Final Compounding Regulations for California

Hazardous Drug Compounding

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FINAL COMPOUNDING REGULATIONS FOR CALIFORNIA: HAZARDOUS DRUG COMPOUNDING

New Pharmacy compounding regulations for California have undergone multiple iterations since last year, with the latest version set to be approved. In February the board of pharmacy voted for these regulations to take effect immediately upon being approved by the CA Office of Administrative Law (OAL) despite commentary from numerous stakeholders requesting a buffer period to account for operational lag time. Most of the push back came from the inclusion in the new regulations of certain parts of the newly published USP <800> for hazardous drugs in health care settings.

The new California regulations for pharmacy compounding are expected to become law as early as January 1, 2017. This gives California compounders and CA-licensed non-resident pharmacies a little over six months to become compliant with the new laws. In addition to new definitions, CA has also added details for facilities and equipment needed for the safe handling and manipulation of hazardous drugs similar to USP <800>. The following is a summary of major highlights compounders should be aware of immediately in order to prepare for the January 1, 2017 live date. In this paper the language in the California regulations is examined to understand what these new requirements are, learn how facilities can be set up to comply with them, answer some frequently asked questions, and differentiate between the CA regulations and USP <800>.

Proposed Reg.	Language	Interpretation & Comment
1735.1	**Compounding Definitions.**	
(c)	"Biological Safety Cabinet (BSC)" means a ventilated cabinet for compounding sterile preparations, having an open front with inward airflow for personal protection, downward HEPA-filtered laminar airflow for product protection and, HEPA-filtered exhausted air for environmental protection. Where hazardous drugs are prepared, the exhaust air from the biological safety cabinet shall be appropriately removed by properly designed external building ventilation. This external venting should be dedicated to one BSC or CACI.	Examples of compliant equipment are Class I BSC (for non-sterile only, externally vented) or Class II BSC Type A1 (not for use with volatile chemicals or radionucleotides), Type A2, Type B1, Type B2, Class III BSC. External venting is not restricted to rooftops in this language or in USP <800>.
(e)	"Cleanroom or clean area or buffer area" means a room or area with HEPA-filtered air that provides ISO class 7 or better air quality where the primary engineering control (PEC) is physically located. (1) For non-hazardous compounding a positive pressure differential of 0.02- to 0.05-inch water column relative to all adjacent spaces is required. (2) For hazardous compounding at least 30 air changes per hour of HEPA-filtered supply air and a negative pressure of between 0.01 to 0.03 inches of water column relative to all adjacent spaces is required.	Similar to USP these regulations require 30 air changes per hour (ACPH) as well as a specified pressure differential for the buffer area used for hazardous sterile compounding. Adapted from USP <800> is an allowance for a non-ISO classified area termed "segregated sterile compounding area" for sterile-to-sterile compounding but with limitations described below.
(f)	"Compounding Aseptic Containment Isolator (CACI)" means a unidirectional HEPA-filtered airflow compounding aseptic isolator (CAI) designed to provide worker protection from exposure to undesirable levels of airborne drug throughout the compounding and material transfer processes and to provide an aseptic environment for compounding sterile preparations. Air exchange with the surrounding environment should not occur unless the air is first passed through a microbial retentive filter (HEPA minimum) system capable of containing airborne concentrations of the physical size and state of the drug being compounded. Where hazardous drugs are prepared, the exhaust air from the isolator shall be appropriately removed by properly designed external building ventilation. This external venting should be dedicated to one BSC or CACI. Air within the CACI shall not be re-circulated or turbulent.	Also referred to as glove boxes or barrier isolators, CACIs used for hazardous drug compounding have the added restriction of HEPA filtered ISO 5 air as well as external venting. Because of these and other operational restrictions, they do not represent a significant advantage over BSCs. However, a BSC in a segregated compounding area used for sterile hazardous preparations would be limited to a 12 hour BUD. If a CACI is used instead, and if certified to meet performance requirements in 1751.4(f)(1)-(3) is not limited to 12 hour BUD.
(r)	"Hazardous" means all anti-neoplastic agents identified by the National Institute for Occupational Safety and Health (NIOSH) meeting the criteria for a hazardous drug and any other drugs, compounds, or materials identified as hazardous by the pharmacist-in-charge.	A major difference between this language and USP <800> is the classification exemption of drugs that are not classified as antineoplastic agents. However, the responsibility lies with the PIC to create SOPs to determine which drugs shall be treated as hazardous.

Proposed Reg.	Language	Interpretation & Comment
1735.1	**Compounding Definitions.**	
(af)	"Segregated sterile compounding area" means a designated space for sterile-to-sterile compounding where a PEC is located within either a demarcated area (at least three foot perimeter) or in a separate room. Such area or room shall not contain and shall be void of activities and materials that are extraneous to sterile compounding… The segregated sterile compounding area shall be restricted to preparing sterile-to-sterile compounded preparations.	The segregated sterile compounding area may be a non-ISO classified environment. CAIs or CACIs that are certified to meet performance requirements in 1751.4(f)(1)-(3) may be utilized in this area and are not limited to a 12 hour BUD. A LAFW may also be used in this area exclusively for sterile-to-sterile preparations and is limited to a 12 hour BUD. This is seen most commonly in hospitals.
1735.6	**Compounding Facilities and Equipment**	
(d)	Any pharmacy engaged in any hazardous drug compounding shall maintain written documentation regarding appropriate cleaning of facilities and equipment to prevent cross contamination with non-hazardous drugs.	Cleaning protocols should include all equipment or cleaning agents used as well as documentation of regular cleaning when hazardous drug compounding is taking place.
(e)	Hazardous drug compounding shall be completed in an externally vented physically separate room with the following requirements: (1) Minimum of 30 air changes per hour except that 12 air changes per hour are acceptable for segregated compounding areas with a BSC or CACI when products are assigned a BUD of 12 hrs or less or when non-sterile products are compounded; and (2) Maintained at at negative pressure of 0.01 to 0.03 inches of water column relative to all adjacent spaces (rooms, above ceiling, and corridors); and (3) Each PEC in the room shall also be external vented; and (4) All surfaces within the room shall be smooth, seamless, impervious, and non-shedding.	The physical area for hazardous compounding may include a modular structure housing an internal separate room, a demarcated area, or a dedicated stand-alone room. In the case of the latter, the segregated room for hazardous drug compounding is fit to compound sterile and non-sterile hazardous preparations providing the requirements pertaining to each are met.

Figure 1.

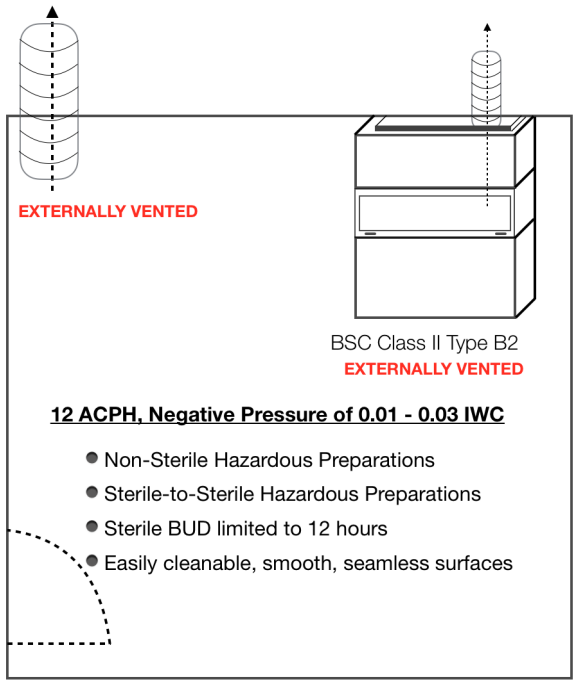

Figure 1. This diagram shows an example of a compliant "segregated compounding area" for hazardous drug compounding pursuant to Section 1735.6(e).

Proposed Reg.	Language	Interpretation & Comment
1735.6	**Compounding Facilities and Equipment**	
(f)	Where compliance with the [insert effective date upon adoption (Jan. 1, 2017 expected date)] amendments to Article 4.5 or Article 7, requires physical construction or alteration to a facility or physical environment, the board or its designee may grant a waiver of such compliance for a period of time to permit such physical change(s). Application for any waiver shall be made by the licensee in writing, and the request shall identify the provisions(s) requiring physical construction or alteration, and the timeline for any such change(s). The board or its designee may grant the waiver when, in its discretion, good cause is demonstrated for such waiver.	The board of pharmacy has included a waiver provision to allow pharmacies who require time to modify facilities additional time to complete the process. Without a waiver, the board may hold a pharmacy in violation if compliance with any of these regulations is not met on or after the expected live date of Jan. 1, 2017. The board has stated publicly that pharmacies making a 'good faith' effort to make physical changes to their facilities will most likely have waivers granted according to the requested timeline. However, this will require advanced planning and close communication with the build-out team.
1751.3	**Sterile Compounding Policies and Procedures**	
(a)(16)	Procedures for handling, compounding and disposal of hazardous agents. The written policies and procedures shall describe the pharmacy protocols for cleanups and spills in conformity with local health jurisdiction standards.	Written policies and procedures should also include details about acquisition and storage of hazardous drugs and reference all equipment and facilities required for doing so.
1751.4	**Facility and Equipment Standards for Sterile Compounding**	
(g)	Pharmacies preparing sterile hazardous agents shall do so in accordance with Section 505.1 of Title 24, Chapter 5, of the California Code of Regulations, requiring a negative pressure PEC. Additionally, each PEC used to compound hazardous sterile agents shall be externally vented. The negative pressure PEC must be certified every six months by a qualified technician who is familiar with CETA Certification Guide for Sterile Compounding Facilities (CAG-003-2006-1, Revised May 20, 2015). Any drug preparation that is compounded in a PEC where hazardous drugs are prepared must be labeled as hazardous, regardless of whether the drug ingredients are considered hazardous. 1. During the hazardous drug compounding that is performed in a compounding aseptic containment isolator, full hand hygiene and garbing must occur. Garbing shall include hair cover, facemask, beard cover (if applicable), polypropylene or low shedding gown that closes in the back, shoe covers, and two pairs of sterile ASTM D6978-05 standard gloves.	All sterile hazardous drugs compounding must utilize an externally vented, ISO 5, HEPA-filtered, negative-pressure PEC in a room that is also externally vented and under a negative pressure of 0.01-0.03 IWC with 30 ACPH. 12 ACPH may be used in the segregated compounding area if assigning a 12 hour BUD.

1751.6	Compounding Consultation, Training of Sterile Compounding Staff	
(b)	The pharmacist-in-charge shall ensure that all pharmacy personnel engaging in compounding sterile drug preparations have training and demonstrated competence in the safe handling and compounding of sterile drug preparations, including hazardous agents if the pharmacy compounding products with hazardous agents.	Training objectives for hazardous drug compounding should include reading the pharmacy's SOPs pertaining to this topic, transport, manipulation, labeling, documentation, cleaning and disinfecting, spill cleanup, and disposal of hazardous drugs. Personnel should also be able to determine which drugs should be treated as hazardous.

Frequently Asked Questions

Q: USP <800> allows for non-sterile hazardous compounding to be redundantly HEPA filtered in the BSC instead of externally vented. Do the new regulations allow this too?

No, redundant HEPA filtering is not permitted. The Primary Engineering Control (PEC), or device providing specific controlled conditions needed for compounding (e.g. BSC), must be externally vented whether for sterile or non-sterile compounding.

Q: My pharmacy compounds a great deal with hormones like estrogens. Will I need to build a negative pressure room and buy a BSC to continue compounding with hormones under the new regulations?

No you do not. Under the CA regulations only NIOSH-classified antineoplastic agents will be considered hazardous drugs; it is up to the PIC to determine if any other drug used in compounding presents a significant risk and should also be treated as hazardous by the pharmacy.

Q: Do the antineoplastic agents I use for sterile compounding need to be stored separately from other inventory in a dedicated negative pressure room?

No, there are no special storage requirements for hazardous drugs in this text. If your pharmacy plans to be compliant with USP <800>, there *are* special storage instructions for certain dosage forms of hazardous drugs.

Q: Can I modify my current cleanroom to meet the new California requirements?

Modification of your current facility will greatly depend on your available space, building restrictions, ability to adjust workflow and other factors. In modular cleanrooms, adding an additional room is a matter of fabricating a panel to insert to the planned space. Creating the new room, negative pressure and venting ducts in these types of facilities is easier than doing the same for built-in cleanroom facilities.

Q: My pharmacy packages and dispenses antineoplastic agents in their final dosage form but we don't compound. Do these regulations apply to me?

No. These regulations apply specifically to the compounding of hazardous drugs; dispensing in final dosage is not considered compounding.