

Compounding Regulations Guidance

Title CCR section 1735 et seq. and CCR section 1751 et seq.

Regulation Effective January 1, 2017

This guidance is not nor is it a substitute for legal advice. It is intended solely to assist pharmacists and pharmacies with understanding the requirements for compounding drug preparations for patients in California. References are provided to aid the users of this document. Licensees are strongly encouraged to read the regulations to have a full understanding of the requirements. All references to California Code of Regulations (CCR) sections are in Title 16 of the California Code of Regulations.

1. What is a “copy or essentially a copy” of a commercially available product?

CCR section 1735.1(k) specifies that this includes all preparations that are comparable in active ingredients to commercially available products EXCEPT when the following conditions are met

- The preparation has been changed for an identified patient AND
- The preparation produces for that patient a clinically significant difference as determined by the prescribing practitioner.

NOTE: The FDA currently has pending guidance in this area.

2. Who determines whether there is a “clinically significant difference” between a compounded preparation and the comparable commercially available drug product?

As stated in CCR section 1735.1(k), the prescribing practitioner determines whether there is a “clinically significant difference”.

3. Are there requirements for the maintenance of equipment used in compounding including minimum standards for such equipment as well as record keeping requirements?

Yes, CCR section 1735.6 states compounding facilities and equipment requirements for all compounding (general and sterile). Included in this section are the record keeping requirements for the maintenance and cleaning of equipment, calibration requirements and specific requirements for hazardous drug compounding. In addition, CCR section 1751.4 establishes additional requirements for facilities and equipment used in sterile

compounding. An entity performing sterile compounding must comply with the requirements in both of these sections.

4. Are there requirements for the establishment of beyond use dates (BUDs)? Are the requirements the same for sterile preparations?

There are several provisions regarding assignments of BUDs:

- CCR section 1735.2(i) establishes general requirements for all compounded preparations.
- For sterile drugs preparations, sections 1735.2(i)(2) and 1751.8 address BUD assignment.

5. Under what conditions can a BUD be extended?

As specified in CCR section 1735.2(i)(3), a BUD can be extended if it is supported by the following:

- Method Suitability Test, AND
- Container Closure Integrity Test, AND
- Stability Studies

6. Is a master formula required for compounded preparations made for an inpatient of a hospital?

Yes, as stated in CCR section 1735.2(e) a master formula is required in all settings and for all compounding. Under the provisions of CCR section 1735.2(f), if a preparation is not routinely compounded, the master formula may be recorded on the prescription document.

Note: As with all pharmacy compounding records, the master formula may be maintained in an electronic form that is readily retrievable. Records recorded or stored electronically, on magnetic media, or in any other computerized form shall be maintained as specified in B&PC section 4070(c). (CCR section 1735.3(d))

7. What are the requirements for a compounding log?

As provided in CCR 1735.3(a)(2), a compounding log shall be a single document containing all of the following:

- Name and strength of the compounded drug preparation;
- The date the drug preparation was compounded;

- The identity of any pharmacy personnel engaged in compounding the drug preparation;
- The identity of the pharmacist reviewing the final drug preparation.
- The quantity of each ingredient used in compounding the drug preparation.
- The manufacturer, expiration date and lot number of each component.
- A pharmacy-assigned unique reference or lot number for the compounded drug preparation;
- The beyond use date or beyond use date and time of the final compounded drug preparation, expressed in the compounding document in a standard date and time format;
- The final quantity or amount of drug preparation compounded for dispensing;
- Documentation of quality reviews and required post-compounding process and procedures.

8. What are expectations with regards to the training of environmental services staff?

As required by CCR section 1735.7(a), the environmental services, housecleaning, maintenance or any other staff in the compounding area must have the skills and training required to properly and accurately perform their assigned responsibility. As required in this section, there must be documentation of this training in or retrievable from the pharmacy.

9. May a sterile compounding pharmacy use a continuous monitoring or recording device to monitor and document air pressure differentials as required under CCR section 1751.1(a)(8) ?

Yes, so long as daily documentation is maintained and readily retrievable.

10. Can a CAI be used outside an ISO Class 7 environment?

Yes, according to CCR section 1751.4(f) a CAI may be used outside an ISO Class 7 environment if certain conditions specified in the section are met.

11. Am I allowed to wear any kind of makeup in a clean room?

No, CCR section 1751.5(a)(6) prohibits cosmetics in ISO Class 5 and ISO Class 7 compounding areas.

Note: Nail polish and artificial nails are prohibited as well.

12. What are the training requirements for sterile compounding staff?

CCR section 1751.6 details training requirements for sterile compounding staff, responsibilities for ensuring training and documentation requirements.

13. Is a nonresident compounding pharmacy held to the same requirements for a drug recall as a compounding pharmacy in California?

Yes, both resident and nonresident sterile compounding pharmacies must notify the board within 12 hours of initiating a recall involving California. (See B&PC section 4127.9(a)(2) and 4127.2(e)(3).)

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

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

- The drugs or compounded drug preparation tested and studied are identical in ingredients.
- The specific and essential compounding steps and quality reviews are identical.
- The packaging of the finished drug or compounded drug preparation is identical.

15. How long will a pharmacy have to get in compliance with the new building requirements for hazardous compounding?

The revised regulation will go into effect January 1, 2017. As provided in CCR section 1735.6(f), a pharmacy may seek a compliance delay for a defined section for requirements that require physical construction or alteration to a facility or physical environment. The process and forms to request such a compliance delay can be found at the following link:

http://www.pharmacy.ca.gov/licensees/facility/compliance_delay.shtml

16. If the hospital pharmacy is located in the basement and there are challenges to venting hoods to outside and ceiling air filter/exchanges are there exemptions available?

There are no exemptions available. If a facility anticipates it will not be compliant with the physical requirements by the effective of January 1, 2017, a compliance delay may be requested to allow additional time for the necessary structural changes to be made (see CCR section 1735.6(f)). The process and forms to request such a compliance delay can be found at the following link:

http://www.pharmacy.ca.gov/licensees/facility/compliance_delay.shtml

17. Under CCR section 1735.1(l), “daily” is defined as “occurring every day the pharmacy is operating.” What happens to monitoring and maintenance requirements when the compounding area is not open on a day the retail area of the pharmacy is open?

If the pharmacy is open, then activities requiring daily monitoring or maintenance are required. There are no exemptions if the compounding area(s) is/are not in use but the pharmacy is open. For instance, a refrigerator and freezer still need to be monitored at least every 24 hours to ensure they are storing dangerous drugs at the correct temperature. Please see required policies and procedures under CCR section 1735.5(c)(9).

18. What drugs are required to be treated as “hazardous drugs?”

As specified in CCR section 1735.1(r), hazardous drugs include all anti-neoplastic agents identified by NIOSH as meeting the criteria for a hazardous drug and any other drugs, compounds, or materials identified as hazardous by the pharmacist-in-charge.

19. The facility’s scales are new and have internal calibration. Staff records performance of the daily calibration by signing an individual’s initials on an online form. Is this acceptable?

According to CCR section 1735.6(c), this is acceptable if the calibration is done prior to use, done per manufacturer’s specification, the records are not alterable and the records are retrievable for 3 years.

20. Is it required that each BSC and Compounding Aseptic Containment Isolator (CACI) have a dedicated external vent?

No, CCR section 1735.1(c) and 1735.1(f) state external venting should be dedicated to one BCS or CACI.

Acronyms:

ACPH: air changes per hour

B&PC: Business and Professions Code

BOP: The California State Board of Pharmacy

BUD: beyond use date

CCR: California Code of Regulations.

CETA: Controlled Environment Testing Association

CFUs: colony-forming units

CSP: Compounded Sterile Preparations

EPA: Environmental Protection Agency

FD&C act: Food Drug and Cosmetic act

FDA: Food and Drug Administration

NIOSH: National Institute for Occupational Safety and Health

P&P: policy and procedure

PIC: Pharmacist- in-Charge

USP <1150>: United States Pharmacopeia Chapter 1150

USP <1207>: United States Pharmacopeia Chapter 1207

USP <797>: United States Pharmacopeia Chapter 797

USP <800>: United States Pharmacopeia Chapter 800