

**ENFORCEMENT AND COMPOUNDING
COMMITTEE REPORT
June 2, 2017**

Amy Gutierrez, PharmD, Licensee Member, Chair
Allen Schaad, Licensee Member, Vice Chair
Greg Lippe, Public Member
Stan Weisser, Licensee Member
Valerie Muñoz, Public Member
Ricardo Sanchez, Public Member

- I. **Call to Order, Establishment of Quorum and General Announcements**
- II. **Public Comments on Items Not on the Agenda/Agenda Items for Future Meetings**

Note: The board may not discuss or take action on any matter raised during this public comment section that is not included on this agenda, except to decide whether to place the matter on the agenda of a future meeting. [Government Code sections 11125, 11125.7(a)]

- III. **Review and Discussion of Board's Compounding Regulations, CCR Section 1735 et seq., and Section 1751 et seq., and Relevant Chapters of USP Pharmacopeia relating to Compounding**

Attachment 1

Relevant Law

CCR section 1735 et seq., and CCR section 1751 et seq., establish the requirements for compounding drug preparation.

Business and Professions Code (BPC) section 4127.1 requires the board to adopt regulations to establish policies, guidelines and procedures to implement Article 7.5, Sterile Drug Products. BCP 7127.1 also requires the board to review any formal revisions to General Chapter 797 of the United States Pharmacopeia and the National Formulary (USP-NF), relating to the compounding of sterile preparations, not later than 90 days after the revision becomes official.

Attachment 1 includes the board's current regulations establishing the requirements for compounding drug preparations.

Background

In April 2015, the board formally initiated a rulemaking to promulgate the board's compounding regulations. The final version of the regulation language was adopted by the board on January 19, 2016, and approved by the Office of Administrative Law on September 13, 2016. The effective date of the regulations was January 1, 2017.

Since adoption by the board, both the committee and board have received public comment regarding the impact of the regulations on patient populations, including animals. Although

comments have been provided in several areas, many of the comments are focused on the board's requirements for the assignment of a Beyond Use Date (BUD).

During the committee's April meeting, a presentation was provided by Road Runner Pharmacy regarding concerns about the board's regulation relating to the requirements for the establishment of the BUD of veterinary products. The committee was advised of some of the challenges for compounding medications for their patient population. The committee was also advised about the cost impacts of the board's current regulations and the resulting impact on consumers and their pets. After hearing the presentation and public comments about the board's regulation, the committee determined it was necessary to schedule a special meeting to focus on several different aspects of the board's compounding regulations.

Further, during the May 2017 board meeting, members heard comments on the issue, including reference to the DQSA and its lack of applicability to veterinary compounding.

Update

Board staff has confirmed that the provision of the DQSA relates specifically to human drug compounding, meaning the compounding provisions for 503A and 503B provisions apply only to human drugs. Staff notes, however, that California pharmacy law does not differentiate between compounding for humans versus animals. Staff has confirmed with UPS that all compounding chapters apply to human and animal patients and that USP <795> includes a section specific for animal patients.

IV. Discussion on Possible Recommended Changes to the Board's Compounding Regulations, CCR Section 1735 et seq, and Section 1751 et seq

During this meeting, committee members will have the opportunity to discuss possible changes to the board's compounding regulations. Provided below are summaries of recommendations being offered by staff and members of the regulated public.

Staff recommends changes to the following sections:

- Section 1735, relating to activities that do not constitute compounding.
- Section 1735.2(i), relating to BUD requirements.
- Section 1751.1, relating to smoke study requirements.
- Section 1751.4, relating to cleaning requirements.

1735 Compounding in Licensed Pharmacies: Board staff does not believe that the mixing of ingredients from a compounding kit purchased from an FDA approved manufacturer needs to be included in definition of compounding if done according to the manufacturer instructions.

Section 1735.2 Compounding Limitations and Requirements; Self-Assessment: Board staff recommends changes to the establishment of the BUD to more closely align with the requirements of USP <795> (for nonsterile products) and USP <797> for sterile products including changes to 1735.2(i)(1), 1735.2(i)(2) and 1735.2(i)(3).

Section 1751.1 Sterile Compounding Recordkeeping Requirements: Staff recommends clarifying the requirements for smoke studies, including both the applicable area where such studies must be performed (ISO Class 5) as well as the frequency in which they must be conducted (semi-annually).

Section 1751.4 Facility and Equipment Standards for Sterile Compounding: Staff recommends clarifying that cleaning must be done whenever hazardous drugs are being compounded as well as clarifying where the cleaning must occur.

In addition to staff recommendations, written comments have been submitted by members of the public. Below is a list of the changes requested by each commenter. A copy of the submissions is included in the identified attachments below.

California Pharmacists Association/International Academy of Compounding Pharmacists

Attachment 2

- 1735.1(l) Amend the definition of “daily.”
- 1735.1 (n) Amend the definition of dosage unit to beyond one administration and allow for the dosage unit to be considered a quantity prescribed.
- 1735.1 Add a definition of sterility.
- 1735.2 (i)(1) – (3) Amend the BUD requirements.
- 1735.2 (4) Change requirements relating to the extension of BUD provisions to what appears to be allowing analogous versus identical ingredients.
- 1735.2 (5) Correct the drafting error where the board inadvertently indicated that shorter dating can be done.
- 1735.2 (6) Request recognition of potency over time study as applicable to the compounded formulations can be used to validate stability and assign extended beyond use dates.
- 1751.1(a)(5) Clarify smoke studies in an ISO Class 5 certified space.
- 1751.4(d) Clarify that cleaning does not need to happen daily, but rather every day the facility is used to prepare sterile drug compounds.
- 1751.4(k) Remove minimum room temperature requirement.
- 1751.6(e) Correct typo by removing redundant “sterile” and indicate that training can vary for someone only directly supervising individuals compounding, not performing it themselves.
- 1751.7(e)(1) Allow for an equivalent method of testing as those described in USP 71 and exempt pyrogen testing from irrigation.

Kaiser

Attachment 3

1. 1735.1(r) and 1735.6(e) Requests changing the hazardous provisions to mirror the requirements in USP 800.
2. Requests clarification on smoke study environments.
3. 1751.4(d) Requests that the regulation specify that ready-to-use germicidal detergent, including sterile water, is acceptable.

4. 1751.4(g)(1) Requests addition of a requirement for two pairs of standard gloves for all hazardous compounding (assuming that HD stands for hazardous).
5. 1751.3 and 1751.4 Request clarification on the need for sampling for the segregated compounding areas outside of the ISO-5 environment. Question: Is the sampling plan and procedures for nonviable particle samples as well as violation air and surface limited to ISO certified areas, or does it also apply to segregated compounding area outside the ISO environment.
6. Request clarification if a pharmacy can contract with another pharmacy for compounded products or just parenteral.

Letco Medical LLC

Attachment 4

- 1735.2(i) The board's interpretation of "identical" is too limiting.

Rite Aid

Attachment 5

- 1735.8 Advising board that costs associated with compliance with these requirements exceed total profitability and therefore it is not fiscally responsible to compound low volumes necessary for their patients.

Rick Rhoads

Attachment 6

- 1735.1(r) Harmonize the definition of hazardous to mirror the USP <800> definition
- 1735.1 Add a definition of "Stability"
- 1735.2(i)(3) Change the requirements to extent a BUD
- 1735.6(e) & 1751.4(g)(1) Create an exception allowing a pharmacy to perform an assessment to determine alternative containment strategies for hazardous drugs that are not antineoplastics
- 1751.3(c) Provide detailed description of the information standard operating procedures (SOP) must include for sterilization and depyrogenation processes
- 1751.11 Add provisions to establish requirements for sterilization and depyrogenation

Road Runner

Attachment 7

- 1735 Far exceeds USP in a number of areas
- 1735.2(a) Remove the require to document a prescriber's authorization to compound a product
- 1735.2 Make stability, container closure, sterility and testing frequency consistent with USP standards

Wedgewood

Attachment 8

- 1735.2(c) Change the prescriber office use provisions to expand the conditions under which prescriber office dispensing can be done and change the definition of reasonable quantity.
- 1735.2(d) Change regulation to indicate that the prohibitions to compound only apply to human drugs.

Attachment 1

Title 16. Professional and Vocational Regulations
Division 17. California State Board of Pharmacy
Article 4.5. Compounding

16 CCR § 1735

§ 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 preparation from chemicals or bulk drug substances

(b) "Compounding" does not include reconstitution of a drug pursuant to a manufacturer's direction(s), 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) The parameters and requirements stated by Article 4.5 (Section 1735 et seq.) apply to all compounding practices. Additional parameters and requirements applicable solely to sterile compounding are stated by Article 7 (Section 1751 et seq.).

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

§ 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 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 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 compounding 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 shall be appropriately removed by properly designed external building ventilation. This external venting should be dedicated to one BSC or CACI.

(d) "Bulk drug substance" means any substance that, when used in the preparation of a compounded drug preparation, processing, or packaging of a drug, 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.

(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.

(1) For nonhazardous compounding a 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 0.01 to 0.03 inches of water column relative to all adjacent spaces is required.

- (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 hazardous drugs are prepared, the exhaust air from the isolator 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 recirculated 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 recirculated nor turbulent.
- (h) "Controlled cold temperature" means 2 degrees to 8 degrees C (35 degrees to 46 degrees F).
- (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.
- (j) "Controlled room temperature" means 20 degrees to 25 degrees C (68 degrees to 77 degrees F).
- (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.
- (l) "Daily" means occurring every day the pharmacy is operating, except when daily monitoring of refrigerator and freezer temperature are required, then daily means every 24 hours.
- (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) "Dosage unit" means a quantity sufficient for one administration to one patient.
- (o) "Equipment" means items that must be calibrated, maintained or periodically certified.
- (p) "First air" means the air exiting the HEPA filter in a unidirectional air stream that is essentially particle free.
- (q) "Gloved fingertip sampling" means a process whereby compounding personnel lightly press each fingertip and thumb 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) "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.
- (s) "Integrity" means retention of potency until the beyond use date provided on the label, so long as the preparation is stored and handled according to the label directions.

- (t) "Lot" means one or more compounded drug preparation(s) prepared during one uninterrupted continuous cycle of compounding from one or more common active ingredient(s).
- (u) "Media-fill test" means a test used to measure the efficacy of compounding personnel in aseptic techniques whereby compounding procedures are mimicked using a growth-based media and then the resulting preparation is evaluated for sterility. The media-fill test must mimic the most complex compounding procedures performed by the pharmacy.
- (v) "Non-sterile-to-sterile batch" means any compounded drug preparation containing two (2) or more dosage units with any ingredient that was at any time non-sterile, regardless of intervening sterilization of that ingredient.
- (w) "Parenteral" means a preparation of drugs administered in a manner other than through the digestive tract. It does not include topical, sublingual, rectal or buccal routes of administration.
- (x) "Personal protective equipment" means clothing or devices that protect the employee from exposure to 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.
- (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 shall be calculated and defined in the master formula.
- (z) "Preparation" means a drug or nutrient compounded in a licensed pharmacy; the preparation may or may not be sterile.
- (aa) "Prescriber's office" or "prescriber office" means an office or suite of offices in which a prescriber regularly sees patients for outpatient diagnosis and treatment. This definition does not include any hospital, pharmacy, or other facility, whether or not separately licensed, that may be affiliated with, adjacent to, or co-owned by, the prescriber's practice environment.
- (ab) "Primary Engineering Control (PEC)" means a device that provides an ISO Class 5 or better environment through the use of non-turbulent, unidirectional HEPA-filtered first air for 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) "Process validation" means demonstrating that when a process is repeated within specified limits, the process will consistently produce preparations complying with predetermined requirements. If any aspect of the process is changed, the process would need to be revalidated.
- (ad) "Product" means a commercially manufactured drug or nutrient evaluated for safety and efficacy by the FDA.
- (ae) "Quality" means the absence of harmful levels of contaminants, including filth, putrid, or decomposed substances, the absence of active ingredients other than those listed on the label, and the absence of inactive ingredients other than those listed on the master formula document.
- (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 preparation 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 it meets the requirements listed in section 1751.4(f)(1)-(3), the assigned BUD shall comply with section 1751.8(a-b) or (d).

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

§ 1735.2. Compounding Limitations and Requirements; Self-Assessment.

(a) Except as specified in (b) and (c), no drug 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 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 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" 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 preparation that:

(1) Is ordered by the prescriber or the prescriber's agent 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 office administration; 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 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

(4) That the pharmacist has a credible basis for concluding it is a reasonable quantity for office use considering the intended use of the compounded medication and the nature of the prescriber's practice; and

(5) With regard to any individual prescriber to whom the pharmacy furnishes, and with regard to all prescribers to whom the pharmacy furnishes, 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 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.

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

- (1) Active ingredients to be used.
- (2) Equipment to be used.
- (3) 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) 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.

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

(g) The pharmacist performing or supervising compounding is responsible for the integrity, potency, quality, and labeled strength of a compounded drug preparation until the beyond use date indicated on the label, so long as label instructions for storage and handling are followed after the preparation is dispensed.

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

(i) Every compounded drug preparation shall be given a 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.

(1) For non-sterile compounded drug preparation(s), 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 compounded drug preparation,
- (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.

(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

(4) In addition to the requirements of paragraph three (3), the drugs or compounded drug preparations tested and studied shall be identical 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.

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

(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 compounding is performed in the pharmacy. The applicable sections of the self-assessment shall subsequently be completed before July 1 of each odd-numbered year, within 30 days of the start date of a new pharmacist-in-charge or change of location, and within 30 days of the issuance of a new pharmacy license. The primary purpose of the self-assessment is to promote compliance through self-examination and education.

(l) Packages of ingredients, 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.

(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.

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

§ 1735.3. Recordkeeping for Compounded Drug Preparations.

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

(1) The master formula document.

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

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

(B) The date the drug preparation was compounded.

(C) The identity of any pharmacy personnel engaged in compounding the drug preparation.

(D) The identity of the pharmacist reviewing the final drug preparation.

(E) The quantity of each ingredient used in compounding the drug preparation.

(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 (l) shall apply.

(i) Exempt from the requirements in this paragraph (1735.3(a)(2)(F)) are sterile preparations compounded in a single lot for administration within seventy-two (72) hours to a 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 (37th Revision, Effective December 1, 2014), hereby incorporated by reference.

(G) A pharmacy-assigned unique reference or lot number for the compounded drug preparation.

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

(I) The final quantity or amount of drug 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 chemicals, bulk drug substances, and drug products used to compound drug preparations shall be obtained, whenever possible, from FDA- registered suppliers. The pharmacy shall acquire and retain certificates of purity or analysis, either written in English or translated into English, for chemicals, bulk drug substances, and drug products 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 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 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).

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

§ 1735.4. Labeling of Compounded Drug 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.

(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.

(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.

(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.

§ 1735.5. Compounding Policies and Procedures.

(a) Any pharmacy engaged in compounding shall maintain written policies and procedures 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 policies and procedures shall be reviewed and such review shall be documented on an annual basis by the pharmacist-in-charge. The policies and procedures shall be updated whenever changes in policies and procedures are implemented.

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

(1) Procedures for notifying staff assigned to compounding duties of any changes in policies or procedures.

(2) A written plan for recall of a dispensed compounded drug preparation where subsequent information demonstrates the potential for adverse effects with continued use. 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) 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) 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.

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

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

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

(8) Dates and signatures accompanying any revisions to the policies and procedures 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.

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

§ 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 compounded drug 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 preparations shall be stored, used, maintained, and cleaned in accordance with manufacturers' specifications.

(c) Any equipment that weighs, measures, or transfers ingredients used to compound drug 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 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 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 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.

(f) Where compliance with the January 1, 2017 amendments to Article 4.5 or Article 7, requires physical construction or alteration to a facility or physical environment, the board or its designee may grant a waiver of such compliance for a period of time to permit such physical change(s). Application for any waiver shall be made by the licensee in writing, and the request shall identify the provision(s) requiring physical construction or alteration, and the timeline for any such change(s). The board or its designee may grant the waiver when, in its discretion, good cause is demonstrated for such waiver.

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

§ 1735.7. Training of Compounding Staff.

(a) A pharmacy engaged in compounding shall maintain documentation demonstrating that personnel involved in compounding have the skills and training required to properly and accurately perform their assigned responsibilities and documentation demonstrating that all personnel involved in compounding 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 compounding process.

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

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

§ 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 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. All qualitative and quantitative analysis reports for compounded drug preparations shall be retained by the pharmacy and maintained along with the compounding log 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 preparation is ever discovered to be 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 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.

Title 16. Professional and Vocational Regulations
Division 17. California State Board of Pharmacy
Article 7. Sterile Compounding

16 CCR § 1751

§ 1751. Sterile Compounding; Compounding Area; Self-Assessment.

(a) Any pharmacy engaged in compounding sterile drug 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 compounding.

(b) Any pharmacy compounding sterile drug preparations shall have a compounding area designated for the preparation of sterile drug preparations that is in a restricted location where traffic has no impact on the performance of the PEC(s). The 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 505.7 of Title 24, Part 4, Chapter 5 of the California Code of Regulations. The environments within the pharmacy shall meet the following standards:

(1) Each ISO environment shall be certified at least every six months by a qualified technician in accordance with Section 1751.4. Certification records must be retained in the pharmacy.

(2) Items related to the compounding of sterile drug preparations within the compounding area shall be stored in such a way as to maintain the integrity of an aseptic environment.

(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 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. 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) the sterile compounding area is exempt from the room requirement listed in 1751(b)(3).

(4) There shall be a refrigerator and, 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.

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.

§ 1751.01. Facility and Equipment Standards for Sterile Injectable Compounding from Non-Sterile Ingredients. [Renumbered]

Note: Authority cited: Section 4005, Business and Professions Code. Reference: Section 4005, Business and Professions Code; and Section 18944(a), Health and Safety Code.

§ 1751.02. Policies and Procedures. [Renumbered]

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

§ 1751.1. Sterile Compounding Recordkeeping Requirements.

(a) In addition to the records required by section 1735.3, any pharmacy engaged in any compounding of sterile drug preparations shall maintain the following records, which must be readily retrievable, within the pharmacy:

- (1) Documents evidencing training and competency evaluations of employees in sterile 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 air and surface sampling.
 - (5) Video of smoke studies in all ISO certified spaces.
 - (6) Documents indicating daily documentation of room, 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.
 - (7) Certification(s) of the sterile compounding environment(s).
 - (8) Documents indicating daily documentation 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.
 - (9) Other facility quality control records specific to the pharmacy's policies and procedures (e.g., cleaning logs for facilities and equipment).
 - (10) Logs or other documentation of inspections for expired or recalled chemicals, bulk drug substances, drug products, or other ingredients.
 - (11) Preparation records including the master formula document, the preparation compounding log, 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, 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).
- Note: Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052 and 4127, Business and Professions Code.

§ 1751.2. Sterile 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 that compounds sterile drug preparations shall include the following information on the label for each such preparation:

- (a) The telephone number of the pharmacy. The telephone number is not required on the label for sterile drug preparations administered to inpatients within the hospital.
- (b) Instructions for storage, handling, and administration.
- (c) 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.

§ 1751.3. Sterile Compounding Policies and Procedures.

(a) Any pharmacy engaged in compounding sterile drug preparations shall maintain written policies and procedures 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)
- (9) Facility management including certification and maintenance of controlled environments and related equipment.
- (10) For compounding aseptic isolators and compounding aseptic containment isolators, documentation of the manufacturer's recommended purge time.
- (11) Hand hygiene and garbing.
- (12) Labeling of the sterile compounded drug preparations based on the intended route of administration and recommended rate of administration.
- (13) Methods by which the supervising pharmacist will fulfill his or her responsibility to ensure the quality of compounded drug preparations.
- (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.
- (15) Preparing sterile compounded drug preparations from non-sterile components (if applicable). This shall include sterilization method suitability testing for each master formula document.
- (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.
- (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.
- (18) Proper use of equipment and supplies.
- (19) Quality assurance program compliant with sections 1711, 1735.8 and 1751.7.
- (20) Record keeping requirements.
- (21) Temperature monitoring in compounding and controlled storage areas.
- (22) The determination and approval by a pharmacist of ingredients and the compounding process for each preparation before compounding begins.
- (23) Use of automated compounding devices (if applicable).
- (24) Visual inspection and other final quality checks of sterile drug preparations.

(b) For lot compounding, the pharmacy shall maintain written policies and procedures 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 documents and compounding logs.

(2) Appropriate documentation.

(3) Appropriate sterility and potency testing.

(c) For non-sterile-to-sterile batch compounding, the pharmacy shall maintain written policies and procedures for compounding that includes, in addition to the elements required by section 1735.5, 1751.3(a), and 1751.7(e), written policies and procedures regarding the following:

(1) Process validation for chosen sterilization methods.

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

(d) Policies and procedures shall be immediately available to all personnel involved in compounding activities and to board inspectors.

(e) All personnel involved must read the policies and procedures before compounding sterile drug preparations. All personnel involved must read all additions, revisions, and deletions to the written policies and procedures. Each review must be documented by a signature and date.

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

§ 1751.4. Facility and Equipment Standards for Sterile Compounding.

(a) No sterile drug 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 drug preparations.

(b) During the compounding of sterile drug preparations, access to the areas designated for compounding must be limited to those individuals who are properly attired.

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

(d) 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, including:

(1) At the beginning of each shift;

(2) At least every 30 minutes when compounding involving human staff is occurring or before each lot;

(3) After each spill; and

(4) When surface contamination is known or suspected.

(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-003-2006-13, Revised May 20, 2015), which is hereby incorporated by reference. Certification records must be retained for at least 3 years. Unidirectional compounding aseptic isolators or compounding aseptic containment isolators may be used outside of an ISO Class 7 cleanroom if the isolator is certified to meet 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 that do not meet the requirements as outlined in this subdivision or are not located within an ISO Class 7 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 sterile hazardous agents shall do so in accordance with Section 505.7.1 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. The negative pressure PEC must be certified every six months by a qualified technician who is familiar with CETA Certification Guide for Sterile Compounding Facilities (CAG-003-2006-13, Revised May 20, 2015), which is hereby incorporated by reference. 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. Garbing shall include hair cover, facemask, beard cover (if applicable), polypropylene or low shedding gown that closes in the back, shoe covers, and two pairs of sterile ASTM D6978-05 standard gloves.

(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.

(j) Viable surface sampling shall be done at least every six months for all sterile-to-sterile compounding and quarterly for all non-sterile-to-sterile compounding. Viable air sampling shall be done by 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 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 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 pursuant to its policies and procedures. Remediation shall include, at minimum, an immediate investigation of cleaning and compounding operations and facility management.

(k) The sterile compounding area in the pharmacy shall have a comfortable and well-lighted working environment, which includes a room temperature of 20-24 degrees Celsius (68-75 degrees Fahrenheit) or cooler to maintain comfortable conditions for compounding personnel when attired in the required compounding garb.

(l) A licensee may request a waiver of these provisions as provided in section 1735.6(f).

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.

§ 1751.5. Sterile Compounding Attire.

(a) When compounding sterile drug preparations the following standards must be met:

(1) Personal protective equipment consisting of a non-shedding gown, head cover, face mask, facial hair covers (if applicable), and shoe covers must be worn inside the designated area at all times. For hazardous compounding double shoe covers are required.

(2) Personal protective equipment must be donned and removed 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.

(4) Compounding personnel shall not wear any wrist, hand, finger, or other visible jewelry, piercing, headphones, earbuds, or personal electronic device.

(5) 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 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.

(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).

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

§ 1751.6. 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 drug preparations and related supplies furnished by the pharmacy.

(b) The pharmacist-in-charge shall ensure that all pharmacy personnel engaging in compounding sterile drug preparations 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.

(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 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 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 preparation compounding documentation.

(D) Quality assurance procedures.

(E) Aseptic preparation procedures.

(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 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 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 performed 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.

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

§ 1751.7. Sterile Compounding Quality Assurance and Process Validation.

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

(1) Procedures for cleaning and sanitization of the sterile preparation area.

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

(3) Documentation justifying the chosen beyond use dates for compounded sterile drug 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.

(c) All sterile compounding personnel must successfully complete an initial competency evaluation. In addition, immediately following the initial hand hygiene and garbing procedure, 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.

(e)(1) Batch-produced sterile drug preparations compounded from one or more non-sterile ingredients, except as provided in paragraph (2), 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 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 topical ophthalmic and inhalation preparations.

(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 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.

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

§ 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, 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 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 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 cleanroom with an ante-area or compounded entirely within a CAI 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 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 cleanroom with an ante-area or compounded entirely within a CAI 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 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:

(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 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 (d), 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 cleanroom, with an ante-area. 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.

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

§ 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 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 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.

§ 1751.10. Sterile Compounding Reference Materials.

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

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

§ 1751.11. Furnishing to Home Health Agencies and Licensed Hospices. [Renumbered]

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

§ 1751.12. Obligations of a Pharmacy Furnishing Portable Containers. [Renumbered]

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

Attachment 2



May 19, 2017

Ms. Virginia Herold
Executive Officer
California Board of Pharmacy
1625 N. Market Blvd, Suite N 219
Sacramento, CA 95834

Dear Ms. Herold,

We thank the California Board of Pharmacy, Compounding & Enforcement Committee for being receptive to scheduling an interim meeting of the Committee to consider modification to certain provisions within 16 CCR § 1735 and 1751 related to the compounding regulations that went into effect January 1, 2017.

As the largest statewide association representing pharmacists in the country, the California Pharmacists Association (CPhA) has been working closely with our members in the compounding pharmacy community on implementing these important measures to ensure optimal patient safety and access to high quality compounded medications.

As with any significant policy and regulatory implementation such as those contained in the new California compounding provisions, we have received significant feedback regarding a few provisions that we believe the Committee and full Board of Pharmacy should consider modifying to ensure that safety and accessibility to compounded medications are optimized. It is understandable and reasonable to suggest that the Board would anticipate the need for modifications now that the regulations have been in place for five months and practitioners have begun to comply with the requirements. Our recommendations are based on best practices in the compounding profession as well as international standards and reference points in the United States Pharmacopeial (USP) for compounding both non-sterile and sterile medications.

In addition to changes related to specific regulatory sections, we are also recommending changes to the compounding Frequently Asked Questions (FAQ) document produced by the Board. We understand that the Board FAQs are not regulations and as such are not enforceable, however they are used by practitioners and Board inspectors as guidance and a beneficial reference in furtherance of complying with the regulations. We have included those recommended changes as well.

We look forward to attending the June 2nd meeting and again appreciate the Committee's time and interest in these matters on behalf of the patients that our members serve.

Best regards,

Jon R. Roth, MS, CAE
Chief Executive Officer

California Pharmacists Association
Recommended Amendments to
16 CCR § 1735 and 1751

1735.1(l) "Daily" means occurring every day the pharmacy is operating, except when daily monitoring of refrigerator and freezer temperature are required, then daily means every 24 hours. Electronic monitoring and recording of daily refrigerator and freezer temperature may be used to satisfy the provisions of this section.

Need for Recommended Change: This change is necessary to provide clarity that electronic monitoring and recording of temperature is acceptable. Further, we believe this ensures a more precise and continuous measure of refrigerator and freezer temperature ranges and allows pharmacies that are not staffed daily to ensure compliance with the requirement.

...

1735.1(n) "Dosage unit" means a quantity prescribed sufficient for ~~one~~ administration to one patient.

Need for Recommended Change: This change is recommended for ensuring the definition of dosage unit is clearly intended to allow the compounding pharmacist to fulfill a prescriber's request for a patient to receive a prescribed course of therapy that involves multiple dose units of medication. An example of this would be a patient whose prescriber writes a prescription for a compounded medication that requires individual dose vials daily for 10 days. Each vial is only used once and discarded resulting in 10 dosage units being needed for the prescribed course of therapy. The existing definition would prohibit this patient access to the prescribed care because it is restricted to one administration.

...

1735.1 proposed new definitions to be added:

For purposes of this section, sterility may be defined as:

- (a) The application of a lethal process to sealed containers to achieve a predetermined sterility assurance level of greater than 10^{-6} or a probability of less than one in one million of a nonsterile unit, or,
- (b) Passage of a fluid or solution through a sterilizing grade membrane to produce a sterile effluent. Membranes must be documented to retain 100% of a culture of 10^7 microorganisms of a strain of *Brevundimonas (Pseudomonas) diminuta* per square centimeter of membrane surface under a pressure of not less than 30 psi (2.0 bar).

Need for Recommended Change: These definitions are derived from the USP 797 glossary and are necessary to clarify the methods for obtaining sterility in compounded sterile preparations.

...

1735.2(i) Every compounded drug preparation shall be given a 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.

(1) For non-sterile compounded drug preparation(s), in the absence of stability information applicable to the compounded formulation, 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 compounded drug preparation,
- (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.

(2) For sterile compounded drug preparations, in the absence of stability information applicable to the compounded formulation, 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) In the absence of sterility testing conducted in accordance with USP Chapter 797, ~~the~~ beyond use date assigned for sterility in section 1751.8.

Need for Recommended Change: Modification to sub-section 2(D) is necessary to clarify that the beyond use dates contained in section 1751.8 are only applicable to sterile compounds that do not undergo sterility testing, consistent with USP 797.

(3) Extension of a beyond use date for sterile compounded drug preparations exceeding those in section 1751.8 is only allowable when supported by the following:

- (A) Sterility testing methods are supported by Method Suitability Tests,
- (B) Container closure types are supported by Container Closure Integrity Tests, and
- (C) ~~Stability Studies~~ Sterility testing performed in accordance with USP 797.

Need for Recommended Change: Modifications to sub-section 3 are necessary to clarify the types of testing needed to ensure sterility beyond the timelines as set forth in section 1751.8, consistent with USP 797.

(4) In addition to the requirements of paragraph one (1) and paragraph three (3), the stability of drugs or compounded drug preparations tested and studied shall be identical in use ingredients, specific and essential compounding steps, quality reviews, and packaging analogous to as the finished drug or compounded drug preparation as demonstrated by scientific publications referenced in the judgement of the pharmacist.

Need for Recommended Change: These modifications are critically important to bring the regulation consistent with USP 797 and are necessary because the standard of meeting “identical” characteristics in a compounded preparation to any studied drug is a nearly impossible standard to achieve.

In particular, USP/NF monographs ensure that active pharmaceutical ingredients (API) and excipients meet specific standards of purity and suitability for use as drugs. However, there can be acceptable slight variances in assay, moisture, and other relevant USP monograph requirements. These variances are within the specific monograph requirements but yield differences that would dictate that the API is not *identical* from lot to lot, yet are analogous to the studied drugs and do not impact the final preparation.

Additionally, stability studies use a specific lot of API and/or excipient for that particular study. It is highly unlikely that any facility, including hospitals, use the *identical* API or drug (same as original study lot) as was used in the study. Stability studies are performed to ensure that the compounded preparation has a predictable potency over a period of time. Requiring that ingredients be identical would disqualify a substantial body of scientific and authoritative data performed and/or published by qualified sources.

Further, very few stability studies outline every compounding step, process and equipment to be used in the preparation of the compounded end-product. For example, Trissel’s Handbook of Injectable Drugs provides tabular charts of expected BUD for particular combinations of API/drug and IV solution. ‘Specific and essential compounding steps’ and ‘quality reviews’ are not listed as a standard in the literature for most studies footnoted.

Similar to APIs, it is believed that the competent compounding pharmacist will have the training and experience to perform the essential compounding steps consistently. Requiring steps be *identical* will again invalidate a large body of stability studies performed and/or published by qualified sources. These include studies published on a wide range of aqueous-containing compounded preparations such as creams and sterile parenteral solutions.

Lastly, removing the standard of *identical* is also necessary because in many cases stability studies simply state that the compounded preparation was placed in a container with only a general description of the container type given. As with the API and compounding steps, it is believed that the pharmacist will use professional judgment to determine if the container is equivalent to produce an analogous preparation. For example, a published study may conclude that compounded preparation XX was stable for YY time in an amber plastic bottle. The type of plastic may not be specified. The use of term identical precludes use of this scientifically valid study to develop an otherwise safe, replicated preparation.

...

(5) ~~Shorter~~ Longer dating than set forth in this subsection may be used if it is deemed appropriate in the professional judgment of the responsible pharmacist.

Need for Recommended Change: We believe this is a drafting error in the original regulation. The judgment of the pharmacist is necessary to establish dating longer than what is set forth in the section, not shorter than what is set forth in the section.

...

(6) For the purpose of sections 1735.2(i)(1) and 1735.2(i)(2), a potency over time study applicable to the compounded formulation may be used to validate stability and assign extended beyond use dates of compounded preparations. [new sub-section]

Need for Recommended Change: Modifications to section 1, 2, and addition of a new section 6 are necessary to bring the regulation regarding potency over time studies consistent with USP 795 (nonsterile) and USP 797 (sterile) standards. This addition also provides clarity to the current regulations that a potency over time study is acceptable for both nonsterile compounding and stability studies for sterile compounded drug preparations.

...

1751.1(a)(5) In addition to the records required by section 1735.3, any pharmacy engaged in any compounding of sterile drug preparations shall maintain the following records, which must be readily retrievable, within the pharmacy:

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

Need for Recommended Change: Specifying smoke studies in Class 5 ISO certified spaces brings the regulation up to standard with Current Good Manufacturing Practices (CGMP). Smoke studies outside of Class 5 spaces are not a standard since the smoke study is isolated to the laminar flow hood to visualize air flow.

...

1751.4(d) All ISO Class 5 surfaces, work table surfaces, carts, counters, and the cleanroom floor shall be cleaned ~~at least daily~~ each day the facility is used to prepare a sterile drug compound. After each cleaning, disinfection using a suitable sterile agent shall occur on all ISO Class 5 surfaces, work table surfaces, carts, and counters.

Need for Recommended Change: The objective of cleaning an ISO Class 5 space is to ensure sterility of the space between sterile drug preparations. However, not all pharmacies engage in sterile compounding daily, therefore requiring daily cleaning on days where no sterile compounding has occurred invites undue contamination risk due to personnel entering a sterile environment in order to comply with the regulation. Inviting risk of unnecessarily entering a sterile environment in order to again clean the sterile space between days where preparations occurred is a greater risk to patient safety.

...

1751.4(k) The sterile compounding area in the pharmacy shall have a comfortable and well-lighted working environment, which includes a room temperature ~~not to exceed of 20-24 degrees Celsius (68-75 degrees Fahrenheit) or cooler~~ to maintain comfortable conditions for compounding personnel when attired in the required compounding garb.

Need for Recommended Change: This change seeks to clarify the ambiguity in complying with the temperature provision of the regulation (range of degrees versus “or cooler”). It is clearer to state the temperature as a maximum and remove reference to the specific range. Doing so also provides flexibility for the pharmacy to meet personnel comfort and carries no risk.

...

1751.6(e) Pharmacies that compound sterile drug preparations must comply with the following training requirements:

(2) Each person engaged in ~~sterile~~ compounding sterile drug preparations 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 performed by the individual. Each pharmacist responsible for, or directly supervising and controlling, aseptic techniques or practices, must ensure each person engaged in compounding sterile drug preparations successfully demonstrates 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.

(3) Each pharmacist responsible for, or directly supervising and controlling persons engaged in compounding sterile drug preparations, aseptic techniques or practices must demonstrate competency in evaluating the skills of those persons engaged in compounding sterile drug preparations.

Need for Recommended Change: Ensuring the person engaged in compounding sterile preparations successfully demonstrates aseptic technique is necessary for contributing to a sterile environment and patient safety. However, it is not necessary for supervising pharmacists, who are not engaged in compounding, to demonstrate aseptic technique, and in fact, invites undue contamination risk due to unnecessary personnel entering a sterile environment in order to comply with the regulation. We do agree that additional regulatory language may be necessary that specifies the manner in which a supervising pharmacist shall demonstrate competency to assess the pharmacist engaged in compounding as having met the aseptic practice skills assessment.

...

1751.7(e)(1) Batch-produced sterile drug preparations compounded from one or more non-sterile ingredients, except as provided in paragraph (2), 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 performed in accordance with USP chapter 71 ~~compliant and or an equivalent method. If sterility testing methods other than those described in USP Chapter 71 are used, the testing method must demonstrate documented equivalent or superior~~

effectiveness as USP chapter 71 methodology. Pyrogens testing shall confirm 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 topical ophthalmic, irrigation, and inhalation preparations.

Need for Recommended Change: This change brings consistency and uses language from USP 797, which allows end product sterility to be achieved using USP 71, or alternative methods that meet or exceed the USP 71 standard. The proposed changes ensure consistency and clarity as to the standard that all sterility testing methods must meet pursuant to USP 797. The addition of irrigation preparations to the exemptions for pyrogen testing are consistent with the other preparations listed for exception. After preparation, irrigations are often placed into nonsterile delivery mechanisms for patient care. Pyrogen testing these medications is therefore unnecessary and delays patient care.

California Pharmacists Association
Recommended Amendments to
California Board of Pharmacy Compounding
Frequently Asked Questions

5. Under what conditions can a BUD be extended?

As specified in CCR section 1735.2(i)(1-6), a beyond use date can be extended if it is supported by a potency over time study applicable to the compounded formulation. In addition, As specified in CCR section 1735.2(i)(3), a BUD for a sterile compounded preparation can be extended if it is supported by the following:

- (A) Sterility testing methods are supported by Method Suitability Tests, AND
- (B) Container closure types are supported by Container Closure Integrity Tests, AND
- (C) ~~Stability Studies~~ Sterility testing performed in accordance with USP 797.

Need for Recommended Changes to FAQ #5: Modifications to this FAQ are necessary to align with the recommended changes pursuant to CCR 1735.2(i).

...

14. Can I use a stability study done by a third party to assign the BUD of my compounded preparation?

The pharmacist performing or supervising the compounding is responsible for exercising his or her professional judgment with regard to beyond use dating. CCR section 1735.2(i)(4) does not prohibit reliance on third-party stability studies, if all of the following conditions are met:

- The drugs or compounded drug preparation tested and studied use are identical-analogous in ingredients.
- ~~The specific and~~ There is no substantial variation in the essential compounding steps ~~and quality reviews are identical.~~
- The packaging of the finished drug or compounded drug preparation is identical-equivalent to the packaging of the drug or compounded drug preparation tested or studied.

Need for Recommended Changes to FAQ #14:

Modifications to this FAQ are necessary to align with the recommended changes pursuant to CCR 1735.2(i)(4).

May 19, 2017

Ms. Virginia Herold
Executive Officer
California Board of Pharmacy
1625 N. Market Blvd, Suite N 219
Sacramento, CA 95834
Sent via Email to: Virginia.Herold@dca.ca.gov

Re: International Academy of Compounding Pharmacists Supports the California Pharmacists Association's Modifications to Sections 1735 and 1751

Dear Ms. Herold:

The International Academy of Compounding Pharmacists (IACP) represents more than 3,600 pharmacists, technicians, students, and members of the compounding community who focus on the specialty practice of pharmacy compounding. Compounding pharmacists work directly with prescribers including physicians, nurse practitioners and veterinarians to create customized medication solutions for patients and animals whose health care needs cannot be met by manufactured medications. IACP works diligently to preserve patient access to these vital compounded medications.

IACP would like to thank the California Board of Pharmacy, Enforcement & Compounding Committee (the "*Committee*") for this opportunity to present thoughts on current regulations applicable to compounding pharmacies. IACP supports the Committee's mission to ensure that patients throughout the State of California receive safe, effective and quality compounded medications. IACP understands and supports the need to protect public health. However, when developing and implementing regulations, it is essential to preserve patient access to vital compounded medications, the physician-patient-pharmacist triad, and the right of a patient to choose their pharmacist. Prescribers must have the right to prescribe medications that best fit the needs of their patients and patients.

IACP has reviewed the current California regulations and has heard from pharmacists as well patients that specific provisions of the regulations are causing significant constraints in patients being able to access care resulting in decreasing patient access to vital compounded medications. Additionally, IACP had the opportunity to review the recommendations being submitted by the California Pharmacists Association (CPhA) and would like to take this opportunity to express full support for the CPhA's proposed modifications to Sections 1735 and 1751 of the California Code of Regulations. The proposed changes are necessary to ensure that Sections 1735 and 1751 conform to other standards currently governing compounding pharmacies. The CPhA's recommendations will safe-guard patient safety and place the regulations in line with best practices while also preserving patient access to compounded medications.

In particular, CPhA's amendments to Section 1735.2(i), related to beyond use dates, are necessary to ensure consistency and clarity among all requirements governing compounding pharmacies. As it stands, the current iteration of Section 1735.2(i) is confusing and compounding pharmacies often struggle to determine what testing requirements apply under the circumstances. In addition, the testing requirements set forth in Section 1735.2(i) appear to exceed USP <795> and <797> standards. In fact, they appear to mimic current Good Manufacturing Practices ("cGMP") requirements, which are applicable to drug manufacturers and not compounding pharmacies.

Unlike drug manufacturers, compounding pharmacies prepare unique medications for particularized medical needs when a prescriber determines a commercially available drug is not suitable for treatment. The Food Drug & Cosmetic Act ("FDCA") requirements for manufactured drugs, including cGMPs, were not designed for these specialized medications. CGMP testing practices are extremely expensive and are therefore not economically practical when small amounts of customized drug product are being produced. This is one of the very reasons why commercial drug manufacturers only produce very large quantities of medication in standardized strengths and dosage forms. Compounding pharmacies cannot, therefore, with any economic feasibility, comply with cGMP testing requirements. If compounding pharmacies were required to comply with cGMP, the increased cost to do so would either be passed on to patients or result in pharmacies discontinuing compounding activities. In either case, patients would suffer due to drastically increased prices and restricted access to necessary medications.

IACP appreciates the opportunity to fully support CPhA's recommendations and request full adoption. IACP wishes to work with the Committee toward the mutual goal of protecting and promoting the health and safety of Californians by pursuing the highest quality of pharmacist's care and the appropriate use of pharmaceuticals while preserving patient access to vital compounded medications.

Sincerely,

A handwritten signature in black ink that reads "Cynthia Blankenship". The signature is written in a cursive, flowing style.

Cynthia Blankenship

Interim Executive Vice President, IACP

Of Counsel, Rose Law Firm

Attachment 3

BOP CCRs 1735 & 1751 – Kaiser Permanente Requests for Clarification

1) Clarify language regarding the definition of a hazardous drug CCR 1735.1(r)

- 1.) USP 800, Section 2 states “an entity must maintain a list of HDs, which must include any items on the current NIOSH list that the entity handles”
- 2.) CCR 1735.1(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.
- 3.) CCR 1735.6(e) requires a negative pressure room for all hazardous drug compounding
- 4.) Compounding of all NIOSH drugs including Table 2/3 drugs requires a negative pressure room if an organization adopts the NIOSH list

Request concordance with USP 800 definition of HD (all NIOSH tables) by 7/1/18.

2) CCR 1751.1(a)(5) - Video of smoke studies in all ISO certified spaces.

- Request to clarify required locations for smoke studies. Does this include ISO 7 and ISO 8 certified spaces?
- Request to clarify frequency of smoke studies. Required every 6 months or only during initial certification?

3) CCR 1751.4(d) - Cleaning shall be done using a germicidal detergent and sterile water.

- Provide a cleared definition of germicidal.
- Request to add after “Cleaning shall be done using a germicidal detergent and sterile water” the following: “The use of a ready-to-use germicidal detergent including sterile water is acceptable.”

4) CCR 1751.4(g)(1) - During the hazardous drug compounding that is performed in a compounding aseptic containment isolator, full hand hygiene and garbing must occur. Garbing shall include hair cover, facemask, beard cover (if applicable), polypropylene or low shedding gown that closes in the back, shoe covers, and *two pairs of sterile ASTM D6978-05 standard gloves*.

- This is the only mention of “two pairs of sterile ASTM D6978-05 standard gloves”.
- Recommend adding a requirement for two pairs of ASTM D6978-05 standard gloves for all HD compounding

5) CCR 1751.3 requires a sampling plan specific to viable air, surface and nonviable particle sampling. Additionally, CCR 1751.4 requires viable surface and air sampling shall be done at least every 6 months for all sterile to sterile compounding.

- Request to clarify need for a sampling plan for the segregated compounding area outside of the ISO-5 environment. Is the sampling plan and procedures for nonviable particle sampling as well as viable air and surface limited to ISO certified areas? OR does the BOP expect to see a sampling plan for segregated compounding area outside the ISO-5 environment?

BOP CCRs 1735 & 1751 – Kaiser Permanente Requests for Clarification

- 6) CCR 1735.6(f) states “Where compliance with the January 1, 2017 amendments to Article 4.5 or Article 7, requires physical construction or alteration to a facility or physical environment, the board or its designee may grant a waiver of such compliance for a period of time to permit such physical change(s).”

CCR 4123. Compounding Drug for Other Pharmacy for Parenteral Therapy; Notice to Board
Any pharmacy that contracts to compound a drug for parenteral therapy, pursuant to a prescription, for delivery to another pharmacy shall report that contractual arrangement to the board. That information shall be reported by the pharmacy performing the compounding services within 30 days of commencing that compounding.

- CCR 4123 allows for compounding of parenteral (sterile) products from one licensed pharmacy to another licensed pharmacy.
- Request to clarify if non-sterile hazardous drugs fall under CCR 4123 for pharmacies with waiver denials.

Attachment 4



QUALITY COMPOUNDING STARTS HERE

DOUGLAS E. BOWMAN
CHIEF EXECUTIVE OFFICER
DIRECT: 1-734-843-4603
FACSIMILE: 1-734-843-7603
DBowman@LetcoMedical.com

CORPORATE OFFICE:
460 E. SWEDES FORD ROAD, SUITE 2040
WAYNE, PA 19087

CENTER OF EXCELLENCE:
17199 N. LAUREL DRIVE, SUITE 315
LIVONIA, MI 48150

SALES OFFICES:
9380 CENTRAL AVENUE
SUITE 260
BLAINE, MN 55434

7400 N. ORACLE ROAD
SUITE 236
TUCSON, AZ 85704

DISTRIBUTION CENTER:
1316 COMMERCE DRIVE
DECATUR, AL 35601
WWW.LETCOMEDICAL.COM

May 22, 2017

VIA FEDERAL EXPRESS

Virginia Herold
Executive Officer
California State Board of Pharmacy
1625 N. Market Blvd., N219
Sacramento, CA 95834

RE: INTERPRETATION OF THE WORD "IDENTICAL" IN COMPOUNDING REGULATIONS

Dear Ms. Herold:

Please accept this letter from Letco Medical LLC ("Letco") in support of the comments to be provided at the June 2, 2017 Enforcement and Compounding Committee Meeting. Letco is a licensed California wholesale distributor (WLS 6763) and appreciates the opportunity to present its concerns to the Board.

We respectfully ask the Enforcement and Compounding Committee and the Board to address its interpretation of the word "identical" in CCR Sections 1735 et seq., and specifically C.C.R. § 1735.2(i). This section of the compounding regulations allows a pharmacy to extend a beyond use date (BUD) if the extension is supported by Method Suitability, Container Closure Integrity and Stability testing. To rely on those studies, subsection 4 requires that "the drugs or compounded drug preparations tested and studied shall be *identical* in ingredients, specific and essential compounding steps, quality reviews, and packaging as the finished drug or compounded drug preparation."

Our request for clarity is focused on the word "identical". It has come to our attention that the Board and/or others in the industry are interpreting that term very narrowly. Specifically, it has been stated that the word "identical" means that a compounder must use the same manufacturers for the active and inactive ingredients, exactly the same container closure, and the same NDC used in the underlying studies to rely on the extended BUD supported by those test results. This interpretation is problematic as it is unnecessarily restrictive, outside of industry standards, limits California patients' access to safely compounded drugs, and benefits only a small number of participants in this market.

Such a narrow interpretation of "identical" is unreasonable and burdensome. Active pharmaceutical ingredients as well as excipients and dietary supplements are often produced by only one manufacturer globally and are then repackaged into smaller containers, resulting in different NDCs for the exact same product. These repackaged products are in smaller, more user-friendly volumes that eliminate pharmaceutical waste and decrease costs to health care consumers. Allowing a pharmacy to rely on third party studies for extended BUDs, but requiring them to use only the exact same components used in the supporting studies limits a pharmacy's ability to source product freely in the marketplace in times of a shortage, product discontinuation and/or to find a better price. Under this narrow reading of the rule, if the pharmacy or hospital itself performed the testing, this interpretation also invalidates those studies if the NDC changes. For example, if the manufacturer holding the NDC stops producing that product, either based on an emergency or a business decision, pharmacies and hospitals would need to conduct their own expensive testing on different analogous products so that they can continue to compound the medication. These restrictions unreasonably limit a compounding pharmacist's ability to

compound a product needed by a patient, when there is no evidence or scientific authority that supports an interpretation that the referenced studies are only reliable when the exact same NDC is used.

Furthermore, this narrow interpretation is unnecessary if the goal is to protect the health and safety of California residents. A broader interpretation of “identical” as referring to analogous products is consistent with <USP 797> and USP/NF monographs that ensure the active pharmaceutical ingredients, excipients, and dietary supplements meet standards for suitability and purity; therefore, ingredients from different manufacturers are safe to use interchangeably. It is for these reasons that the prevailing standard nationwide is to allow pharmacies to rely on third-party studies but use analogous underlying components – and not solely the same NDCs – a prevailing standard that has shown to be safe and effective.

Finally, there are only a few entities in our industry who are large enough to afford such studies, making this narrow interpretation hurtful to smaller wholesalers, pharmacies and hospitals who cannot produce their own studies. Larger wholesalers who can conduct their own studies using their own product lines benefit, as the narrow interpretation of “identical” would require pharmacies to use that wholesaler’s products to adopt the extended BUDs from the studies that the wholesaler performed or commissioned. Smaller wholesalers cannot afford to conduct these studies for all of their products, and smaller hospitals and pharmacies cannot afford to conduct these studies on their own. This interpretation would have a significant effect on smaller wholesalers that provide the exact same product to pharmacies now, only with different NDCs. These smaller wholesalers may be forced to leave the California market, decreasing availability and increasing the price of the product for California pharmacies and the patients that receive these medications. Pharmacies have been using analogous products interchangeably for years safely and effectively; forcing them to alter their relied-upon suppliers and compounding processes to strictly replicate these studies may be difficult, expensive or even impossible based on availability.

All of these arguments also apply to the interpretation of “identical” as it applies to container closure systems. Different manufacturers can make analogous closure systems, or a pharmacy may elect to use a closure system that is analogous or *better* per USP standards, yet a strict interpretation of the word “identical” would limit the pharmacy to using the exact same closure system. As noted above, if that container manufacturer should have supply chain issues or cease manufacturing that container closure, the pharmacy would have to find a different study of that compounded drug using a different container closure. The pharmacy would then have to look at the remaining components of the new study to ensure that it has or can obtain access to that study’s components, and may find that it has to purchase all new API and inert ingredients (hoping that all of those are still on the market) so that what they compound is strictly “identical” to the components in the new study.

In conclusion, we ask the Committee and the Board to adopt a more reasonable definition of “identical”, either via rulemaking or through the adoption of a practical interpretation of the rule as written, that allows “identical” to be interpreted as it has been for decades and across the country in <USP 797> and traditional compounding resources. We ask the Board for an interpretation that the word “identical” means that the components in the compounded drug be of an analogous strength, form, and container closure as the product in the underlying study, and not that they be *exactly* identical to the components in the underlying study. Any different interpretation would affect the health and safety of California residents by arbitrarily and unnecessarily restricting a pharmacy’s ability to rely on third party studies and components proven to be safe and effective, therefore restricting their ability to provide safe, effective, prompt and economical care to California patients.

We thank you for your thoughtful consideration of this request.

Sincerely,

LETCO MEDICAL, LLC:

By: 
Douglas E. Bowman
Chief Executive Officer

Attachment



Daniel Miller
SVP, Pharmacy Regulatory Affairs

MAILING ADDRESS
P.O. Box 3165
Harrisburg, PA 17105

GENERAL OFFICE
30 Hunter Lane
Camp Hill, PA 17011

717.214.2541
e-mail: dmiller1@riteaid.com

March 13, 2017

Virginia Herold
Executive Officer
Board of Pharmacy
1625 North Market Blvd, Suite N219
Sacramento, CA 95834

Dear Executive Officer Herold:

Due to the new regulatory requirements enacted by your Board of Pharmacy, and the associated cost to maintain compliance, Rite Aid is considering discontinuing the practice of compounding in approximately 506 of our 583 California pharmacy locations. This difficult decision has been made after a thorough review of the amendments to §1735 in Article 4.5 of Division 17 of Title 16 of the California Code of Regulations, as well as Rite Aid business practices and fiscal responsibilities. The intent of this letter is to inform you of the financial implications of the newly amended regulation, and its potential consequences that restrict access to patient care. Please recognize that only *simple and moderate, non-sterile* compounding (e.g. magic mouthwash prepared from a kit or the mixing of 2 creams from a manufacturer's packaging) is currently permitted at Rite Aid pharmacies.

Section 1735.8 of the amended regulation titled Compounding Quality Assurance states that "*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.*" It has been determined that the cost associated with such required annual testing and analysis for 506 of our pharmacies far exceeds the total profitability of prescriptions compounded annually in the majority of our pharmacies. Therefore, it is not fiscally responsible for Rite Aid pharmacies that compound low volumes of necessary prescriptions for their patients to continue to do so.

Rite Aid will continue to prioritize and promote patient safety in all aspects of pharmacy practice. It is our hope that the said component of the newly amended regulation will be reconsidered in the near future to enhance patient care access to simple and moderate non-sterile prescription compounding for all California residents. Rite Aid and its predecessors have been serving California patients for over 50 years by compounding their prescribed non-sterile medications safely. Today, our pharmacies provide convenient access for all professional services in the community setting for immunization, dispensing, medication counseling, and compounding, when necessary. Pharmacists are highly educated professionals who are trained in Pharmacy School or College to compound many types of medications, and it is unfortunate that we may have to restrict their practice around this valuable patient service in the near future.

Sincerely,

A handwritten signature in cursive script that reads "Daniel Miller".

Daniel Miller, R.Ph.
SVP, Pharmacy Regulatory Affairs

Attachment 6

Proposed Changes to California Compounding Regulations
April 25th, 2017
Rick Rhoads, Pharm.D.

Introduction: The new California Compounding Regulations were a step in the right direction to protect patient safety in California, but there are still gaps pertaining to quality that should be addressed. There are also potential inconsistencies with the USP which may contribute to confusion in the industry. Although the best approach would be to adopt USP chapters <795>, <797>, and <800>, there may be good reasons it is not feasible for the board to do so.

As a “next step” to address the most pressing issues related to gaps and inconsistencies, the following changes to CCR 1735 and 1751 are proposed.

Proposal 1: Add detail to the process validation requirements in the policies and procedures section. This is important as there are currently no standards given in the regulations for verifying the effectiveness of sterilization and depyrogenation methods.

Proposed 1751.3 (c)

(c) For non-sterile-to-sterile batch compounding, the pharmacy shall maintain written policies and procedures for compounding that includes, in addition to the elements required by section 1735.5, 1751.3(a), and 1751.7(e), written policies and procedures regarding the following:

- (1) ~~Process validation for chosen sterilization methods.~~
- (1) **A description of the sterilization and depyrogenation process, including the temperature, pressure (if applicable), duration, and permissible load conditions for each cycle.**

(A) In addition, the SOPs must include a schedule and method for establishing and periodically verifying the effectiveness of the sterilization and depyrogenation methods selected, as well as the method for maintaining and cleaning the sterilizers and depyrogenation equipment.

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

Reference: Proposed Revision USP <797>

Proposal 2: Add a new section in 1751 for Sterilization and Depyrogenation requirements. Again, there are no current requirements in California regulations for sterilization and depyrogenation methods. Although there were many problems at NECC, some of the disastrous consequences could have been prevented if they followed the standards for cleaning, operating, and verifying the sterilizing cycles of their

autoclaves. These standards are needed for all the major methods of drug and component sterilization. The following language is essentially verbatim from the proposed revision of USP 797, which is very similar to the current version.

1751.11 Sterilization and Depyrogenation

(a) When selecting the sterilization method for each non-sterile to sterile CSP, personnel must take into consideration the nature of the components, its physical and chemical properties, and the intended container– closure system.

(b) The sterilization method used must sterilize the CSP while maintaining its physical and chemical stability (i.e., appropriate strength, purity, quality), and the packaging integrity of the CSP.

(c) Utensils and materials in direct contact with the components, the CSP, and the container–closure system must be sterilized and depyrogenated using appropriate methods. If sterilization and depyrogenation of container–closure systems is performed on site, the efficacy of each process must be established and documented, and the process must be shown to be reproducible.

(d) The following sections provide minimum requirements on specific sterilization methods.

(1) Sterilization by Filtration

(A) Commercially available sterile filters must be certified by the manufacturer as suitable for pharmaceutical use when used to sterilize CSPs. Sterilizing filters must be sterile and pyrogen-free and have a nominal pore size of 0.2 or 0.22 μm . They must be certified by the manufacturer to retain at least 10^7 microorganisms of a strain of *Brevundimonas diminuta* per square centimeter of upstream filter surface area under conditions similar to those in which the CSPs will be filtered (i.e., pressure, flow rate, and volume filtered).

(B) The supervising pharmacist must ensure, directly or from appropriate documentation from the supplier, that the sterilizing grade filters 1) are chemically and physically stable at the pressure and temperature conditions that will be used; 2) have enough capacity to filter the required volumes; and 3) will yield a sterile filtrate while maintaining pre-filtration pharmaceutical quality, including strength of ingredients of the specific CSP.

(C) The filter dimensions and the preparation to be sterilized by filtration should permit the sterilization process to be completed without the need for replacement of the filter during the process.

(D) When CSPs are known to contain excessive particulate matter, to maximize the efficiency of the final sterilizing filtration, a pre-filtration step should be performed using a filter of larger nominal pore size, or a separate filter of larger nominal pore size should be placed upstream of (i.e., prior to) the sterilizing filter to remove gross particulate contaminants before the CSP is passed through the sterilizing grade filter.

(E) Filter units used to sterilize CSPs must be subjected to the manufacturers' recommended post-use integrity test, such as a bubble point test.

(2) Sterilization by Steam Heat

(A) The process of thermal sterilization using saturated steam under pressure (i.e., autoclaving) is the preferred method for terminal sterilization of aqueous preparations in their final, sealed container-closure system. Steam heat sterilization is not an option if moisture, pressure, or the temperatures used would degrade the CSP. Steam heat sterilization is also used to sterilize many components (e.g., elastomeric closures) and some types of equipment.

(B) To achieve sterility, all materials must be directly exposed to steam under adequate pressure for the length of time necessary, as determined by use of appropriate biological indicators, to render the items sterile (i.e., kill any microorganisms, including bacterial spores that might be present). This is usually between 20 and 60 minutes at 121° saturated steam under a pressure of 15 psi. The duration of the exposure period must include sufficient time for the CSP or other items to reach the sterilizing temperature. The CSP and other items must remain at the sterilizing temperature for the duration of the sterilization period.

(C) The sterilization cycle should be designed to achieve a SAL of 10^{-6} . CSPs must be placed in suitable trays to allow steam to reach the CSPs without entrapment of air. Flat, stainless steel trays with low sides or ventilated bottoms will permit steam contact. When preparing plastic, glass, and metal devices or other items for steam sterilization, the items must be wrapped in low-lint protective fabric or paper or sealed in envelopes that will permit steam penetration and prevent post sterilization microbial contamination.

(D) Immediately before filling ampuls and vials that will be steam sterilized, solutions must be passed through a filter having a nominal pore size of not larger than 1.2 μm for removal of particulate matter.

(E) Sealed containers must be able to generate steam internally. Stoppered and crimped empty vials must contain a small amount of moisture to generate steam. Deep containers, such as beakers and graduated cylinders, should be placed on their sides to prevent air entrapment, or should have a small amount of water placed in them when steam sterilized.

(F) Porous materials and those items with occluded pathways (e.g., tubing) should only be sterilized by steam if the autoclave chamber has suitable cycles for dry goods, such as a pre-vacuum process to remove air before steam is sent into the chamber. Elastomeric closures and many other dry goods will need a drying cycle after steam exposure to remove condensed or absorbed moisture.

(G) The effectiveness of steam sterilization must be established and verified with each sterilization run or load by using appropriate biological indicators, such as spores of *Geobacillus stearothermophilus*, ATCC 12980, ATCC 7953 or equivalent, and other confirmation methods such as physicochemical indicators and integrators.

(H) The steam supplied must be free of contaminants and generated using clean water.

(I) The seals on the doors of autoclave chambers should be examined visually every day they are used for cracks or other damage, and the seal surfaces should be kept clean. A data recorder or chart must be used to monitor each cycle and to examine for cycle irregularities (e.g., deviations in temperature or pressure).

(J) Because the temperatures used to achieve sterilization by steam heat are lower than those used to achieve depyrogenation, materials in direct contact with the CSP (e.g., the container–closure system) must first undergo a depyrogenation process (e.g., dry heat or rinsing with pyrogen-free water) before being sterilized using steam heat, unless the materials used are certified to be pyrogen-free.

(3) Sterilization by Dry Heat

(A) Dry heat can be used only for those items that cannot be sterilized by steam or other means, when either the moisture would damage the material or the wrapping material is impermeable.

(B) Sterilization by dry heat requires higher temperatures and longer exposure times than sterilization by steam. The duration of the exposure period must include sufficient time for the CSP or other items to reach the sterilizing temperature. The CSP and other items must remain at the sterilizing temperature for the duration of the

sterilization period. Dry heat sterilization is usually done in an oven designed for sterilization at a temperature of 160° or higher, although sterilization processes at lower temperatures have been developed and validated. If lower temperatures are used, they must be shown to achieve effective sterilization.

- (C) Heated air must be evenly distributed throughout the chamber, which is typically done by an air blower. The oven must be equipped with temperature controls and a timer. During sterilization, sufficient space must be left between materials to allow for good circulation of the hot air. A data recorder or chart must be used to monitor each cycle and the data must be reviewed to identify cycle irregularities (e.g., deviations in temperature or exposure time).
- (D) The effectiveness of the dry heat sterilization method must be established and verified with each sterilization run or load using appropriate biological indicators such as spores of *Bacillus atrophaeus*, ATCC 9372, and other confirmation methods (e.g., temperature-sensing devices). Because the temperatures used to achieve sterilization by dry heat are lower than those used to achieve depyrogenation, materials in direct contact with the CSP (e.g., the container–closure system) must first undergo a depyrogenation process (e.g., dry heat or rinsing with pyrogen-free water) before being sterilized using dry heat, unless the materials used are certified to be pyrogen-free.

(4) Depyrogenation by Dry Heat

- (A) Dry heat depyrogenation must be used to render glassware and other thermostable containers pyrogen-free.
- (B) Depyrogenation processes typically operate at a range of temperatures from approximately 170° up to about 400°, depending on the exposure time. For example, a typical cycle would hold the items at 250° for 30 minutes. The duration of the exposure period must include sufficient time for the items to reach the depyrogenation temperature. The items must remain at the depyrogenation temperature for the duration of the depyrogenation period.
- (C) The effectiveness of the dry heat depyrogenation cycle must be established and verified annually using endotoxin challenge vials (ECVs) to demonstrate that the cycle is capable of achieving a ≥3-log reduction in endotoxins.

Reference: Proposed Revision USP <797>

Proposal 3: The current definition of hazardous drugs in CA regulations creates uncertainty and confusion. NIOSH drugs other than anti-neoplastics are not included in the definition, but there is an implication they should be dealt with in a certain way, either by classifying as hazardous or conducting an assessment of risk. I have heard of enforcement issues related to this confusion as well. A better approach would be to harmonize the definition with USP <800> and allow for an AOR for drugs that are not antineoplastic. This makes it very clear and is consistent with the pharmacy's obligations under federal regulations. Currently if these drugs are classified as hazardous, there is no provision in the CA regulations to modify work practices based on the safety profile of the drug and dosage form. Several sections of the HD regulations are affected.

Proposed 1735.1 (r)

(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

Proposed 1735.6 (e)

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

- (1) Minimum of 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 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~~ **exhausted**, and
- (4) All surfaces within the room shall be smooth, seamless, impervious, and non-shedding.

(5) Exception: For dosage forms of other HDs on the NIOSH list that are not antineoplastics, the pharmacy may perform an assessment of risk to determine alternative containment strategies and/work practices to the above requirements.

(A) The assessment of risk must, at a minimum, consider the following: Type of HD (e.g., antineoplastic, non-antineoplastic, reproductive risk), Risk of exposure, Packaging, Manipulation)

(B) If an assessment of risk approach is taken, the pharmacy must document what alternative containment strategies and/or work practices are being employed for specific dosage forms to minimize occupational exposure. If used, the assessment of risk must be reviewed at least annually and the review documented.

Reference: USP <800>

1751.4. Facility and Equipment Standards for Sterile Compounding

(g) 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. The negative pressure PEC must be certified every six months by a qualified technician who is familiar with CETA Certification Guide for Sterile Compounding Facilities (CAG-003-2006-13, Revised May 20, 2015), which is hereby incorporated by reference. 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) **Exception: For dosage forms of other HDs on the NIOSH list that are not antineoplastics, the pharmacy may perform an assessment of risk to determine alternative containment strategies and/work practices to the above requirements.**

(A) The assessment of risk must, at a minimum, consider the following: Type of HD (e.g., antineoplastic, non-antineoplastic, reproductive risk), Risk of exposure, Packaging, Manipulation)

(B) If an assessment of risk approach is taken, the entity must document what alternative containment strategies and/or work practices are being employed for specific dosage forms to minimize occupational exposure. If used, the assessment of risk must be reviewed at least annually and the review documented.

Reference: USP <800>

Proposal 4: Modify and clarify the testing requirements for extending BUDs. These should be more specific and appropriate based on the type of compound. Also, it is not clear what is meant by 'method suitability test'. Generally, this term refers to a test associated with USP <71> sterility testing. Although method suitability is necessary for all USP <71> sterility testing, it seems to be an unnecessary requirement for extending the BUD.

Proposed 1735.2 (i)(3)

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

(A) ~~Method Suitability Test,~~

(A) Studies demonstrating chemical, physical, and microbiological stability, and

(B) Anti-Microbial Effectiveness Testing for multi dose containers, and

(C) Container Closure Integrity Testing for sterile preparations.

Reference: USP <1191> Stability Considerations in Dispensing Practice

Proposal 5: Add a definition for stability.

Proposed 1735.1

“Stability” is defined as the extent to which a preparation retains, within specified limits, and throughout its period of storage and use (i.e., its shelf-life), the same properties and characteristics that it possessed at the time of its compounding.

Reference: USP <1191> Stability Considerations in Dispensing Practice

Attachment 7

Dear Board Member

Thank you for the opportunity to speak before the subcommittee on the ramifications of recent pharmacy regulations within the compounding industry.

Given the lateness of the meeting we did not have the chance to address concerns addressed by the enforcement team. At least 32 states have essentially adopted USP as their guidance in proper compounding procedures. With its GMP-like standards for ***non-sterile compounds***, 1735 far exceeds USP in a number of areas that, as noted in the meeting, are unwarranted and very expensive.

Stability

USP	1735
	There is no clarity about the nature of the stability testing. Our fear is that CA will insist on forced degradation testing for compounds which is inappropriate, unnecessary and sometimes misleading.

Container Closure

USP	1735
While compounders shall ensure containers meet USP requirements, "compounders are not expected to perform the tests".	Regardless of sterile versus non-sterile, 1735.2 requires BUD extension ONLY in the presence of Container Closure Integrity testing , Stability Studies and Method Suitability testing (addressed in USP 797 for STERILE items).

Sterility

USP	1735
No reference in USP for sterility of non-sterile compounds	Regardless of sterile versus non-sterile, 1735.2 requires BUD extension ONLY in the presence of Container Closure Integrity test, Stability Studies and Method Suitability testing (addressed in USP 797 for STERILE items).

Testing Frequency

USP	1735
No mention of annual testing	Specifies annual testing, regardless of consistency of formulation.

In 1735.2, "the prescriber has approved use of a compounded drug either orally or in writing. Where approval is given orally, that approval shall be noted on the prescription prior to compounding."

Documentation of the use for a compound is equally problematic, especially in veterinary medicine, where there are many off-label conditions that can be associated with the use of a compound. Even the AVMA recommends this action might be best left to the individual medical record where quantity, lot number and rationale for the use of a compound can be noted.

In 1735.2, *"...using a purchase order or other documentation...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 office administration."*

USP makes no reference toward mandating forecasts for office stock items—an impossibility in the veterinary community.

Lastly, as you may know, the President has signed the Congressional Omnibus bill into law, H.R. 244. The language calls on FDA to release new guidance to allow **503A** pharmacists to compound for "office-use" for prescribers, hospitals and other health systems. Congress expressed concern that patient access is decreasing to compounded medications, due to FDA's implementation actions of prohibiting all office-use compounding even where "this practice is authorized in the vast majority of states and was intended to be allowable under DQSA."

California wisely allows for office stock for veterinary practitioners for acute needs until a follow-on prescription can be obtained. Clinics should be afforded the best possible dating for these medications, hence the need to pursue optimum Beyond Use Dating.

Thank you for your consideration of these issues in the June emergency meeting. I'm confident compounders will provide you with even more insight than these points.

Regards,

Bruce Dell, R.Ph.
General Manager

Attachment

SENT VIA EMAIL

May 19, 2017

Ms. Virginia Herold
Executive Officer
California Board of Pharmacy
1625 N. Market Blvd, Suite N 219
Sacramento, CA 95834

Dear Ms. Herold:

Wedgewood Village Pharmacy, LLC ("*Wedgewood*") would like to thank the California Board of Pharmacy, Enforcement & Compounding Committee (the "*Committee*") for this opportunity to present its thoughts on current regulations applicable to compounding pharmacies. Wedgewood believes in the Committee's mission to ensure that patients throughout the State of California receive safe, effective and quality compounded medications. With that in mind, Wedgewood fully supports the California Pharmacy Association's ("*CPhA*") proposed modifications to Sections 1735 and 1751 of the California Code of Regulations. The proposed changes ensure that Sections 1735 and 1751 conform to other standards currently governing compounding pharmacies.

In particular, CPhA's amendments to Section 1735.2(i), related to beyond use dates, are necessary to ensure consistency and clarity among all requirements governing compounding pharmacies. As it stands, the current iteration of Section 1735.2(i) is confusing and compounding pharmacies often struggle to determine what testing requirements apply under the circumstances. In addition, the testing requirements set forth in Section 1735.2(i) appear to exceed USP <795> and <797> standards. In fact, they appear to mimic current Good Manufacturing Practices ("*cGMP*") requirements, which are applicable to drug manufacturers and not compounding pharmacies.

Unlike drug manufacturers, compounding pharmacies prepare unique medications for particularized medical needs when a prescriber determines a commercially available drug is not suitable for treatment. The Food Drug & Cosmetic Act ("*FDCA*") requirements for manufactured drugs, including cGMPs, were not designed for these specialized medications. cGMP testing practices are extremely expensive and are therefore not economically practical when small amounts of customized drug product are being produced. This is one of the very

reasons why commercial drug manufacturers only produce very large quantities of medication in standardized strengths and dosage forms. Compounding pharmacies cannot, therefore, with any economic feasibility, comply with cGMP testing requirements. If compounding pharmacies were required to comply with cGMP, the increased cost to do so would either be passed on to patients or result in pharmacies discontinuing compounding activities. In either case, patients would suffer due to drastically increased prices and restricted access to necessary medications.

In addition, Wedgewood wishes to submit its own proposed amendments to Section 1735.2(c), related to office use, and Section 1735.2(d) (Attachment A). Wedgewood believes its proposed changes are necessary to ensure patient access to needed compounded medication. A copy of the proposed amendments are attached hereto. With respect to office use, prescribers are often presented with patients who have an immediate need for compounded medication. These patients cannot wait for a pharmacist to fill a prescription. As a result, prescribers must have office stock on hand to treat patients that present with urgent medical needs. In turn, compounding pharmacies must be allowed to dispense compounded medication for office use so that prescribers have access to compounded medication in advance of examining patients. The California Board of Pharmacy acknowledges the need for this practice within Section 1735.2(c), however within that section there is some office use quantity requirements that are unclear and potentially not practical.

For example, a veterinarian sees a variety of animal species and sizes on any given day. As a result, medication dosage amounts and frequencies vary greatly. It is neither practical nor reasonable to expect the veterinarian, in advance of knowing the species and size of the animal patient, to: (1) anticipate the quantity of drug sufficient to treat the patient; and (2) anticipate the amount of drug needed to be administered to the patient versus the amount of drug that constitutes a 120 hour supply for the patient. Wedgewood's proposed changes to Section 1735.3(c) ensure that California's regulations allow for the practical application of office use compounding.

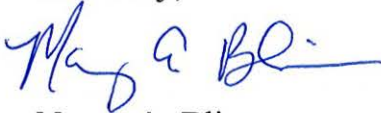
As for Wedgewood's proposed amendment to Section 1735.2(d), Wedgewood has added the word "human" to clarify that the limitations of sub-sections (1) through (3) are applicable to only human health compounding. The language currently used in sub-sections (1) through (3) mirrors the language of the Drug Quality Security Act ("DQSA"), which only applies to human health compounding. DQSA was explicitly not intended for veterinary compounding. Moreover, the ASHP drug shortage list does not include veterinary drugs. The inclusion, therefore, of the term "human" in Section 1735.2(d) will ensure consistency with federal law.

Wedgewood is aware that other compounding pharmacies have stopped dispensing into California as a result of California's restrictive regulations. As a result, patients throughout the State of California may not be able to get the

compounded medications they need and may be forced to go untreated. Wedgwood believes the CPhA's proposed amendments, along with Wedgwood's own proposed amendments, will provide consistency and clarity among all requirements governing compounding pharmacies and allow patients who depend on compounded medications to continue to have full access.

Wedgwood appreciates the opportunity to present its proposed amendments to the Committee and is available to answer any questions the Committee may have. Wedgwood wishes to work with the Committee toward the mutual goal of protecting and promoting the health and safety of Californians by pursuing the highest quality of pharmacist's care and the appropriate use of pharmaceuticals.

Sincerely,



Marcy A. Bliss
President & CEO



Anthony Grzib
Director of Pharmacy Compliance

cc: A. Lynch – Pharmacist-in-Charge

Attachment: Attachment A

WEDGEWOOD VILLAGE PHARMACY, LLC ATTACHMENT A

CCR 1735.2(c) A “reasonable quantity” 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 preparation that:

(1) Is ordered by the prescriber or the prescriber’s agent 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 office use ~~administration~~; 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 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

(4) That the pharmacist has ~~a credible basis for concluding it~~ concurred is a reasonable quantity for office use as determined by the prescriber considering the potential intended use of the compounded medication and the nature of the prescriber’s practice; and

(5) With regard to any individual prescriber to whom the pharmacy furnishes, and with regard to all prescribers to whom the pharmacy furnishes, is an amount which the pharmacy is capable of compounding in compliance with ~~pharmaceutical~~ compounding standards for integrity, potency, quality and strength of the compounded drug preparation; and

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

Need for Recommended Changes:

- Alterations to sub-section (1) are needed to account for the fact that compounded medications ordered for office use are often medications needed to treat immediate medical needs of patients who have not yet presented to the prescriber. As such, these medications are typically ordered by prescribers in advance of examining patients. Because of the variation of animal species and sizes that may present to the prescriber, medication dosage amounts and frequencies vary greatly. Therefore, it's neither practical nor reasonable to expect a prescriber, in advance of knowing the species and size of veterinary patients yet to be seen, to:
 - Anticipate the quantity of drug sufficient to treat each patient, and
 - Anticipate the amount of drug needed to be administered to each patient versus the amount of drug that constitutes a 120 hour supply for each patient.
- For the same reason, sub-section (3) needs to be altered to remove the requirement that the prescriber document these yet-to-be determined quantities of drug sufficient to treat each patient.

- Alterations to sub-section (4) are needed to remove the requirement that pharmacist establish and document a creditable basis for the quantity of compounded medication being ordered by the prescriber. In sub-section (1) and sub-section (3), the prescriber is permitted

to determine the amount of medication they're ordering from the pharmacy for office use based on the number of anticipated patients they may see and estimated quantities of medication they may need. It's unclear how a pharmacist can be accountable for establishing and documenting a creditable basis for the prescriber's patient forecast and medication quantity estimates.

- Alterations to sub-section (5) are needed to clarify that the standards used by the compounding pharmacy to produce the compounded medication are standards applicable to pharmacy compounding, not standards applicable to pharmaceutical manufacturing.

CCR 1735.2(d) No pharmacy or pharmacist shall compound a human 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.

Need for Recommended Change: The addition of the word "human" to section (d) is required to clarify the limitations of sub-sections (1) through (3) are applicable to only human health. The language used in sub-sections (1) through (3) mirror the language in the Federal DQSA, which itself is applicable to only human health. In addition, the ASHP drug shortage list does not include veterinary drugs.