

## Compounding Questions and Answers

SEPTEMBER 5, 2013

**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, expiration date and lot number of each component. If the manufacturer name is demonstrably unavailable, the name of the supplier may be substituted. Exempt from the requirements of this paragraph are sterile products compounded on a one-time basis for administration within seventy-two hours and stored in accordance with the standards for "Redispensed CSPs" found in Chapter 797 of the United States Pharmacopeia – National Formulary (USP-NF) 35<sup>th</sup> Revision, Effective May 1, 2012) to an in-patient in a health care facility.
- (7) A pharmacy assigned reference or lot number for the compounded drug product.
- (8) The expiration date of the final compounded drug product.
- (9) 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. **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, expiration date 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, expiration date and lot number of each component. If the manufacturer name is demonstrably unavailable, the name of the supplier may be substituted. Exempt from the requirements of this paragraph are sterile products compounded on a one-time basis for administration within seventy-two hours and stored in accordance with the standards for “Redispensed CSPs” found in Chapter 797 of the United States Pharmacopeia – National Formulary (USP-NF) 35<sup>th</sup> Revision, Effective May 1, 2012) to an in-patient in a health care facility.
- (7) A pharmacy assigned reference or lot number for the compounded drug product.

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

- 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, expiration date and lot number required?**

**Answer:** No.

The regulations provide for an exemption for sterile products compounded on a one-time basis for administration within seventy-two hours and stored in accordance with the standards for “Redispensed CSPs” found in Chapter 797 of the United States Pharmacopeia – National Formulary (USP-NF) )35<sup>th</sup> Revision, Effective May 1, 2012)

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

- 14. Question: When must the manufacturer, expiration 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 72 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 1735.2 defines what must be recorded for each compounded drug product. CCR 1735.2(d)(2) states, “Equipment to be used.” Does this include tubing sets, spikes, needles, syringes, etc.?**

**Answer:** No, equipment is defined in CCR 1735.1(a) as items that must be calibrated, maintained or periodically certified – TPN compounders, homogenizers, scales, etc. Syringes, needles, tubing sets, spikes, filters, mortar and pestle are considered to be ancillary compounding supplies and it is not necessary to document them on the compounding record. However, the ancillary compounding supplies to be used to compound a drug product should be identified on the master formula record.

Reference: CCR 1735.1(a) 1735.2(d)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: What type of auxiliary labels needs to be placed on a**

**cytotoxic or chemotherapy agent?**

**Answer:** CCR 1751.2 provides direction for sterile injectable labeling requirements. CCR 1751.2(d) states, "All cytotoxic agents shall bear a special label with states 'Chemotherapy – Dispose of Properly' or 'Cytotoxic – Dispose of Properly.'"

Reference: CCR 1751.2(d)

26. **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.

27. **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.

28. **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.

29. **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.

**30. 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.

**31. 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)