



**California State Board of Pharmacy**  
1625 N. Market Blvd, Suite N 219, Sacramento, CA 95834  
Phone (916) 574-7900  
Fax (916) 574-8618  
www.pharmacy.ca.gov

STATE AND CONSUMER SERVICES AGENCY  
DEPARTMENT OF CONSUMER AFFAIRS  
GOVERNOR EDMUND G. BROWN JR.

## COMPOUNDING REGULATION SUBCOMMITTEE

Stan Weisser, RPh, Chairperson, Board President  
Randy Kajioka, PharmD, Board Vice-President  
Anil Badlani, RPh, Board Member

Report of the Meeting Held August 22, 2011

This subcommittee was formed to respond to inquiries regarding implementation of the board's compounding regulations, sections 1735-1735.8 and 1751-1751.8. Copies of these regulation requirements are provided as **Attachment 1**. As you will remember, these regulations were developed following formation of the board's Committee on Compounding in 2004, and the regulation provisions have gone through various iterations since and before they took effect (although some of the provisions existed before the 2009 rulemaking).

For the past year, the board has been discussing implementation of these requirements which became effective July 2010. A series of questions and answers have been developed by the board, and are available in **Attachment 2**. However, questions remain from some of the board's licensees.

Minutes of the Compounding Subcommittee Meeting are provided as **Attachment 3**,

The regulations are very important for public safety. There are general provisions for compounding in sections 1735-1735.8 that apply to all compounding activities. Provisions for compounding for sterile injectable products are provided in sections 185-1751.8. Many of the provisions for sterile injectable compounding were promulgated after California's public health event in 2001 where a pharmacy compounded contaminated injectable products that killed three patients and put more than 30 in the hospital. Some of these provisions also existed as parenteral compounding requirements that were in place before 1990.

The board's Compounding Subcommittee met on August 22, 2011. Minutes of this meeting are provided in **Attachment 3**. From this meeting there were several recommendations that will be presented to the board at this meeting. During this board meeting, the board also will have an opportunity to hear public comments regarding the board's compounding regulations.

First, from the hospital setting, Rita Shane, Pharm.D., FASHP, Director, Pharmacy Services, Cedars-Sinai Medical Center, will provide an overview of how hospital pharmacies compound injectable products for patients.

Issues:

1. Current: Question and Answer 23:

Q: CCR section 1735.3 defines what must be recorded for each compounded drug product. CCR 1735.3(a)(7) states, "The equipment used in compounding the drug product." Does this include tubing sets, spikes, needles, syringes, etc.?

A: Yes, all equipment used for compounding the drug product must be recorded – TPN compounders, homogenizers, scales, syringes, needles, tubing sets, spikes, filters, mortar and pestle, pill making device, infusion devices. If there is more than one of the same device (e.g., scales, laminar flow hoods) it is recommended to label them in some manner to distinguish which one was used in the process for appropriate completion for the compounding record.

Reference: CCR 1735.3(a)(7).

Problem: the answer interpreting the regulation requires that a great deal of equipment used in compounding must be recorded and this is perhaps too broad without corresponding consumer protection benefit, and than what the regulation requires. For example, recording the lot number and expiration date of discarded syringes is time consuming. Moreover, a review of actual section 1735(a)(7) requires that equipment used must be documented, but not the expiration date or lot number.

Resolution: Recast answer to question 23 to include record only equipment used where that equipment must be calibrated or maintained per manufacturer's guidelines, and does not require expiration date and lot number.

---

2. Can a patient-specific medication, compounded for use on a one-time basis for administration within 24 hours for one patient in a hospital, be returned to the pharmacy for redispensing to another patient.

Problem:

1735.3 (a) For each compounded drug product, the pharmacy records shall include:

...

(6) The manufacturer and lot number of each component. If the manufacturer name is demonstrably unavailable, the name of the supplier may be substituted. **Exempt from the requirements in this paragraph are sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.**

Resolution:

No, not if the exemption from recordkeeping is followed as specified in 1735(a)(6).

---

3. In Section 1751.2 (d): All cytotoxic agents shall bear a special label which states “Chemotherapy – Dispose of Properly.”

Problem: not all cytotoxic agents are used for chemotherapy.

Resolution: Amend Section 1751.2(d) to read:

All cytotoxic agents shall bear a special label which states “~~Chemotherapy~~ Cytotoxic product – ~~Dispose of Properly.~~”

- 
4. In Section 1735.3, there is a list of elements that the pharmacy must record when compounding.

Problem: Missing from the list is a requirement to record the expiration date of each substance used to compound drug products.

Resolution: Add expiration date to the list of elements that must be recorded when a pharmacy compounds medication. Specifically:

**1735.3. Recordkeeping of Compounded Drug Products** (Effective 07/06/10)

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

- (1) The master formula record.
  - (2) The date the drug product was compounded.
  - (3) The identity of the pharmacy personnel who compounded the drug product.
  - (4) The identity of the pharmacist reviewing the final drug product.
  - (5) The quantity of each component used in compounding the drug product.
  - (6) The expiration date of each component.
  - (7) The manufacturer and lot number of each component. If the manufacturer name is demonstrably unavailable, the name of the supplier may be substituted. Exempt from the requirements in this paragraph are sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.
  - (7) The equipment used in compounding the drug product.
  - (8) A pharmacy assigned reference or lot number for the compounded drug product.
  - (9) The expiration date of the final compounded drug product.
  - (10) The quantity or amount of drug product compounded.
- (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) Chemicals, bulk drug substances, drug products, and components used to compound drug products shall be obtained from reliable suppliers. The pharmacy shall acquire and retain any available certificates of purity or analysis for chemicals, bulk drug substances, drug products, and components used in compounding. Certificates of purity or analysis are not required for products that are approved by the Food and Drug Administration.
- (d) Pharmacies shall maintain and retain all records required by this article in the pharmacy in a readily retrievable form for at least three years from the date the record was created.

---

Another issue involving compounding:

5. In the interests of patient safety when compounding stock solutions from nonsterile to sterile ingredients, do the stock solutions need to undergo sterility and pyrogen testing?

Reference: 1751.7(c) Batch-produced sterile injectable drug products compounded from one or more non-sterile ingredients 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.

Problem:

The concern is the interpretation of what is a “batch-produced” sterile injectable drug product and what is the “end product” that requires testing for sterility and pyrogens. Many compounding pharmacies are compounding a stock solution made from one or more non-sterile ingredients. The stock solution is used over a period of time to compound multiple prescriptions by withdrawing an amount from the stock solution to be compounded with other non-sterile or sterile ingredients as prescriptions are received. The compounding pharmacies are filtering the stock solution and the final compounded drug product that has the additional ingredients added. The compounding pharmacy considers the product with all the ingredients to be the “end product”. The compounding pharmacy is also considering, once the stock solution is filtered, it is sterile and does not consider it to be a nonsterile ingredient, even though it is not tested to confirm sterility.

Because the compounding pharmacy is adding additional ingredients with an amount from the stock solution as they receive a prescription, the compounding pharmacy does not consider the final compounded drug as being “batch produced” and therefore, not subject to end-product testing for sterility and pyrogens. This practice of compounding can result in multiple patients being affected by a stock solution that is not tested to confirm sterility. In the case involving Doc’s Pharmacy, a stock solution was compounded and sterilized, but it was not tested for sterility and pyrogens. As a result, this untested stock solution resulted in 3 deaths and 30 or more hospitalizations.

Solution: The board needs to discuss and determine its interpretation of the regulations regarding end-product testing of non-sterile to sterile injectable compounds and whether this requires sterility and pyrogen testing of stock solutions.

---

Following this page are two pages of comments provided by Dr. Shane.

Submitted by Dr. Shane, 10/11/11:

## Recommended Definitions for 1735.3.a.6 Hospital Patient Specific and Batch Compounding

### Specific Board of Pharmacy (BOP) Code of Regulation: 1735.3. Records of Compounded Products

#### 1735.3. Recordkeeping of Compounded Drug Products (Effective 07/06/10)

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

(6) The manufacturer and lot number of each component. If the manufacturer name is demonstrably unavailable, the name of the supplier may be substituted. Exempt from the requirements in this paragraph are sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

### Proposed Definitions for the Hospital Setting:

**Patient-specific compounded medications in the hospital setting:** Medications compounded using sterile products for an individual patient based on a physician order (prescription) intended to be given within 24 hours.

**Batches in the hospital setting:** Preparation of compounded products for multiple patients in anticipation of physicians' orders.

Example: Preparation of 200 doses of vancomycin 1 gram on a weekly basis. Expiration: 14 days refrigerated per USP 797.

### Hospital Compounding of Sterile Products

- In the hospital setting, the majority of sterile compounded medications are patient-specific and often prepared multiple times during each 24 hour period since patients condition change requiring modifications in the medications or doses.
  - For example, an antibiotic ordered to be given every 6 hours may be prepared at 4 different times each day the patient is in the hospital. In the community and home infusion settings, the entire quantity for a prescription is generally prepared at one time.
- The number of sterile products compounded in a hospital per day is approximately equal to the number of beds. A 300 bed hospital will prepare approximately 300 sterile products per day for adults; in pediatric patients, the number of sterile products prepared per patient is higher since they often cannot take medications by mouth.
- Currently, the manufacturer and lot number (7-10 characters/lot number) of each component needs to be handwritten for each dose which represents several hundred transcriptions a day in order to be able to use the medication beyond 24 hours.
- Current hospital computer systems do not support an automated way to capture this information.

### Harmful Patient Events from Sterile Compounding

- A 20 year review of publicly reported harmful patient events from sterile compounded medications demonstrates that the events are primarily due to contamination by the personnel or facility during the preparation process or mathematical errors rather than recalls from the manufacturer.
- Recording the lot number and manufacturer for each component would not have prevented harm to patients.

### Timely Preparation to Treat Hospital Patient Conditions

- There are numerous medications where national guidelines require availability within an hour or less. Examples include antibiotics, medications for stroke or myocardial infarction, clotting factors and pain medications.

- Hospitalized patients' conditions change throughout each 24 hour period which necessitates last minute modifications to medication orders (prescriptions). Therefore, in order to ensure patient safety, many hospitals compound medications close to the time that they need to be given.
- Recording the manufacturer and lot number each time the medication is compounded delays the availability of the medication for patient care.

### Drug Shortages and Wastage

- Drug shortages have been recognized as a national health crisis.
- There have been more than 160 injectable drug shortages this year.
- An evaluation of medications not used within 24 hours (due to changes in patients' conditions) demonstrated that 50% of the wastage involved drugs that are on shortage. The actual drugs discarded included cancer medications, antibiotics, heart failure and critical care medications.

### Recall Management

- Until such time as technology enables the recording of manufacturer and lot number via either RFID (radio frequency identification) or bar coding or other means, the requirement for recording of manufacturer and lot number should be limited to batches and sterile compounding from non-sterile ingredients.
- Recommended recall process (Class 1 or recalls with the potential for patient harm) for patient-specific compounded medications:
  - To ensure patient safety and prevent delays associated with retrieving handwritten manufacturer and lot numbers for compounded products, hospitals will immediately quarantine all patient-specific compounded products not yet administered which contain recalled medications.
  - Any remaining medications that have not been compounded would be evaluated to determine if any of the recalled lot numbers are in stock.
  - Physicians whose patients may have potentially received medications that have been recalled would be notified if the recall level indicated the potential for patient harm.

### **Summary of Recommendations:**

1. **Patient-specific compounded medications in the hospital setting:** Medications compounded using sterile products for an individual patient based on a physician order (prescription) intended to be given within 24 hours.

Patient-specific medications should not require the recording of manufacturer and lot numbers for the following reasons:

- The need to handwrite the manufacturer and lot number of each medication component slows the preparation of medications to treat critical patient conditions.
- Harmful events with sterile compounded medications have not been due to recalled medications or components but rather due to contamination during preparation or human error.
- Critical medications that are on shortage (or may be in the future) are being discarded even though they are still sterile and stable, based on national standards.
- Quarantining all recalled products would ensure patient safety and timely management of the recall.
- Sterile compounded medications discontinued due to changes in the patient's condition that meet standards for sterility and stability could be dispensed for another patient based on a specific medication order.

Example: 1 dose of vancomycin 1.5 gram prepared for patient A, discontinued and used for patient B on the same day or within 14 days if refrigerated per USP 797.

Compounding of batches or sterile products from non-sterile ingredients would require recording of lot number and



## Article 4.5 Compounding

### **1735. Compounding in Licensed Pharmacies** (Effective 07/06/10)

(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 drug product from chemicals or bulk drug substances

(b) “Compounding” does not include reconstitution of a drug pursuant to a manufacturer’s direction(s) for oral, rectal topical, or injectable administration, nor does it include tablet splitting or the addition of flavoring agent(s) to enhance palatability.

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

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

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

**1735.1. Compounding Definitions** (Effective 07/06/10)

- (a) “Integrity” means retention of potency until the expiration date noted on the label.
- (b) “Potency” means active ingredient strength within +/- 10% of the labeled amount.
- (c) “Quality” means the absence of harmful levels of contaminants, including filth, putrid, or decomposed substances, and absence of active ingredients other than those noted on the label.
- (d) “Strength” means amount of active ingredient per unit of a compounded drug product.

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

**1735.2. Compounding Limitations and Requirements** (Effective 07/06/10)

- (a) Except as specified in (b) and (c), no drug product shall be compounded prior to receipt by a pharmacy of a valid prescription for an individual patient where the prescriber has approved use of a compounded drug product either orally or in writing. Where approval is given orally, that approval shall be noted on the prescription prior to compounding.
- (b) A pharmacy may prepare and store a limited quantity of a compounded drug product 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) Pursuant to Business and Professions Code section 4052(a)(1), a “reasonable quantity” of compounded drug product may be furnished to a prescriber for office use upon prescriber order, where “reasonable quantity” is that amount of compounded drug product that:
  - (1) is sufficient for administration or application to patients in the prescriber’s office, or for distribution of not more than a 72-hour supply to the prescriber’s patients, as estimated by the prescriber; and
  - (2) is reasonable considering the intended use of the compounded medication and the nature of the prescriber’s practice; and
  - (3) for any individual prescriber and for all prescribers taken as a whole, is an amount which the pharmacy is capable of compounding in compliance with pharmaceutical standards for integrity, potency, quality and strength of the compounded drug product.
- (d) A drug product shall not be compounded until the pharmacy has first prepared a written master formula record that includes at least the following elements:
  - (1) Active ingredients to be used.
  - (2) Inactive ingredients to be used.
  - (3) Process and/or procedure used to prepare the drug.
  - (4) Quality reviews required at each step in preparation of the drug.
  - (5) Post-compounding process or procedures required, if any.
  - (6) Expiration dating requirements.

- (e) Where a pharmacy does not routinely compound a particular drug product, the master formula record for that product may be recorded on the prescription document itself.
- (f) The pharmacist performing or supervising compounding is responsible for the integrity, potency, quality, and labeled strength of a compounded drug product until it is dispensed.
- (g) All chemicals, bulk drug substances, drug products, and other components used for drug compounding shall be stored and used according to compendial and other applicable requirements to maintain their integrity, potency, quality, and labeled strength.
- (h) Every compounded drug product shall be given an expiration date representing the date beyond which, in the professional judgment of the pharmacist performing or supervising the compounding, it should not be used. This “beyond use date” of the compounded drug product shall not exceed 180 days from preparation or the shortest expiration date of any component in the compounded drug product, unless a longer date is supported by stability studies of finished drugs or compounded drug products using the same components and packaging. Shorter dating than set forth in this subsection may be used if it is deemed appropriate in the professional judgment of the responsible pharmacist.
- (i) The pharmacist performing or supervising compounding is responsible for the proper preparation, labeling, storage, and delivery of the compounded drug product.
- (j) Prior to allowing any drug product to be compounded in a pharmacy, the pharmacist-in-charge shall complete a self-assessment form for compounding pharmacies developed by the board (form 17m-39 rev. 10/07). That form contains a first section applicable to all compounding, and a second section applicable to sterile injectable compounding. The first section must be completed by the pharmacist-in-charge before any compounding is performed in the pharmacy. The second section must be completed by the pharmacist-in-charge before any sterile injectable compounding is performed in the pharmacy. The applicable sections of the self-assessment shall subsequently be completed before July 1 of odd-numbered each year, within 30 days of the start of a new pharmacist-in-charge, 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.

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 of Compounded Drug Products** (Effective 07/06/10)

- (a) For each compounded drug product, the pharmacy records shall include:
  - (1) The master formula record.
  - (2) The date the drug product was compounded.
  - (3) The identity of the pharmacy personnel who compounded the drug product.
  - (4) The identity of the pharmacist reviewing the final drug product.
  - (5) The quantity of each component used in compounding the drug product.
  - (6) The manufacturer and lot number of each component. If the manufacturer name is demonstrably unavailable, the name of the supplier may be substituted. Exempt from the requirements in this paragraph are sterile products compounded on a one-time basis for

administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

(7) The equipment used in compounding the drug product.

(8) A pharmacy assigned reference or lot number for the compounded drug product.

(9) The expiration date of the final compounded drug product.

(10) The quantity or amount of drug product compounded.

(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) Chemicals, bulk drug substances, drug products, and components used to compound drug products shall be obtained from reliable suppliers. The pharmacy shall acquire and retain any available certificates of purity or analysis for chemicals, bulk drug substances, drug products, and components used in compounding. Certificates of purity or analysis are not required for products that are approved by the Food and Drug Administration.

(d) Pharmacies shall maintain and retain all records required by this article in the pharmacy in a readily retrievable form for at least three years from the date the record was created.

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

#### **1735.4. Labeling of Compounded Drug Products** (Effective 07/06/10)

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

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

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

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** (Effective 07/06/10)

(a) Any pharmacy engaged in compounding shall maintain a written policy and procedure manual for compounding that establishes procurement procedures, methodologies for the formulation and compounding of drugs, facilities and equipment cleaning, maintenance, operation, and other standard operating procedures related to compounding.

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

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

- (1) Procedures for notifying staff assigned to compounding duties of any changes in processes or to the policy and procedure manual.
- (2) Documentation of a plan for recall of a dispensed compounded drug product where subsequent verification demonstrates the potential for adverse effects with continued use of a compounded drug product.
- (3) The procedures for maintaining, storing, calibrating, cleaning, and disinfecting equipment used in compounding, and for training on these procedures as part of the staff training and competency evaluation process.
- (4) Documentation of the methodology used to test integrity, potency, quality, and labeled strength of compounded drug products.
- (5) Documentation of the methodology used to determine appropriate expiration dates for compounded drug products.

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

**1735.6. Compounding Facilities and Equipment** (Effective 07/06/10)

- (a) Any pharmacy engaged in compounding shall maintain written documentation regarding the facilities and equipment necessary for safe and accurate compounded drug products. Where applicable, this shall include records of certification(s) of facilities or equipment.
- (b) Any equipment used to compound drug products shall be stored, used, and maintained in accordance with manufacturers' specifications.
- (c) Any equipment used to compound drug products for which calibration or adjustment is appropriate shall be calibrated prior to use to ensure accuracy. Documentation of each such calibration shall be recorded in writing and these records of calibration shall be maintained and retained in the pharmacy.

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** (Effective 07/06/10)

- (a) Any pharmacy engaged in compounding shall maintain written documentation sufficient to demonstrate that pharmacy personnel have the skills and training required to properly and accurately perform their assigned responsibilities relating to compounding.
- (b) The pharmacy shall develop and maintain an on-going competency evaluation process for pharmacy personnel involved in compounding, and shall maintain documentation of any and all training related to compounding undertaken by pharmacy personnel.
- (c) Pharmacy personnel assigned to compounding duties shall demonstrate knowledge about processes and procedures used in compounding any drug product.

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** (Effective 07/06/10)

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

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

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

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

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

## **Article 7. Sterile Injectable Compounding**

### **1751. Sterile Injectable Compounding; Compounding Area**

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

(b) Any pharmacy doing sterile injectable compounding shall have a designated area for the preparation of sterile injectable products which shall meet the following standards:

(1) Clean Room and Work Station Requirements, shall be in accordance with Section 490A.3.1 of Title 24, Part 2, Chapter 4A of the California Code of Regulations.

(2) Walls, ceilings and floors shall be constructed in accordance with Section 490A.3 of Title 24, Part 2, Chapter 4A of the California Code of Regulations.

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

(4) Be certified annually by a qualified technician who is familiar with the methods and procedures for certifying laminar air flow hoods and clean room requirements, in accordance with standards adopted by the United States General Services Administration. Certification records must be retained for at least 3 years.

(5) The pharmacy shall be arranged in accordance with Section 490A.3 of Title 24, Part 2, Chapter 4A of the California Code of Regulations. Items related to the compounding of sterile injectable products within the compounding area shall be stored in such a way as to maintain the integrity of an aseptic environment.

(6) A sink shall be included in accordance in Section 490A.3.4 Title 24, Part 2, Chapter 4A of the California Code of Regulations.

(7) There shall be a refrigerator and/or freezer of sufficient capacity to meet the storage requirements for all material requiring refrigeration.

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

Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4036, 4037, 4051, 4052, 4127 and 4127.7, Business and Professions Code; and Section 18944, Health and Safety Code.

#### **1751.1. Sterile Injectable Recordkeeping Requirements.**

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

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

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

(2) Refrigerator and freezer temperatures.

(3) Certification of the sterile compounding environment.

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

(5) Inspection for expired or recalled pharmaceutical products or raw ingredients.

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

(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.

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 Injectable Labeling Requirements.**

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

(a) Telephone number of the pharmacy, except for sterile injectable products dispensed for inpatients of a hospital pharmacy.

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

(c) Instructions for storage and handling.

(d) All cytotoxic agents shall bear a special label which states "Chemotherapy - Dispose of Properly."



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

**1751.3. Sterile Injectable Policies and Procedures.**

- (a) Any pharmacy engaged in compounding sterile injectable drug products shall maintain a written policy and procedure manual for compounding that includes, in addition to the elements required by section 1735.5, written policies and procedures regarding the following:
- (1) Compounding, filling, and labeling of sterile injectable compounds.
  - (2) Labeling of the sterile injectable product based on the intended route of administration and recommended rate of administration.
  - (3) Equipment and supplies.
  - (4) Training of staff in the preparation of sterile injectable products.
  - (5) Procedures for handling cytotoxic agents.
  - (6) Quality assurance program.
  - (7) Record keeping requirements.
- (b) The ingredients and the compounding process for each preparation must be determined in writing before compounding begins and must be reviewed by a pharmacist.
- (c) Pharmacies compounding sterile injectable products shall have written policies and procedures for the disposal of infectious materials and/or materials containing cytotoxic residues. The written policies and procedures shall describe the pharmacy protocols for cleanups and spills in conformity with local health jurisdiction standards.
- (d) Pharmacies compounding sterile injectable products from one or more non-sterile ingredients must have written policies and procedures that comply with the following:
- (1) All written policies and procedures shall be immediately available to all personnel involved in these activities and board inspectors.
  - (2) All personnel involved must read the policies and procedures before compounding sterile injectable products, and any additions, revisions, and deletions to the written policies and procedures must be communicated to all personnel involved in sterile compounding.
  - (3) Policies and procedures must address at least the following:
    - (A) Competency evaluation.
    - (B) Storage and handling of products and supplies.
    - (C) Storage and delivery of final products.
    - (D) Process validation.
    - (E) Personnel access and movement of materials into and near the controlled area.
    - (F) Use and maintenance of environmental control devices used to create the critical area for manipulation of sterile products (e.g., laminar-airflow workstations, biological safety cabinets, class 100 cleanrooms, and barrier isolator workstations).
    - (G) Regular cleaning schedule for the controlled area and any equipment in the controlled area and the alternation of disinfectants. Pharmacies subject to an institutional infection control policy may follow that policy as it relates to cleaning schedules and the alternation of disinfectants in lieu of complying with this subdivision.
    - (H) Disposal of packaging materials, used syringes, containers, and needles to enhance sanitation and avoid accumulation in the controlled area.
    - (I) For sterile batch compounding, written policies and procedures must be established for the use of master formulas and work sheets and for appropriate documentation.
    - (J) Sterilization.
    - (K) End-product evaluation and testing.

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 Injectable Compounding**

- (a) No sterile injectable product shall be compounded if it is known, or reasonably should be known, that the compounding environment fails to meet criteria specified in the pharmacy's written policies and procedures for the safe compounding of sterile injectable drug products.
- (b) During the preparation of sterile injectable products, access to the designated area or cleanroom must be limited to those individuals who are properly attired.
- (c) All equipment used in the designated area or cleanroom must be made of a material that can be easily cleaned and disinfected.
- (d) Exterior workbench surfaces and other hard surfaces in the designated area, such as walls, floors, ceilings, shelves, tables, and stools, must be disinfected weekly and after any unanticipated event that could increase the risk of contamination.
- (e) Pharmacies preparing parenteral cytotoxic agents shall do so in accordance with Section 4-1106(b) of Title 24 of the California Administrative Code, requiring a laminar air flow hood. The hood must be certified annually by a qualified technician who is familiar with the methods and procedures for certifying laminar air flow hoods and cleanroom requirements, in accordance with National Sanitation Foundation Standard 49 for Class II (Laminar Flow) Biohazard Cabinetry, as revised May, 1983 (available from the National Sanitation Foundation, 3475 Plymouth Road,

P.O. Box 1468, Ann Arbor, Michigan 48106, phone number (313) 769-8010) or manufacturer's specifications, Certification records must be retained for at least three years.

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

#### **1751.5. Sterile Injectable Compounding Attire.**

- (a) When preparing cytotoxic agents, gowns and gloves shall be worn.
- (b) When compounding sterile products from one or more non-sterile ingredients the following standards must be met:
  - (1) Cleanroom garb consisting of a low-shedding coverall, head cover, face mask, and shoe covers must be worn inside the designated area at all times.
  - (2) Cleanroom garb must be donned and removed outside the designated area.
  - (3) Hand, finger, and wrist jewelry must be eliminated. If jewelry cannot be removed then it must be thoroughly cleaned and covered with a sterile glove.
  - (4) Head and facial hair must be kept out of the critical area or be covered.
  - (5) Gloves made of low-shedding materials are required.
- (c) The requirements of subdivision (b) do not apply if a barrier isolator is used to compound sterile injectable products from one or more non-sterile ingredients.

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 Training of Sterile Injectable Compounding Staff, Patient, and Caregiver**

- (a) Consultation shall be available to the patient and/or primary caregiver concerning proper use of sterile injectable products and related supplies furnished by the pharmacy.
- (b) The pharmacist-in-charge shall be responsible to ensure all pharmacy personnel engaging in compounding sterile injectable drug products shall have training and demonstrated competence in the safe handling and compounding of sterile injectable products, including cytotoxic agents if the pharmacy compounds products with cytotoxic agents.

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

- (d) The pharmacist-in-charge shall be responsible to ensure the continuing competence of pharmacy personnel engaged in compounding sterile injectable products.
- (e) Pharmacies that compound sterile products from one or more non-sterile ingredients must comply with the following training requirements:
- (1) The pharmacy must establish and follow a written program of training and performance evaluation designed to ensure that each person working in the designated area has the knowledge and skills necessary to perform their assigned tasks properly. This program of training and performance evaluation must address at least the following:
    - (A) Aseptic technique.
    - (B) Pharmaceutical calculations and terminology.
    - (C) Sterile product compounding documentation.
    - (D) Quality assurance procedures.
    - (E) Aseptic preparation procedures.
    - (F) Proper gowning and gloving technique.
    - (G) General conduct in the controlled area.
    - (H) Cleaning, sanitizing, and maintaining equipment used in the controlled area.
    - (I) Sterilization techniques.
    - (J) Container, equipment, and closure system selection.
  - (2) Each person assigned to the controlled area must successfully complete practical skills training in aseptic technique and aseptic area practices. Evaluation must include written testing and a written protocol of periodic routine performance checks involving adherence to aseptic area policies and procedures. Each person's proficiency and continuing training needs must be reassessed every 12 months. Results of these assessments must be documented and retained in the pharmacy for three years.

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

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

- (a) Any pharmacy engaged in compounding sterile injectable drug products 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) Cleaning and sanitization of the parenteral medication preparation area.
  - (2) The storage of compounded sterile injectable products in the pharmacy and periodic documentation of refrigerator temperature.
  - (3) Actions to be taken in the event of a drug recall.
  - (4) Written justification of the chosen expiration dates for compounded sterile injectable products.
- (b) Each individual involved in the preparation of sterile injectable products must first successfully complete a validation process on technique before being allowed to prepare sterile injectable products. The validation process shall be carried out in the same manner as normal production, except that an appropriate microbiological growth medium is used in place of the actual product used during sterile preparation. The validation process shall be representative of all types of manipulations, products and batch sizes the individual is expected to prepare. The same personnel, procedures, equipment, and materials must be involved. Completed medium samples must be incubated. If microbial growth is detected, then the sterile preparation process must be evaluated, corrective action taken, and the validation process repeated. Personnel competency



must be revalidated at least every twelve months, whenever the quality assurance program yields an unacceptable result, when the compounding process changes, equipment used in the compounding of sterile injectable drug products is repaired or replaced, the facility is modified in a manner that affects airflow or traffic patterns, or whenever improper aseptic techniques are observed. Revalidation must be documented.

(c) Batch-produced sterile injectable drug products compounded from one or more non-sterile ingredients 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.

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

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

#### **1751.8. Sterile Injectable Compounding Reference Materials.**

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

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

#### **1751.10. Furnishing to Parenteral Patient at Home.**

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

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

*Sec.*

## Compounding Questions and Answers

JANUARY 10, 2011

**1. Question: What is a “reliable supplier?”**

**Answer:** Some examples of reliable suppliers are FDA licensed manufacturers, CA Department of Public Health – Food and Drug Branch licensed drug repackagers; CA licensed pharmacies and wholesalers; CA licensed non-resident wholesalers.

Prior to making a purchase, it is recommended to check the board’s website – [www.pharmacy.ca.gov](http://www.pharmacy.ca.gov) – to verify if the wholesaler or non-resident pharmacy is licensed by the board.

If purchasing chemicals from another country, obtain a certificate issued by the FDA authorizing shipment of the product into the U.S. and a certificate of analysis printed in English.

As a reminder, any pharmacy purchasing, trading, selling, or transferring drugs to an entity not licensed by the board could be cited and fined up to \$5000 per transaction

Reference: B&P §§ 4160, 4163, 4126.5, 4169(a)(1); CCR §§ 1780, 1783, 1735.3(c)

**2. Question: Do cytotoxic agents and other hazardous substances have the same requirements for qualitative and quantitative analysis?**

**Answer:** Yes.

**3. Question: Is a non-resident pharmacy (NRP) that provides compounded product into CA required to meet the same staffing requirements as CA pharmacies?**

**Answer:** No.

A non-resident pharmacy (NRP) is a pharmacy located in another state that furnishes dangerous drugs to patients in CA, and is required to be licensed with the board. Part of the licensure requirement is that the NRP be in compliance with pharmacy laws in the state where it is located.

The board has no authority to dictate staffing requirements for pharmacies located in states other than CA. The board expects the NRP to be staffed in accordance with requirements where it is located.

Reference: Business and Professions Code § 4112(a); 4112(d)

**4. Question: What constitutes sterile compounding?**

**Answer:** First, let's define "compounding" in general:

"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 drug product from chemicals or bulk drug substances

With the above in mind, sterile compounding is a specific sub-type of general compounding whereby there is a requirement for the compounded drug product to be sterile. Sterile compounding almost exclusively involves sterile parenteral compounding for which there are additional requirements.

Reference: CCR §§ 1735(a) 1735(d); 1751 et seq.5.

**5. Question: Is the adding of 20 mEq of potassium chloride to 1000cc of normal saline for intravenous administration considered sterile compounding.**

**Answer:** Yes, and this is also considered sterile parenteral compounding.

Reference: CCR 1735(a)6.

**6. Question: Can a pharmacy mix three liquids (Maalox, Benadryl, and Xylocaine) in equal parts or two creams in equal parts, and would this be considered compounding.**

**Answer:** Yes in the examples given, a pharmacy may mix those products in equal parts. And yes, it is considered compounding.

Reference: CCR 1735(a)7.

7. **Question:** What happens in a situation where an IV is made to be used on a one-time basis for administration within 24 hours for a registered in-patient of a health care facility and the IV product is not used and returned to the pharmacy? Can it be reused?

**Answer:** No.

The compounding regulations require specific records for compounded drug products. For each compounded drug product, the pharmacy records shall include:

- (1) The master formula record.
- (2) The date the drug product was compounded.
- (3) The identity of the pharmacy personnel who compounded the drug product.
- (4) The identity of the pharmacist reviewing the final drug product.
- (5) The quantity of each component used in compounding the drug product.
- (6) The manufacturer and lot number of each component. If the manufacturer name is demonstrably unavailable, the name of the supplier may be substituted. Exempt from the requirements of this paragraph are sterile products compounded on a one-time basis for administration within twenty-four hours to an in-patient in a health care facility.
- (7) The equipment used in compounding the drug product.
- (8) A pharmacy assigned reference or lot number for the compounded drug product.
- (9) The expiration date of the final compounded drug product.
- (10) The quantity or amount of drug product compounded.

If all the information is not recorded [as provided by the exemption in (6)] then there is a lack of complete traceability and accountability for the compounded drug product and thus it cannot be reused.

Reference: CCR 1735.3(a)8.

8. **Question:** Our medical center's policies and procedures have the initial dose of an IV admixture compounded in the pharmacy satellite to assure timely initiation of therapy, with all subsequent doses mixed in the central pharmacy.

**Is the initial IV admixture compounded in the satellite pharmacy subject to the record keeping requirements?**

**Answer:** Yes, with the possible exception of documenting the manufacturer and lot number of each component of the admixture.

Reference: CCR 1735.3(a)(6)9.

9. **Question:** Is a master formula record equivalent to a "recipe card?"

**Answer:** Basically, yes.

Like a recipe card the master formula record includes the active and inactive ingredients to be used, the process and/or procedure used to prepare the drug, quality reviews required at each step in the preparation of the drug, post-compounding process or procedures required, and the expiration dating requirements.

The master formula record must be created prior to compounding the drug product.

The prescription document itself may be used as the master formula record if a pharmacy does not routinely compound a particular drug product.

Reference: CCR 1735.2(d)10.

10. **Question:** When compounding a product, is it required to have master formula record available and used when the product is compounded?

**Answer:** Yes, the master formula record must be created prior to compounding the drug product and its use will provide guidance for compounding personnel and consistency in the product produced.

Reference: CCR 1735.2(d)11.

**11. Question: Is it required to review the master formula record as part of pre-check process?**

**Answer:** The law is silent on a “pre-check process.” However, the master formula record will provide guidance to compounding personnel in what to use and how to compound the particular drug product. So the master formula record could be used in a “pre-check” process to insure consistency in the compounding process.

Reference: CCR 1735.3 12.

**12. Question: What are the requirements for compounding documentation?**

**Answer:** The compounding regulations require specific records for compounded drug products. For each compounded drug product, the pharmacy records shall include:

- (1) The master formula record.
- (2) The date the drug product was compounded.
- (3) The identity of the pharmacy personnel who compounded the drug product.
- (4) The identity of the pharmacist reviewing the final drug product.
- (5) The quantity of each component used in compounding the drug product.
- (6) The manufacturer and lot number of each component. If the manufacturer name is demonstrably unavailable, the name of the supplier may be substituted. Exempt from the requirements of this paragraph are sterile products compounded on a one-time basis for administration within twenty-four hours to an in-patient in a health care facility.
- (7) The equipment used in compounding the drug product.
- (8) A pharmacy assigned reference or lot number for the compounded drug product.
- (9) The expiration date of the final compounded drug product.
- (10) The quantity or amount of drug product compounded.

Reference: CCR 1735.313.

- 13. Question: When using the record-keeping exemption in 1735.3(a)(6) to compound a one-time Vancomycin IV with a seven-day expiration date and to be used within 24 hours, is the manufacturer and lot number required?**

**Answer:** No.

The regulations provide for an exemption for sterile products compounded on a one-time basis for administration within twenty-four hours to an in-patient of a health care facility.

Reference: CCR 1735.3(a)(6)14.

- 14. Question: When must the manufacturer and lot number be recorded?**

**Answer:** This information must be documented if the product is not for a one-time use for a specific patient to be used within 24 hours.

Reference: CCR 1735.3(a)(6)15.

- 15. Question: How will the board insure compliance by non-resident pharmacies (NRP's) that provide compounded drug products into CA?**

**Answer:** The board does not have the ability to inspect NRPs. However, NRPs are required to be licensed with the board and to maintain compliance with pharmacy regulations of their home state. Also, a NRP performing sterile parenteral compounding as a condition of renewal will be encouraged to submit a completed Compounding Self Assessment Form.

Reference: B&P §§ 4112, 4127.216.

- 16. Question: Is the dilution per the manufacturer's instructions and adding to the IV solution considered compounding?**

**Answer:** Yes, if done in a pharmacy. However, statute provides for exemption from sterile compounding licensure if the sterile powder was obtained from a manufacturer and the drug is reconstituted for administration to patients by a health care professional licensed to administer drugs by injection.

Reference: CCR 1735(a)(1); B&P 4127.1(e)17.

**17. Question: Are proprietary drug delivery systems such as ADD-Vantage, Mini-Bag Plus, and At-Eas considered compounded products after the vials have been attached to the IV bags?**

**Answer:** These types of delivery systems are exempt from the compounding requirements if the sterile powder was obtained from a manufacturer and the drug is reconstituted for administration to patients by a health care professional licensed to administer drugs by injection.

Reference: CCR 1735(a)(1); B&P 4127.1(e) 18.

**18. Question: What specifically will be required or what process is acceptable to achieve quality assurance?**

**Answer:** Quality assurance, as the term implies, is designed to monitor and ensure the integrity, potency, quality, and labeled strength of compounded products.

A quality assurance plan will touch all parts of the compounding process – drug product and equipment acquisition/storage; compounding processes; documentation of compounding and related analysis; employee training and monitoring; recall procedure; etc

Reference: CCR §§ 1735.8; 1735.3; 1735.5; 1735.6; 1735.7; 1751 et seq19.

**19. Question: When recycling an IV that was previously compounded by the pharmacy, can the previous lot number of the recycled IV be used as long as the lot number can be traced to all the requirements listed in section 1735.3(a)?**

**Answer:** Yes.

Reference: CCR 1735.3(a)20.

**20. Question: Does every product and/or formulation compounded by a pharmacy have to undergo qualitative and quantitative analysis? If not, can the board provide guidance for selecting products to be analyzed?**

**Answer:** The pharmacy, and the pharmacist, are responsible for insuring the compounded product complies quantitatively and qualitatively

with the prescriber's prescription.

For compounded product that is compounded on a one-time basis for immediate dispensing, it would not be likely there would be a quantitative or qualitative analysis conducted.

For products compounded for on-going therapy it would be expected there would be analysis done initially and on a periodic basis to validate the product and compounding process.

The same holds true for sterile injectable drug products too.

However, if two or more sterile injectable drug products being compounded from one or more non-sterile ingredients, these end-products shall be quarantined until end-product testing confirms sterility and acceptable levels of pyrogens.

Reference: CCR §§ 1735.2(f); 1735.2(i); 1751.7(a); 171621.

- 21. Question: Does CCR section 1735.5 require a pharmacy to test each and every compounded product for integrity, potency, quality, and labeled strength of the compounded product?**

**Answer:** No. However, if the compounded product involves a complex process it would seem prudent to have documentation of the final product. This is even more important when the product is compounded on a more routine basis.

Compounding involves not just the QA process, but staff training, equipment maintenance, proper documentation and appropriate analysis of products compounded.

Reference: CCR 1735.8; 1735.3; 1735.5; 1735.6; 1735.7; 1751 et seq.22.

- 22. Question: For the purposes of CCR section 1735.3(a)(6) and 1751.2(a), would patients receiving chemotherapy administered in an infusion center that is part of a health care facility be considered "in-patients" and exempt from the labeling requirements?**

**Answer:** If the infusion center is part of the licensed health care facility and the patients receiving care there are registered as hospital in-patients, then yes the exemption provided by CCR 1735(a)(6) would apply. However, the labeling requirements as defined in

CCR 1751.2 would apply and compliance would be expected.

Reference: B&P §§ 4027, 4019, 4029; CCR 1735.3(a)(6), 1751.223.

- 23. Question: CCR section 1735.3 defines what must be recorded for each compounded drug product. CCR 1735.3(a)(7) states, “The equipment used in compounding the drug product.” Does this include tubing sets, spikes, needles, syringes, etc.?**

**Answer:** Yes, all equipment used for compounding the drug product must be recorded – TPN compounders, homogenizers, scales, syringes, needles, tubing sets, spikes, filters, mortar and pestle, pill making device, infusion devices. If there are more than one of the same device (e.g. - scales, laminar flow hoods) it is recommended to label them in some manner to distinguish which one was used in the process for appropriate completion of the compounding record.

Reference: CCR 1735.3(a)(7)24.

- 24. Question: Where would the lot number, manufacturer, and expiration date be recorded?**

**Answer:** The law does not specify where or how the information is to be recorded. A pharmacy may develop its own form(s) for the proper documentation. The pharmacy shall maintain the record for three years from the date it was created.

Reference: CCR 1735.325.

- 25. Question: CCR section 1751.2(d) states, “All cytotoxic agents shall bear a special label which states ‘Chemotherapy – Dispose of Properly.’” This appears to give no wiggle room for the text of the message.**

**Answer:** There are no exceptions. If a drug is classified as a cytotoxic agent then the special label must be used.

Reference: CCR 1751.2(d)26.

**26. Question: Gancyclovir is a cytotoxic agent but is not a chemotherapeutic agent. Does the special label need to be applied?**

**Answer:** Yes, the regulation does not provide for exceptions. However, nothing prevents the pharmacist from consulting the patient on the drugs classification and use.

Reference: CCR 1751.2(d)27.

**27. Question: CCR section 1751.5(b)(1) states, in pertinent part, "Cleanroom garb consisting of low-shedding coverall, head cover...must be worn inside the designated area at all times." USP 797 does not require the use of a coverall, only a gown.**

**Answer:** The board does not enforce USP 797, but expects compliance with board regulations.

A coverall is much more encompassing than a gown and would provide better protection during the compounding process.

Reference: CCR 1751.5(b)(1)28.

**28. Question: For a compounded drug product can a pharmacy use an expiration date, or beyond use date, of greater than 180 days?**

**Answer:** Yes, if the longer date is supported by stability studies of finished drugs or compounded drug products using the same components and packaging.

Reference: CCR 1735.2(h)29.

**29. Question: If a pharmacy makes a compounded drug product and does the qualitative and quantitative testing that demonstrates it has a stability expiration dating greater than 180 days, can another pharmacy use the same formula, with minor changes, use the same extended expiration date?**

**Answer:** No. To use another pharmacy's extended expiration date the formula must use the same components and packaging.

Reference: CCR 1735.2(h)30.

**30. Question: Master formulas and compounding records are filed in separate locations, can easily be linked together, and are readily retrievable. Is it an absolute requirement to file these documents together?**

**Answer:** No, there is no such requirement for the above records to be maintained together as long as they are readily retrievable and available for inspection. These records may be maintained in a paper or electronic manner.

However, qualitative and quantitative analysis reports for compounded drug products shall be retained by the pharmacy and collated (kept together) with the compounding record and master formula.

Any records that are maintained electronically shall be maintained so that the pharmacist-in-charge or the pharmacist on duty shall during business hours be able to produce a hard copy and electronic copy.

Reference: CCR 1735.8(c); B&P 4105(d)31.

**31. Question: Is record keeping for compounding just referring to products that are administered intravenously or intraocular (e.g. where sterile preparation is imperative) or does it extend to oral and topical compounding?**

**Answer:** The regulations apply to all forms of compounding – oral, inhalation, topical, sterile parenteral, etc. The record keeping requirements for sterile compounding are more extensive

Reference CCR §§ 1735 et seq & 1751 et seq.32.

**32. Question: What is meant by proper acquisition?**

**Answer:** Records of proper acquisition of dangerous drugs and dangerous devices would include purchase records that correctly give the date, the names and address of the supplier and the buyer, the drug or device, and its quantity.

Also, refer to Question #1 and its answer.

Reference: B&P § 4059(b)



**California State Board of Pharmacy**

1625 N. Market Blvd, N219, Sacramento, CA 95834

Phone: (916) 574-7900

Fax: (916) 574-8618

www.pharmacy.ca.gov

STATE AND CONSUMER SERVICES AGENCY

DEPARTMENT OF CONSUMER AFFAIRS

GOVERNOR EDMUND G. BROWN JR.

**STATE BOARD OF PHARMACY  
DEPARTMENT OF CONSUMER AFFAIRS  
COMPOUNDING REGULATION SUBCOMMITTEE MEETING  
MINUTES**

**DATE:** August 22, 2011

**LOCATION:** Department of Consumer Affairs  
El Dorado Room, 2<sup>nd</sup> Floor, N-220  
1625 N. Market Boulevard  
Sacramento, CA 95834

**SUBCOMMITTEE**

**MEMBERS PRESENT:** Stan Weisser, RPh  
Randy Kajioka, PharmD  
Neil Badlani, RPh

**STAFF**

**PRESENT:** Virginia Herold, Executive Officer  
Anne Sodergren, Assistant Executive Officer  
Robert Ratcliff, Supervising Inspector  
Janice Dang, Supervising Inspector  
William Young, Supervising Inspector  
Carolyn Klein, Legislation and Regulation Manager  
Tessa Miller, Staff Analyst

---

**Call to Order**

Board President Stan Weisser appointed himself to the Subcommittee.

Chair Randy Kajioka called the meeting to order at 10:07 a.m.

**Discussion Including Questions and Answers from Hospital Pharmacies and the Public on the Board's Implementation of 16 California Code of Regulations Sections 1735-1735.8, Pharmacies That Compound, and Sections 1751-1751.8, Pharmacies That Compound Sterile Injectable Medications**

Chair Kajioka provided that the board has received questions regarding the new compounding regulations that took effect in July 2010. He stated that the answers to these questions have been compiled into a document and are available on the board's

Web site. Chair Kajioka discussed that the Subcommittee has convened in order to provide additional clarification on the implementation of the compounding regulations.

### **Presentation**

Rita Shane, representing Cedars-Sinai Hospital, provided a presentation on sterile compounding to ensure patient safety. A copy of the presentation is attached, following this meeting summary.

Dr. Shane provided an overview of sterile compounding and an analysis of current requirements in this area. She reviewed U.S. reported events and recalls associated with sterile compounding from 1991 to present and indicated that 65 percent of these events were caused by contamination.

Katherine Palmer, representing Cedars-Sinai Hospital, reviewed epidural medication components and the 38 elements of documentation required to compound this medication. She discussed the balance between meeting compounding requirements while also providing timely patient care.

MJ Ziadeuin, representing Cedars-Sinai Hospital, reviewed a patient example of a Vancomycin order for five days of therapy as well as specific considerations for compounded medications for hospital patients.

Dr. Shane provided an overview on the comprehensive guidelines for sterile compounding and dating of such products pursuant to US Pharmacopeia Chapter 797 (USP 797).

Dr. Shane reviewed results from a survey on hospital compounding practices in California regarding USP 797 guidelines, safety strategies, training, drugs shortages, error prevention, and hospital pharmacy computer systems. She stated that survey responses indicated that most commercial systems do not have the ability to support documentation of lot number and manufacturer information.

Dr. Shane discussed dating for sterile compounded medications. She indicated that 24-hour dating of these products and change in patient condition or medication dose contributes to product waste, including waste of medications that are part of a drug shortage. Dr. Shane stated that the medication cannot be reused if recording requirements are not met due to time limitations for immediate use medications.

### **Discussion**

Katy Marconi provided an overview on DoseEdge, a pharmacy workflow system that has been implemented at Doctors Hospital of Manteca. (DoseEdge performs the selecting, compounding, inspecting, tracking, and reporting of IV or oral doses and records the entire dose preparation and dispensing process including photo imaging.) Dr. Marconi reviewed the time required to operate the system for photo imaging as well as the cost to operate the system including an expense per label. She indicated that this system is not used for immediate use medications due to the cumbersome process.

Executive Officer Virginia Herold provided comment on AB 377 (Solorio). She stated that the bill would allow for anticipatory unit-dose packaging to ensure patient care.

Lynn Paulsen, representing UCSF, provided comment on “just-in-time” compounding. She stated that this process is becoming more common in hospitals across the country. Dr. Paulsen reviewed processes that have been implemented at UCSF in this area.

Supervising Inspector Robert Ratcliff advised that documentation of all recording requirements is required in order to reuse a compounded product. He stated that sterile products compounded on a one-time basis for administration within 24-hours to an in-patient in a health care facility are exempt from recording of the manufacturer and lot number of each component.

Steve Gray, representing Kaiser Permanente, suggested that the board clarify its intent for implementing the records requirements. He also suggested that clear definitions be provided for “components” and “equipment.”

Public comment was provided regarding the definition of “equipment.” It was recommended that the board revisit its interpretation of this term in the regulation.

Dr. Shane reviewed challenges associated with quantitative and labeled strength analysis such as overfills. She also discussed that cytotoxic medications are being inappropriately labeled as chemotherapy.

A member of the public discussed that appropriate labeling is critical as chemotherapy and cytotoxic medications are to be administered by specially trained staff.

Dr. Shane summarized her presentation and reiterated the importance of quality assurance and training programs to prevent errors and harmful events. She also reiterated the need for clarity regarding the definitions for “quantitative analysis,” “cytotoxic,” “equipment,” and “non-sterile products.”

Steve Gray, representing Kaiser Permanente, provided comment on quality assurance programs. He discussed that the regulations require that pharmacies develop their own policies and procedures for quality assurance and record and verify the accuracy of the compounded products.

Dr. Gray discussed that there has also been a lot of discussion on the definition of a “batch.” He stated that this term should be clarified, possibly through a regulatory revision process.

A representative from the UCSF School of Pharmacy suggested that the discussion focus on the available evidence regarding compounding errors to identify possible problems and to identify goals to alleviate these issues.

Chair Kajioka discussed that the board should look at whether the regulations are enhancing healthcare for patients or imposing unnecessary, labor intensive requirements.

Board Member Anil Badlani asked whether there is any other compounding software currently being used.

A representative from Kaiser Permanente provided that Kaiser has developed its own software, similar to the DoseEdge system, in response to the regulations to record the actual ingredients of a compounded sterile product. He discussed that the system is easy to use and can be searched to identify patients who have received a compounded drug with specific ingredients, manufacturer, and lot number. The system does not interface with the existing electronic medical record system. He stated that the system is currently being piloted and should be fully implemented by the end of the year.

A member of the public provided comment regarding PK software, a system that is proprietary for compounding pharmacies that tracks active and inactive ingredients, lot number, manufacturer, etc. He advised that this software cannot track what syringe was used but can track at the patient level and can track ingredients that have been recalled.

There was discussion on § 1751.3 regarding sterile injectable policies and procedures for cleanups and spills in conformity with local health jurisdiction standards. Input received indicated that hospital pharmacies have policies and procedures in place to address this requirement.

Chair Kajioka discussed that under § 1735.3, sterile products compounded on a one-time basis for administration within 24-hours to an in-patient in a health care facility are exempt from the specific records requirements. He suggested that the record requirement be clarified.

Dr. Shane provided that 24-hour dating is used for these products.

Dr. Fujimoto discussed that the board has previously discussed and clarified that a “batch” is made for more than one patient.

A member of the public suggested that the group look at the definition of a “batch” versus a “product” that is compounded for a specific patient to provide clarification in this area. He indicated that he interprets a “batch” to be a large quantity of a product created to be used and designated to a specific patient in the future.

Dan Wills spoke in opposition to the proposed definition. He stated that USP has interpreted that a “product” that is compounded for 10 or more patients constitutes a “batch.”

Ms. Herold asked if the number of patients is known in advance of the preparation of the medication.

Ms. Sherpa clarified the difference between USP 795 and 797 regarding sterile and non-sterile products.

Dr. Paulsen discussed that irrespective of the regulations, it has been typical practice to record the lot number and expiration date of the drug when preparing a batch.

Chair Kajioka encouraged pharmacists to use their professional judgment in this area. He discussed that rather than being overly prescriptive, “gray area” is beneficial as it allows pharmacists to best serve their patients. Chair Kajioka stated that guidelines have been established to provide direction and to ensure the safety of the public.

Ms. Herold indicated that the minutes of this meeting will be brought to the full board. She advised that any action on this issue will come from the board itself and not from today’s discussion. Ms. Herold discussed that this meeting is an opportunity to provide comments to the board, to explore and discuss the topic to better understand the comments of industry, and to provide some consideration regarding problems that have developed. She discussed that regulations must be clear and consistent and where such clarity does not exist, the pharmacy must be in a position to explain how or why a decision or action was made.

A member of the public suggested that the discussion focus on the risk of the product. He stated that low and medium risk products should have a different quality plan than high risk products. He suggested that the board provide each pharmacy with some latitude on what quality and quantitative analysis is necessary.

Mr. Badlani suggested that the board define the terms “equipment” and “supplies” and provide clarification on what documentation is to be maintained. He stated that a master formula could include the equipment as well as the supplies being used for a particular compounded drug product. Mr. Badlani suggested that some items currently required, may not need to fall under the definition of equipment and provided an example of the IV syringe.

A member of the public sought clarification regarding the board’s goal in requiring the recording of this information and how this goal can be best achieved.

A member of the public provided comment on the outsourcing of compounded drug products and another approach to risk assessment.

Dr. Gray spoke to the limitations on the data provided and the challenges that could be presented if an internal recall was necessary and provided some historical perspective on this.

Dr. Shane spoke in support of the need for internal processes and indicated that patients are kept safe by the quality of the people performing the work.

A member of the public discussed that hospital pharmacies have spent several years focusing on USP 797 compliance and risk assessment. He stated that as reconsideration of the regulation is being sought, harmonization with USP 797 would be beneficial as hospital administration has already bought off on this compliance as important. He spoke in support of leveraging USP 797 as the foundation of the regulations.

Dr. Marconi requested that the board look at USP 797 as the best practice. She suggested that the board allow industry to demonstrate how they can achieve patient safety with their 797 policies and procedures. Dr. Marconi discussed approaches to tracking and reacting to a recall.

Dr. Fujimoto sought clarification regarding whether the master formula should include the supplies being used.

Dr. Kajjoka responded that the terms “supplies” and “equipment” will need to be discussed and brought to the full board. He discussed that documenting the equipment used is beneficial when conducting a root cause analysis.

A member of the public comment spoke in opposition to the documentation of supplies being used and provided an example of two different staff using different syringe sizes while performing the same task.

Dr. Shane discussed that hospitals use prep labels and indicated that the amount that is being added to a solution is known prior to preparation. She stated that the focus should be on the amount of the solution and spoke in support of the previous public comment.

Dr. Gray provided that “supplies” is only mentioned in § 1751 and clarified that the regulation does not state that the master formula needs to include the supplies being used. Dr. Gray did indicate that Kaiser found benefit in recording such information and indicated that such documentation should be determined by each institution. He underscored that as long as the policies and procedures are appropriate, patient safety will be met because risk assessment considerations can be a determining factor in the level of documentation for each type of product.

A public comment was received indicating that there are very specific policies and procedures for pediatric compounds. She spoke in support of flexibility and professional judgment in this area.

Dr. Shane clarified that the group’s request of the board is to relax some of the recording requirements for patient specific medicine.

Mr. Wills reviewed the recording requirements that are clarified in the Q&A document for each compounded drug product pursuant to § 1735.3.

Dr. Ratcliff explained how the definition of “equipment” was arrived upon as well as the definition of a “batch,” as both are not defined in statute or by regulation. He indicated that both of these definitions may be action items by the board.

Dr. Gray suggested that the board look at the definition of “supply” versus “equipment” and determine whether these terms have been defined under the Good Manufacturing Practice Regulations (GMP) by the U.S. Food and Drug Administration (FDA). Dr. Gray also specified that the regulations require the recording of the equipment, but not the lot number. He recommended that the current interpretation of the regulation in this area be revisited.

Dr. Fujimoto reviewed a section of USP 797 which appears to define equipment as related to compounding. She suggested that USP 797 can be cross-referenced.

Discussion continued regarding the requirements under USP 797.

Dr. Shane provided an example of the master formula versus a chart order.

Dr. Young suggested that the group look at § 1735.3 in terms of components that are helpful and components that are not necessary in the interest of patient safety.

Ms. Sherpa suggested that the discussion focus on batches that are non-patient specific for anticipatory needs versus onetime patient specific doses for immediate use. She confirmed that the group agrees that anticipatory batches require all necessary recording. Ms. Sherpa suggested that immediate use doses should be exempt from all recording requirements.

Dr. Marconi reviewed the recording requirements under § 1735.3 and indicated that recording the manufacturer and lot number and the equipment, as required in subdivision (a), paragraphs (6) and (7), poses the greatest challenge and difficulty.

Ms. Sherpa provided that these items are currently being recorded in prescription records, and not in a separate documentation log.

Ms. Herold advised that USP is a guideline. She reviewed possible implications of referring to USP via regulation.

Dr. Paulsen indicated that hospital pharmacies are required to meet both the requirements of the board and the USP guidelines as required by the California Department of Public Health.

Discussion continued regarding the required documentation with regards to patient safety and necessity when trying to meet patient care demands. Public comment

suggested that the recording requirements may not be addressed if the drugs are dispensed via a Pyxis machine. Possible consequences to recalls were also evaluated.

Dr. Shane discussed the challenges and time limitations when adding additional recording requirements given all of the other processes that must occur as part of the compounding process.

Dr. Paulsen suggested that policies and procedures should allow for the development of a process to address a recall versus recording the lot number for recall purposes and provided an example of a recent alcohol wipe recall. She indicated that it is easier and faster to re-compound than to try to identify and recall impacted IV bags.

Ms. Herold clarified that the group is requesting an exemption to the recording requirements under § 1735.3 (a) (6) and (7) for patient-specific compounded medications for immediate use.

Public comment requested that the exemption be granted for settings other than hospitals including outpatient oncology infusion practices.

Dr. Shane provided comment on pharmacists' dedication to patient safety and reiterated that adding additional recording requirements will complicate the process and the ability of pharmacists to provide patient care.

Mr. Wills requested that the definition of "equipment" be re-evaluated for all settings, not just the inpatient setting, and questioned how a problem can be fixed if good records are not maintained.

Dr. Kajioka summarized the issue and indicated that the information will be presented to the board. He discussed that the solution needs to focus on the patient and must be workable.

Ms. Herold provided some historical perspective on the compounding regulations and discussed the ultimate goal of patient safety. She stated that the ability to reconstruct records is necessary for patient care. Ms. Herold requested that additional comments be directed to her attention.

### **Public Comment on Matters Not on the Agenda**

No public comment was provided.

The meeting was adjourned at 1:45 p.m.