupted continuous cycle of compounding from one or more common active ingredient(s).~~ OR Alternatively, recommend changing definition of "lot" to "greater than one dose" in order to ensure timely preparation of compounded drugs to treat emergency patients' conditions where immediate administration of medications is essential. When medications are prepared as single doses, time is of the essence and documentation requirements for a lot would delay patient treatment. "Lot" means ~~one or more~~ "**greater than one dose of compounded drug preparation prepard in anticipation of immediate patients needs**. ~~compounded drug preparation(s) during one uniterrupted continuous cycle of compounding from one or more common active ingredient(s).~~
1735.1(v)	**P. Kim Peterson** University of California, Davis Medical Center	Recommendation/ Comments: we had several people review this statement to determine the intent. The range in answers was an exact copy of the process to make a critical product which many not have complex manipulations versus a complex serial dilution for a neonate. The complexity changes in an ever changing environment and staff are tested throughout the year. We would like to update the process on an annual basis based on what we would determine to be complex and error prone.
1735.1(x)	**Jeffrey Nehira** Dignity Health	Suggest redefining this term. Confusion can result by defining the term "parenteral" other than what it actually is. For example, the transdermal route of administration was omitted. Suggest using a more common definition of the term parenteral and removing specifics added in the new language.

1735.1(x)	**Rachel Taggs** **Shauna Doherty** Precision Pharmacies	The phrase ". . . administration into the eye" can include ophthalmic drops. The phrase ". . . administration into the eye" should be changed to "injection into the eye".
1735.1(z)	**Jeffrey Nehira** Dignity Health	Suggest adding an appendix of USP34-NG32, 37th Revision referencing "Potency" to the policy for easier referencing of USP version required in CA Pharmacy Law. This has changed since the last draft and should be reviewed through the BOP for adoption when changes are made.
1735.1(z)	**Doug O'Brien** Kaiser Permanente	Recommendation: "Sterile injectable preparations compounded solely from commercially manufactured sterile pharmaceutical products are exempt from this definition. For those exempt, the range may be calculated and defined in the master formula." Rationale: All pharmacies with sterile compounding permits should be able to benefit from the exemption Consistency of the regulations
1735.1(z)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: USP 797 only describes potency in terms of ensuring potency by monitoring controlled storage areas. In addition, considering the many drugs that could be compounded (biosimilars, immune mediators, blood derivatives, etc) it may be too arbitrary to put such a hard limit on this definition. Solution: Remove section that defines "potency" altogether.
1735.1(ab)	**Doug O'Brien** Kaiser Permanente	Recommendation: Eliminate from the Proposed Regulation this unsafe narrowing of the definition of a "Prescriber's Office". Rationale: Prescribers have not provided care for several decades in what once was a solo practitioner's medical office facility. In fact for decades there have been many additional categories of "prescribers" that are authorized under State statutes to dispense or "furnish" and administer medications to their own patients in their practice sites, e.g. Nurse Practitioners. Such additional dispensing clinicians have not, however been trained in safe and appropriate compounding required by current standards. Also many categories of sites of clinician practice have come to rely on pharmacists to compounded products to provide medical care for special patient needs and or in special situations. These sites include but are not limited to Licensed Clinics and small hospitals (99 beds or less) such as rural and/or specialty hospitals that are not required to have a pharmacy or pharmacist. This proposed Regulatory definition would lead to dangerous compounding and/or sub-optimal care in such facilities by either compounding by less qualified personnel or deferral of the care provided by pharmacist-compounded products. The Board's intent may be to force such facilities/clinicians to obtain such products that are not available from traditional suppliers (e.g. FDA registered manufacturers.), from FDA or State licensed "Outsourcing" facilities/entities. However there are and will be many situations when based on the cGMP rules such facilities or entities will have to follow, supplying these true "prescriber's offices" will neither be a reality within the time needed nor a commercial practicality. Thus the ability of properly trained and qualified pharmacies in properly designed and equipped facilities to supply these clinician practice sites is vital to safe and effective patient care. Decreases patient safety Encourages sub-optimal medication therapy.
1735.1(ac)	**Jeffrey Nehira** Dignity Health	Recommend removing the wording "...through the use of unidirectional HEPA filtered first air." from the definition as it also is not in USP797. Although it is implied that through the PEC directional flow would be one way, most negative pressure glove boxes can be configured for both positive and negative pressure.

1735.1(ac)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: The inherent definition of a PEC is that it has the ability to produce/provide ISO Class 5 or better air environment. Many Sterile Compounding Automated Robots that are available and that are in production have no intention of being able to create/produce/provide an ISO Class 5 (or any air class for that matter). These automated robots are made to be simply put or placed in the appropriate air environment (ISO Class air). Solution: Remove sterile compounding automated robots from the PEC definition and just make the stipulation that they should be used in an appropriate ISO Class 5 or 7 environments.
1735.1(ag)	**Jeffrey Nehira** Dignity Health	The USP 797 definition of a Segregated compounding area is "a designated space, either a demarcated area or room, that is restricted to preparing low-risk level CSPs with 12 hour or less BUD". The proposed language does not correspond to standard of practice which exist and is defined.
1735.1(ag)	**Doug O'Brien** Kaiser Permanente	Recommendation: Allow compounding of hazardous drugs in a segregated compounding area within a CACI by removing the language “non-hazardous”. The applicable sentence would read, “The segregated sterile compounding area shall be restricted to preparing non-hazardous sterile to sterile compounded preparations.” Rationale: The USP Chapter 797 definition of a segregated compounding area is “a designated space, either a demarcated area or room, that is restricted to preparing low-risk level CSPs with 12 hour or less BUD”. USP Chapter 797 allows placement of a CACI (used for hazardous drug compounding) in less clean than ISO Class 7 areas if the following conditions are met: -The isolator shall provide isolation from the room and maintain ISO Class 5 during the dynamic operating conditions, including transferring ingredients, components, and devices into and out of the isolator and during preparation of CSPs -Particle counts sampled approximately 6 to 12 inches upstream of the critical exposure site shall maintain ISO Class 5 levels during compounding operations -Not more than 3520 particles per m3 shall be counted during material transfer, with the particle count probe located as near to the transfer door as possible without obstructing the transfer. Section 1735.6(e) delineates requirements for hazardous drug compounding facilities. The requirements described in this section are referring to a segregated compounding area as described in the draft language of USP Chapter 800. This section implies that it is appropriate to compound hazardous drugs within a segregated compounding area with the appropriate engineering controls. Concordance with USP Chapter 797 National Standards and the current version of USP Chapter 800 National Standards Consistency of the regulations

1735.1(ag)	**Douglas Barcon** Barcon & Associates	The current draft of USP 800 (C151881) permits hazardous sterile preparations in a containment segregated compounding area (C-SCA), which is a separate room with negative pressure and at least 12 air changes per hour. It further states that low- and medium-risk HD compounded sterile preparations may be prepared in a BSC or compounding aseptic containment isolator (CACI) located in a C-SCA, provided the BUD of the CSP does not exceed 12 hours. There is no reference to a CACI tested by the manufacturer to comply with USP 797 in air worse than ISO Class 7, ISO Class 8, or unclassified air quality permitting full USP 797 beyond-use-dates for low and medium risk HDs as is specified for non-HDs in USP 797. I discussed this with and submitted my comment on this to the USP 800 committee for review in the current revision (C151881) of USP 800 that closed for comments on May 31, 2015. There has been no reason given that a hazardous preparation should be given a 12-hour BUD, while a non-hazardous preparation can have the full BUD duration. Hazardous drug preparation compounding should be permitted in a CACI with manufacturer compliance with USP 797 when located in a segregated sterile compounding area provided the area is negative pressure, externally vented, and has at least 12 ACPH.
1735.1(ag)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: Many hospitals have established pharmacy satellites nearby patient care areas to serve our most vulnerable patients (e.g. Intensive Care Units). The central pharmacy is too far from these patient care areas and the pharmacy satellites provide a venue to provide patient care that is closer to the patients. These pharmacy satellites are one room that provides a place for the pharmacy to perform order verification, drug storage, and drug preparation. Many of the pharmacy satellites have very limited room, thus the pharmacy will place compounding aseptic containment isolators (CACIs) which are enclosed to the surrounding environment and should have evidence from the manufacturer that they meet USP chapter 797 and Controlled Environment Testing Association (CETA) requirements. If one were to believe that this is an unverified study then one would have to question most of the conclusions derived from USP 797 as many of the conclusions taken from there are not based on “randomized controlled trials”. We believe that we can remove the 3 foot no sink/drain requirement when CACIs are used to support pharmacy satellites. The alternative would be to close these pharmacy satellites that do not have the room to abide by the 3 foot no sink/drain rule which is not consistent with a patient centered care model. Solution: Make an exception that if the ISO Class 5 PEC is a CACI, that the three foot sink/drain rule does not apply while maintaining that sinks and drains should not be placed in a buffer area or in ISO class 7 or better.
1735.1(ah)	**Douglas Barcon** Barcon & Associates	Paragraph needs to be relabeled as (ah) because the previous paragraph is labeled (ag).
1735.2(c)(1)	**P. Kim Peterson** University of California, Davis Medical Center	**Recommendation/ Comments:** In the health system, purchase orders and payment is processed by the University accounts payable or other systems, not by the physician directly.
1735.2(c)(1)	**Rachel Taggs** **Shauna Doherty** Precision Pharmacies	The phrase “. . . and paid for by the prescriber” suggests that only the prescriber may pay for the medication. Many prescribers belong to a practice and as with any business entity the entity pays for purchases, not the individual member or employee. We suggest the following: (1) Is ordered by the prescriber or the prescriber’s agent and paid for by the prescriber or their practicing entity.

1735.2(c)(1) & 1735.2(c)(3)	**Doug O'Brien** Kaiser Permanente	Recommendation #1: Clarify that the prescriber does not have to personally pay for the medication supplied to the prescriber for office use by adding the phrase “or the prescriber’s agent” as shown below. Rationale: Not all prescriber’s are in private solo practice and the medications they use in the prescriber’s office are actually paid for by either the prescriber’s group entity or another entity that is responsible for the cost of the patient’s care, e.g. a county or city government, the State or even a private health plan or clinic. “1) Is ordered by the prescriber or the prescriber’s agent and paid for by the prescriber or the prescriber’s agent…” Recommendation #2 Do not eliminate the ability of pharmacies to compound for prescriber’s office use by changing decades of vital history that has allowed a prescriber to dispense from the prescriber’s office up to at least a 72-hour supply of pharmacy compounded medication. In fact, as the Board’s rationale of acceptance for allowing “...a 120-hour supply for veterinary medical practices…” should be also allowed for human medical care. Rationale: For over 30 years, the Legislature’s authorization for pharmacists' ability to compound preparations for prescriber "for office use by the prescriber" (B&P Code 4052(1)(a) has been interpreted to include BOTH for administration in the office and for DISPENSING to a patient for up to a 72-hour supply. Under State law prescriber’s are allowed to dispense prescription medications to their own patients. This Board proposed will effectively narrow the scope of practice of physicians and other prescribers without a discussion via the Legislature of that vital State policy. The proposed regulation language will remove the allowance for pharmacists to compound for any prescriber for dispensing - except for veterinarians. [See Proposed regulation Section 1735.2(c)(3)] **Continued in Next Row**
1735.2(c)(1) & 1735.2(c)(3)	**Doug O'Brien** Kaiser Permanente	**Continued from Previous Row** This change in pharmacy scope of practice could hinder appropriate and safe human therapy in some situations where, by definition, the prescriber has asked a pharmacy to compound a product to either keep on hand for a potential human need (just like the Board’s rationale for allowing the compounding for animal therapy). It will also encourage medication compounding by practitioners or health professionals with less education and training in compounding than pharmacists, e.g. physicians, dentists, etc. and nurses, etc., respectively. These potential adverse consequences were exactly what the Legislature was trying to avoid when the Statute was enacted decades earlier after it was alerted to such tragedies. Some examples of the need for allowing prescriber dispensing of pharmacy-compounded products, include when medication is unavailable for a type of patient with special needs, (such as an eye drop without preservatives) or when a commonly available critical medication is in reality not available from usual sources. Another increasing reason for allowing a prescriber to dispense a reasonable supply of a pharmacy compounded drug is to avoid unnecessarily increasing the cost of care or increasing the waste of safe and effective medication and the avoidable adverse effects on the environment of its unnecessary disposal. One example, is when the prescriber could administer a few drops of a pharmacy—compounded eye solution in the office but under the regulation change would have to discard the remainder of the container instead of dispensing it to the patient even though the patient would only need a few day’s therapy or who would be unlikely to procure a continuous supply directly from a compounding pharmacy in the remaining 72 to 120 hours of therapy **Continued in Next Row**

1735.2(c)(1) & 1735.2(c)(3)	**Doug O'Brien** Kaiser Permanente	**Continued from Previous Row** The Board's apparent intent will be to discipline the pharmacy, Pharmacist-In-Charge and dispensing pharmacist if they knew or should have known that the prescriber was going to dispense the remainder of the bottle to the patient. Consequently it won't be done and prescriber's and patients will be denied this option without discussion via the Legislature. Just as for animal treatment, which the Board intends to allow, the ability for prescribers to dispense pharmacy-compounded mediations is also important to situations where a compounding pharmacy will not be reasonably available, e.g. because of holidays, distance, expertise, proper equipment for sterile compounding, etc.. The Regulation will delay or interrupt vital therapy, such as immediate and continuous treatment of infections or relief of suffering. Situations that most likely can be avoided with the dispensing of the 72 to 120 hour supply. This change in statutory intent could also make care substantially more expensive for the patient whom would have to buy another supply of compounded medication at the pharmacy and/or for the organization responsible for the drug cost.
1735.2(d)(2)	**Rachel Taggs** **Shauna Doherty** Precision Pharmacies	Subdivision (2) does not reference "human" drugs. As such, this would not allow veterinary preparations to be compounded that have been removed for human use, but are not necessarily unsafe or not effective for veterinary use. We recommend the following: (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 for human use; or
1735.2(d)(3)	**Rachel Taggs** **Shauna Doherty** Precision Pharmacies	Subdivision (3) does not take into consideration medications needed for veterinary use. While some medications may appear on the ASHP list, the FDA list of veterinary drugs includes five drugs and is not updated on a regular bases. There is no other formal list of short supply or backordered veterinary drugs. We recommend the following: (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), FDA list of drugs that are in short supply at the time of compounding, or for veterinary products the pharmacy shall document unavailability by the wholesaler or manufacturer, and at the time of dispensing, 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.

1735.2(i)	**University Compounding Pharmacy** Joe Grasela	Definition should be changed to the following: This “beyond use date” of the compounded drug preparation shall not exceed the shortest expiration date of any ingredient in the compounded drug preparation, nor shall it exceed 180 days for non-aqueous formulations, 14 days for water-containing oral formulations, and 30 days for water-containing topical/dermal and mucosal liquid and semisolid formulations, unless a later date is supported by stability studies of finished drugs or compounded drug preparations using similar ingredients, specific and essential compounding steps, quality reviews, and similar packaging made from the same materials (ie: plastic, glass, etc). Reasons: (1) The extreme number of variations in customized, yet similar preparations, would prevent us from providing an adequate supply of compounds to the patient. This wording removes pharmacists judgment and is unnecessarily restrictive to the patient, affecting continuity of therapy. (2)This would inhibit our ability to compound for anticipatory prescriptions which we have on record that these patients are using for routine therapy. (3) Increased delay in therapy to the patient. (4) Patients will have to come back every 30 days for their prescriptions (5) Overall, unnecessary burden to the patient, and affects continuity of therapy/care. (6) The law is unenforceable for out of state pharmacies because they follow their state laws. BOP does not inspect out of state pharmacies for non-sterile compounded preparations which is the majority of the compounding business. (7) Patients that prefer their medications mailed to them (~5-7 days to mail), the drug would be expired if we sent a 30 day supply with a 30 day expiration date by the time they receive in in the mail. In effect they would get a 21 day supply and have to get their prescription filled every 21 days due to mailing delay

1735.2(i)	**Rachel Taggs** **Shauna Doherty** Precision Pharmacies	The use of the word "identical" in the phrase ". . . unless a later date is supported by stability studies of finished drugs or compounded drug preparations using identical ingredient, specific and essential compounding steps, quality reviews and packaging" is extremely limiting. USP states the following regarding BUDs: "BUDs should be assigned conservatively. When assigning a BUD, compounders shall consult and apply drug-specific and general stability documentation and literature when available and should consider: • the nature of the drug and its degradation mechanism • the dosage form and its components • the potential for microbial proliferation in the preparation • the container in which it is packaged • the expected storage conditions • the intended duration of therapy (see General Notices and Requirements, Preservation, Packaging, Storage, and Labeling, Labeling, Expiration Date and Beyond-Use Date). We recommend the following: ". . . unless a later date is supported by stability studies of finished drugs or compounded drug preparations. The pharmacy shall assign BUDs conservatively. When assigning a BUD, compounders shall consult and apply drug-specific and general stability documentation and literature when available and should consider: (1) the nature of the drug and its degradation mechanism (2) the dosage form and its components (3) the potential for microbial proliferation in the preparation (4) the container in which it is packaged (5) the expected storage conditions, and; (6) the intended duration of therapy
1735.2(i)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: Many CSP's (e.g. reconstituted vials) that are a result of following manufacturer's directions have labeling (supported by the manufacturer) that exceeds what is listed in this section for water containing formulations and water containing topical/dermal formulations. Furthermore, to expect that stability studies will be provided by the manufacturer in lieu of a general statement by the manufacturer stating the stability/sterility is not feasible. Many generic manufacturers do not have the infrastructure to accommodate inquiries by many pharmacies to provide them stability studies. Solution: Retract the examples of water containing oral formulations and water containing topical/dermal formulations from this section and replace the language with what was in the previous version. In addition, add the stipulation that a later date may be used for a CSP if the manufacturer provides communication regarding stability and sterility to support that claim.
1735.3(a)(2)(E)	**Rachel Taggs** **Shauna Doherty** Precision Pharmacies	(a) (2) (E) Requires that if an expiration date is not provided by the manufacturer the pharmacy shall document the date of receipt on the compounding document. Section 1735.2 subdivision (k) restricts when the said component cannot be used. Requiring both the expiration and acquisition date of components on documents will lead to confusion and inconsistent record keeping. We recommend the following: (E) If the manufacturer does not supply an expiration date for any component, the records shall include the date beyond which the component shall not be used as the limitations of section 1735.2, subdivision (k) shall apply.

1735.3(a)(2)(E)(i)	**Doug O'Brien** Kaiser Permanente	Recommendation: Include ambulatory oncology clinic pharmacies in the seventy-two (72) hour exception language, in a manner similar to inpatient pharmacies. Rationale: Ambulatory oncology clinic pharmacies compound preparations in a similar manner to inpatient pharmacies
1735.3(a)(2)(H)	**P. Kim Peterson** University of California, Davis Medical Center	Recommendation/ Comments: Drugs are stored according to USP or manufacturer recommendations. We do not record the storage of each drug. This would be a labor intensive requirement to maintain these records and is not provided by electronic pharmacy inventory management systems in a readily retrievable format.
1735.3(c)	**Rachel Taggs** **Shauna Doherty** Precision Pharmacies	The term “supplier” implies “wholesaler” consequently excluding manufacturers. We recommend the following: (c) Active ingredients shall be obtained from a wholesaler or manufacturer registered with the Food and Drug Administration (FDA).
1735.4(b)	**Douglas Barcon** Barcon & Associates	Should also include sterile drug preparations compounded in a centralized hospital packaging pharmacy for use with patients at affiliated health care facilities under common ownership as per B&PC regulation 4128.
1735.4(c)	**Jeffrey Nehira** Dignity Health	With regard to drug labeling I believe this regulation requiring both the names of the compounding pharmacy and dispensing pharmacy, if different, should also state, "if not apparent from the container". Products may come from multiple sources and this requirement currently states that the pharmacy label should have both names. This is impracticle if the original pharmacy label is apparent from the product and has the information required. (ex. TPN formulations prepared at an outsourced facility)
1735.4(e)	**Candace Fong** **Clara Evans** Dignity Health	Add: Alternate cleaning schedules may be submitted to the Board for fully automated robots CHA appreciates the addition of robotics into the regulations and now requests to add alternate cleaning schedules to address their specific disinfecting needs. Cleaning at 30 minute intervals is unobtainable with robots that are totally contained.
1735.4(e)	**BJ Bartleson** California Hospital Association	Add: Alternate cleaning schedules may be submitted to the Board for fully automated robots Dignity Health appreciates the addition of robotics into the regulations and requests to add alternate cleaning schedules to address specific disinfecting needs. Cleaning the robots at 30 minute intervals is unrealistic with robots that are totally contained
1735.5(a)	**P. Kim Peterson** University of California, Davis Medical Center	Recommendation/ Comments: Change shall to may or eliminate as unnecessary as regulations give the Board authority to take disciplinary actions.
1735.5(a)	**Douglas Barcon** Barcon & Associates	Suggest defining “material” and “material failure.” The definitions used by the board in disciplinary actions would suffice, or alternatively the definitions from Black’s Law Dictionary 6th and 9th Editions including such terms as significant, substantial, important, necessary, and essential.
1735.5(c)(4)	**Jeffrey Nehira** Dignity Health	Reference to "disinfecting the facility (physical plant) used for compounding" needs clarification. Regulations already exist for the requirements of cleaning walls, ceilings, etc. The reference to "the facility (physical plant)" is not defined in the definitions at the beginning of the document.
1735.5(c)(7-8)	**Jeffrey Nehira** Dignity Health	Recommend removal of the requirement for annual review. Although this is in current policy, this differs from other regulatory body requirements for hospitals. Request review, "at least every 3 years" or to similar verbiage in Title 22. Reference to "signed and dated by the pharmacist-in-charge" should be updated to include electronic signatures.
1735.5(c)(9)	**Douglas Barcon** Barcon & Associates	Suggest adding at end after the word pharmacy: “and as specified in 1735.8 (e) for health care facilities” for continuity

1735.5(c)(9)	**Jeffrey Nehira** Dignity Health	Need further clarification regarding room temperature storage. Currently regulation state that medications are stored at controlled room temperature, but there is no requirement for daily monitoring. Request an extended implementation date is this is now required for hospital settings.
1735.5(c)(10)	**Jeffrey Nehira** Dignity Health	Suggest and exemption for health care settings with a facility services policy regarding appropriate function of refrigeration devices.
1735.5(c)(10)	**Douglas Barcon** Barcon & Associates	Suggest adding at end after the word pharmacy: “and as specified in 1735.8 (e) for health care facilities” for continuity
1735.6(e)	**Rachel Taggs** **Shauna Doherty** Precision Pharmacies	Subdivision (e), including points (1), (2) and (3), are all included in the USP <800> draft, which has yet to be published. We ask that this section is removed until the new chapter has been made effective and no changes can occur.
1735.6(e)	**Jeffrey Nehira** Dignity Health	A physcially separate room for low risk, low volume hazardous compounding is not required according to current standards of practice and does not take into account the use of CASis. This statement does not correspond with current CETA engineering requirements compared with USP<797>. Recommend ceiling, reclassifying this requirement according to CETA flowchart of Engineering Control Requirements for Hazardous Drugs revised May 2009 (see attached document).
1735.6(e)	**Brian Warren** California Pharmacist Association	(e) Beginning no later than January 1, 2020, Hazardous drug compounding shall be completed in a physically separate room with the following requirements: (1) Minimum of 12 air changes per hour; and (2) Maintained at a negative pressure of at least 0.01 inches of water column relative to all adjacent spaces (rooms, above ceiling, and corridors); and (3) All surfaces with the room shall be smooth, seamless, impervious, and non-shedding. During discussion by the Board of Pharmacy of the proposed modifications that added these requirements, the Board expressed an interest in an exemption process or delayed implementation of the hazardous room requirements. We support requirements that will protect pharmacy personnel and others from potential contact with hazardous drugs, though we would like to reiterate that USP <800> is still in draft form and caution against enacting regulations before USP finalizes the standard. Promulgating a separate rulemaking package to enact USP <800> standards after they are finalized would be a more prudent process. If the Board is intent on moving forward with these requirements as part of this rulemaking package, we recommend placing delayed implementation in the regulation until 2020. Given the extensive changes that these requirements could necessitate for some hospitals and pharmacies, some time will be necessary to allow for compliance. Delayed implementation is preferable to some sort of exemption process, because the latter would require detailed parameters that exemptions would have to be granted or denied based upon. Delayed implementation, on the other hand, allows pharmacies to begin compliance over a period of time, with a deadline of January 1, 2020
1735.6(e)	**P. Kim Peterson** University of California, Davis Medical Center	Recommendation/ Comments: This would require physical plant alterations and would need a lead time of a minimum of 3-5 years to implementation given space and cost considerations and extent of mechanical systems to handle the venting and negative pressure requirements. We started an evaluation based on USP 800 proposed regs and are in active architect level design work and estimated completion is currently out 2-3 years if space and funding can be secured. There is equipment available that allows for containment and protection of staff which, if allowed by the board, provide an alternative either short or long term.

1735.6(e)	**Doug O'Brien** Kaiser Permanente	Recommendations: 1. Delay implementation of the requirement for a negative pressure buffer area for compounding hazardous drugs until USP Chapter 800 is finalized. 2. If a negative pressure room will continue to be included in the Regulation, allow an adequate period for the phase-in of this design. For some facilities, this redesign process could take several years due to numerous factors including physical constraints within the facility, cost of the redesign, and time to obtain the appropriate permits from regulatory agencies such as OSHPD. 3. Eliminate or reword item(3) Rationale: USP Chapter 797 allows the compounding of low volumes of hazardous drugs within a positive pressure buffer area with appropriate primary engineering controls. The language of Item(3) is ambiguous and confusing.
1735.6(e)	**Douglas Barcon** Barcon & Associates	(1), (2), and (3) are fine, but should add an additional numbered line to include the proposed requirement in USP 800 for the room to be externally vented and the PEC to be externally vented. May want to shift current (3) to (4) to accommodate change.
1735.6(e)(1)	**Rheta Sandoval** Kaweah Delta Health Care	As proposed, appears to conflict with 1735.1(e)(2). Is this section addressing sterile hazardous drug compounding in a segregated compounding area that is negative pressure?
1735.6(e)(2)	**Rheta Sandoval** Kaweah Delta Health Care	Please strike the words within the parenthesis or provide guidance on how the pressure differential is monitored between the negative pressure room and the ceiling above it.
1735.6(e)(3)	**Rheta Sandoval** Kaweah Delta Health Care	Typographical error change the word “with” to “within”
1735.6(e)(1-3)	**Rheta Sandoval** Kaweah Delta Health Care	If the BOP adopts the modified text as proposed, please consider establishing reasonable timelines and expectations for compliance so as not to severely limit patient access to needed cancer care or place tremendous burdens on patients and those supporting their care to travel to a facility that is compliant with the regulation. Additionally, please establish a process for waiver application that would allow compounding pharmacies to continue to provide services out of their existing pharmacies as they work to gain regulatory compliance. Outside of the costs and time necessary to complete facility modifications to meet this requirement, there could be negative impacts if a pharmacy could not continue to provide the potentially life-saving “hazardous” medications needed as a facility works towards gaining compliance with the requirement. Some geographic areas of the State may not have a nearby health facility to provide this type of service or the ability to handle the order volume currently managed by the Pharmacy.
1735.6(e)(1)	**Michael Tou** Providence Health	Proposed Text: (e) Hazardous drug compounding shall be completed in a physically separate room with the following requirements: (1) Minimum of 12 air changes per hour; and Providence requests the board issue exemptions to hospital pharmacies which are unable to immediately comply with the requirements of section 1735.6(e)(1)(2)(3).

1735.6(e)(2)	**Michael Tou** Providence Health	Proposed Text: (2) Maintained at a negative pressure of at least 0.01 inches of water column relative to all adjacent spaces (rooms, above ceiling, and corridors); and Providence requests the board issue exemptions to hospital pharmacies which are unable to immediately comply with the requirements of section 1735.6(e)(1)(2)(3).
1735.6(e)(3)	**Michael Tou** Providence Health	Proposed Text: (3) All surfaces with the room shall be smooth, seamless, impervious, and non-shedding. Providence requests the board issue exemptions to hospital pharmacies which are unable to immediately comply with the requirements of section 1735.6(e)(1)(2)(3).
1735.6(e)(1-3)	**Lauren Berton** CVS Health	Rule language proposed in 1735.6(e)(1-3) reflects draft language found in USP 800 – Hazardous Drugs – Handling in Healthcare Settings. USP Chapter 800 draft language was released on 10/31/14 with a comment submission period until 5/31/15 and is currently pending final draft. It is our understanding that this particular USP chapter will undergo significant language changes due to comments received. It is recommended that the Board remove the proposed language found in 1735.6(e)(1-3) for Compounding Facilities and Equipment and await the final language release for USP Chapter 800 before amending the regulation in regards to hazardous drug compounding.
1735.7	**Jeffrey Nehira** Dignity Health	Time frame for the record keeping requirement should be specified and further clarification should be included specifYing the training of pharmacy staff, as this is a BOP requirement. Pharmacies do not have direct oversight of the training of personnel with institutional contracts; outsourced cleaning services are not taken into account with this added language. Request exemption of instituations with contracts for environmental cleaning services as the outsourced compancies should maintain documenation of their assigned staff. Pharmacies should have oversight of the processes and contracts themselves.
1735.8(c)	**Bruce Lepley** Community Regional Pharmacy	Reason for concern: This section describes the requirement of a quality assurance plan including “written standards for qualitative and quantitative analysis of compounded drug preparations…including the frequency of testing”. The verbiage is not specific and appears to imply that all products compounded by a pharmacy must be tested for integrity, potency, quality and labeled strength at least annually. Given the wide range and various dosage forms of products compounded in any given hospital pharmacy, as well as the limitations of some end-product testing laboratories to only be able to test certain medications, we recommend that facilities should be allowed to adopt a methodology and frequency (at least annually) for testing specific products for potency. Solution: Reword the statement to use “shall include a program for routine testing and analysis of designated compounded drug preparations on at least an annual basis”.
1735.8(c)	**Doug O'Brien** Kaiser Permanente	Recommendation: “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, of compounded drug preparations. The criteria by which preparations would be tested for potency, quantitative analysis, and labeled strength analysis shall be described in the quality assurance plan. All qualitative and quantitative analysis reports for compounded drug preparations shall be retained by the pharmacy and maintained along with the compounding record and master formula. Rationale: This proposed language would encompass non-sterile compounding of preparations such as creams and ointments, for which quantitative testing methods do not exist or are exorbitantly expensive. This language could be interpreted to require that quantitative and qualitative analysis be performed on all compounded products regardless of cost, availability of the actual assay, or scientific validity. Or, it could be interpreted to mean that one or two compounded drug preparations could be tested annually. **Continued in Next Row**

1735.8(c)	**Doug O'Brien** Kaiser Permanente	**Continued from Previous Row** Let's consider the latter scenario, since the former scenario is completely unrealistic. If one or two compounded drug preparations were tested annually, what is the value of those results to the pharmacist in charge? What are the benefits to the public? Those test results would show that a compounded drug prepared at a specific time on a specific date by a specific pharmacist did (or did not) meet potency and labeled strength requirements. Those test results can NOT be applied, however, to an identical compounded drug prepared the following day using the same master formula by another pharmacist, or even if it is prepared the following day by the same pharmacist (unless that product was tested as well – a highly unlikely occurrence). It seems like the Board is attempting to apply the systematic testing approach used in the pharmaceutical industry, in which large batches of finished products are systematically manufactured, and where samples from multiple batches are tested. By its very nature – preparing a compounded drug based on an individual prescription - pharmacy compounding is an episodic process. Therefore, testing for potency and labeled strength must be approached differently. It is important that there be a quality assurance plan, with criteria for end product examination in the master formula; as well as criteria and circumstances by which end products are tested for potency or labeled strength.
1735.8(e)	**Jeffrey Nehira** Dignity Health	Suggest and exemption for health care settings with a facility services policy regarding appropriate function of refrigeration devices.
1735.8(e)	**P. Kim Peterson** University of California, Davis Medical Center	1735.8(e) Agree with Doug O'Brien of Kaiser written comments in 45 Comment document. Additionally could create a push for increased use of 503B facility produced products due to the substantial increase in cost for implementing this onerous of a program as defined and left to interpretation by inspectors.
1751(b)	**Jeffrey Nehira** Dignity Health	This requirement for venting may provide a challenge for DSH and rural hosptials. Request exemption for these settings. Referencing this code of regulations as an appendix in the CA law book would be helpful as the referenced chapter may change.

1751(b)(3)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: Many hospitals have established pharmacy satellites nearby patient care areas to serve our most vulnerable patients (e.g. Intensive Care Units). The central pharmacy is too far from these patient care areas and the pharmacy satellites provide a venue to provide patient care that is closer to the patients. These pharmacy satellites are one room that provides a place for the pharmacy to perform order verification, drug storage, and drug preparation. Many of the pharmacy satellites have very limited room, thus the pharmacy will place compounding aseptic containment isolators (CACIs) which are enclosed to the surrounding environment and should have evidence from the manufacturer that they meet USP chapter 797 and Controlled Environment Testing Association (CETA) requirements. If one were to believe that this is an unverified study then one would have to question most of the conclusions derived from USP 797 as many of the conclusions taken from there are not based on "randomized controlled trials". We believe that we can remove the 3 foot no sink/drain requirement when CACIs are used to support pharmacy satellites. The alternative would be to close these pharmacy satellites that do not have the room to abide by the 3 foot no sink/drain rule which is not consistent with a patient centered care model. Solution: Make an exception that if the ISO Class 5 PEC is a CACI, that the three foot sink/drain rule does not apply while maintaining that sinks and drains should not be placed in a buffer area or in ISO class 7 or better.
1751(b)(3)(A)	**Douglas Barcon** Barcon & Associates	Current proposed text does not include manufacturer documentation of Chapter 797, USP-38 NF-33, 38th Revision, Effective May 1, 2015 compliance in air quality worse than ISO Class 7. The text in (A) should be amended to include this depending on whether the BUD is 12-hours or longer. Suggest adding after 1751.4(f)(1)-(3): "in air quality worse than ISO Class 7 or is non-ISO classified air quality "
1751(b)(4)	**Douglas Barcon** Barcon & Associates	Suggest adding: "products or" before "compounded drug preparations
1751.1(a)	**P. Kim Peterson** University of California, Davis Medical Center	Recommendation/ Comments: Please amend length of time within the pharmacy versus outside of the department or offsite storage. If 3 years within the pharmacy for personnel (>100 staff members) and compounding records would impact critical space available for operational and distributive needs.
1751.1(a)(5)	**Jeffrey Nehira** Dignity Health	Need further clarification regarding room temperature storage. Currently regulations state that medications are stored at controlled room temperature but there is no requirement for daily monitoring. Request an extended implementation date ifthis is now required for hospital settings.
1751.1(a)(7)	**Jeffrey Nehira** Dignity Health	Currently the technology does not exist for mobile isolation chambers and barrior isolators to measure the pressure differential ofthe 150-7 area of the divices. Only the pressure associated with the 150-5 compounding area. Clarification needs to be made regarding this requirement. For areas/rooms utilizing laminar flow hoods, it is impracitcal for daily monitoring of the pressure differential between areas. There has been no studies done indicating that a drop in pressure leads to an increase in contaminated preparations. Recommend removing the requirement for MICs/Barrior Isolators and changing the requirement for testing to every 6 months for room compliance.
1751.1(a)(7)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: USP 797 allows for at least daily documentation or by using a continuous recording device. We would like to continue to allow the use of a continuous recording device as an alternative which would also give the facility better "real time" data. Solution: Reword the section to state "Documents indicating daily documentation or by continuous recording device of air pressure differentials…"
1751.1(b)	**Douglas Barcon** Barcon & Associates	Suggest adding: "license type" before or after "license number" and shifting placement of "and."

1751.2(c)	**Douglas Barcon** Barcon & Associates	Suggest adding protection from light at end to read: “Instructions for storage and handling, including protection from light.”
1751.2(d)	**Douglas Barcon** Barcon & Associates	Insert between hazardous agents and shall:” “and non-hazardous preparations compounded in a PEC that is also used for compounding hazardous preparations” to bring into harmony with 1751.4(g).
1751.2(a)(2) Incorrect Section listed. Should be 1751.2(d)	**Jeffrey Nehira** Dignity Health	Cytotoxic and Hazardous drugs have very specific definitions not necessarily interchangeable. The NIOSH list 2014 states refer to Antineoplastic medications while other Hazardous agents are to be evaluated at each faciilty setting. Recommend leaving the comment, "if applicable" at the end of the statement that was removed.
1751.3	**P. Kim Peterson** University of California, Davis Medical Center	Recommendation/ Comments: Change shall to may or eliminate as unnecessary as regulations give the Board authority to take disciplinary actions.
1751.3(a)	**Douglas Barcon** Barcon & Associates	Consider adding definition of “material” or “material failure” as in suggestion for 1735.5(a).
1751.3(a)(2)	**Jeffrey Nehira** Dignity Health	Currently the technology does not exist for mobile isolation chambers and barrior isolators to measure the pressure differential ofthe 150-7 area of the divices. Only the pressure associated with the 150-5 compounding area. Clarification needs to be made regarding this requirement. For areas/rooms utilizing laminar flow hoods, it is impracitcal for daily monitoring of the pressure differential between areas. There has been no studies done indicating that a drop in pressure leads to an increase in contaminated preparations. Recommend removing the requirement for MICs/Barrior Isolators and changing the requirement for testing to every 6 months for room compliance.
1751.3(a)(7)	**Jeffrey Nehira** Dignity Health	Language should state, "Cleaning and disinfection schedule for the controlled areas and any equipment in the controlled area as specified in section 1751.4." as the frequecy is specified elsewhere regluations.
1751.3(a)(9)	**Jeffrey Nehira** Dignity Health	Purge time for some CACI's is indicated by an LED light or lockout mechanism. An exemption should be written in, "if applicable"
1751.3(a)(16)	**Jeffrey Nehira** Dignity Health	Infection control policies in health care institutions cover procedures around infectious materials. An exemption should be written for instituations, such as hospitals, with manditory Infection Control and Safety policies. Most pharmacies do not handle infectious materials; so "if applicable" should be added to the verbiage.
1751.3(a)(20)	**Jeffrey Nehira** Dignity Health	Need further clarification regarding room temperature storage. Currently regulations state that medications are stored at controlled room temperature but there is no requirement for daily monitoring. Request an extended implementation date if this is now required for hospital settings. Monitoring of medications at room temperature is also not required from distribution centers or during transport. Daily monitoring is impractical and does not correspond to current industry practice. Room temperature monitoring should first go to the FDA and manufacturers/distributors for consistency of practice. To require this at a local pharmacy level does not take into account any chain of custody until the final storage location.
1751.3(c)	**Douglas Barcon** Barcon & Associates	Change text: "section 1735.5 and 1751.3(a)" to "section 1735.5, 1751.3(a), and 1751.7(e)"
1751.3(e)	**P. Kim Peterson** University of California, Davis Medical Center	Recommendation/ Comments: Please amend to allow for electronic capture. We use and online learning system to manage distributing to employees and documenting their learning.

1751.3(e)	**Bruce Lepley** Community Regional Pharmacy	Reason for concern: We acknowledge that any material or significant changes to written policies and procedures for sterile compounding should be communicated to all personnel involved in compounding. However, this section implies that personnel must review all changes to all compounding policies and procedures, even if they do not directly impact their job duties in a material fashion. Additionally, our pharmacy and organization holds personnel responsible for abiding by all policies and procedures whether they are related to compounding or not; it is a standard expectation, and signature and date are not collected except in rare cases where the practice change is deemed significant. We believe a signature and date should only be required if there is a significant practice change being implemented as a result of any changes in policies and procedures. Solution: Change the first sentence to "…any material or significant additions, revisions and deletions…must be communicated to all personnel involved in sterile compounding". Change the last sentence to "If changes to the written policies and procedures result in a significant change in practice for compounding personnel, the review must be documented by a signature and date".
1751.4(d)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: USP 797 does not make any stipulation or requirement of mandatory use of a sterilizing agent (i.e. sporicidal: EPA definition). It only makes the stipulation of sanitizing and disinfecting. Furthermore, when sterilizing (i.e. killing spores) is mentioned as recommendation in the literature it is limited to general floor cleaning. The way it is written in this section could lend itself to believe that all items in the IV room have to be sterilized (i.e. use of a sporicide; EPA definition) at least monthly which is not a recommendation that cannot be found anywhere for a pharmacy that compounds sterile products (using sterile to sterile compounding methodology). Solution: Remove the requirement that the use of a sporicidal agent is required monthly and ensuring that there continues to be requirements for sanitizing and disinfecting at appropriate intervals. If the sporicidal requirement is not removed at least add verbiage that specifies that this requirement is for the cleaning of floors.
1751.4(d)(1-2)	**Jeffrey Nehira** Dignity Health	Use of a sporicidal agent is not required or standard of practice for surfaces other than IS0-5 environments in institutional settings, and is not mentioned in USP<797>. This regulation implies that a sporicdal agent is used on all surfaces and floors daily, which is not based on practice or evidenced based infection control practices. Frequency of cleaning also goes beyond/contradicts the requirements of weekly cleaning as specified in earlier regulation. Recommend removing this requirement of, "work table surfaces, carts, counters, and the clean room floor" as well as "walls, ceilings, storage shelving, tables, stools, and all other items in the ISO Class 7 or ISO Class 8 environment." Fungal contamination takes weeks of incubation, and through montioring of surface sampling and standard infection control practices risk is minimal.
1751.4(d)(4)	**Jeffrey Nehira** Dignity Health	An exemption should be made for instituations regarding storage of cleaning supplies in a clean room or ante-area as there are conflicting regulatory requirements for the storage of cleaning products under safety and environment of care. Suggest removal of the last statement, " and shall not be removed from these areas except for disposal."
1751.4(e)	**Jeffrey Nehira** Dignity Health	This requirement is not listed in USP<797> and not based in evidence practice. Implementation of this practice would severely impede workflow, especially in an institutional setting where there are requirements of timely delivery of monthly... Disinfection, using a suitable sterile agent, shall also occur on administration. This requirement encourages the all surfaces in the ISO Class 5 PEC frequently (at least every 30 minutes): preparation of compounded products by non-pharmacy personnel as delays patient care. If this requirement of every 30 minute cleaning is implemented in the hospital pharmacy practice setting, it would severely compromise the integrity of the pharmacy profession.

1751.4(e)	**William Stuart** Hartley Medical	Recommend: (d) Disinfection of the ISO Class 5 PEC, using a suitable sterile agent, shall also occur frequently, including: (1) At the beginning of each work shift; (2) Before each batch preparation is started; (3) Every 30 minutes during continuous compounding periods of individual CSPs; (4) After each spill; and (5) When surface contamination is known or suspected. Rationale: The proposed language does not differentiate between different compounding activities. A “lot” that requires longer than 30 minutes to complete would force an operator complying with this policy to cease compounding and disinfect the PEC. This would require unnecessary interventions into the PEC, therefore greatly increasing the risk of contamination of the lot either by moving the components outside of the PEC (biological contamination risk) or by cleaning while the components are inside the PEC (chemical contamination risk). The definition of 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).” would could classify each patient specific prescription as a lot. This would require an operator to disinfect the entire PEC before the start of every prescription. Disinfecting the PEC before the start of every single prescription would be an unreasonable burden for the operators and would decrease productivity significantly. We recommend introducing the definition of a “batch” to differentiate between patient specific prescriptions and larger quantity compounded preparations. Our recommendation to the proposed legislation follows USP <797> more closely to accurately represent the intent of the guideline. (Source: Cleaning and Disinfecting Compounding Area, February 2015 USP Compounding Compendium)
1751.4(e)	**Doug O'Brien** Kaiser Permanente	Recommendation: Delete 1751.4(e)(2) Rationale: Consider a typical scenario in a clean room in a hospital pharmacy. During a 15-minute period of compounding operations, pharmacy personnel could compound four doses of azithromycin 500 mg/250mL dextrose 5% for four different patients, two doses of famotidine 40 mg in 250mL dextrose 5% 250mL for one patient, and five doses of furosemide 100mg/100mL dextrose 5% for five different patients. Under the definition of “lot”, pharmacy personnel would be required to clean and disinfect the ISO Class 5 PEC before each lot – four times in 15 minutes. If one considers the number of lots that would be compounded in four hours, the PECs would need to be cleaned and disinfected 50 to 60 times. Subsections 1751.4(e)(1) , 1751.4(e)(3), and 1751.4(e)(4) are sufficient.
1751.4(e)	**Rheta Sandoval** Kaweah Delta Health Care	Please consider inserting the verbiage “when ongoing compounding activities are occurring” after the word “minutes”. This verbiage is consistent with USP Chapter <797>. Rational: some sterile compounding pharmacies are not open 24-7.

1751.4(e)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: The language in this sentence uses disinfectant and sterile agent in the same sentence which could be interpreted as the use of a sterilizing agent to disinfect. According to EPA and other regulatory standards disinfect and sterilize have two distinct meanings. There could be confusion if these two words are used in the same sentence. Solution: Remove the words “using a suitable sterile agent” to “using a suitable disinfecting agent” to mitigate the risk of confusion that the use of a sterilizing agent is required to disinfect the PEC.
1751.4(e)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: The language here states that disinfection should occur at least every 30 minutes. Please know that the Phenol and Quaternary Ammonia compounds used for disinfecting state that once these chemicals are used they are to be air dried for up to 10 minutes. If we are making the requirement to disinfect at least every 30 minutes then that means that the PEC can only be used for 40 minutes of every hour if you take into consideration the time to allow to dry when cleaning with disinfectants. In addition, if we are to disinfect upon spill, before each lot, etc,.. as stipulated in this same section this only further diminishes the time we can use our PEC. This could potentially mean that we could be disinfecting so often that we could only be using the PEC for less than 30 minutes for each hour the PEC is available when you consider the drying time needed after the application of the Phenol or Quaternary Ammonium compounds that are used. This would impair pharmacy’s ability to meet turnaround times for medications that are essential for a patient centered care model of service established for hospitals that produce “STAT” medications. Solution: Remove the requirement to disinfect (the PEC) at least every 30 minutes. Maintain the stipulations in this section that describe disinfecting at the beginning of each shift….items (1),(2),(3), and (4).
1751.4(e)(2)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: The most recent USP 797 regulations state that cleaning of the ISO 5 PEC should occur at the beginning of each work shift, before each batch (USP 797 only uses the word batch in referencing high-risk compounding) preparation is started, every 30 minutes during continuous compounding periods of individual CSPs, when there are spills, and when surface contamination is known or suspected from procedural breaches. With the new proposed definition of “lot,” interruption of workflow of hospital compounding in order to clean before and after each lot may impact the timeliness of medication delivery to patient and could introduce potential for medication errors. Solution: Remove “before and after each lot” and keep items (1), (2), (3), and (4) which will ensure proper intervals for disinfection are still in place.
1751.4(f)	**Jeffrey Nehira** Dignity Health	Recommend updating the second sentance to state, "Certification and testing of primary and secondary engineering controls shall be the performed no less than every six months. Certification and testing will also occur when ver the device or area designated for compounding is altered or a service to the facility is performed that would impact the device or area." Barrier isolators are self-contained by definition and manufacturer specification and should not require recertification if moved.
1751.4(f)(1)	**Jeffrey Nehira** Dignity Health	This secton requires clarification and exemption should be made for Barrior Isolators for this requirement as the airflow displacement is different than laminar flow hoods. The requirements for measuring the particle counts apply to lamnar flow hoods.
1751.4(f)(2)	**Jeffrey Nehira** Dignity Health	Recommend clarification of this requirement. If this is requiring testing of Barrior Isolators during material transfer this is impracticle and not part of testing for recertification of the hoods.
1751.4(f)(3)	**Jeffrey Nehira** Dignity Health	Recommend clarification of this requirement. CACI's are by definition contained isolators that should not need to be located in an IS0-7 cleanroom. If this is requiring testing of in Barrior Isolators during material transfer this is impracticle and also not part of testing for recertification of the hoods. Barrior isolators have manufacturer recommended purge times prior to aseptic manipulation. Perhaps this regulation should defer to manufacturer specifications.

1751.4(g)	**Jeffrey Nehira** Dignity Health	Request exemption of the labeling requirement for DSH hospitals and rural hospitals as this places a tremendous cost on the organization/facility. The third sentence states that during hazardous compounding performed using a compounding asceptic containment isolator full garbing must occur, which includes two layers of gloves... this contradicts some manufacturers recommendation of mobile isolation chamber use. This also does not correspond to the ASHP recommendations of Hazardous Drug Preparation. Clarification needs to be made since manufacturers recommend an intermediary cloth glove that allows for easy removal of the hand from the containment glove. Please note that most sterile gloves do not meet ASTM D6978-05 standards and those that are used for chemotherapy handling that most facilities utilize are typically the non-sterile nitrile gloves. The non-sterile gloves are then sterilized with the appropriate disinfecting agent. Recommend adding that non-sterile nitrile gloves that meet ASTM D6978-05 standard can be used if steriled with the appropriate disinfecting agent. This statement does not correspond with current CETA engineering requirements compared with USP<797>. Recommend reclassifying this requirement according to CETA flowchart of Engineering Control Requirements for Hazardous Drugs revised May 2009 (see attached document).
1751.4(g)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: We just want to be sure that when we use the definition of “hazardous” drugs we are referring to agents used to treat neoplasms. We want to be sure that we are not using the NIOSH definition of hazardous drugs that include non-antineoplastic drugs that meet one or more of the NIOSH criteria for a hazardous drug including those with manufacturers’ safe handling guidance (MSHG). Solution: Modify the definition of “hazardous” to mean “all anti-neoplastic agents used to treat neoplasms identified by the National Institute for Occupational Safety (NIOSH)…….”
1751.4(g)	**Katherine Palmer** **Rita Shane** Cedars-Sinai Medical Center	Pharmacies preparing sterile hazardous agents shall do so in accordance with Section 505.5.1 of Title 24, Chapter 5, of the California Code of Regulations, requiring a negative pressure PEC. ~~Additionally, each PEC used to compound hazardous agents shall be externally vented~~. Include timeframe (ex.5 years) to allow facility changes to be made for external venting of PEC before enforcing.
1751.4(g)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: This statement would include CACI’s that are used as PEC’s to compound hazardous drugs. USP 797 does not make it required that CACI’s that are used to compound hazardous drugs to be externally vented. In fact, USP 797 recognizes that many hazardous have sufficient vapor pressures that allow volatilization at room temperature and that environmental sampling in the CACI to detect uncontained hazardous drugs can be performed and analyzed to help determine if there is a need for a CACI to be externally vented. Solution: Add the stipulation that a PEC does not have to be externally vented if it is a CACI unless environmental sampling cannot be provided or proved that there is no detection of uncontained hazardous drugs on the CACI work surfaces.
1751.4(g-l)	**University Compounding Pharmacy** Joe Grasela	It is unnecessary to have the gown close in the back so long as the employee is fully covered, front closure with zippers or snaps should be allowed Gloves tested to meet ASTM 6978-05 are standard practice for assessment of resistance of medical gloves to permeation by chemotherapy drugs. Double gloves should only be required when working with NIOSH Anti-neoplastics and shouldn't be a requirement for NIOSH NON Anti-neoplastics. USP 800 doesn't require or propose a double glove when working with hazardous compounds non-antineoplastics. Please explain your reasoning for two layers of gloves when they are not needed

1751.4(h)	**Jeffrey Nehira** Dignity Health	This statement says when using a compounding asceptic containment isolator full garbing must occur, which includes two layers of gloves... Two layers of gloves are not consistent with most PEC operational guidelines and deviate from manufacturer recommendations. Clarification needs to be made since manufacturers recommend an intermediary cloth glove that allows for easy removal of the hand from the containment glove. Donning of sterile gloves with asceptic islolators also does not make sense since the outside portion of the glove and the barrier isolator can be maintained in a non-sterile environment.
1751.4(h)	**Ernest Pieper** Glenn Medical Center	For compounding in cleanroom environments, sterile gloves may be donned in the ante area or the cleanroom which have ISO 8 or ISO 7 air standards respectively. 1715.5 (5) states: "…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 nonsterile objects. Gloves shall also be routinely inspected for holes, punctures, or tears and replaced immediately if such are detected." Sterile gloves used in cleanrooms are exposed to relatively dirty air versus ISO 5. The gloves may come in contact with a variety of supplies and objects, even the attire of the preparer. There seems to be no time limit to the use of these gloves, as long as the preparer remains in the ante area or cleanroom. Inspection of holes or tears is subjective to the diligence of the preparer. In great contrast, the attached gloves in a containment aseptic isolator are continually exposed to ISO 5 air quality in the interior of the isolator. They cannot touch the variety of dirty objects that are accessible to gloves worn on the hand. The integrity of isolator gloves can also be assured by monitoring the pressure differential of the CAI. There is no logic or evidence that donning sterile gloves over intact, sanitized isolator gloves provides any additional protection to the public. The paper package for sterile gloves might even introduce potentially harmful particulate matter into the compounding area with a loss if ISO 5 air quality.
1751.4(h)	**Douglas Barcon** Barcon & Associates	In order to include a CACI, after "compounding aseptic isolator" consider adding "or a compounding aseptic containment isolator
1751.4(k)	**Brian Warren** California Pharmacist Association	~~(j)~~(k) The sterile compounding area ~~is~~ of the pharmacy shall have a comfortable and well-lighted working environment, which includes a room temperature of 20-~~22~~ 24 degrees Celsius (68-75 degrees Fahrenheit) or cooler to maintain comfortable conditions for compounding personnel when attired in the required compounding garb. Technical fix to change "is" to "of." Also, fix Celsius to Fahrenheit conversion error. 75 degrees Fahrenheit is 23.9 degrees Celsius (which could be rounded to 24 degrees Celsius).
1751.4(k)	**Douglas Barcon** Barcon & Associates	Change "is" to "in"
1751.4(k)	**Jeffrey Nehira** Dignity Health	The requirement of 20-22 degree C room temperature for compounding sterile preparations puts undo burden on pharmacies with a narrow temperature range smaller than the definition of controlled room temperature defined above. ("Controlled room temperature" means 20 degrees to 25 degrees C (68-77 degrees F.) Request leaving room temperature as defined in previous sections.
1751.4(k)	**BJ Bartleson** California Hospital Association	The degree conversion between Celsius and Fahrenheit needs to be changed from Celsius 20-22, to, 20-24. CHA would like to offer that since this range closely mirrors the controlled room temperature already required for the drugs, perhaps eliminating the specific temperature range would be reasonable.
1751.4(k)	**Candace Fong** **Clara Evans** Dignity Health	The conversion factor from Fahrenheit to Centigrade is inaccurate and should be updated from 20-22C to 20-24C. In addition, since this range closely mirrors the controlled room temperature already required for drug storage Dignity Health recommends eliminating the specific temperature range all together.

1751.4(k)	**University Compounding Pharmacy** Joe Grasela	Please correct the Celsius to Fahrenheit conversion error 22 degrees Celsius = 71.6 degrees Fahrenheit
1751.5(a)(1)	**Jeffrey Nehira** Dignity Health	"...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 are not required." Recommend removal of this statement since the use of any PEC should be according to manufacturer specification. PECs go through a certification process and manufacturered accordingly. Products are sampled using these PECs and environmental testing is done by the pharmacy every 6 months according to the manufacturer recommendations. Manufacturers would not take on the liability of the product since it is dependent on the environment they are used. The environmental sampling done every 6 months should validate the necessity tor PPE beyond manufacturer recommendation.
1751.5(a)(4)	**Jeffrey Nehira** Dignity Health	Request addition of statement, "If jewelry cannot be removed, then it must be thoroughly cleaned and covered."
1751.5(a)(5)	**Jeffrey Nehira** Dignity Health	Recommend removing the first word, "sterile". If gloves have been tested tor compatibility with disinfection with isopropul alcohol, the gloves should not need to be "sterile" before disinfection. Once sterile gloves are donned, they will immediately become contaminated when products are picked up for sterile preparation. This would require disinfection regardless of the original sterility of the glove.
1751.5(a)(6)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: Prohibiting the use of nail polish in an ISO Class 5 or 7 area supersedes the nationally enforceable USP 797 regulation that only makes the stipulation that artificial nails or extenders are prohibited. In fact, there are studies that have reviewed nail polish used in these areas and have found no direct correlation that nail polish increases the number of particles shed from compounding personnel which lead to an increased risk of microbial contamination of critical sites of CSP's. Solution: Remove "nail polish" from this section.
1751.5(b)	**Rheta Sandoval** Kaweah Delta Health Care	Please verify the correct code is being cited here. There are not any apparent exceptions listed in 1751.4(g). Perhaps referring to the exceptions listed in 1751.5(a)(1)?
1751.6(e)	**Douglas Barcon** Barcon & Associates	Paragraph (e) is embedded in (d). Add a line feed to shift (e) to next line.
1751.6(e)(1)(E)	**Bruce Lepley** Community Regional Pharmacy	Reason for concern: The statement "which contain the same amount or greater of volume transferred during the selected manipulations" implies that the media-fill test performed by personnel must involve a volume transfer the same size or greater than the largest volume transfer performed by the pharmacy when compounding sterile products. It would be difficult to establish this threshold; furthermore, media-fill test kits are commercially manufactured and designed with specific volume transfers and procedures to mimic the most complex manipulation performed by the pharmacy. Solution: Remove the portion of the sentence stating "and which contain the same amount or greater of volume transferred during the selected manipulations".
1751.6(e)(1)	**Douglas Barcon** Barcon & Associates	Suggest adding "Hazardous and non-hazardous spills and knowledge of MSDS information" as a lettered paragraph; perhaps as (K)

1751.7(b)	**P. Kim Peterson** University of California, Davis Medical Center	Recommendation/ Comments: Materials could imply the drugs and diluents. We use non drug products and media in order to test staff. Please consider exploring language that would separate those preparing (technicians) from those checking (pharmacists) in completing this hands on testing. Didactic instruction and knowledge validation could be used for pharmacists that would allow alignment with new electronic systems for validating the preparation by technicians of the product prior to release of the preparation to the patient. This meets the intent and allows the pharmacist with physical limitations or working outside of the area to not have to perform the media fill tests. Of note, schools of pharmacy do not necessarily routinely train pharmacists in sterile compounding in a working or lab environment to perform these manipulations.
1751.7(e)	**Douglas Barcon** Barcon & Associates	On first line of text change “preparation” to “preparations” Delete (1) immediately following (e) on first line because (1) is used again in second paragraph.
1751.7(e)	**Katherine Palmer** **Rita Shane** Cedars-Sinai Medical Center	1751.7 (e) Sterile Compounding Quality Assurance and Process Validation In a circumstance where a 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, (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 **and patient's** written consent to dispense. (2) And subsequent to dispensing: **(A)Send random sample for sterility and pyrogen testing as part of process validation** **(B) Notify physician if results demonstrate microbial growth or pyrogens** **(C) Have protocol approved by the Pharmacy & Therapeutics Committee** Would recommend including this section back into the regulation revision to avoid patient loss of life or intense suffering due to the inability to provide emergency medications to patients. In rare circumstances medications such as Alum and Formalin are needed to treat hemorrhagic cystitis that can be life- threatening. Evidence supports that these drugs are needed when other measures fail. The patient could bleed to death without this provision.

1751.7(e)	**Brian Warren** California Pharmacist Association	~~(c)~~ (e)(1) Batch-produced sterile injectable drug preparation compounded from one or more non-sterile ingredients except as provided in paragraph (2), 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. Exempt from pyrogen testing are non-injectable ophthalmic and inhalation preparation. ~~(1)~~ (2) The following non-sterile-to-sterile batch drug preparations do not require end product testing for sterility and pyrogens: (A) Preparations for self-administered ophthalmic drops in a quantity sufficient for administration to a single patient for 30 days or less. (B) Preparations for self-administered inhalation in a quantity sufficient for administration to a single patient for 14 ~~5~~ days or less. (C) Preparations compounded for administration to a single patient that meet all of the following criteria: (i) Are needed for emergency administration to prevent the loss of life or intense suffering, as determined by the prescriber or institution, and only in a quantity sufficient for an emergency course of therapy. (ii) Have a chemical stability of 14 days or less according to a nationally recognized reference, such as Trissel's Stability of Compounded Formulations, the Merck Manual, or the American Society of Health-System Pharmacists' Compounding Sterile Preparations. (iii) Are intended to fill a need for a drug classified as currently in shortage on the list of Current and Resolved Drug Shortages and Discontinuations maintained by the federal Food and Drug Administration, listed on the Current Drug Shortage Bulletins maintained by the American Society of Health-System Pharmacists, or on backorder with the institution. **Continued on Next Row**
1751.7(e)	**Brian Warren** California Pharmacist Association	**Continued from Previous Row** First, we recommend a technical fix to renumber what should be paragraph (2) of subsection (e), which is currently numbered as a second paragraph (1). Second, we recommend modifying subparagraph (B) of paragraph (2) to allow for no more than a 14-day course of therapy. Testing for sterility and pyrogens takes up to 14 days to complete. Allowing an exemption from end-product testing for a course of therapy sufficient for administration to a single patient for 14 days ensures that the patient has access to the medication while a longer course of therapy awaits release from quarantine following receipt of end-product testing results. Third, we recommend exempting a narrow class of preparations from end-product testing to ensure patient access. We propose exempting emergency use preparations that are for drugs experiencing shortage or on back-order and where chemical stability is 14 days or less. Our proposed exemption is for preparations that meet all three of these criteria. A number of sterile preparations have chemical stability of 14 days or less. Some of these are needed in emergency situations, so they cannot be compounded in advance for patient-specific use, and compounding in advance for office use can be difficult to accurately predict. Additionally, some of these preparations are compounded due to need for drugs experiencing a shortage or are on backorder. Key examples include epinephrine, sodium bicarbonate, and IV calcium (gluconate and chloride). For further examples of CSPs with abbreviated chemical stability, see Trissel's Stability of Compounded Formulations, the Merck Manual, or the American Society of Health-System Pharmacists' Compounding Sterile Preparations.

1751.7(e)(1)	**Michael Tou** Providence Health	Proposed Text: (e)(1) Batch-produced sterile injectable drug preparation compounded from one or more non-sterile ingredients except as provided in paragraph (2), 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… (1) The following non-sterile-to-sterile batch drug preparations do not require end product testing for sterility and pyrogens Providence requires that it be renumbered to (e)(2): ~~(1)~~(2) The following non-sterile-to-sterile batch drug preparations do not require end product testing for sterility and pyrogens
1751.7(f)	**Judith Brosz**	On January 27, 2015, a sterile compounding inspection took place at El Camino Hospital in Mountain View, CA. Certain informal statements made by the inspectors in an e-mail exchange implied that all pharmacists in the department, regardless of whether or not they actually worked in the sterile processing environment, had to pass the rigorous practical test involving long standing times and repeated manipulation of needles. This universal requirement will make it difficult or impossible for those with disabilities to work in any capacity in a hospital pharmacy. Specifically, the testing requirement was broadened to include not only pharmacists producing the sterile product, and pharmacists directly supervising technicians inside the sterile environment, but those pharmacists whose duties only include checking final sterile products remotely using computerized systems such as DoseEdge. These are quite different tasks. The latter is also a duty more accommodating to a disabled pharmacist. To correct this situation, for myself and other disabled pharmacists, I have recommended adding 1751.7 (f) or an equivalent statement to clarify that that remote computer checking should not have identical training requirements to the actual production or direct supervision of sterile drug preparations in the controlled sterile processing environment. DoseEdge and similar systems have no mechanism for supervision of pharmacy technicians to ensure the proper sterile processing procedures are followed. It is not a direct supervision method. Written competency tests are appropriate, but practical tests of cleaning and needle handling should not be necessary if a pharmacist has no actual duties inside the controlled environment.
1751.8	**Doug O'Brien** Kaiser Permanente	Recommendation: “Multiple dose vials of allergen extracts, when compounded in accordance with the section of USP Chapter 797 entitled “Allergen Extracts as CSPs”, shall be assigned the beyond use dates recommended by the manufacturer.” Rationale: Allergen extracts are specialized CSPs and are frequently not subject to the standard BUD rules delineated in USP Chapter 797.
1751.8	**Jeffrey Nehira** Dignity Health	This section of Title 16 seems to try and copy the definitions of low, medium, and high risk compounding. Recommend using verbiage straight from USP797 to eliminate confusion.
1751.8(a)(1)	**Douglas Barcon** Barcon & Associates	An ISO Class 5 PEC is also a CAI or CACI. With that said, after “1751.4(f)(1)-(3)” insert “and manufacturer documentation shows compliance with USP 797 when located in an area where air quality is worse than ISO Class 7 or is non-ISO classified” …, using only…

1751.8(a)(3)	**Douglas Barcon** Barcon & Associates	After “penetrating disinfected stoppers on vials with sterile needles and syringes” add “or spiked transfer devices” to not exclude use of such devices
1751.8(e)	**Douglas Barcon** Barcon & Associates	Add at end after “ante-area”: “or within a segregated compounding area” If I interpreted this correctly, without this change to exclude a segregated compounding area, a compounded product may be given either a 12-hour BUD or an immediate use BUD depending on compounding staff choice. There will be no continuity.
1751.8(e)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: Many large health care facilities already employ the use of an “immediate use only” label for reasons other than a 1 hour BUD (e.g. criticality of the drug, cost of the drug, etc.) In addition, other regulatory agencies (i.e. The Joint Commission) have stipulations in existence for labeling “immediate use” sterile products (i.e. medication name, strength, quantity, diluent and volume, expiration date when not used within 24 hours, and expiration time when expiration occurs in less than 24 hours). To avoid confusion, it would be beneficial to specifically remove the requirement of labeling the product for “immediate use only” and impose the existing regulation of the expiration time when expiration occurs in less than 24 hours. Solution: Replace the requirement of labeling for “immediate use only” with the exact one hour beyond use date and time.
1751.8(e)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: This section does not stipulate as to whether this applies to all healthcare professionals who are qualified to engage in immediate use sterile compounding drug preparation outside the profession of pharmacy. Solution: Please clarify and insert verbiage to make clear of whether or not this stipulation applies to all professions outside of pharmacy who are qualified to engage in immediate use sterile compounding (e.g. RN).
1751.8(e)(1)	**Bruce Lepley** Community Regional Pharmacy	Reason for Concern: Other regulatory agencies (i.e. The Joint Commission) have stipulations in existence for one to compound immediate use sterile products which include: “…a delay could harm the patient …or the products stability is short. To mitigate risk of confusion we recommend adopting similar language that would accomplish the intent of this section. Solution: Reword section to use “a delay could harm the patient” or “the products stability is short”.
1751.9(a)	**Jeffrey Nehira** Dignity Health	Exemptions should be made for use during a procedure. Most ampules are used in the operating room and are used on the sterile field.

1751.9(b)	**Katherine Palmer** **Rita Shane** Cedars-Sinai Medical Center	~~(c)~~ **(3)** 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. **(4) The use of technologies, techniques, materials, and procedures other than those described in this sterile compounding section is not prohibited so long as they have been proven to be equivalent or superior with statistical significance to those described herein" (USP 797 page 1).** Additionally, as a result, counterfeit chemotherapy is an area of national concern, until such time as E-Pedigree is available. Closed system transfer devices (CTSD) protect the vial from entry of external bacteria after initial puncture beyond the USP 797 approved 6 hour time limit. It has been shown that one of these systems maintains sterility of the vials to which it is attached for up to 168 hours (7 days). Recommendation: Allowance to use CTSDs with supporting literature to extend the beyond use date of single dose vials of chemotherapy to 24 hours or use through the end of the shift, whichever is shorter. This recommendation is more conservative than the timeframe of 7 days listed in the CTSD study and would assist institutions in conserving scarce chemotherapy medications. Metzger ML, Billett A, Link MP. The Impact of Drug Shortages on Children with Cancer- The Example of Mechlorethamine. New Eng/ 1 Med, 2012; 367:2461-3. Giorgi D, Sadeghipour F, Favet J, et al. Sterility validity period of vials after multiple sampling under vertical laminar airflow hood. 1 Oneal Pharm Practice, 2005; 11:57-62. Edwards M, Solimando D, Grollman F, et al. Cost savings realized by use of the PhaSeaiTM closed-system transfer device for preparation of antineoplastic agents. 1 Oneal Pharm Practice. 2013; 19:338-47.
1751.9(a)(b)(c)	**Doug O'Brien** Kaiser Permanente	Recommendation: Include above language from USP 797 allowing the use of proven technologies with quality assurance procedures (for example, Closed System Transfer Devices) allowing for extension of BUD for single-dose vials. Rationale: One of the hallmarks of USP and Current Good Manufacturing Practices (cGMP) is the ability of entities under the guidelines to be innovative and advance practice with validated processes that differ from the current standards. The advancement of knowledge, technology, and validation processes in a very fluid environment must be allowed to flourish; thus the ability to design programs that meet or exceed current outcomes is essential. The key statement allowing this within the USP 797 is as follows: “The use of technologies, techniques, materials, and procedures other than those described in this chapter is not prohibited so long as they have been proven to be equivalent or superior with statistical significance to those described herein.”
Overall Comment	**Michael Tou** Providence Health	Allow exemptions from compliance: The modified text intends to align state regulations with proposed USP 800 national guidance for the preparation of hazardous drugs. We request the board issue exemptions to hospital pharmacies unable to immediately comply with the new requirements, including external ventilation. Our pharmacies wish to continue providing life-saving therapies to our most vulnerable patients as they implement a corrective action plan. The board should consider the lengthy regulatory approval required by OSHPD for any modifications to our hospital pharmacies when granting exemptions. Additionally, hospitals must go through a lengthy internal governance process to obtain financing for these types of projects. The board’s guidance in allowing temporary exemptions from compliance should be developed with hospital pharmacy input prior to enforcement of the final rule

Overall Comment	**Judith Brosz**	Indiscriminate use of “employees,” “personnel” “staff,” “compounding personnel, and “sterile compounding personnel.” The broad range of terms leaves too much room for interpretation, as some of these terms could be used to generate a “universal” requirement for specific training that is not actually necessary for all staff in a pharmacy. This was addressed in greater detail in comments presented at the last comment cycle.
Overall Comment	**BJ Bartleson** California Hospital Association	At the June 25, 2015, Board meeting, during discussion of the sterile compounding modified regulations, the Board clearly stated hospitals that do not presently meet the proposed regulations for physical plant and venting issues, and/or who will not meet by the regulatory mandated date, could be granted a program waiver. The program waiver would be considered based on the development of a detailed plan of correction and corresponding timeline of planned implementation, and full completion of updated requirements as determined in the plan of correction. CHA agrees the containment of hazardous drug residue during hazardous sterile compounding is necessary, reasonable and in full alignment with forthcoming USP 800 guidance. With that being said, the proposed requirement for a separate negative pressure room for all hazardous sterile drug compounding, and the requirement for external venting, will require many hospitals to make significant physical plant changes, ventilation reconfigurations, along with potential purchase and or procurement of new or modified equipment, to perform successfully under the newly revised guidelines. Specifically, section 1735.1 (c) requiring BSC or CACI to be vented externally, 1735.6(e) requiring a physically separate room with negative pressure, and, 1751.4(i) requiring unidirectional airflow in CAI/CACI. These changes could range widely across our diverse hospital pharmacies relative to cost and time required for changes **Continued on Next Row**
Overall Comment	**BJ Bartleson** California Hospital Association	**Continued from Previous Row** CHA and its members would appreciate involvement in any Board activity that may occur defining the program waiver process and its components, especially as specific details are determined such as plan of correction requirements, forms, permits, approvals, timelines, etc. CHA is putting an ad hoc team of pharmacists, facilities experts, OSPHD and others, to assist in member support as we move through the final phases of the regulatory process. We are updating the sterile compounding matrixes developed by the CHA/CSHP work group, covering such items as physical plant requirements, policies, procedures and frequency of documentation, lab testing and temperature monitoring requirements. We plan to implement a member webinar that will discuss the USP transition from 797 to 800, the proposed and finalized regulations, along with tools and solutions, including a gap analysis, and best practice examples from the field. We appreciate the Board’s flexibility and accommodating approach to afford all stakeholders a voice in creation and design of sterile compounding regulations that both meet the ultimate goal of patient safety, as well as recognizing the flexibility necessary to address the varied complexities of health care systems, hospitals and organizations across the state

Overall Comment	**Candace Fong** **Clara Evans** Dignity Health	While Dignity Health agrees containment of hazardous drug residue during hazardous sterile compounding is necessary, reasonable and in full alignment with USP 800 guidance, the proposed requirement for a separate negative pressure room for all hazardous sterile drug compounding, and the requirement for venting to the outside, will require significant physical plant changes, ventilation reconfigurations, and investment in new or modified equipment. For Dignity Health, at least 15 of our hospitals in California will require a build out of separate negative pressure rooms, with ventilation outside, to compound hazardous drugs. The remaining facilities with existing negative pressure rooms will require assessment of their ability to comply with new regulations. Total cost estimated to build and/or retrofit negative pressure rooms is estimated conservatively at $3 million for construction costs alone, in addition to the additional time it will take to plan and seek approval from OSHPD, which often takes at least six months. Dignity Health respectfully requests the Board to provide program flexibility to allow hospitals to assess, plan and implement venting requirements and room construction, and time to move those changes through the complicated Office of Statewide Health Planning and Development (OSHPD) approval process. Thus, Dignity Health respectfully requests the Board solicit stakeholder input when establishing program flexibility, particularly in the development of specific plan of correction requests, templates, and timelines
Overall Comment	**Katherine Palmer** **Rita Shane** Cedars-Sinai Medical Center	Ability to provide emergency therapy to patients to avoid patient loss of life or intense suffering when other hemorrhagic cystitis treatments have failed
Overall Comment	**Katherine Palmer** **Rita Shane** Cedars-Sinai Medical Center	Ability to provide chemotherapy to patients in the setting of continued drug shortages of cancer medications by using equivalent or superior technologies for preserving medication vials
Overall Comment	**University Compounding Pharmacy** Joe Grasela	Sections that address Hazardous compounding seem to have been derived from the proposed language in USP 800 which has yet to pass and become a standard. They are still in the early stages of their submission/revisions. It is in CaBOP's best interest to wait until the language in USP 800 is finalized prior to making it law. Adding the language prematurely and then having to potentially change it again once USP 800 is final may certainly cause unnecessary distress, construction, and financial burden for many hospitals, compounding pharmacies, and other facilities/institutions that compound preparations.

Attachment 4

Title 16. Board of Pharmacy

Modified Text

Changes made to the originally proposed language are shown by ~~double strike-through~~ for deleted language and double underline for added language. (The changes are also indicated in red font)

Changes made to the modified proposed language are shown by ~~double strike-through/bold underline~~ for deleted language and curved underline for added language. (The changes are also indicated in blue font)

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 area with 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. ISO Class 7 or better air quality is required for ante-areas providing air to a negative pressure room.

(b) "Beyond use date" means the date, or date and time, after which administration of a compounded drug preparation shall not ~~be begun~~ begin, 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. Where hazardous drugs are prepared, the exhaust air from the biological safety cabinet ~~should~~ shall be appropriately removed by properly designed external building ventilation. This external venting should be dedicated to one BSC or CACI.

~~(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.~~

~~(c)~~(d) "Bulk drug substance" means any substance that, when used in the preparation of a compounded drug preparation, processing, or packaging of a drug, ~~becomes~~ is 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)~~(e) "Cleanroom or clean area or buffer area" means a ~~physically separate~~ room or area ~~with walls and doors~~ with HEPA-filtered air that provides ~~at least an~~ ISO Class 7 or better air quality where the primary engineering control (PEC) is physically located.

(1) For nonhazardous compounding a ~~A~~ ~~minimum~~ ~~differential~~ positive pressure differential of 0.02- to 0.05-inch water column relative to all adjacent spaces is required.

(2) For hazardous compounding at least 30 air changes per hour of HEPA-filtered supply air and a negative pressure of between ~~at least~~ 0.01 to 0.03 inches of water column relative to all adjacent spaces is required.

~~(h)~~(f) "Compounding Aseptic Containment Isolator (CACI)" means a unidirectional HEPA-filtered airflow 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~~ shall be appropriately removed by properly designed external building ventilation. This external venting should be dedicated to one BSC or CACI. Air within the CACI shall not be re-circulated nor turbulent.

(g) "Compounding Aseptic Isolator (CAI)" means a form of isolator specifically designed for non-hazardous compounding of pharmaceutical ingredients or preparations while bathed with

unidirectional HEPA-filtered air. 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. Air within the CAI shall not be re-circulated nor turbulent.

~~(i)~~(h) "Controlled cold temperature" means 2 degrees to 8 degrees C (35~~-6~~ degrees to 46~~-4~~ degrees F).

~~(j)~~(i) "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(s) for that product.

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

~~(l)~~(k) "Copy or essentially a copy" of a commercially available drug product includes all preparations that are comparable in active ingredients to commercially available drug products, except that it does not include any preparations in which there has been a change, made for an identified individual patient, which produces for that patient a clinically significant difference, as determined by a prescribing practitioner, between that compounded preparation and the comparable commercially available drug product.

~~(m)~~(l) "Daily" means occurring every day ~~that a~~ the pharmacy is operating, except when daily monitoring of refrigerator and freezer temperature are required, then daily means every 24 hours.

~~(n)~~(m) "Displacement airflow method"~~:~~ means a concept which utilizes a low pressure differential, high airflow principle to maintain segregation from the adjacent ante-area by means of specific pressure differentials. This principle of displacement airflow shall require an air velocity of 40 ft per minute or more, from floor to ceiling and wall to wall, from the clean area across the line of demarcation into the ante-area. The displacement concept may not be used to maintain clean area requirements for sterile compounds which originate from any ingredient that was at any time non-sterile, regardless of intervening sterilization of the

ingredient, or for hazardous compounds.

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

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

~~(q)~~~~(r)~~(q) "Gloved fingertip sampling" means a process whereby compounding personnel lightly press each fingertip and thumb of each hand 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)~~~~(s)~~(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)~~~~(c)~~~~(t)~~(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)~~~~(u)~~(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)~~~~(v)~~(u) "Media-fill test" means a test used to measure the efficacy of compounding personnel in aseptic techniques whereby ~~that mimics~~ compounding procedures are mimicked using a growth-based media and then the resulting preparation is evaluated for sterility. ~~to demonstrate the competency of compounding personnel in aseptic techniques.~~ The media-fill test must mimic the most complex compounding procedures performed by the pharmacy ~~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)~~~~(w)~~(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)~~~~(x)~~(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.~~ It does not include topical, sublingual, rectal or buccal routes of administration.

~~(x)~~~~(y)~~(x) "Personal protective equipment" means clothing or devices that protect the employee from exposure to ~~drug products~~ compounding ingredients and/or potential toxins and minimize the contamination of compounded preparations. These include shoe covers, head and facial hair covers, face masks, gowns, and gloves.

~~(c)~~~~(y)~~~~(z)~~(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. Sterile injectable products compounded solely from commercially manufactured sterile pharmaceutical products in a health care facility licensed under section 1250 of the Health and Safety Code are exempt from this definition. For those exempt, the range ~~may~~ shall be calculated and defined in the master formula.

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

~~(aa)~~~~(ab)~~(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)~~~~(ac)~~(ab) "Primary Engineering Control (PEC)" means a device that provides an ISO Class 5 or better environment through the use of non-turbulent, 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, sterile compounding automated robots, compounding aseptic isolators, and compounding aseptic

containment isolators.

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

~~(d)~~~~(ae)~~~~(af)~~(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~~ document.

~~(af)~~~~(ag)~~(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~~ of sterile-to-sterile compounded preparations.

(1) The BUD of a sterile drug preparation made in a segregated sterile compounding area is limited to 12 hours or less as defined by section 1751.8(d).

(2) When the PEC in the segregated sterile compounding area is a CAI or a CACI and the documentation provided by the manufacturer shows its meet~~ing~~ the requirements listed in section 1751.4(f)(1)-(3), the assigned BUD shall comply with section 1751.8(a-b) or (d) ~~(b)~~.

~~(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) ~~I~~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 veterinary 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 it is a reasonable quantity for office use ~~the quantity provided for office use 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~~ document 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 and essential 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 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 a~~n expiration~~ beyond use date representing the date or date and time beyond which the compounded drug preparation should not be used, stored, transported or administered, ~~.~~ and determined based on the professional judgment of the pharmacist performing or supervising the compounding. ~~, in the professional judgment of the pharmacist performing or supervising the compounding, it should not be used, stored, transported, or administration begun.~~

(1) For non-sterile compounded drug preparation(s), the beyond use date ~~This "beyond use date" of the compounded drug product preparation~~ shall not exceed any of the following: ~~180 days from preparation or~~

(A) the shortest expiration date or beyond use date of any ~~component~~ ingredient in the compounded drug ~~product~~ preparation, ~~nor shall it exceed 180 days~~

(B) the chemical stability of any one ingredient in the compounded drug preparation;

(C) the chemical stability of the combination of all ingredients in the compounded drug preparation,

(D) 180 days for non-aqueous formulations,

(E) 14 days for water-containing oral formulations, and

(F) 30 days for water-containing topical/dermal and mucosal liquid and semisolid formulations.

~~from preparation~~

(2) For sterile compounded drug preparations, the beyond use date shall not exceed any of the following:

(A) The shortest expiration date or beyond use date of any ingredient in the sterile compounded drug product preparation,

(B) The chemical stability of any one ingredient in the sterile compounded drug preparation,

(C) The chemical stability of the combination of all ingredients in the sterile compounded drug preparation, and

(D) The beyond use date assigned for sterility in section 1751.8.

(3) Extension of a beyond use date is only allowable when supported by the following:

(A) Method Suitability Test,

(B) Container Closure Integrity Test, and

(C) Stability Studies

~~unless a longer later date is supported by stability studies of~~

(4) In addition to the requirements of paragraph three (3), the ~~finished~~ drugs or compounded drug ~~products~~ preparations tested and studied shall be ~~using the same~~ identical ~~components~~ in ingredients, specific and essential compounding steps, quality reviews, and packaging as the finished drug or compounded drug preparation.

(5) 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 (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)~~(l) 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~~ document.

(2) A compounding log consisting of a single document containing all of the following: ~~The compounding document shall include the following:~~

(A) Name and Strength of the compounded drug preparation.

~~(2)~~(A)(B) The date the drug ~~product~~ preparation was compounded.

~~(3)~~(B)(C) The identity of ~~the~~ any pharmacy personnel ~~who compounded the~~ engaged in compounding the drug ~~product~~ preparation.

~~(4)~~(C)(D) The identity of the pharmacist reviewing the final drug ~~product~~ preparation.

~~(5)~~(D)(E) The quantity of each ~~component~~ ingredient used in compounding the drug ~~product~~ preparation.

~~(6)~~(E)(F) 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.

(i) Exempt from the requirements in this paragraph (1735.3(a)(2)(E)) are sterile ~~products~~ preparations compounded ~~on a one-time basis~~ in a single lot for administration within seventy-two (72) hours to a~~n in~~patient 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)~~~~(F)~~(G) A pharmacy-assigned unique reference or lot number for the compounded drug ~~product~~ preparation.

~~(8)~~~~(G)~~(H) The ~~expiration~~ beyond use date or beyond use date and time of the final compounded drug ~~product~~ preparation, expressed in the compounding ~~record~~ document in a standard date and time format.

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

(J) Documentation of quality reviews and required post-compounding process and procedures.

(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~~ chemical, bulk drug substance, or drug products 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~~ last in effect. If only recorded and stored electronically, on magnetic media, or in any other computerized form, the records shall be maintained as specified by Business and Professions Code section 4070 subsection (c).

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) Each compounded drug preparation shall be affixed with a container label prior to dispensing that contains at least:

(1) Name of the compounding pharmacy and dispensing pharmacy (if different);

(2) Name (brand or generic) and strength, volume, or weight of each active ingredient. For admixed IV solutions, the intravenous solution utilized shall be included;

(3) Instructions for storage, handling, and administration. For admixed IV solutions, the rate of infusion shall be included;

(4) The beyond use date for the drug preparation;

(5) The date compounded; and

(6) The lot number or pharmacy reference number.

~~In addition to the labeling information required under Business and Professions Code section 4076 and under California Code of Regulations section 1707.5, the label of a compounded drug product preparation shall contain the generic or brand name(s) of the principal all active ingredient(s)~~.

(b) Any compounded drug preparation dispensed to a patient or readied for dispensing to a patient shall also include on the label the information required under Business and Professions Code section 4076 and California Code of Regulations, title 16, section 1707.5.

~~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 a patient of the facility. To be treated as such, the "health care facility" must be licensed under Health and Safety Code section 1250.~~

(c) Any compounded drug preparation dispensed to a patient or readied for dispensing to a patient shall also include, on the container label or on a receipt provided to the patient, a

statement that the drug has been compounded by the pharmacy. ~~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 and shall not be subject to minimum font size requirements.~~

(d) Prior to dispensing drug preparations compounded into unit-dose containers that are too small or otherwise impractical for full compliance with subdivisions (a), (b), and (c) 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), strength, volume or weight of the preparation, pharmacy reference or lot number, and beyond use date, and shall not be subject to minimum font size requirements. Once dispensed, outer packaging must comply with 1735.4(a) – (c).

(e) All hazardous agents shall bear a special label which states "Chemotherapy - Dispose of Properly" or "Hazardous – Dispose of Properly."

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~~y~~ies 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 material failure to follow the pharmacy's written policies and procedures shall constitute a basis for

disciplinary action.

(b) The policy~~y~~ies 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 policy~~y~~ies 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~~ policy~~y~~ies 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 and shall provide steps to identify which patients received the affected lot or compounded drug preparation(s).

(3) ~~The p~~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 p~~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~~5) 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~~6) 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.

(11) Policies and procedures for proper garbing when compounding with hazardous products. This shall include when to utilize double shoe covers.

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 compounding of ~~ed~~ 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.

(e) Hazardous drug compounding shall be completed in an externally vented physically separate room with the following requirements:

(1) Minimum of ~~12~~ 30 air changes per hour except that 12 air changes per hour are acceptable for segregated compounding areas with a BSC or CACI when products are assigned a BUD of 12 hrs or less or when non sterile products are compounded; and

(2) Maintained at a negative pressure of ~~at least~~ 0.01 to 0.03 inches of water column relative to all adjacent spaces (rooms, above ceiling, and corridors); and

(3) Each PEC in the room shall also be externally vented; and

(4) All surfaces within the room shall be smooth, seamless, impervious, and non-shedding.

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) A pharmacy engaged in compounding shall maintain documentation ~~that demonstrates~~ demonstrating that personnel involved in compounding have the skills and training required to properly and accurately perform their assigned responsibilities and documentation ~~that~~ demonstrating that all personnel involved in compounding ~~was~~ are trained in all aspects of policies and procedures. This training shall include but is not limited to support personnel (e.g. institutional environmental services, housekeeping), maintenance staff, supervising pharmacist and all others whose jobs are related to the ~~sterile~~ compounding process. ~~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~~. All qualitative and quantitative analysis reports for compounded drug ~~products~~ preparations shall be retained by the pharmacy and ~~collated~~ maintained along with the compounding log ~~record document~~ and master formula document. The quality assurance plan shall include a schedule for routine testing and analysis of specified 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~~ outside 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~~ and 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, with the exception of emergency eye-rinsing stations. A sink may be located in an ante-area. ~~(A)~~ When the PEC in the segregated sterile compounding area is a CAI or CACI and the documentation provided by the manufacturer shows it meets the requirements listed in 1751.4(f)(1)-(3) ~~they~~ the sterile compounding area is ~~are~~ exempt from the room requirement listed in 1751(b)(3).

~~(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~~ maintain the following records, which must be ~~must be made and kept by~~ readily retrievable, 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.

(5) Video of smoke studies in all ISO certified spaces.

~~(2)~~ ~~(5)~~(6) Documents indicating daily ~~recordation~~ documentation 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.

(B) Controlled cold temperature.

(C) Controlled freezer temperature.

~~(3)~~ ~~(6)~~(7) Certification(s) of the sterile compounding environment(s).

~~(7)~~(8) Documents indicating daily documentation ~~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)~~ ~~(9)~~(9) Other facility quality control ~~logs~~ records specific to the pharmacy's policies and procedures (e.g., cleaning logs for facilities and equipment).

~~(5)~~ ~~(9)~~(10) Logs or other documentation of ~~I~~inspections for expired or recalled ~~pharmaceutical products or raw ingredients~~ chemicals, bulk drug substances, drug products, or other ingredients.

~~(6)~~ ~~(10)~~(11) Preparation records including the master formula document ~~work sheet~~, the preparation compounding log ~~document~~~~work sheet~~, and records of end-product evaluation testing and 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 type and 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, title 16, sections 1707.5 and 1735.4, a pharmacy ~~which~~ that compounds sterile ~~injectable~~ drug ~~products~~ preparations shall include the following information on the label~~s~~ for each such ~~those 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~~ administered ~~for~~ to inpatients ~~of a~~ within the hospital ~~pharmacy~~.

~~(b) Name (brand or generic) and concentration strength, volume, or weight of each active ingredients contained in the sterile injectable drug product preparation.~~

(~~c~~b) Instructions for storage, ~~and~~ handling, and administration.

(~~d~~c) 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 drug preparations shall maintain ~~a~~ written policies and procedures ~~manual~~ for compounding. Any material failure to follow the pharmacy's written policies and procedures shall constitute a basis for disciplinary action. In addition to the elements required by section 1735.5, there shall be written policies and procedures regarding the following:

(1) Action levels for colony-forming units (CFUs) detected during viable surface sampling, glove fingertip, and viable air sampling= and actions to be taken when the levels are exceeded.

(2) Airflow considerations and pressure differential monitoring.

(3) An environmental sampling plan and procedures specific to viable air, surface and gloved fingertip sampling as well as nonviable particle sampling.

(4) Cleaning and maintenance of ISO environments and segregated compounding areas.

(5) Compounded sterile drug preparation stability and beyond use dating.

(6) Compounding, filling, and labeling of sterile drug preparations.

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

(8) Depyrogenation of glassware (if applicable)

~~(8)~~(9) Facility management including certification and maintenance of controlled environments and related equipment.

~~(9)~~(10) For compounding aseptic isolators and compounding aseptic containment isolators, documentation of the manufacturer's recommended purge time.

~~(10)~~(11) Hand hygiene and garbing.

~~(11)~~(12) Labeling of the sterile compounded drug preparations based on the intended route of administration and recommended rate of administration.

~~(12)~~(13) Methods by which the supervising pharmacist will fulfill his or her responsibility to ensure the quality of compounded drug preparations. ~~Media-fill testing procedure~~.

~~(13)~~(14) 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, demonstrated through the use of a media-fill test performed by applicable personnel; and aseptic area practices.

~~(14)~~(15) Preparing sterile compounded drug preparations from non-sterile components (if applicable). This shall include sterilization method suitability testing for each master formula document.

~~(15)~~(16) 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.

~~(16)~~(17) 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.

~~(17)~~(18) Proper use of equipment and supplies.

~~(18)~~(19) Quality assurance program compliant with sections 1711, 1735.8 and 1751.7.

~~(19)~~(20) Record keeping requirements.

~~(20)~~(21) Temperature monitoring in compounding and controlled storage areas.

~~(21)~~(22) The determination and approval by a pharmacist of ingredients and the compounding process for each preparation before compounding begins.

~~(22)~~(23) Use of automated compounding devices (if applicable).

~~(23)~~(24) Visual inspection and other final quality checks of sterile drug preparations.

~~(a) Any pharmacy engaged in compounding sterile injectable drug products preparations shall maintain a written policyies and procedures manual for compounding. Any material failure to follow the pharmacy's written policies and procedures shall constitute a basis for disciplinary action. that includes, i~~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). This shall include sterilization method suitability testing for each master formula document.~~

~~(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, sampling, glove fingertip, and volumetric viable 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 formula~~s~~ documents and compounding logs ~~documents 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), and 1751.7(e), written policies and procedures regarding the following:

(1) Process validation for chosen s~~S~~terilization methods ~~and shall include sterilization method suitability testing for each master formula document~~.

(2) End-product evaluation, quantitative, and qualitative testing.

(d)~~(1) All written p~~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~~ All personal involved must read all additions, revisions, and deletions to the written policies and procedures ~~must be communicated to all personnel involved in sterile compounding~~. ~~This~~ Each 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:~~ Cleaning shall be done using a germicidal detergent and sterile water. The use of a sporicidal agent is required to be used at least monthly.

(1) All ISO Class 5 surfaces, work table surfaces, carts, counters, and the cleanroom floor shall be cleaned at least daily. After each cleaning, disinfection using a suitable sterile agent shall occur on all ISO Class 5 surfaces, work table surfaces, carts, and counters.

(2) Walls, ceilings, storage shelving, tables, stools, and all other items in the ISO Class 7 or ISO Class 8 environment shall be cleaned at least monthly.

(3) Cleaning shall also occur after any unanticipated event that could increase the risk of contamination.

(4) All cleaning materials, such as wipers, sponges, and mops, shall be non-shedding and dedicated to use in the cleanroom, or ante-area, and segregated sterile compounding areas and shall not be removed from these areas except for disposal.

(e) Disinfection, using a suitable sterile agent, shall also occur on all surfaces in the ISO Class 5 PEC frequently ~~(at least every 30 minutes)~~, including:

(1) At the beginning of each shift;

(2) At least every 30 minutes when compounding involving human staff is occurring or ~~B~~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-003-2006-131, Revised January 31, 2012May 20, 2015). Certification records must be retained for at least 3 years. Unidirectional Ccompounding aseptic isolators or compounding aseptic containment isolators may be used outside of an ISO Class 7 buffer area or cleanroom if the isolator is certified to 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 cleanroom 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. Additionally, each PEC used to compound hazardous agents shall be externally vented.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-003-2006-131, Revised January 31, 2012May 20, 2015). 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.

(1) During the hazardous drug compounding that is performed in a compounding aseptic containment isolator, full hand hygiene and garbing must occur ~~complete with~~. Garbing shall include 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~~ two pairs of sterile ASTM D6978-05 standard gloves. ~~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) Compounding aseptic isolator and compounding aseptic containment isolator used in the compounding of sterile drug preparations shall use non-turbulent unidirectional air flow patterns. A smoke patterned test shall be used to determine air flow patterns.

~~(i)~~(j) Viable surface sampling shall be done at least ~~quarterly~~ every six months for all sterile-to-sterile compounding and ~~monthly~~ quarterly for all non-sterile-to-sterile compounding. ~~Volumetric~~ Viable air sampling shall be done by ~~impaction~~ volumetric air sampling procedures which test a sufficient volume of air (400 to 1,000 liters) at each location and shall be done at

least once every six months. Viable surface and ~~volumetric~~ viable 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. Viable s~~S~~urface 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 pursuant to its policies and procedures. Remediation shall include, at minimum, an immediate investigation of cleaning and compounding operations and facility management.

~~(i)~~(k) The sterile compounding area ~~is~~in the pharmacy shall have a comfortable and well-lighted working environment, which includes a room temperature of 20-2~~3~~4 degrees Celsius (68-75 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. For hazardous compounding double shoe covers are 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 any wrist, Hhand, finger, and or wrist other visible jewelry or piercing must be eliminated jewwlry, piercing, headphones, earbuds, or personal electronic device. 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 exposed rashes, sunburn, weeping sores, conjunctivitis, active respiratory infections or other communicable disease, or those wearing cosmetics, nail polish, or artificial nails 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). ~~Exceptions are as listed in 1751.4(g).~~

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 (aseptic area practices).

(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 using models that are comparable to the most complex manipulations to be performs by the individual. Each pharmacist responsible for, or directly supervising and controlling, aseptic techniques or practices, must demonstrate the skills needed to ensure the sterility of compounded drug preparations. 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~~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)(1) The pharmacy and each individual involved in the compounding of sterile drug preparations must successfully demonstrate competency on aseptic technique and aseptic area practices before being allowed to prepare sterile drug 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 the types of manipulations, products and batch sizes the individual is expected to prepare and include a media-fill test. The validation process shall be as complicated as the most complex manipulations performed by staff and contain the same amount or greater amount of volume transferred during the compounding process. The same personnel, procedures, equipment, and materials must be used in the testing. Media used must have demonstrated the ability to support and promote

growth. Completed medium samples must be incubated in a manner consistent with the manufacturer's recommendations. If microbial growth is detected, then each individual's sterile preparation process must be evaluated, corrective action taken and documented, and the validation process repeated.

(2) Each individual's competency must be revalidated at least every twelve months for sterile to sterile compounding and at least every six months for individuals compounding sterile preparations from non-sterile ingredients.

(3) The pharmacy's validation process on aseptic technique and aseptic area practices must be revalidated whenever:

(A) the quality assurance program yields an unacceptable result,

(B) there is any change in the compounding process, the Primary Engineering Control (PEC), or the compounding environment. For purposes of this subsection, a change includes, but is not limited to, when the PEC is moved, repaired or replaced, when the facility is modified in a manner that affects airflow or traffic patterns, or when improper aseptic techniques are observed.

(4) The pharmacy must document the validation and revalidation process.

~~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~~ each individual who may be required to do so in practice must successfully complete a gloved fingertip (all fingers on both hands) 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)(1) Batch-produced sterile ~~injectable~~ drug preparations compounded from one or more non-sterile ingredients, except as provided in paragraph (2), ~~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. Sterility testing shall be USP chapter 71 compliant and pyrogens testing shall confirm acceptable levels of pyrogen~~.~~ 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. Exempt from pyrogen testing are ~~non-injectable~~ topical ophthalmic and inhalation preparation.

(12) The following non-sterile-to-sterile batch drug preparations do not require end product testing for sterility and pyrogens:

(A) Preparations for self-administered ophthalmic drops in a quantity sufficient for administration to a single patient for 30 days or less pursuant to a prescription.

(B) Preparations for self-administered inhalation in a quantity sufficient for administration to a single patient for 5 days or less pursuant to a prescription.

~~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 shortest expiration date or beyond use date of any ingredient in sterile compounded drug preparation, nor the chemical stability of any one ingredient in the sterile compounded drug preparation, nor the chemical stability of the

combination of all ingredients in the sterile compounded drug preparation ~~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~~ an 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~~ in solid frozen state, 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 or compounded entirely within a CAI ~~or CACI~~ which meets the requirements in 1751.4(f)(1)-(3), 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 or spiked transfer devices, 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~~ in solid frozen state, 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 or compounded entirely within a CAI ~~or CACI~~ which

meets the requirements in 1751.4(f)(1)-(3), 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~~ in solid frozen state, where the sterile compounded drug preparation is compounded solely with aseptic manipulations using non-sterile ingredients, regardless of intervening sterilization of that ingredient and the following applies: ~~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.~~

(1) The preparation is compounded entirely within an ISO Class 5 PEC located in an ISO Class 7 cleanroom with an ante-area or compounded entirely within a CAI ~~or CACI~~ which meets the requirements in 1751.4(f)(1)-(3).

(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.

(f) The beyond use date for any compounded allergen extracts shall be the earliest manufacturer expiration date of the individual allergen extracts.

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 shall be labeled with a beyond use date ~~BUD~~ and 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. A container must remain within the ISO Class 5 or better air quality to be used for the full six hours, unless otherwise specified by the manufacturer.

(3) If the puncture time is not noted on the container, the container must immediately be discarded.

(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 shall be labeled with a beyond use date ~~BUD~~ and 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. If any open container is not labeled with a beyond use date or the beyond use date is not correct, the container must immediately be discarded.

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 1:1,000;

(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~~ 1753.

(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~~ 1753.

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