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.

NOTICE OF MEETING AND AGENDA

Compounding Subcommittee

March 19, 2013

Contact Person: Laura Hendricks
(916) 574-7918

This committee meeting is open to the public and is accessible to the physically disabled. A person who needs a disability-related accommodation or modification in order to participate in the meeting may make a request by contacting Laura Hendricks at (916) 574-7918, by emailing laura.hendricks@dca.ca.gov or sending a written request to Ms. Hendricks at the Board of Pharmacy, 1625 N. Market Blvd., Suite N-219, Sacramento, CA 95834. Providing your request at least five business days before the meeting will help to ensure availability of the requested accommodation.

DATE: March 19, 2013

PLACE: NOTE LOCATION:
DCA Headquarters Building Two
1747 North Market Blvd Room 186
Sacramento, CA 95834

This meeting may be cancelled without notice. For verification of the meeting, call (916) 574-7900 or access the Board's Web site at www.pharmacy.ca.gov.

Discussion and action may be taken on any item on the agenda. The committee may discuss agenda items in any order. Time limitations for discussion and comment will be determined by the Committee Chair.

Agenda

Call to Order **10 a.m.**

I. General Background of Compounding Pharmacies in California

II. Discussion Regarding California's Amended Compounding Regulations to Take Effect April 1, 2013 – Amendments to 16 California Code of Regulations, Sections 1735.1, 1735.2 and 1751.2

III. Discussion Regarding the Introduction of the Board of Pharmacy's Sponsored Legislation on Sterile Compounding, Senate Bill 294 (Emmerson)

IV. Discussion Regarding USP's 797 Standards and Regulation Requirements of the Board of Pharmacy

Meeting Materials will be available on the board's Web site at www.pharmacy.ca.gov by March 18, 2013

V. Discussion Regarding "Batches"

VI. Discussion of the Board of Pharmacy's Questions and Answers Document on Compounding

VII. General Discussion

VIII. Closing Comments

X. Public Comment on Items Not on the Agenda/Agenda Items For Future Meetings

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

ADJOURNMENT **4 p.m.**

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

March 15, 2013

To: Members, Compounding Subcommittee

Subject: Agenda Item I – Discussion Compounding In California

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Compounding of medications by pharmacies is a long-time function of the care provided by pharmacies to patients and their providers.

In California, compounding has specific additional requirements. For a number of years, California has recognized and regulated pharmacies that compound parenteral therapy medications under an additional separate class of regulation requirements. More recently in 2001, the board sponsored legislation and eventually promulgated requirements for pharmacies that compound sterile injectable compounds as part of the board's response to a contaminated compounded medication that killed three patients and injured others in Northern California.

Regulation requirements exist for any pharmacy that compounds, and there are additional requirements for pharmacies that do sterile compounding, and even more for pharmacies that do nonsterile to sterile compounding. The main provisions are in Title 16 California Code of Regulations sections 1735 et seq. and 1751 et seq.

California law has also for a number of years authorized a pharmacy to compound for prescriber office use (Business and Professions Code section 4052(a) and (a)(1)):

> **4052. Furnishing to Prescriber; Permitted Procedures by Pharmacist**
> (a) Notwithstanding any other provision of law, a pharmacist may:
> (1) Furnish a reasonable quantity of compounded drug product to a prescriber for office use by the prescriber.

This authority and clarifying regulations that exist in 16 California Code of Regulations Section 1735.2 do allow pharmacies to compound larger quantities of non-patient specific medication.

> **1735.2. Compounding Limitations and Requirements; Self-Assessment**
> (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.

But the question has been for years, at what point is a pharmacy no longer compounding medication but rather manufacturing medication?

This year, the board is sponsoring legislation to rev up the statutory requirements for any pharmacy that compounds sterile medication that will be made or used in California (Senate Bill 294, Emmerson).

Since the fall of 2012, the country has become aware of the impact of contaminated medication compounded by the New England Compounding Center In Massachusetts and distributed nationwide , where more than 45 patients have died and more than 700 patients seriously injured. The FDA is looking at perhaps creating a new classification of compounding – a "nontraditional compounding pharmacy" that would likely be more restrictive than California's current structure for "prescriber office use." Otherwise pharmacies that do large scale production of medication would be considered manufacturers and regulated by the FDA, and in California Department of Public Health.

The board is again reopening the discussion in California of compounding and California's requirements.

Provided in **Attachment Agenda I** are:

- the recent 60 Minutes transcript,
- A Preliminary Report from the fall on NECC
- The ASHP Discussion Guide for Compounding Sterile Preparations

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DEPARTMENT OF CONSUMER AFFAIRS
GOVERNOR EDMUND G. BROWN JR.

March 15, 2013

To: Members, Compounding Subcommittee

Subject: Agenda Item II – Discussion Regarding California's Amended Compounding Regulations to Take Effect on April 1, 2013

On April 1, new amendments affecting both general and sterile compounding approved last year by the board will take effect. These requirements are shown on the next page in underscore (new provisions) and strikeout (deleted provisions).

Order of Adoption
Board of Pharmacy
California Code of Regulations

Amend Section 1735.1 in Article 4.5 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

§ 1735.1. Compounding Definitions.

(a) "Equipment" means items that must be calibrated, maintained or periodically certified.

~~(a)~~ (b) "Integrity" means retention of potency until the expiration date noted on the label.

~~(b)~~ (c) "Potency" means active ingredient strength within +/- 10% of the labeled amount.

~~(c)~~ (d) "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)~~ (e) "Strength" means amount of active ingredient per unit of a compounded drug product.

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

Amend Section 1735.2 in Article 4.5 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

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

(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) A "reasonable quantity" as used in Business and Professions Code section 4052(a)(1) means 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) Equipment to be used.

(3) Expiration dating requirements.

~~(2)~~ (4) Inactive ingredients to be used.

~~(3)~~ (5) Process and/or procedure used to prepare the drug.

~~(4)~~ (6) Quality reviews required at each step in preparation of the drug.

~~(5)~~ (7) 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 for compounding pharmacies developed by the board. (Incorporated by reference is "Community Pharmacy & Hospital Outpatient Pharmacy Compounding Self-Assessment" Form 17M-39 Rev. ~~01/11~~ 02/12.) 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 each odd-numbered 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.

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

To Amend Section 1735.3 of Article 4.5 of Division 17 of Title 16 of the California Code of Regulations to read as follows:

§ 1735.3. Records of Compounded Drug Products.

(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, 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 in this paragraph are sterile products compounded on a one-time basis for administration within ~~twenty-four~~ seventy-two (72) hours and stored in accordance with standards for "Redispensed CSPs" found in Chapter 797 of the United States Pharmacopeia – National Formulary (USP-NF) (35th Revision, Effective May 1, 2012), hereby incorporated by reference, 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)~~ (7) A pharmacy assigned reference or lot number for the compounded drug product.

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

~~(10)~~ (9) 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 drug 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.

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

To Amend Section 1751.2 of Article 7 of Division 17 of Title 16 to read as follows:

§ 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 injectable products shall include the following information on the labels for those products:

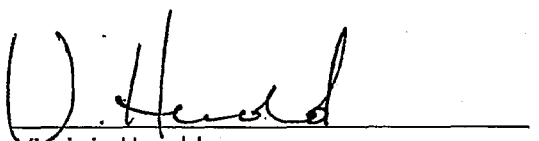
(a) Telephone number of the pharmacy, except for sterile injectable products dispensed for inpatients of a hospital pharmacy.

(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." or "Cytotoxic – Dispose of Properly."

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



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

March 15, 2013

To: Members, Compounding Subcommittee

Subject: Agenda Item III – Discussion Regarding the Introduction of the Board of Pharmacy's Sponsored Legislation on Sterile Compounding, SB 294 (Emmerson)

Following two massive public health emergencies last year regarding the products compounded by two pharmacies out of state that were shipped nationwide, staff suggested the modification of existing sterile compounding requirements. The board agreed and worked to develop the components for the legislation that has been authored by Senator Emmerson as Senate Bill 294.

A copy of this proposal follows this page.

BILL NUMBER: SB 294 INTRODUCED
BILL TEXT

INTRODUCED BY Senator Emmerson

FEBRUARY 15, 2013

An act to amend Sections 4127.1, 4127.2, and 4400 of, to amend the heading of Article 7.5 (commencing with Section 4127) of Chapter 9 of Division 2 of, and to repeal and add Section 4127 of, the Business and Professions Code, relating to pharmacy.

LEGISLATIVE COUNSEL'S DIGEST

SB 294, as introduced, Emmerson. Sterile drug products.

The Pharmacy Law provides for the licensure and regulation of pharmacists and pharmacy corporations in this state by the California State Board of Pharmacy. Existing law requires the board to adopt regulations establishing standards for compounding injectable sterile drug products in a pharmacy. Existing law requires pharmacies to obtain a license from the board, subject to annual renewal, in order to compound injectable sterile drug products. A similar licensing requirement applies to nonresident pharmacies compounding injectable sterile drug products for shipment into California. A violation of the Pharmacy Law is a crime.

This bill would expand these provisions to prohibit a pharmacy from compounding or dispensing, and a nonresident pharmacy from compounding for shipment into this state, sterile drug products for injection, administration into the eye, or inhalation, unless the pharmacy has obtained a sterile compounding pharmacy license from the board. The bill would specify requirements for the board for issuance or renewal of a license, and requirements for the pharmacy as a licensee. By adding additional requirements to the Pharmacy Law concerning sterile drug products, the violation of which is a crime, the bill would impose a state-mandated local program.

Existing law specifies the fee for issuance or renewal of a nongovernmental license to compound sterile drug products.

This bill would provide that the fee for a nonresident sterile compounding pharmacy license shall also require payment of the travel expenses incurred by the board in inspecting the pharmacy at least once annually.

The California Constitution requires the state to reimburse local agencies and school districts for certain costs mandated by the state. Statutory provisions establish procedures for making that reimbursement.

This bill would provide that no reimbursement is required by this act for a specified reason.

Vote: majority. Appropriation: no. Fiscal committee: yes. State-mandated local program: yes.

THE PEOPLE OF THE STATE OF CALIFORNIA DO ENACT AS FOLLOWS:

SECTION 1. The heading of Article 7.5 (commencing with Section

4127) of Chapter 9 of Division 2 of the Business and Professions Code is amended to read:

Article 7.5. ~~Injectable~~ Sterile Drug Products

SEC. 2. Section 4127 of the Business and Professions Code is repealed.

~~4127. The board shall adopt regulations establishing standards for compounding injectable sterile drug products in a pharmacy.~~

SEC. 3. Section 4127 is added to the Business and Professions Code, to read:

4127. A pharmacy that compounds sterile drug products for injection, administration into the eye, or inhalation shall possess a sterile compounding pharmacy license as provided in this article before dispensing the compounded medication.

SEC. 4. Section 4127.1 of the Business and Professions Code is amended to read:

4127.1. (a) A pharmacy shall not compound ~~injectable~~ sterile drug products ~~in this state~~ unless the pharmacy has obtained a *sterile compounding pharmacy* license from the board pursuant to this section. The license shall be renewed annually and is not transferable.

(b) A license to compound ~~injectable~~ sterile drug products ~~may only~~ *shall* be issued ~~for~~ *only to* a location that is licensed as a pharmacy. Furthermore, the license to compound ~~injectable~~ sterile drug products ~~may only~~ *shall* be issued *only* to the owner of the pharmacy ~~license~~ *licensed* at that location. A license to compound ~~injectable~~ sterile drug products ~~may~~ *shall* not be issued until the location is inspected by the board and found in compliance with this article and regulations adopted by the board.

(c) A license to compound ~~injectable~~ sterile drug products ~~may~~ *shall* not be *issued or* renewed until the ~~location has been inspected by the board and found to be in compliance with this article and regulations adopted by the board.~~ *board does all of the following:*

~~(d) Pharmacies operated by entities that are licensed by either the board or the State Department of Public Health and that have current accreditation from the Joint Commission on Accreditation of Healthcare Organizations, or other private accreditation agencies approved by the board, are exempt from the requirement to obtain a license pursuant to this section.~~

(1) Performs an onsite inspection of the premises, and any deficiencies noted are corrected.

(2) Reviews a current copy of the pharmacy's policies and procedures for sterile compounding.

(3) Reviews the pharmacy's completed self-assessment form required by Section 1735.2 of Title 16 of the California Code of Regulations.

(4) Is provided with copies of all inspection reports conducted of the pharmacy's premises, and any reports from a private accrediting

agency, conducted in the prior 12 months documenting the pharmacy's operations.

(5) Receives a list of all sterile medications compounded by the pharmacy since the last license renewal.

(d) A pharmacy licensed pursuant to this section shall do all of the following:

(1) Provide to the board a copy of any disciplinary or other action taken by another state within 10 days of the action.

(2) Notify the board within 10 days of the suspension of any accreditation held by the pharmacy.

(3) Provide to the board, within 24 hours, any recall notice issued by the pharmacy for sterile drug products it has compounded.

(e) Adverse effects reported or potentially attributable to a pharmacy's sterile drug product shall be immediately reported to the board and the MedWatch program of the federal Food and Drug Administration.

~~(e)~~

(f) The reconstitution of a sterile powder shall not require a license pursuant to this section if both of the following are met:

(1) The sterile powder was obtained from a manufacturer.

(2) The drug is reconstituted for administration to patients by a health care professional licensed to administer drugs by injection pursuant to this division.

SEC. 5. Section 4127.2 of the Business and Professions Code is amended to read:

4127.2. (a) A nonresident pharmacy ~~may~~ *shall* not compound ~~injectable~~ sterile drug products for shipment into ~~the State of California~~ *this state* without a *sterile compounding pharmacy* license issued by the board pursuant to this section. The license shall be renewed annually and shall not be transferable.

(b) A license to compound ~~injectable~~ sterile drug products ~~may only~~ *shall* be issued ~~for~~ *only to* a location that is licensed as a nonresident pharmacy. Furthermore, the license to compound ~~injectable~~ sterile drug products ~~may only~~ *shall* be issued *only* to the owner of the nonresident pharmacy ~~license~~ *licensed* at that location. A license to compound ~~injectable~~ sterile drug products ~~may~~ *shall* not be issued ~~or renewed until the board receives the following from the nonresident pharmacy:~~ *until the location is inspected by the board and found in compliance with this article and any regulations adopted by the board.*

~~(1) A copy of an inspection report issued by the pharmacy's licensing agency, or a report from a private accrediting agency approved by the board, in the prior 12 months documenting the pharmacy's compliance with board regulations regarding the compounding of injectable sterile drug products.~~

~~(2) A copy of the nonresident pharmacy's proposed policies and procedures for sterile compounding.~~

~~(c) Nonresident pharmacies operated by entities that are licensed as a hospital, home health agency, or a skilled nursing facility and have current accreditation from the Joint Commission on Accreditation~~

~~of Healthcare Organizations, or other private accreditation agencies approved by the board, are exempt from the requirement to obtain a license pursuant to this section.~~

~~(d) This section shall become effective on the earlier of July 1, 2003, or the effective date of regulations adopted by the board pursuant to Section 4127.~~

(c) A license to compound sterile drug products shall not be issued or renewed until the board does all of the following:

(1) Performs an onsite inspection of the premises, and any deficiencies noted are corrected. The nonresident pharmacy shall be responsible for payment of reasonable travel expenses incurred by the board in connection with inspecting the pharmacy at least once annually pursuant to subdivision (v) of Section 4400.

(2) Reviews a current copy of the nonresident pharmacy's policies and procedures for sterile compounding.

(3) Reviews the pharmacy's completed self-assessment form required by Section 1735.2 of Title 16 of the California Code of Regulations.

(4) Is provided with copies of all inspection reports conducted of the nonresident pharmacy's premises, and any reports from a private accrediting agency, conducted in the prior 12 months documenting the nonresident pharmacy's operations.

(5) Receives a list of all sterile drug products compounded by the pharmacy within the prior 12 months.

(d) A pharmacy licensed pursuant to this section shall do all of the following:

(1) Provide to the board a copy of any disciplinary or other action taken by its state of residence or another state within 10 days of the action.

(2) Notify the board within 10 days of the suspension of any accreditation held by the pharmacy.

(3) Provide to the board, within 24 hours, any recall notice issued by the pharmacy for sterile drug products it has compounded that have been shipped into, or dispensed in, California.

(4) Advise the board of any complaint it receives from a provider, pharmacy, or patient in California.

(e) Adverse effects reported or potentially attributable to a nonresident pharmacy's sterile compounded drug products shall be immediately reported to the board and the MedWatch program of the federal Food and Drug Administration.

SEC. 6. Section 4400 of the Business and Professions Code is amended to read:

4400. The amount of fees and penalties prescribed by this chapter, except as otherwise provided, is that fixed by the board according to the following schedule:

(a) The fee for a nongovernmental pharmacy license shall be four hundred dollars ($400) and may be increased to five hundred twenty dollars ($520). The fee for the issuance of a temporary nongovernmental pharmacy permit shall be two hundred fifty dollars ($250) and may be increased to three hundred twenty-five dollars ($325).

(b) The fee for a nongovernmental pharmacy license annual renewal shall be two hundred fifty dollars ($250) and may be increased to three hundred twenty-five dollars ($325).

(c) The fee for the pharmacist application and examination shall be two hundred dollars ($200) and may be increased to two hundred

sixty dollars ($260).

(d) The fee for regrading an examination shall be ninety dollars ($90) and may be increased to one hundred fifteen dollars ($115). If an error in grading is found and the applicant passes the examination, the regrading fee shall be refunded.

(e) The fee for a pharmacist license and biennial renewal shall be one hundred fifty dollars ($150) and may be increased to one hundred ninety-five dollars ($195).

(f) The fee for a nongovernmental wholesaler license and annual renewal shall be six hundred dollars ($600), and may be increased to seven hundred eighty dollars ($780). The application fee for any additional location after licensure of the first 20 locations shall be two hundred twenty-five dollars ($225) and may be increased to three hundred dollars ($300). A temporary license fee shall be five hundred fifty dollars ($550) and may be increased to seven hundred fifteen dollars ($715).

(g) The fee for a hypodermic license and renewal shall be one hundred twenty-five dollars ($125) and may be increased to one hundred sixty-five dollars ($165).

(h) (1) The fee for application, investigation, and issuance of license as a designated representative pursuant to Section 4053 shall be two hundred fifty-five dollars ($255) and may be increased to three hundred thirty dollars ($330).

(2) The fee for the annual renewal of a license as a designated representative shall be one hundred fifty dollars ($150) and may be increased to one hundred ninety-five dollars ($195).

(i) (1) The fee for the application, investigation, and issuance of a license as a designated representative for a veterinary food-animal drug retailer pursuant to Section 4053 shall be two hundred fifty-five dollars ($255) and may be increased to three hundred thirty dollars ($330).

(2) The fee for the annual renewal of a license as a designated representative for a veterinary food-animal drug retailer shall be one hundred fifty dollars ($150) and may be increased to one hundred ninety-five dollars ($195).

(j) (1) The application fee for a nonresident wholesaler's license issued pursuant to Section 4161 shall be six hundred dollars ($600) and may be increased to seven hundred eighty dollars ($780).

(2) For nonresident wholesalers who have 21 or more facilities operating nationwide the application fees for the first 20 locations shall be six hundred dollars ($600) and may be increased to seven hundred eighty dollars ($780). The application fee for any additional location after licensure of the first 20 locations shall be two hundred twenty-five dollars ($225) and may be increased to three hundred dollars ($300). A temporary license fee shall be five hundred fifty dollars ($550) and may be increased to seven hundred fifteen dollars ($715).

(3) The annual renewal fee for a nonresident wholesaler's license issued pursuant to Section 4161 shall be six hundred dollars ($600) and may be increased to seven hundred eighty dollars ($780).

(k) The fee for evaluation of continuing education courses for accreditation shall be set by the board at an amount not to exceed forty dollars ($40) per course hour.

(l) The fee for an intern pharmacist license shall be ninety dollars ($90) and may be increased to one hundred fifteen dollars ($115). The fee for transfer of intern hours or verification of

licensure to another state shall be twenty-five dollars ($25) and maybe increased to thirty dollars ($30).

(m) The board may waive or refund the additional fee for the issuance of a license where the license is issued less than 45 days before the next regular renewal date.

(n) The fee for the reissuance of any license, or renewal thereof, that has been lost or destroyed or reissued due to a name change shall be thirty-five dollars ($35) and may be increased to forty-five dollars ($45).

(o) The fee for the reissuance of any license, or renewal thereof, that must be reissued because of a change in the information, shall be one hundred dollars ($100) and may be increased to one hundred thirty dollars ($130).

(p) It is the intent of the Legislature that, in setting fees pursuant to this section, the board shall seek to maintain a reserve in the Pharmacy Board Contingent Fund equal to approximately one year's operating expenditures.

(q) The fee for any applicant for a nongovernmental clinic license shall be four hundred dollars ($400) and may be increased to five hundred twenty dollars ($520) for each license. The annual fee for renewal of the license shall be two hundred fifty dollars ($250) and may be increased to three hundred twenty-five dollars ($325) for each license.

(r) The fee for the issuance of a pharmacy technician license shall be eighty dollars ($80) and may be increased to one hundred five dollars ($105). The fee for renewal of a pharmacy technician license shall be one hundred dollars ($100) and may be increased to one hundred thirty dollars ($130).

(s) The fee for a veterinary food-animal drug retailer license shall be four hundred five dollars ($405) and may be increased to four hundred twenty-five dollars ($425). The annual renewal fee for a veterinary food-animal drug retailer license shall be two hundred fifty dollars ($250) and may be increased to three hundred twenty-five dollars ($325).

(t) The fee for issuance of a retired license pursuant to Section 4200.5 shall be thirty-five dollars ($35) and may be increased to forty-five dollars ($45).

(u) The fee for issuance or renewal of a nongovernmental *sterile compounding pharmacy* license ~~to compound sterile drug products~~ shall be six hundred dollars ($600) and may be increased to seven hundred eighty dollars ($780). The fee for a temporary license shall be five hundred fifty dollars ($550) and may be increased to seven hundred fifteen dollars ($715).

(v) The fee for a nonresident sterile compounding pharmacy license shall also require payment of the travel expenses incurred by the board in inspecting the pharmacy at least once annually. Failure to pay this fee within 30 days shall result in the suspension of the nonresident sterile compounding pharmacy license.

SEC. 7. No reimbursement is required by this act pursuant to Section 6 of Article XIII B of the California Constitution because the only costs that may be incurred by a local agency or school district will be incurred because this act creates a new crime or infraction, eliminates a crime or infraction, or changes the penalty for a crime or infraction, within the meaning of Section 17556 of the Government Code, or changes the definition of a crime within the meaning of Section 6 of Article XIII B of the California Constitution.

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

March 15, 2013

To: Members, Compounding Subcommittee

Subject: Agenda Item IV – Discussion Regarding USP 797 and the California's Requirements for Compounding

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For a number of years, California has had its own statutory and regulation requirements for those pharmacies that compound medication or perform parenteral compounding. Since 2001, again through legislation as well as through regulations, the board has several times developed additional requirements to respond to emergent public health or regulatory concerns.

Today, many states rely upon USP 797 components to regulate compounding activities. California instead relies on its own standards for compounders and sterile compounding.

During this segment of the meeting, the committee will review the components in a crosswalk comparing the two sets of requirements. This crosswalk has been prepared by the Los Angeles County Department of Health Services, and is provided as **Attachment Agenda IV**.

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

March 15, 2013

To: Members, Compounding Subcommittee

Subject: Agenda Item V – Discussion Regarding Batches

During modifications in 2012 to the board's compounding regulations, there was discussion about the term "batch" and what batch applies to.

USP defines it as more than 25 units, ASHP has another definition and the board references batch as:

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.
(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.

The board has discussed that batch could mean more than one dose, or for use on more than one patient.

At this meeting, the committee will initiate a new discussion of "batch."

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

March 15, 2013

To: Members, Compounding Subcommittee

Subject: Agenda Item VI – Compounding Questions and Answers

The board has questions and answers it has developed in response to questions from practitioners about the board's compounding regulations. With the modifications to take effect April 1, it is time to amend the Qs and As.

Below are the modified questions.

7. Question: **What happens in a situation where an IV is made to be used on a one-time basis for administration within 72 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))35th Revision, Effective May 1, 2012)** to an in-patient in a health care facility.
~~(7) The equipment used in compounding the drug product~~.

(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 admixture compounded in the satellite pharmacy subject to the recordkeeping 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.

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))35th Revision, Effective May 1, 2012)** to an in-patient in a health care facility.
~~(7) The equipment used in compounding the drug product~~.
(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 72 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))35th 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.

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, filers, 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.

~~**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.~~

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 reuirements. 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)

Attachment Ia

March 10, 2013 7:01 PM

Lethal medicine linked to meningitis outbreak

The following script is from "Lethal Medicine" which aired on March 10, 2013. Scott Pelley is the correspondent. Michael Radutzky, Oriana Zill de Granados and Michael Rey, producers.

60 Minutes Web Extra

Clues to a mom's mysterious death »

Last fall, 17,000 vials of a steroid were shipped to clinics and hospitals in 23 states. The drug had to be sterile because patients would have it injected into their joints or their spines to relieve chronic pain. What happened next is the worst pharmaceutical disaster in decades.

The steroid was contaminated with fungus. Forty-eight people have been killed, 720 are being treated for persistent fungal infections. The tragedy has exposed a failure in drug safety. And, in a moment, you will hear the commissioner of the FDA acknowledge that she can no longer guarantee the safety of many high risk drugs.

The steroid was produced by New England Compounding Center and in the six months since the first deaths, no one at New England Compounding has revealed what happened. But tonight they will. As for the victims, this has been an unrelenting horror after just one injection of lethal medicine.

Julie Otto: I've been in the hospital seven times, total of 75 days. I've missed Thanksgiving and Christmas and my son's birthday.

Julie Otto is one of 13 injured patients who met us at St. Joseph Mercy Hospital outside Detroit.

Willard Mazure: I'm on 60 milligrams of morphine a day with no cure in sight. There is no cure in sight for me.

Willard Mazure's morphine is to kill the pain from the fungal infection. We asked the patients to sit down in the first two rows and many of them brought family to the auditorium. Michigan is a hotspot for the toxic steroid, one of 23 states that received the drug from Massachusetts. St. Joseph Mercy has treated 189 patients -- all of whom endure brutal anti-fungal drugs.

Willard Mazure: The medicine is just unbearable. You know, they talk about cancer treatments, and I'm sure they're unbearable too. But this is some unbearable stuff.

This is the fungus. It is a sample that has been grown from the spinal fluid of a patient. The fungus is a form of mold that attacks bone and nerves. The patients who had it injected in the spine have an infection called meningitis which can also reach the brain.

Scott Pelley: Have the doctors told any of you that the fungus is gone and you never have to worry about it again?

Voices: No. Absolutely not. No.

The steroid, methylprednisolone acetate, made by New England Compounding Center, known as NECC, came from this industrial park near Boston which houses the pharmacy and an outfit that recycles construction debris -- both owned by the family of Barry Cadden, a pharmacist, and president of NECC.

Cadden's New England Compounding Center was what's known as a compounding pharmacy. By law, compounding pharmacies are not allowed to manufacture pharmaceuticals for the mass market. That would require the oversight of the FDA. Instead, states license compounding pharmacies to make drugs for individuals. For example, a doctor might order a liquid form of a medication for a patient who can't swallow a pill. Compounding pharmacies are bound by one rule: they must have a prescription for each individual patient.

But NECC was shipping tens of thousands of vials from its lab called Clean Room One. Investigators shot video inside NECC. This is the first time the public has seen it. And this is the first interview with a technician from Clean Room One.

Joe Connolly: The underlying factor is that the company got greedy and overextended and we got sloppy, and something happened.

Joe Connolly started in Clean Room One in 2009. He remembers, in 2011, a salesman came by with a boast and a warning.

Joe Connolly: He was walking through and says, "Oh, I got-- I got a bunch of stuff coming for you guys. You guys are gonna be busy. You're gonna-- I'm gonna keep you guys movin'." And that just meant compound it, process it, get it out the door.

Connolly says, over months, the lab was overwhelmed with orders. Output of drugs that he made increased by a factor of 1,000.

Joe Connolly: We became a manufacturer overnight. So we were basically trying to have the best of both worlds. It was trying to manufacture without the oversight of a manufacturer. And it was just, we all got overtaxed and everything.

Which made it harder, he says, to follow the strict procedures that kept drug preparation sterile.

Scott Pelley: They would occasionally find mold in the clean room?

Joe Connolly: Occasionally. Yes.

Scott Pelley: How often?

Joe Connolly: I would say maybe a dozen times in three years we would find it.

He told us they would clean up and keep moving. But a month before the first steroid death, he says he warned his supervisor.

Joe Connolly: Something's going to happen. Something's going to get missed. And we're going to get shutdown.

Scott Pelley: What did you mean by that?

Joe Connolly: We were going to hurt a patient. We were just thinking-- hurt a patient. We weren't compounding anymore, we were manufacturing.

Scott Pelley: When you went to your supervisor and told him that, he said what?

Joe Connolly: That's verbatim. He shrugged. That was his response for a lot of our questions or comments or concerns, was a shrug.

Scott Pelley: Meaning?

Joe Connolly: Just do it. He'd-- either he didn't care, or he was powerless to change it.

NECC was growing explosively and so was the compounding industry. It started in 1998 when Congress exempted compounding pharmacies from the oversight of the Food and Drug Administration. The theory was, mixing drugs one prescription at a time shouldn't require federal inspection. The law passed, over the strong objections of then-FDA Commissioner David Kessler.

Scott Pelley: You as FDA commissioner testified before them and you said, "Don't do this."

David Kessler: If you're not going to have oversight, one day people are going to die.

Scott Pelley: That day's arrived.

David Kessler: This should not happen in 2013. Maybe at the turn of the previous century where we didn't have institutions like the FDA. There is no reason why people had to die.

Without FDA supervision compounding took off. State health departments are responsible for regulating what is now nearly a $2 billion industry. Dr. Margaret Hamburg is FDA commissioner now and she told us, because of the 1998 law, she doesn't know how many compounders there are or what they're making.

Scott Pelley: You know, I can just hear the folks at home saying, "Wait a minute. I thought every pharmaceutical drug in this country was approved by the FDA." And you seem to be telling me in this interview that that's not the case?

Margaret Hamburg: Well, compounded drugs are not FDA approved.

Scott Pelley: So if a patient goes into a clinic and the doctor or the nurse pulls out a vial of something, that patient has no way to know whether that drug has been approved by the FDA or not?

Margaret Hamburg: Well, I think that's right under the current system. And what I think emerged in the meningitis outbreak was that many patients and their health care providers didn't realize that they in fact were using a compounded product.

Scott Pelley: As commissioner of the FDA then you can't tell us sitting here now that every drug being used in the United States is safe and effective?

Margaret Hamburg: No. I really cannot.

It was up to the Massachusetts Board of Pharmacy to inspect NECC. Records show occasional problems with sterility. But the pharmacy passed a board inspection in 2011. Still there is no indication that the state fully realized how big and dangerous NECC had become. This is an NECC salesman, speaking for the first time. And we were surprised when he told us how many hospitals and clinics were clients.

Salesman: Close to 3,000, I'd say.

Scott Pelley: Three thousand clients, all across the country?

Salesman: Yeah.

The salesman asked us to disguise him and not use his name. He fears the connection to NECC will ruin his career. He left NECC a year before the steroid disaster. He says he was replaced by a competing salesman. He told us that many of NECC's clients were in on a fraud at the heart of the company's growth. The law required NECC to have a name on a prescription so clinics provided names -- any names.

Salesman: Bart Simpson, Homer Simpson, that we-- those ones did raise red flags, and we told to call our client back, and say, "Hey, give us different names." The follow-up names would be like a John Doe, Jane Doe, Bill Doe, you know, Jane Smith, Bill Smith, et cetera.

Scott Pelley: These weren't real people?

Salesman: As far as I know. I mean, how many Jane Does and John Does do you know? I mean--

Scott Pelley: And when you got the prescriptions with Bart Simpson's name, and Homer Simpson's name you went back to that client and said what?

Salesman: Can you please, you know, give us legitimate names, or people that you know? Sometimes they'd take a phone directory within their office, and scribble out their extensions, and fax it over to us.

Scott Pelley: It's obvious what was going on, and it was obvious to them?

Salesman: Yeah.

Scott Pelley: That this wasn't above board?

Salesman: Right, I mean, if you're in your position, if you're buyer, and your job is to save money, and you're going to get a brand name for $40, and we offer you a $20 vial for the same drug, same size, same everything? What are you going to do? You're going to go and get two for the price of one, using us. So, they-- most of them knew that. I mean, some of them wouldn't do business with us. The ones that we didn't have as clients are the ones that knew, "Hey, you guys can't be doing this. You're not doing it right." And we'd run into that a lot. But we'd move on to the next one. There's more big fish out there.

Big fish kept a big sales team busy. But the salesman told us Barry Cadden, the president, hid that fact during state inspections.

Salesman: So, Barry would notify the managers of the sales team, "Hey, don't let the sales team either come in today, or if they're already in the building, don't let them leave." If the FDA went upstairs, or the Board of Pharmacy went up there and saw 30 sales reps making phone calls, 100 calls a day, they'd wonder what was going on, and why are you so big when you're supposed to be a mom and pop specialty pharmacy, and you're not?

That sales force sold methylprednisolone to a pain clinic in Michigan which treated George Cary's wife and Anita Baxter's mother.

Lilian Cary and Karina Baxter were among the first to die. We've pulled together pictures of about half of the 48 dead. The most recent fatality was last month. Death often comes when the fungus reaches the brain.

George Cary: By the time the hospital determined that she had suffered a stroke it was too late.

Karina Baxter: Same here.

George Cary: She died five days later.

Lilian Cary died before doctors figured out what was happening. So, while she was in the hospital, her husband George decided to do something about a nagging pain in his back. He went to the same clinic she had. And now the fungus is in him too.

Scott Pelley: What has the treatment been like?

George Cary: You're not able to function. You're not able to concentrate. You, you, the staff called us the walking zombies.

On September 26th, after patients started dying, state officials came to inspect NECC.

Scott Pelley: What happened that day?

Joe Connolly: We were told that we're being inspected, so, "Everybody stop what you're doing, start cleaning."

Scott Pelley: So you started cleaning the clean room?

Joe Connolly: Yeah.

Scott Pelley: Now, at this point, there is a federal investigation underway.

Joe Connolly: I did-- we didn't know that.

Scott Pelley: You didn't know that, but the company knew that.

Joe Connolly: I would assume, yeah.

Scott Pelley: A prosecutor investigating this case might consider that to be obstruction of justice.

Joe Connolly: I would very much agree.

Scott Pelley: The evidence was getting cleaned up.

Joe Connolly: It seemed like it.

Despite the cleanup, the FDA tested 50 left over vials of methylprednisolone and all were contaminated. They noted the intake for NECC's ventilation was 100 feet from the recycling plant.

Barry Cadden, New England Compounding's founder was subpoenaed by Congress.

[Barry Cadden: I respectfully decline to answer on the basis of my constitutional rights and privileges, including the Fifth Amendment to the United States Constitution.]

Scott Pelley: I wonder what you would say to him today.

Patient: I'd hope it'd be through bars. Whatever I said to him I hope it'd be through bars.

After this interview, Willard Mazure lost feeling in both legs. He's back in the hospital and so is George Cary. Margaret Hamburg, commissioner of the FDA now wants Congress to return authority over compounding pharmacies to her agency.

Margaret Hamburg: We need clear, strong, consistent federal standards that will be applied across the board, all 50 states. We need to be able to go in and inspect these facilities and get access to all of the information that we need.

Scott Pelley: What are the chances of this happening again?

Margaret Hamburg: I'm sad to say that if we do not put in place the comprehensive legislation that really defines roles and responsibilities, we will have other similar problems.

Barry Cadden and others are targets of a criminal investigation. Cadden declined to be interviewed. His lawyer told us that Cadden is saddened by all of this, but does not know how the drug was contaminated. NECC has gone into bankruptcy and we noticed in the court papers that Cadden and his partners withdrew $16 million from the company over the last year, some of it as people were beginning to die.

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Attachment Ib

THE COMMONWEALTH OF MASSACHUSETTS
EXECUTIVE OFFICE OF HEALTH AND HUMAN SERVICES
Massachusetts Department of Public Health

New England Compounding Center (NECC)

Preliminary Investigation Findings

BOARD OF REGISTRATION IN PHARMACY REPORT

October 23, 2012

INTRODUCTION

Since September 24, 2012 a widespread outbreak of fungal meningitis has affected people in 17 states and caused 23 deaths at the time of this report. The outbreak originated from a medication compounded by New England Compounding Center (NECC), a facility licensed by the Massachusetts Board of Registration in Pharmacy (Board). The Massachusetts Department of Public Health (DPH) has taken immediate action to protect public health and safety. In collaboration with investigators from the U.S. Food and Drug Administration (FDA), DPH investigators have worked to identify the root causes of these events. While the complete scope and severity of this outbreak will not be fully understood for many weeks, to ensure the utmost transparency, DPH is releasing these preliminary findings from its ongoing investigation of NECC. This report constitutes early findings that may be subject to revision as the investigation unfolds.

Medication compounding involves the practice of taking commercially available products and modifying them to meet the needs of an individual patient pursuant to a prescription from a licensed provider. Nearly all retail pharmacies in Massachusetts perform compounding, however only 25 compounding pharmacies meet the standards necessary to produce sterile injectable products. By terms of their license with the Board, every Massachusetts pharmacy must comply with Massachusetts laws and regulations, including compliance with the United States Pharmacopeia Standards. Compounding pharmacies may only perform compounding upon receipt of a patient-specific prescription. These requirements and restrictions are consistent with the rules in place in other states.

Upon beginning the joint on-site investigation of NECC early in this outbreak, DPH and FDA investigators identified serious deficiencies and significant violations of pharmacy law and regulations that clearly placed the public's health and safety at risk.

KEY FACTS

DATE(S) OF INVESTIGATION: *September 26, 2012 to Present*
PHARMACY LICENSE NUMBER AND INITIAL ISSUE DATE: *DS2848; July 16, 1998*
LICENSE STATUS: *Voluntary Surrender, October 3, 2012*
CORPORATION NAME: *New England Compounding Pharmacy, Inc.*
DBA NAME: *New England Compounding Center (NECC)*
ADDRESS: *697 Waverly Road, Framingham, MA, 01702*
MANAGER OF RECORD AND LICENSE NUMBER: *Cadden, Barry J; PH21239*
DEA REGISTRATION NUMBER AND EXPIRATION DATE: *BNS927819, July 31, 2013*
PRACTICE SETTING: *Specialty Pharmacy*
PREVIOUS INSPECTION DATE: *May 24, 2011*
PREVIOUS INSPECTION DOCKET OR STAFF ASSIGNMENT NUMBER: *ISP-738*

INVESTIGATIVE METHODOLOGY

The NECC on-site investigation process consisted of DPH investigators obtaining documentary evidence (including photographs), reviewing and obtaining copies of Standard Operating Procedures, observational findings, reviewing and obtaining copies of all policies and procedures, reviewing batch records and interviewing NECC staff. The FDA conducted product testing and investigators took environmental samples of various areas of the facility to test for contaminants.

DPH investigators principally communicated with three NECC staff members during the on-site investigation (Barry J. Cadden, Glenn A. Chin and Lisa Conigliaro-Cadden) along with FDA investigators. After September 26, 2012, the majority of NECC employees were no longer on site. As has publicly been documented, NECC terminated many of their staff. The continuing investigation will include interviews of NECC employees.

SELECTED PRELIMINARY FINDINGS

During the facility inspections, investigators documented serious health and safety deficiencies related to the practice of pharmacy. All pertain to violations of 247 CMR 9.01(3) or 247 CMR 6.01(5)(a):

- NECC distributed large batches of compounded sterile products directly to facilities apparently for general use rather than requiring a prescription for an individual patient.
  - Records show that NECC had lists of potential patient names but did not have patient-specific prescriptions from an authorized practitioner when compounding and dispensing medication, as required by state law.
  - Manufacturing and distributing sterile products in bulk was not allowed under the terms of its state pharmacy license. If NECC was appropriately licensed as a manufacturer with the FDA the company would have been subject to additional levels of scrutiny.
  - NECC did not conduct patient-specific medication history and drug utilization reviews as required by regulations.

- NECC distributed two of the recalled lots of methylprednisolone acetate (PF) 80 MG/ML prior to receiving results of sterility testing:
  - Lot *06292012@26* was prepared on June 29, 2012. Final sterility testing was completed on July 17, 2012. Two shipments of product were made prior to the final sterility tests results being received.
  - Lot *08102012@51* was prepared on August 10, 2012. Final sterility testing was completed on August 28, 2012. Eleven shipments of product were made prior to the final sterility tests results being received.
  - While NECC's records show the sterility tests found no contamination, the adequacy of NECC's sterility testing methods are currently under examination.
- Final sterilization of product did not follow proper standards for autoclaving (sterilization through high pressure steam) pursuant to United States Pharmacopeia Standard 797 (USP 797) and NECC's own Standard Operating Procedures:
  - Examination of NECC records indicated a systemic failure to keep products in the autoclave for the required minimum 20-minute sterilization period necessary to ensure product sterility.
- NECC did not conduct proper validation of autoclaves pursuant to USP 797:
  - NECC failed to test their autoclaves to ensure proper function.
- Visible black particulate matter was seen in several recalled sealed vials of methylprednisolone acetate from Lot *08102012@51*.
- Powder hoods, intended to protect pharmacists from inhaling substances during medication preparation, within the sterile compounding area were not thoroughly cleaned pursuant to USP 797.
  - Residual powder was visually observed within the hood during inspection. This contamination may subsequently lead to contamination of compounded medications.
- Condition of "Tacky" mats, which are used to trap dirt, dust, and other potential contaminants from shoes prior to clean room entry, violated the USP 797.
  - Mats were visibly soiled with assorted debris.

- A leaking boiler adjacent to the requisite clean room created an environment susceptible to contaminant growth:
  - A pool of water was visually observed around the boiler and adjacent walls, creating an unsanitary condition; the culture results of this potential contaminant are still pending.

CHRONOLOGY OF THE OUTBREAK & DEPARTMENT OF PUBLIC HEALTH ACTIONS

Monday September 24, 2012 – The Massachusetts Department of Public Health (DPH) was notified by Tennessee Department of Health in late evening about a cluster of six rare fungal meningitis cases, with onset of symptoms between July 30 and September 18, 2012. These patients had several risk factors in common, including an epidural injection of steroid (methylprednisolone acetate 80 mg/ml preservative free) compounded at New England Compounding Center (NECC) located in Framingham. Tennessee also reviewed three other products not made by NECC as potential contaminants.

Tuesday September 25, 2012 – DPH planned an investigation of NECC given growing concerns of linkage to infections. The DPH's Bureau of Health Care Safety and Quality, Board of Registration in Pharmacy (Board), and Bureau of Infectious Diseases began rapid response planning on September 25, and convened a multi-agency meeting between the Tennessee Department of Health, the U.S. Centers for Disease Control and Prevention (CDC), the U.S. Food and Drug Administration (FDA), and the New England Compounding Center (NECC). At the demand of DPH staff, Barry Cadden and Gregory Conigliaro, principal owners of NECC, immediately provided documentation of all facilities in the nation that had received medications from three lots of methylprednisolone acetate that were suspected by the CDC as being linked to the fungal infections ("suspect lots"). Distribution lists were provided to public health authorities across the country, including CDC and FDA. The suspected product was distributed to more than 14,000 patients in 23 states.

Suspect Lots of Methylprednisolone Acetate (PF) 80 mg/ml Injection identified by TN DOH:

Lot #05212012@68 prepared by NECC on 5/21/2012
Lot #06292012@26 prepared by NECC on 6/29/2012
Lot #08102012@51 prepared by NECC on 8/10/2012

17,676 total doses

Wednesday September 26, 2012 – DPH began an onsite investigation of NECC and instituted a recall of all suspect lots of methylprednisolone acetate. Investigators confirmed that all non-distributed methylprednisolone products were quarantined, and that methylprednisolone acetate was no longer being produced. Approximately 3,000 doses were quarantined or returned through recall. Upon arriving at NECC, investigators found NECC employees cleaning sterile compounding areas and conducting environmental testing. DPH investigators also detected signs of bleach decontamination in the compounding areas.

Thursday September 27, 2012 to Sunday September 30, 2012 – DPH coordinated with FDA to plan a collaborative investigation of NECC.

Monday October 1, 2012 – DPH and FDA began a joint investigation at NECC. Findings supported by the epidemiological work of the CDC prompted DPH to issue a formal Quarantine Notice pursuant to M.G.L. c. 94C, §§ 13 and 189A, and M.G.L. c. 112, §§ 30 and 42A. This legally formalized the September 26 quarantine action. The Notice directed that all methylprednisolone acetate raw materials (chemicals), all non-sterile and sterile products located at NECC used in the compounding of methylprednisolone acetate, and all inventory on the premises prepared for dispensing and stored at the pharmacy, or received by recall should be quarantined and not disposed of without the express approval of the DPH. Investigators were shown examples of methylprednisolone products that were labeled as patient specific. The associated documents were not individual prescriptions but lists of patients generated by a clinical facility and provided to NECC to obtain the product. NECC stated the list of names was considered to be an authorized prescription by the physician. This practice is not in accordance with Massachusetts regulations.

Tuesday October 2, 2012 – DPH and FDA observed visible black particulate matter in sealed vials (of purportedly sterile methylprednisolone acetate) returned to NECC. Inconsistencies in sterilization processes of materials were identified through review of NECC's records. The Board voted to obtain a Voluntary Surrender of NECC's license or to initiate action to issue a Temporary Order of Summary Suspension.

Wednesday October 3, 2012 – DPH secured voluntary surrender of NECC's license, effective 12 pm (noon), and instituted a voluntary recall of all intrathecal products (those injected into the area around

the spinal cord or brain). DPH also notified Massachusetts providers to cease use of all NECC products.

Thursday October 4, 2012 – DPH and FDA publicly announced that black particulate matter, tentatively identified by microscopy as fungal contamination, was seen in a sealed, purportedly sterile vial of methylprednisolone acetate from a suspect lot. CDC and FDA recommended that all health care professionals cease use and remove from their pharmaceutical inventory any material produced by NECC. Massachusetts State Epidemiologists contacted nine Massachusetts health care facilities that received non-implicated lots of methylprednisolone acetate, instructing them to contact recipient patients to determine whether there were any unusual infections or other complications. No infections from the non-implicated lots sent to Massachusetts facilities have been identified at this time. DPH and FDA investigators continued with their on-site investigation and evaluated standard operation procedures and batch records related to sterile compounding. FDA investigators took environmental samples of various areas of the facility to test for contaminants.

Friday October 5, 2012 – DPH and FDA investigators noted visible contaminants in additional sealed recalled vials of methylprednisolone acetate. The particulate matter was noted in vials labeled in conformance with Massachusetts pharmacy regulations with patient-specific information. Additionally, particulate matter was noted in recalled vials that were labeled without patient-specific names, in clear violation of Massachusetts regulations. DPH and FDA each issued an alert to providers and facilities across the country stating the identification of particulate matter.

Saturday October 6, 2012 – DPH secured an immediate recall of all NECC products.

Monday October 8, 2012 – At the request of DPH, Barry Cadden and Glenn Chin, leaders at NECC, voluntarily ceased practice as pharmacists pending completion of the investigation.

Wednesday October 10, 2012 – Based on their shared ownership and leadership with NECC, DPH requested that Ameridose and Alaunus Pharmaceutical cease all pharmacy operations and any dispensing, manufacturing or wholesale distribution of any products starting at 3 p.m. on October 10 and continuing until 5 p.m. on October 22. DPH and FDA staff began an on-site investigation of Ameridose, a pharmacy, distributor and wholesaler regulated by the FDA. At the demand of DPH, Barry J. Cadden agreed to immediately resign as manager, director and from any other management

position at NECC, Ameridose, and Alaunus. DPH began working with the Massachusetts Hospital Association to ensure that the supply chain of medications would not be disrupted. The Board issued an advisory to all pharmacies and pharmacists in Massachusetts emphasizing that all of their actions must be performed in accordance with the United States Pharmacopeia. The advisory also reiterated that state law requires compounding pharmacies and
pharmacists to have a patient-specific prescription from an authorized practitioner when compounding and dispensing medication. Compounding pharmacies and pharmacists were required to submit an affidavit asserting that they are following state law in this regard.

Sunday October 14, 2012 – DPH staff began on-site investigation of Alaunus Pharmaceuticals, a wholesale distributor affiliated with Ameridose and NECC.

Monday October 15, 2012 – FDA issued an advisory that a patient may have acquired fungal meningitis from a different NECC steroid injection, triamcinolone acetonide. DPH epidemiologists began outreach to all 192 facilities in Massachusetts who received any NECC injectable products and supported providers in patient outreach. In addition, the FDA reported a transplant patient with an *Aspergillus fumigatus* infection who received a NECC cardioplegic solution during surgery. The CDC is actively working to confirm the presence of fungal contaminants in cardioplegic solutions. DPH asked Massachusetts providers to contact any patients who received any injectable product, including ophthalmic drugs or cardioplegia solutions prepared by NECC after May 21, 2012.

Thursday October 18, 2012 – FDA released definitive laboratory confirmation of the presence of fungal contaminants in sealed vials of methylprednisolone acetate in a suspect lot prepared by NECCDPH and FDA collected samples from sealed vials of completed product at Ameridose. Results are currently pending with the FDA.

Friday October 19, 2012 – DPH and FDA investigators scrutinized business practices of Alaunus Pharmaceuticals, and potential for inappropriate distribution of NECC or Ameridose products. At the request of DPH, Ameridose and Alaunus Pharmaceuticals extended their cessation of operations until November 5, 2012.

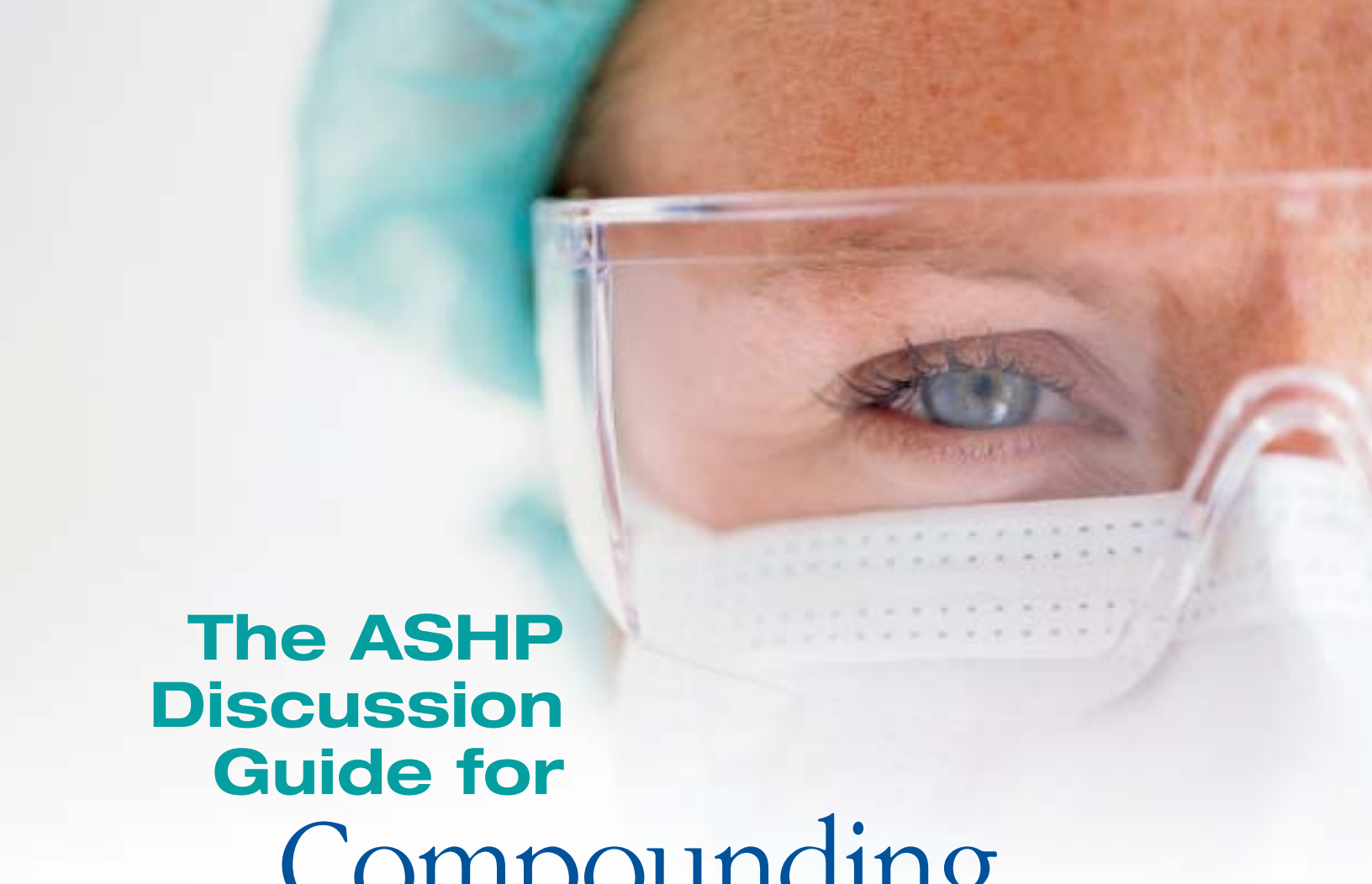
Monday October 22, 2012 – The Board authorized DPH staff to request voluntary permanent surrender of the licenses of Barry J. Cadden, Glenn A. Chin, and Lisa Conigliaro-Cadden, as well as

NECC. If the three pharmacists and NECC do not comply, the Board authorized staff to proceed with permanent revocation. All three individuals are currently prevented from practicing as pharmacists, and would be so prohibited throughout the appeal process.

ONGOING INVESTIGATION

The Department's collaborative investigation with the FDA is comprehensive and will continue until investigators have all information needed to determine what, if any, further action should be taken against NECC and its leadership. This investigation also extends to NECC's business practices and environmental conditions surrounding the business, including the presence of a nearby recycling center that shares ownership with NECC. Investigators are also looking into NECC's corporate entity, including, but not limited to, corporate ownership and governance structures at both NECC and sister companies, Ameridose and Alaunus. DPH will analyze and incorporate all evidence and information gathered by the FDA and the Board of Registration in Pharmacy into a final, comprehensive report. This report will be presented to the Board of Registration in Pharmacy, which will determine appropriate regulatory sanctions under administrative law. DPH will also assist with any investigation, federal or state, that explores the actions of NECC and its principals. DPH will continue to support and cooperate with federal policymakers in addressing gaps in oversight of compounding pharmacies, including leaders on the U.S. Senate Health, Education, Labor, and Pensions Committee, and the U.S. House of Representatives Energy and Commerce Committee, and members of the Massachusetts Congressional delegation, including Congressman Ed Markey. DPH will also work closely with the Massachusetts General Court to explore state-specific policy solutions. Findings of these investigations will be used to inform these state and federal actions to address regulatory gaps within the quickly evolving compounding industry.

Attachment Ic



The ASHP Discussion Guide for Compounding Sterile Preparations

SUMMARY AND IMPLEMENTATION OF USP CHAPTER <797>

Developed by the American Society of Health-System Pharmacists
in collaboration with Baxter Healthcare Corporation

American Society of Health-System Pharmacists®

Medication Delivery

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The information and its applications contained in this guidance document are constantly evolving because of ongoing research and improvements in technology, and are subject to the professional judgment and interpretation of the practitioner due to the uniqueness of each pharmacy's role in compounding sterile preparations. The writer, reviewers, editors, ASHP, and Baxter have made reasonable efforts to ensure the accuracy and appropriateness of the information presented in this document. However, any reader of this information is advised that the writer, reviewers, editors, ASHP, or Baxter are not responsible for the continued currency of the information, for any errors or omissions, and/or for any consequences arising from the use of the information in the document in any and all practice settings. Any reader of this document is cautioned that ASHP and Baxter make no representation, guarantee, or warranty, express or implied as to the accuracy and appropriateness of the information contained in this document, and will bear no responsibility or liability for the results or consequences of its use.

The ASHP Discussion Guide on USP Chapter <797>

Compounding Sterile Preparations

Eric S. Kastango, M.B.A., R.Ph., FASHP

The recently published *USP Chapter <797>, Pharmaceutical Compounding: Sterile Preparations,* became effective January 1, 2004. This discussion guide is intended to assist health-system pharmacists with implementation of USP Chapter <797> requirements.

The United States Pharmacopeia, 27th rev., and the National Formulary 22nd ed. USP General Information Chapter. Pharmaceutical Compounding–Sterile Preparations. Rockville, MD: The United States Pharmacopeial Convention, 2003.

Executive Summary

Over the past three decades, several pharmacy practice documents have been published in hopes of establishing a standard of practice for compounding sterile preparations that could be universally adopted. None of these documents was successful in achieving this goal. However, on January 1, 2004, USP Chapter <797>, Pharmaceutical Compounding: Sterile Preparations, which is published in USP 27/NF 22, came into effect. USP Chapter <797> details the procedures and requirements for compounding sterile preparations and sets standards that are applicable to all practice settings in which sterile preparations are compounded. These standards may be adopted and enforced by state boards of pharmacy and surveyable by accreditation organizations. This discussion guide will provide important information about Chapter <797> and its procedures and requirements. As pharmacists, we have been given the right to compound, but as professionals, we have the obligation to compound right.

Chapter Overview and History

During the 1960s and 1970s, the practice of pharmacy was evolving and emphasis was placed on patient safety factors as a result of patient injuries and deaths that had occurred because of problems with medication delivery and sterile compounding. One of the first groups to address these patient safety issues was the National Coordinating Committee on Large Volume Parenterals (NCCLVP). NCCLVP was established by the US Pharmacopeial Convention, Inc., and subsequently developed and recommended standards of practice for the preparation, labeling, and quality assurance of hospital pharmacy admixture services.[1-7]

After the dissolution of NCCLVP in the 1980s, the profession of pharmacy was under pressure by the Food and Drug Administration (FDA) to address problems with contamination in hospitals in the United States.

In the early 1990s, several pharmacy organizations, including the American Society of Health-System Pharmacists (ASHP), United States Pharmacopeia (USP), and National Association of Boards of Pharmacy (NABP), issued practice recommendations in an effort to provide a professional mandate and practice assistance to pharmacists and technicians responsible for compounding sterile preparations. The central theme in each of the

documents was that the pharmacist was responsible for ensuring that compounded sterile preparations (CSPs) were properly prepared, labeled, stored, dispensed and delivered.

In 1992, the USP issued a draft recommendation entitled USP <1074>, Dispensing Practices for Sterile Drug Products Intended for Home Use. The intent of this general information chapter within the USP/NF was "to detail the various procedures necessary to prepare and dispense sterile drug preparations intended for home use: the validation of sterilization and aseptic processes, the quality and control of environmental conditions for aseptic operations, personnel training, aseptic techniques, finished product release testing, storage and expiration dating, the control of product quality beyond the pharmacy, patient or caregiver training, patient monitoring and complaints, and finally, a quality assurance program."[8] The United States Pharmacopeial Convention, Inc. adopted a finalized version of the draft and numbered it <1206>, Sterile Drug Products for Home Use, to provide specific practice standards and operating guidelines for CSPs.[9] The chapter was only a guideline and not enforceable; the pharmacy profession did not have any accountability to the USP as a regulatory agency.

In 1993, ASHP issued a Technical Assistance Bulletin (TAB) entitled "Quality Assurance for Pharmacy-Prepared Sterile Products."[10] This document defined the level and extent of recommended quality assurance measures that should be utilized by pharmacy operations when compounding sterile preparations. These recommendations also addressed operating parameters such as physical plant, types of products utilized, and length of product storage. This TAB was developed to be applicable in a variety of practice settings, including hospitals, community retail pharmacies, long-term-care facilities, and home care organizations. The TAB spawned the ASHP Risk Level categories (I-III) which, for some, have become the unofficial standard for the pharmacy profession. However, the recommendations in the TAB fell short with respect to the degree of specificity that most pharmacy practitioners wanted, which impeded its integration and general acceptance by the pharmacy community. Among the reasons for not following the recommendations in the TAB was the perception that they were unnecessary, excessive, costly, and too time-consuming. In addition, some practitioners did not think that the TAB added value to the process since there was insufficient evidence to support the recommended changes. As a result, the FDA's concerns were not alleviated by the ASHP QA TAB.

In 1998, former President Clinton signed into law the US Food and Drug Administration Modernization Act (FDAMA) of 1997. Section 503A of the FDAMA, which is titled "Pharmacy Compounding," defined the limits of legitimate compounding. This law limited the scope of pharmacy compounding and was designed to protect patients from the unnecessary use of extemporaneously compounded drugs by pharmacists. FDAMA granted FDA power to identify certain drug products that were difficult to compound and for which compounding could adversely affect safety or effectiveness. In 2001, the U.S. Supreme Court ruled that section 503A was unconstitutional, creating a vacuity of regulation for the pharmacy profession and the FDA.

In 1995, ASHP conducted a national survey of quality assurance for pharmacy-prepared sterile preparations as a follow-up to ASHP QA TAB.[11, 12] Results of the survey indicated that few pharmacies were equipped with adequately controlled compounding environments, which are essential for dispensing sterile preparations. The survey also documented that many pharmacists were not performing critical quality assurance checks, such as environmental monitoring, end-product testing, and process validation.[12]

Another national survey was conducted in 2002.[13] Unfortunately the findings were similar to the 1995 survey, demonstrating that ASHP's QA TAB guidelines had not produced significant changes in sterile compounding practices in the 10 years since publication of the document.[13]

Efforts to improve the quality of pharmacy-prepared sterile preparations have been ongoing. The first official and enforceable sterile preparation compounding requirement in the United States took effect on January 1, 2004, when USP published USP Chapter <797>.

Legal and Regulatory Basis

That USP would initiate a sterile preparation requirement is logical, considering its long history. In 1906, the Food and Drugs Act, passed by the US Congress and the US Pharmacopeia (USP/NF), became the official standard for drugs in the United States. In 1938, Congress passed the Federal Food, Drug, and Cosmetic (FD&C) Act, which was a revision of the 1906 Act. The FD&C Act recognized the USP/NF as the official compendia of drug standards. The US Food and Drug Administration is responsible for the enforcement of the FD&C Act.

Each general chapter of the USP/NF is assigned a number, which appears in brackets along with the chapter name. The general chapters numbered <1> to

<999> are considered requirements and official monographs and standards of the USP/NF, whereas general chapters numbered from <1000> to <1999> are considered informational and chapters above <2000> apply to nutritional supplements.[14] Since USP Chapter <797> is considered a requirement, pharmacies may be subject to inspection against these standards by boards of pharmacy, FDA, and accreditation organizations, such as the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), Accreditation Commission for Health Care, Inc. (ACHC), and Community Health Accreditation Program (CHAP). Pharmacists are strongly encouraged to contact their respective boards of pharmacy for information on state enforcement criteria and activities. The FDA is exercising enforcement discretion during routine inspections but will intervene when patient injury or deaths associated with compounded sterile preparations have occurred. Since 1990, FDA has become aware of more than 55 quality problems associated with compounded preparations, many of which have resulted in recalls, patient injury, and deaths.[15-29]

Areas of Likely Concern

The following points review issues that are most likely to be of concern for pharmacy administrators, pharmacists and technicians:

- **Applicability in all healthcare settings:** The principles of contamination control and proper compounding procedures are not unique to the practice setting where sterile preparations are compounded. USP <797> requirements must be met in all healthcare settings that compound sterile preparations and by all disciplines associated with these settings; including physicians, nurses, and pharmacists in office practices, clinics, hospital care units, and main and satellite pharmacies. The enforcement of this chapter by boards of pharmacy is limited to licensed pharmacies.
- **Risk Levels Criteria:** The practices, policies, procedures and physical plant of pharmacies where sterile compounding occurs vary so widely that USP <797> was written to give the pharmacist, as the individual with the ultimate responsibility for sterility and accuracy of CSPs, flexibility in determining actual risk levels for preparations being compounded. The following examples better illustrate this point (See Table 1).

The checklist on page 4 provides an overview of the various factors that can be used when determining risk levels. The most important factor in determining risk level is sound professional judgment based on knowledge of aseptic compounding principles.

- **Environmental Quality Controls:** The cleanliness or quality of air in critical compounding areas is one factor influencing the likelihood of microbial contamination. The need to control the quality of critical operating environments dates back more than a century, when the etiologic role of bacteria in infection was discovered. Cleanrooms were developed to minimize or eliminate bacteria and to control

Table 1

Compounding Activity	Location	USP <797> Risk Level Determination
Reconstitution of several vials of lyophilized powder with a specific volume of sterile diluent for transfer to a small-volume minibag or large-volume parenteral solution *one at a time*	In the pharmacy using appropriate engineering controls (ISO Class 5 hood in an ISO Class 8 cleanroom)	Low-Risk Level
Reconstitution of several vials of lyophilized powder with a specific volume of sterile diluent; the resulting solution is then aggregated into an evacuated bottle for transfer to several small-volume minibags or large-volume parenteral solutions	In the pharmacy using appropriate engineering controls (ISO Class 5 hood in an ISO Class 8 cleanroom)	Medium-Risk Level
Reconstitution of a single vial of lyophilized powder with a specific volume of sterile diluent for transfer to a small-volume minibag or large-volume parenteral solution	Nursing station, ambulatory care center or at the patient bedside without any engineering controls	High-Risk Level

Pharmacy Compounding-USP <797> Risk Level Assessment

Classification	Requirements	Yes	No
Low-Risk Compounding	■ Simple admixtures compounded using closed system transfer methods ■ Prepared in International Organization for Standardization (ISO) Class 5 (Class 100) laminar airflow workbench (hood) ■ Located in ISO Class 8 (Class 100,000) buffer room (Cleanroom) with ante area ■ Examples include reconstitution of single-dose vials of antibiotics or other small-volume parenterals (SVPs), preparation of hydration solutions		
Medium-Risk Compounding	■ Admixtures compounded using multiple additives and/or small volumes ■ Batch preparations (e.g. syringes) ■ Complex manipulations (e.g. TPN) ■ Preparation for use over several days ■ Prepared in ISO Class 5 (Class 100) ■ Located in ISO Class 8 (Class 100,000) Cleanroom with ante area ■ Examples include pooled admixtures, parenteral nutrition solutions using automated compounders, batch-compounded preparations that do not contain bacteriostatic components		
High-Risk Compounding	■ Non-sterile (bulk powders) ingredients ■ Open system transfers ■ Prepared in ISO Class 5 (Class 100) ■ Located in ISO Class 8 (Class 100,000) Cleanroom with separate ante area ■ Examples include CSPs prepared from bulk, nonsterile components (morphine or other narcotics) or final containers that are nonsterile and must be terminally-sterilized (nuclear pharmaceuticals)		

the incidence of infection in hospitals (especially in operating rooms). It was realized that by providing proper ventilation to critical areas in hospitals, the incidence of airborne infections could be greatly reduced. Another observation was that the airborne particles generated from the environment (dust, dirt, pollen, viable and nonviable microorganisms) and from people (skin flakes, lint, cosmetics, and respiratory gases) negatively influenced patient outcomes.[30] Compounding areas must be routinely monitored to determine the level of cleanliness. The appropriate combination of work areas, "cleanrooms", ante rooms, LAFW (laminar airflow workbenches), or the use of barrier-isolators to achieve desired cleanliness levels based on risk classification and work loads need to be determined. The costs associated with correcting or achieving appropriate levels of cleanliness in accordance with USP <797> can be significant (in the tens of thousands of dollars). Guidance from qualified persons who have experience and expertise with cleanrooms should be sought prior to "fixing the problem." A variety of facility/engineering controls can be employed to ensure that the proper environmental controls are in place, such as installing integrated high efficiency particulate air (HEPA) filters in the ceiling fans, replacing current ceiling tiles with plastic covered "clean room grade" tiles, removing refrigerators, computers, and printers from the compounding area, and replacing existing flooring with seamless vinyl floor covering (e.g., Medintech by Armstrong).

- **Process and Preparation Quality Controls:** Pharmacists and technicians must understand that compounding processes and personnel who perform the compounding (and whether they are following appropriate written policies and procedures) have an impact on the quality assurance of the final compounded sterile preparation. These controls are the cornerstone in ensuring CSP sterility and accuracy. The desired outcome of USP <797> is being able to determine where failures can occur in a process, followed by implementation of methods to control and monitor these critical points of failure, thereby increasing the likelihood of *consistently* producing a quality CSP. Quality cannot be inspected into the final product; it must be built into CSP through process and preparation quality controls. Many resources and guidance documents are available and should be used in order to better understand appropriate aseptic techniques, process validation procedures, and methods for end-process content accuracy, sterility, and other quality measures.
- **Sterility and Beyond-Use Dating:** Two factors are critical in establishing beyond-use dating (formerly known as expiration dating) for CSPs. The first is the chemical stability of the chemical entity in solution. A number of textbook references are available and should be consulted to demonstrate the chemical stability of medications in solution. The second factor is the sterility of the CSP. By definition, sterility is the absence of viable microorganisms in the CSP. Unlike pyrogenicity, sterility is an absolute concept. A CSP is either sterile or it is not. There are acceptable levels of pyrogens permitted in CSPs although the desired goal is to compound a pyrogen-free preparation. Since patient injury and death following administration of CSPs have been associated with microbial contamination, the assignment of risk levels and operating principles outlined in USP Chapter <797> serves to prevent CSP microbial contamination. Unless sterility testing is performed for the CSP, the beyond-use dating of the preparation CANNOT exceed the published limits found in USP <797> (Table 2). If sterility testing is performed according to USP <71> Sterility Tests, the CSP can be assigned beyond-use dating based on the maximum chemical stability of the drug in solution as permitted by valid references.
- **Staff Training, Competency, and Performance:** Pharmacy administrators, pharmacists and technicians are being asked to do more with less every day. This vicious cycle takes a great toll on one of the most crucial aspects of ensuring sterility and accuracy of CSPs: formal training and periodic competency assessment. Properly trained employees are the foundation for ensuring that procedures are followed correctly when compounding sterile preparations.

Compounding Accuracy and Sterility to Ensure the Safety of Patients

There is ample evidence that improperly compounded sterile and nonsterile preparations injure and kill patients.[15-29] The references cited here are not all-inclusive on the subject. Several state boards of pharmacy have made significant revisions to their pharmacy practice acts by expanding regulatory provisions for oversight of compounding. In the United States, the practice of compounding sterile preparations is now dictated by requirements published as a component of the Federal Food, Drug and Cosmetic Act. Subsequently, boards of pharmacy, attorneys, accreditation organizations, and the FDA may utilize and reference these requirements during inspections, surveys, and enforcement actions.

If the profession of pharmacy continues on the path of not looking for problems, it won't find any. However, the fact is that pharmacists are making errors. There have been several studies that have demonstrated the prevalence of pharmacists' compounding errors.[25, 31] It is highly probable that the incidence of vascular access

Table 2

Risk Level	Room Temp	Refrigeration	Freezer (≤-20 °C)
Low	48 hours	14 days	45 days
Medium	30 hours	7 days	45 days
High	24 hours	3 days	45 days

Source: USP <797> Pharmaceutical Considerations: Sterile Preparations.

device phlebitis, septicemia, and other nosocomial infections has not been investigated by taking into account the microbial flora in the sterile compounding areas in pharmacies. Analyzing a potential relationship between hospital infections and the hospital pharmacy might result in a startling find.

Careful supervision and double-checking of calculations, measurements, and compounding are necessary to reduce the risk of medication errors. In 2002, a study on medication errors in hospitals revealed that serious mistakes involving prescription drugs occur in 3% to 7% of hospital inpatients. These findings suggest that more than 90,000 patients are harmed by medication errors in our nation's hospitals each year.[32]

Since adverse events have not motivated significant change in how sterile preparations are compounded, there are three others—economics, publicity, and regulations—that could. Examples of how these three variables could initiate change follow:

Economics: At some point in the future, both payers and liability underwriters may demand evidence of compliance with the new USP chapter as a condition of continued coverage. For instance, insurance premiums could be increased solely on the basis that a facility prepares sterile compounds, making it high-risk. Liability coverage may be dropped altogether, resulting in difficulty obtaining insurance. Some liability underwriters have already begun assessing their tolerance of risk with respect to sterile compounding in certain pharmacy practice settings.[33] Accreditation organizations will survey pharmacies against USP Chapter <797>, and failure to comply may potentially affect accreditation status, subsequently limiting the ability of healthcare organizations to bill and collect from payers.[34]

Publicity: When problems occur, the media attention on such events damages the credibility of the profession and diminishes the confidence of regulators. As a result, additional regulatory actions by local, state and federal authorities may restrict compounding to specialty pharmacies and board certified pharmacists.

Regulations: Many states have changed their practice standards in response to the national publicity of pharmacy compounding errors. For example, Missouri has adopted standards that are more stringent than USP Chapter <797>. In fact, Missouri pharmacists will be conducting end-preparation evaluation for sterility, pyrogenicity, and potency on CSPs.

First Steps on the Road to Compliance

- Determine Risk Level of Compounding using Risk Level Assessment Checklist, Chapter <797> and professional judgment
- Perform Gap Analysis by comparing <797> requirements line by line with pharmacy operational procedures and facilities
- Develop action plan for <797> compliance from prioritized Gap Analysis (See Table 3)
- Communicate results of Gap Analysis and Action Plan with pharmacy staff
- Implement non-facility requirements and revise Policies and Procedures for CSPs, then address changes needed for facility and equipment compliance
- Communicate action plan and demonstrated improvements in patient care with staff
- Evaluate use of alternative products and reassess workload demands for all compounding sites
- Document all measures of quality performance and communicate improvements in <797> compliance with staff, administration, and accreditation organizations

State boards of pharmacy are citing pharmacies for failure to comply with existing sterile compounding regulations and are assessing significant financial penalties. Lawyers have successfully quoted USP/NF chapters as evidence of standards of practice during lawsuits.[34, 35] From a professional standpoint, pharmacists should do the right thing because patients deserve our best efforts. There is clear and compelling evidence that the old ways of compounding sterile preparations must be changed to meet the requirements of USP Chapter <797>. The focus on developing, implementing, using and maintaining good compounding practices and quality systems continues to be critical in ensuring the health and well-being of patients as well as the professional enrichment of pharmacists and technicians. Now is the time for professionals working in the practice of pharmacy (pharmacists and technicians) to embrace the scientific facts that good compounding practices will yield quality preparations (accurate and sterile). This professional responsibility—to consistently meet or exceed state regulatory requirements when compounding sterile preparations—can be a matter of life and death.

First Steps on the Road to Compliance

Healthcare organizations that prepare CSPs may have significant practice standard gaps relative to compliance with USP Chapter <797> in several areas, particularly in regards to facility and equipment needs. As a first step, the risk level of the compounding that is being performed in the pharmacy needs to be determined. Most pharmacies perform low- and medium-risk level compounding. The checklist ("Pharmacy Compounding-USP <797> Risk Level Assessment") shown on page 4 of this guide can be used to identify and document the facility's risk level.

After the level of risk has been determined, the next step is to determine how current pharmacy compounding operations compare with those in USP Chapter <797>. This evaluation is known as a gap analysis. To perform a gap analysis, the requirements of <797> are compared line by line with current practices and operational facilities in order to identify differences or "gaps". The gap areas should be analyzed to identify specific practices causing the greatest risks or differences from <797> requirements, then these gaps should be prioritized by fiscal and human resource costs (Table 3). Developing an action plan from the prioritized gap list identifies options for immediately improving CSP practices, thus reducing vulnerability to microbial contamination and inaccurate compounded preparations.

Having a completed "Pharmacy Compounding-USP <797> Risk Level Assessment" and gap analysis can be used to demonstrate to accreditation organizations, boards of pharmacy and other regulatory authorities that current operating deficiencies are understood and corrective action is being taken to achieve compliance. The immediate corrective action plan should address all non-facility, low-cost requirements identified during the gap analysis. Revised policies and procedures should reflect *actual* day-to-day operations and practices, such as handwashing, gloving and gowning, didactic and skill-based training and competency of staff, aseptic technique media fill validation, proper housekeeping (cleaning and sanitizing), and microbial environmental monitoring. Non-facility issues can be addressed immediately after gap analysis and require little more than time, attention and vigilance. Large capital expenditures may require more time and planning to secure approval. By focusing on positive communication with pharmacy staff of improved quality and patient-care outcomes resulting from <797> requirements, procedural changes can be successfully achieved, establishing employee ownership and buy-in to change old habits.

Another effective means of reducing the level of risk for CSPs is the use of alternative products or product configurations, such as manufacturer ready-to-use premixed medications and unit-of-use closed transfer packaging (Minibag Plus® and Add-Vantage®). Pharmacists can reassess compounding demands based on risk-level requirements and by consolidating workloads from point-of-care locations (main pharmacies versus satellite pharmacies). Questions such as "Could compounding responsibilities be centralized as a means of reducing costs (employee competency, facility requirements) and medium- or high-risk levels (eliminate or minimize decentralized compounding)?" need to be asked. In addition, all aspects of compounding sterile preparations need to be considered during the <797> compliance

Table 3

USP <797> Quality Domains	Impact to CSP Quality	Relative Cost
Compounding Conditions	N/A	N/A
QA Program	++++	$$
QA Practices	++++	$
Reports/Documents	++++	$
Outcomes (ADR) Monitoring	+++	$$
Patient Training	++++	$$
Maintaining Product Quality & Control	++++	$$$
Storage & Beyond Use Dating	+++	$$
Finished Product Release Checks & Tests	++++	$$
CSP Work Environment	+++	$$$$
Equipment and Supplies	++++	$$
Components	++++	$
Processing: Aseptic Technique	++++	$
Environmental Control	+++	$
Verification Processes		
Sterility Testing	+++	$$$
Environmental Monitoring	++++	$$
Personnel Training and Education	++++	$$

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evaluation, including personnel time, equipment and facility options (cleanrooms vs. barrier-isolators) for the central pharmacy, satellite pharmacies, clinics, procedure rooms, and nursing work stations.

The advice of W. Edwards Deming, one of the world's top quality experts, can be applied to compounded sterile preparations. Deming created the 85/15 Rule, a concept that attributes 85% of organizational problems to system failures, and 15% to human factors. Systems failures include poor or nonexistent plans, procedures, measurable performance criteria, and work processes. Deming and others established that the potential to eliminate mistakes and errors in the workplace lies mostly in improving the systems through which work is done, not in blaming the individual workers. These observations have evolved into the "rule of thumb" that approximately 85% of work problems can be corrected by changing the work system and less than 15% can be corrected by changing individual workers. Current research now indicates that the percent ratio leans even farther towards the system component. The rule might be restated as "95/5" or perhaps "97/3". Dr. Deming, through his famous Red Bead Experiment, proved that the only way to improve a product or service is for management to improve the system that creates that product or service.[36] Theodore Roosevelt's words also apply. Roosevelt said, *"In any moment of decision, the best thing you can do is the right thing. The worst thing you can do is nothing."*

USP Chapter <797> Summary

The following points highlight each of the major areas within USP Chapter <797>. These summaries should not serve as a substitute for the actual text of the USP chapter. It is imperative that this chapter be purchased from USP, either in stand-alone format or as a component of the new USP 27/NF 22. It is strongly encouraged that the entire USP 27/NF 22 reference book be purchased since several other important chapters are referenced in Chapter <797>.

Introduction

The definition of sterile compounding is placed in the introduction and is clearly different than nonsterile compounding, which falls under USP Chapters <795>, Pharmaceutical Considerations-Nonsterile Preparations and <1075>, Good Compounding Practices. The intent of Chapter <797> as written in the introduction is "to prevent harm and fatality to patients that could result from microbial contamination (nonsterility), excessive bacterial endotoxins, large content errors in strength of correct ingredients, and incorrect ingredients in CSPs." It is important to realize that this chapter applies to all healthcare settings where sterile preparations are compounded. The introduction also provides the definition of a CSP (compounded sterile preparation). According to Chapter <797>, a CSP is a dosage unit with any of the following characteristics:

- Preparations prepared according to manufacturer's labeled instructions
- Preparations containing nonsterile ingredients or employing nonsterile components and devices that must be sterilized before administration
- Biologics, diagnostics, drugs, nutrients, and radiopharmaceuticals that possess either of the above two characteristics and which include, but are not limited to, baths and soaks for live organs and tissues, implants, inhalations, injections, powder for injection, irrigations, metered sprays and ophthalmic and otic preparations

The introduction to Chapter <797> also discusses the three risk level classifications for CSPs, based on the potential for microbial, chemical and physical contamination (including low, medium and high-risk level compounding conditions).

Responsibility of Compounding Personnel

This section of the chapter details the responsibility of personnel involved in compounding sterile preparations. It states that "compounding personnel are responsible for ensuring that CSPs are accurately identified, measured, diluted and mixed, and are correctly purified, sterilized, packaged, sealed, labeled, stored, dispensed, and distributed." These performance responsibilities include maintaining appropriate cleanliness conditions and providing labeling and supplementary instructions for the proper clinical administration of CSPs. It further discusses the responsibilities of the compounding supervisor to ensure:

a. Personnel are adequately educated, instructed, and skilled to perform their functions
b. Ingredients have correct identity, quality, amount
c. Open/partial containers are properly stored
d. Bacterial endotoxins are minimized
e. Proper and adequate sterilization is used
f. Equipment is clean, accurate, and appropriate
g. Potential harm from added substances is evaluated prior to dispensing

h. Packaging is appropriate for sterility and stability

i. Compounding environment maintains the sterility of presterilized items

j. Labels are appropriate and complete

k. Beyond-use dates are appropriate and based on valid scientific criteria

l. Correct compounding procedures are used

m. Deficiencies in compounding can be rapidly identified and corrected

n. Compounding is separate from quality evaluation

Microbial Contamination Risk Levels

This section defines the three different microbial contamination risk levels. It is important to realize that the determination of compounding risk levels is the responsibility of the compounder. The chapter was written in the broadest terms using general descriptive states; therefore, no single "iron-clad" determination of risk exists with respect to practice settings or compounding procedures. Risk level classification in <797> is, in general, not prescriptive, with one exception: *CSPs prepared from bulk, nonsterile components will always be a high-risk level procedure*. Ultimately, assigning the appropriate risk level to a CSP requires the professional judgment of the pharmacist. Microbial contamination risk levels are defined as follows:

Low-Risk Level

- CSPs compounded from sterile commercial drugs using commercial sterile devices
- Compounding occurs in ISO Class 5 (formerly known as Class 100) environment at all times
- Compounding procedures involves only a few closed-system basic, simple aseptic transfers and manipulations
- Routine disinfection and air quality testing to maintain ISO Class 5 occurs
- There is adequate personnel garb for sterile preparation
- A review for correct identity and amounts of components occurs before and after compounding
- There is a final visual inspection of each sterile preparation
- Annual media-fill test procedure for each person who compounds is performed to validate proper aseptic technique

Medium-Risk Level

- Involves using multiple pooled sterile commercial products for multiple patients or one patient multiple times (batched antibiotics or other small volume parenterals)
- Involves complex aseptic manipulations (TPN or other multiple-ingredient CSPs)
- Compounding occurs over a prolonged period of time (complex procedures)
- No bacteriostatic agents are added to the preparation and it is administered over several days (chemotherapy or pain management administered via infusion device)
- Quality assurance procedures include all steps for low-risk level
- Requires more challenging annual media-fill evaluation of compounding personnel technique that simulates the most challenging or stressful conditions

High-Risk Level

- Prepared from non-sterile ingredients
- Preparation from sterile ingredients but exposed to less than ISO Class 5
- More than 6-hour delay from compounding to sterilization
- Purity of components is assumed but not verified by documentation
- Quality assurance procedures include all steps for low-risk level
- Requires a semiannual media-fill evaluation of compounding personnel technique that simulates the most challenging or stressful conditions using dry nonsterile media verification of compounding personnel technique
- Requires simulation of each high-risk level compounding sterilization process using dry nonsterile media verification

Verification of Compounding Accuracy and Sterilization

The quality (sterility and accuracy) of the CSP is directly related to ensuring that methods used to compound the sterile preparation achieve the desired goal of purity, potency and sterility. CSPs that require some form of terminal sterilization, either by filtration, steam or ionizing radiation have to be validated to ensure that each CSP is void of microbial contamination. There must be proof that the CSP is accurate and sterile.

Personnel Training and Evaluation in Aseptic Manipulation Skills

It is important to realize that many pharmacists and technicians have little or no didactic training in the area of sterile compounding. This section of the chapter requires that all personnel be properly trained by the following means:

- Prior to commencing any compounding, perform thorough didactic instruction in the theory and practice of sterile preparations, with evaluation of technique annually (for low- and medium-risk level) and semiannually (for high-risk level)
- Compounder evaluations should include a formal written exam and practical evaluation of aseptic technique using growth media (media fills)

Environmental Quality and Control

This section of the chapter specifies in great detail the physical plant and environmental requirements for each of the CSP risk levels. These requirements include:

- The need for laminar airflow workbenches (LAFW) and cleanrooms or barrier isolators
- The compounding area must be separated from the general pharmacy and must be a controlled (particle, temperature, humidity) environment.
- Must have an ISO Class 5 (formerly Class 100) environment for critical area where CSP is exposed to air in physical environment
- Must have an ISO Class 8 (formerly Class 100,000) environment for buffer zone or cleanroom (the terms cleanroom and buffer zone are interchangeable)
- There must be detailed cleaning and sanitizing procedures in order to maintain the cleanliness of the compounding environment.
- Compounding personnel must be properly garbed according to the risk level of compounding.
- There must be written, properly-approved policies and procedures for the activities that occur in the compounding environment.
- Environmental monitoring must be routinely performed in order to prove that the compounding environment is properly maintained. There must be documentation to prove control.

Processing

This section calls for a written employee-training and evaluation program specific to preparation of the CSP in each healthcare setting to ensure that compounding personnel are knowledgeable and properly trained. As discussed previously in this guide, training is the cornerstone of ensuring quality and safety of CSPs.

Verification of Automated Compounding Devices (ACDs) for Parenteral Nutrition Compounding

The complexity in preparing parenteral nutrition can be aided with automated compounding devices. It is important to recognize that in order for these devices to accurately deliver the desired volume of ingredients, users must be adequately trained, and the ACDs must be properly calibrated, setup (correct solution containers hung on the correct solution inlet tubing), verified and maintained. This section of the chapter details suggested procedures on ensuring the accuracy and precision of ACDs.

Finished Preparation Release Checks and Tests

All finished CSPs must be checked by a pharmacist prior to dispensing to ensure that the preparation is sterile and accurate. There are several methods that can be employed to meet this requirement. They include:

- Physical visual inspection for preparation integrity (e.g. absence of cores, other particulate matter, phase changes, and discoloration).
- Verification of compounding accuracy conducted by someone other than the compounder to ensure proper measurement, reconstitution, and component usage.
- High-Risk Level CSPs in groups of >25 must be tested according to USP Chapter <71> Sterility Test and <85> Bacterial Endotoxin test.
- Low- and Medium-Risk Level CSPs that exceed the USP chapter guidelines for beyond-use dating (formerly referred to as expiration dating) must be tested according to USP Chapter <71>.

Storage and Beyond-Use Dating

In many healthcare settings, CSPs are often prepared in anticipation of use and as such may be stored for extended periods of time. This section of the chapter focuses on the microbiological limits of CSPs based on risk level and duration of storage. When a CSP is stored for a prolonged period of time prior to use, there is potential for microbial growth and pyrogen formation. As mentioned earlier in the discussion guide, two components—chemical stability and microbial sterility—are described.

- Microbiological limits based on risk level (See Table 2)
- Chemical stability limits obtained from literature or testing using validated equipment (e.g. HPLC, TLC and Flame Spectrophotometry)
- USP Chapter <795> provides guidance for instances where bulk nonsterile components do not have expiration dates.
- Solids and nonaqueous liquids—25% of the remaining expiration period or 6 months (whichever is less)
- USP bulk nonsterile components (Alum)—no more than (NMT) 6 months.
- Aqueous formulations—14 days refrigerated
- All Others—NMT 30 days or intended duration of therapy

Maintaining Product Quality and Control After the CSP Leaves the Pharmacy

Pharmacists are responsible for ensuring that CSP quality and integrity are maintained during transit and regardless of physical location within the health system (hospital, home or ambulatory infusion center). This responsibility includes the use of appropriate packaging (coolers, wet ice blocks, dry ice) that is capable of maintaining proper temperature and conditions (refrigerated or frozen state) during shipment via common carrier (FedEx, UPS, or USPS). Quality control responsibilities during transit also include the delivery of CSPs within a healthcare organization via courier or pneumatic tube system. Specific considerations in the following subsections are also covered:

- Packaging, Handling and Transport
- Use and Storage
- Administration
- Redispensed CSPs
- Education and Training
- Packing CSPs for Transit
- Storage in Locations Outside CSP Facilities

Patient or Caregiver Training

It is crucial that the patient or caregiver (e.g. nurse, physician, spouse, and parent) clearly understands how to store, administer and dispose of the CSP at all times. A formal training program is required to ensure that all persons involved in the handling and use of the CSP are knowledgeable and properly trained.

Patient Monitoring and Adverse Events Reporting

A key component in the pharmaceutical care delivery model is monitoring the patient's response (appropriate and adverse) to therapy. This section focuses on ensuring that patients are clinically monitored when receiving CSPs. Also required is the provision of an effective feedback mechanism for patients and caregivers to report concerns regarding CSPs or administration devices. Review and evaluation of adverse event reports can serve as a quality indicator to improve patient care.

Quality Assurance Program

Many of the elements of USP Chapter <797> focus on formalizing the policies, processes and procedures used in preparing CSPs. One element of quality that may not be routinely performed in pharmacies is documentation, or written "proof" that compounding personnel are trained, equipment is being maintained and calibrated routinely, the compounding environment is being properly maintained and tested, and CSPs are prepared using the correct components in the correct ratios/volumes. The essence of quality assurance is proving that you are really doing what you say you are doing.

References

1. National Coordinating Committee on Large Volume Parenterals. Recommended methods for compounding intravenous admixture in hospitals. *Am J Hosp Pharm.* 1975; 32:261–70.
2. National Coordinating Committee on Large Volume Parenterals. Recommended system for surveillance and reporting of problems with large volume parenterals in hospitals. *Am J Hosp Pharm.* 1975; 34: 1251–3.
3. National Coordinating Committee on Large Volume Parenterals. Recommendations for the labeling of large volume parenterals. *Am J Hosp Pharm.* 1978; 35:49–51.
4. National Coordinating Committee on Large Volume Parenterals. Recommended procedures for in-use testing of large volume parenterals suspected or of producing reactions in a patient. *Am J Hosp Pharm.* 1978; 35:678–82.
5. National Coordinating Committee on Large Volume Parenterals. Recommended guidelines for quality assurance in hospital centralized admixtures in hospitals. *Am J Hosp Pharm.* 1980; 37:645–55.
6. National Coordinating Committee on Large Volume Parenterals. Recommended standard of practice, policies and procedures for intravenous therapy. *Am J Hosp Pharm.* 1980; 37:660–3.
7. Barker KN, ed. Recommendations of the NCCLVP for the compounding and administration of intravenous solutions. Bethesda, MD. American Society of Hospital Pharmacists; 1981.
8. Anon. Pharmacopeial Forum, Vol. 18, Number 2, Mar–Apr 1992, pages 3053.
9. The United States Pharmacopeia, 23rd rev., and the National Formulary 19th ed. USP General Information Chapter <1206>. Sterile Drug Products for Home Use. Rockville, MD: The United States Pharmacopeial Convention, 1995.
10. American Society of Health-System Pharmacists. ASHP Technical Assistance Bulletin on Quality Assurance for Pharmacy-Prepared Sterile Products. *Am J Hosp Pharm.* 1993; 50:2386–98.
11. Santell JP, Kamalich RF. National survey of quality assurance activities for pharmacy-prepared sterile products in hospitals and home infusion facilities—1995. *Am J Health-Syst Pharm.* 1996; 53:2591–605.
12. Myers CE. Needed: Serious attention to sterile products. *Am J Health Syst Pharm* 1996; 53:2582.
13. Morris AM, Schneider PJ, Pedersen CA et al. National survey of quality assurance activities for pharmacy-compounded sterile preparations. *Am J Health-Syst Pharm.* 2003; 60:2567–76.
14. US Pharmacopeial Convention, Inc. General Notices. United States Pharmacopeia 27/National Formulary 22. Rockville, MD: US Pharmacopeial Convention, Inc; 2004, p. 4.
15. Solomon SL, Khabbaz RF, Parker RH, et al. An outbreak of Candida parapsilosis bloodstream infections in patients receiving parenteral nutrition. *J Infect Dis* 1984; 149:98–102.
16. Hughes CF, Grant AF, Leckie BD, et al. Cardioplegia solution: A contamination crisis. *J Thorac Cardiovasc Surg* 1986; 91:296–302.
17. Associated Press. Pittsburgh woman loses eye to tainted drug; 12 hurt. *Baltimore Sun.* November 9, 1990:3A.
18. Dugleaux G, Coutour XL, Hecquard C, et al. Septicemia caused by contaminated parenteral nutrition pouches: The refrigerator as an unusual cause. *J Parenter Enteral Nutr* 1991; 15:474–475.
19. Perrin J. Unsafe activities of compounding pharmacists. *Am J Health-Syst Pharm* 1995;52:2827–2828.
20. Pierce LR, Gaines A, Varricchio R, et al. Hemolysis and renal failure associated with use of sterile water for injection to dilute 25% human albumin solution. *Am J Health-Syst Pharm* 1998;55:1057–1070.
21. Food and Drug Administration. Hazards of precipitation with parenteral nutrition. *Am J Health-Syst Pharm* 1994; 51:427–428.
22. Hallissy E, Russell S. Who's Mixing Your Drugs? Bad medicine: Pharmacy mix-ups a recipe for misery; Some Drugstores operate with very little oversight. San Francisco Chronicle, June 23, 2002.
23. North Carolina Department of Health and Human Services. Painkiller suspected in fourth N.C. meningitis case. www.dhhs.state.nc.us/pressrel/10-18-02.htm (Accessed 2002 Nov 22).
24. Centers for Disease Control and Prevention. *Exophiala* infection from contaminated injectable steroids prepared by a compounding pharmacy—United States, July–November 2002. www.cdc.gov/mmwr/preview/mmwrhtml/mm5149a1.htm (Accessed 2003 Jan 8).
25. US Food and Drug Administration Website. Report: Limited FDA Survey of Compounded Drugs. Available online at: http://www.fda.gov/cder/pharmcomp/survey.htm. Accessed on January 3, 2004.
26. United States Department of Justice, Federal Bureau of Investigation Website, April 22, 2002. Available online at: http://kansascity.fbi.gov/kcmostate042202.htm. Accessed on July 6, 2002.
27. Trissel LA. Compounding our problems-again. *Am J Health-Syst Pharm.* 2003; 60:432. Editorial.
28. Selenic D, Dodson DR, Jensen B et al. *Enterobacter cloacae* bloodstream infections in pediatric patients traced to a hospital pharmacy. *Am J Health-Syst Pharm.* 2003; 60:1440–6.
29. Niedowski, E, Bor,J. State to probe Hopkins death: 2-year-old cancer patient died after receiving improper IV mixture. December 20, 2003. Baltimore Sun, Baltimore, MD.
30. Kastango, ES, DeMarco, S. Pharmacy Cleanroom Project Management Considerations: An Experience-Based Perspective. *Int J Pharm Compd.* 2001; 5: 221–225.
31. Flynn, EA, Pearson, RE, Barker, KN. Observational study of accuracy in compounding IV admixtures at five hospitals. *Am J Health-Syst Pharm.* 1997 Apr 15; 54: 904–912.
32. Bond, CA, et. al. Clinical Pharmacy Services, Hospital Pharmacy Staffing, and Medication Errors in the United States Hospitals, *Pharmacotherapy* 22(2): 134–147, 2002.
33. Personal conversation between Ken Baker, Vice President and General Counsel, Pharmacists Mutual, and Eric S. Kastango, Clinical IQ, LLC. January 2004.
34. Rich, DS. NHIA 13th Annual Conference: Sterile Product Preparations: Meeting New USP Guidelines, Regulations and Standards of Practice for Compounding Sterile Preparations. March 2004.
35. Personal correspondence between Loyd Allen, R.Ph., Ph.D., Oklahoma City, Oklahoma and Eric S. Kastango, Clinical IQ, LLC. October, 2003.
36. Barnes BJ, Van Wormer JM. *Process Thinking and the 85:15 Rule Applied to Education.* Available online at: http://www.grandblanc.k12.mi.us/qip/ProcessThinking.htm. Accessed on July 6, 2002.

Additional Resources

Accreditation Commission for Health Care, Inc. (ACHC) www.achc.org

American Society of Clinical Oncology (ASCO.) Criteria for Facilities and Personnel for the Administration of Parenteral Systemic Antineoplastic Therapy. Journal of Clinical Oncology 1997; 15(11): 3416–17.

American Society of Health-System Pharmacists (ASHP). www.ashp.org

Anon. New National Standards on Pharmaceutical Compounding. Infusion. 2003; 10(1):-20-22. (This article includes the full NHIA Position statement on USP <797>)

ASHP Guidelines on Quality Assurance for Pharmacy-Prepared Sterile Products. Am J Health-Syst Pharm. 2000; 57:1150–69.

ASHP Technical Assistance Bulletin on Handling Cytotoxic and Hazardous Drugs. Am J Hosp Pharm 1990; 47:1033–49.

American Society for Parenteral and Enteral Nutrition (ASPEN). Safe Practices for Parenteral Nutrition Formulation. Journal of Parenteral and Enteral Nutrition. 1998 Vol. 22, No. 2.

Bing, C (ed.) Extended Stability for Parenteral Drugs, 2nd ed . Bethesda, MD: American Society of Health-System Pharmacists; 2003.

Buchanan EC, McKinnon BT, Scheckelhoff DJ, Schneider PJ. Principles of Sterile Product Preparation, revised first edition. Bethesda, MD: American Society of Health-System Pharmacists; 2002. (Second edition in production for 2004)

Centers for Disease Control. Guideline for Hand Hygiene in Health-Care Settings. Morbidity and Mortality Weekly Report. October 25, 2002 / Vol. 51 / No. RR-16. http://www.cdc.gov/mmwr/PDF/rr/rr5116.pdf

Community Health Accreditation Program (CHAP): www.chapinc.org

Cooper, JC, Thoma, LA. Screening Extemporaneously compounded intraspinal injections with bacterial endotoxins test. Am J Health-Syst Pharm. 2002; 59:2426–2433.

FDA. Sterile Drug Products Produced by Aseptic Processing—Current Good Manufacturing Practice. DRAFT guidance issued August 2003 for comments, pending final release. http://www.fda.gov/cder/guidance/1874dft.htm

FDA. Sterility Requirement for Aqueous-Based Drug Products for Oral Inhalation — Small Entity Compliance Guide, November 2001. http://www.fda.gov/cder/guidance/4774fnl.pdf

Food and Drug Administration Modernization Act of 1997,£127. Application of Federal Law to Practice of Pharmacy Compounding. http://www.fda.gov/cdrh/modact97.pdf

Joint Commission on Accreditation of Healthcare Organizations (JCAHO): www.jcaho.org

Kastango, ES. USP <797> Gap Analysis Tool. Clinical IQ website: www.clinicaliq.com.

Kastango, ES, DeMarco, S. Pharmacy Cleanroom Project Management Considerations: An Experience-Based Perspective. Int J Pharm Compd. 2001; 5: 221–225.

Kastango, ES, Douglass, K. Improving the Management, Operations and Cost Effectiveness of Sterile-Product Compounding—Improve the ability to predict employee efficiency, cost of service and product wastage while simultaneously improving quality. Int J Pharm Compd. 1999; 3:253–258.

Kastango, ES, Bradshaw, B. Sterile Product Compounding: Developing Quality-Based Standards for Pharmacy Practice. Infusion. 2002; 8: 23–27.

Kastango, ES, Douglass, K. Quality Assurance for Sterile Products. Int J Pharm Compd. 2001; 5: 246–253.

Kastango, ES, Trissel, LA, Bradshaw, B. An Ounce of Prevention: Controlling Hazards in Extemporaneous Compounding Practices. Int J Pharm Compd. 2003; 5: 401–416.

Kastango, ES. Sterile Product Preparation: A Multimedia Learning Tool. Bethesda, MD: American Society of Health-System Pharmacists, 2002. (CD-ROM)

Kastango, ES. Compounding Containment Devices: Buyer Be Aware. Int J Pharm Compd. 2001; 5: 384–388.

Kastango, ES. The Cost of Quality for Sterile Products, Int J Pharm Compd. 2002; 6: 404–407.

Levy L. Get ready for new sterile compounding regulations. Drug Topics 2003; 147:41.

Morris AM, Schneider PJ, Pedersen CA et al. National survey of quality assurance activities for pharmacy-compounded sterile preparations. Am J Health-Syst Pharm. 2003. 60:2567–76.

National Association of Boards of Pharmacy. Model State Pharmacy Practice Act and Model Rules of the National Association of Boards of Pharmacy. Fall 2002. www.nabp.net

NHIA 12th Annual Conference Advanced Specialty Workshop Regulatory Issues Focus: Sterile Product Preparation (2 Tape Set) February 2003—120 minutes (2 cassettes) Speakers: Eric Kastango, RPh, MBA, FASHP and Gloria Lee Wilder, Pharm.D.

NHIA Audio Conference tape from October 22, 2003n"Meeting the Future Challenges in Sterile Product Compounding" Speaker: Eric Kastango, R.Ph., MBA, FASHP.

O'Neal BC, Schneider PJ, Pedersen, et al. Compliance with safe practices for preparing parenteral nutrition solutions. Am J Health-Syst Pharm. 2002; 59:264–9.

OSHA Technical Manual Section VI, Chapter 2. Controlling Occupational Exposure to Hazardous Drugs (HD's). www.osha.gov/dts/osta/otm/otm_vi/otm_vi_2.html

Pharmaceutical Compounding—Sterile Preparations (General Information Chapter 797) in United States Pharmacopeia, 27th rev., and the National Formulary 22nd ed, Rockville, MD: The United States Pharmacopeial Convention; 2003.

Quality Assurance for Pharmacy-Prepared Sterile Products. Videotape & Workbook. Bethesda, MD: American Society of Health-System Pharmacists; 1994.

Safe Handling of Cytotoxic and Hazardous Drugs Videotape. Bethesda, MD: American Society of Health-System Pharmacists; 1990.

Sterile Drug Products for Home Use, Chapter 1206. . USP 24–NF 19. Rockville, MD: USP Convention, Inc.; 1999. p. 2130–43.

Sterility Testing (General Information Chapter 71) in United States Pharmacopeia, 27th rev., and the National Formulary 22nd ed, Rockville, MD: The United States Pharmacopeial Convention; 2003.

Talley RC. Sterile compounding in hospital pharmacies. Am J Health-Syst Pharm. 2003; 60:2563. Editorial.

Tamer HR, Sweet BV. Management Consultation: Compounding pharmaceuticals for investigational use. Am J Health-Syst Pharm. 2002; 59:1716–19.

Thompson CA. News: USP publishes enforceable chapter on sterile compounding. Am J Health-Syst Pharm. 2003; 60:1814–17.

Trissel, LA. Compounding our problems—again. Am J Health-Syst Pharm. 2003; 60:432. Editorial.

Trissel, LA. Handbook on Injectable Drugs, 12th ed. Bethesda, MD: American Society of Health-System Pharmacists; 2003.

Trissel LA, Ogundele AB, Ingram DS, et al. Using a media fill simulation to establish a benchmark microbiological contamination rate for low-risk-level compounding. Am J Health-Syst Pharm. 2003; 60:1853–5.

Trissel's 2 Clinical Pharmaceutics Database: www.trissels.info

United States Pharmacopeia (USP) web site: www.usp.org

Young D. News: Compounding sterile preparations raises informed consent issues. Am J Health-Syst Pharm. 2003; 60:1209–10.

Young D. News: Outsourced compounding can be problematic. Am J Health-Syst Pharm. 2002; 59:2261–4.

Attachment IV

Sterile Compounding Crosswalk: USP 797 vs. California State Law

USP 797 information extracted from both USP Chapter 797 and Appendix 1: Principal Competencies, Conditions, Practices, and Quality Assurances that are Required († "shall") and Recommended (‡ "should") in USP Chapter <797>
California State Law extracted from 2013 California Law Book for Pharmacy

USP 797 Topic	USP 797 Description	California State Law
Compounding Personnel Responsibilities, Training, and Competencies		
Responsibility of Compounding Personnel	† Practices and quality assurances required to prepare, store, and transport CSPs that are sterile, and acceptably accurate, pure, and stable. Compounding personnel are responsible for ensuring that CSPs are accurately identified, measured, diluted, and mixed and are correctly purified, sterilized, packaged, sealed, labeled, stored, dispensed, and distributed. These performance responsibilities include maintaining appropriate cleanliness, conditions and providing labeling and supplementary instructions for the proper clinical administration of CSPs. All personnel who prepare CSPs shall be responsible for understanding these fundamental practices and precautions, for developing and implementing appropriate procedures, and for continually evaluating these procedures and the quality of final CSPs to prevent harm.	**1751. Sterile Injectable Compounding; Compounding Area; Self-Assessment** (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. (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.
Personnel Training and Evaluation in Aseptic Manipulations Skills	† Pass didactic, practical skill assessment and media-fill testing initially, followed by an annual assessment for a low- and medium-risk level compounding and semi-annual assessment for high-risk level compounding.	**Risk Levels are Not Specifically Defined in California State Law** **1735.7. Training of Compounding Staff** (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. **1751.3. Sterile Injectable Policies and Procedures.** (a) Any pharmacy engaged in compounding sterile injectable drug products shall

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		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: (4) Training of staff in the preparation of sterile injectable products. (d) Pharmacies compounding sterile injectable products from one or more non-sterile ingredients must have written policies and procedures that comply with the following: (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. **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. (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

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		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. **1751.7. Sterile Injectable Compounding Quality Assurance and Process Validation.** (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.
	† Compounding personnel who fail written tests, or whose media-fill test vials result in gross microbial colonization, shall be immediately reinstructed and re-evaluated by expert compounding personnel to ensure correction of all aseptic practice deficiencies.	**1735.8. (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. **1751.7. Sterile Injectable Compounding Quality Assurance and Process Validation.** (b) … If microbial growth is detected, then the sterile preparation process must be evaluated, corrective action taken, and the validation process repeated.
PATIENT OR CAREGIVER TRAINING	† Multiple component formal training program to ensure patients and caregivers understand the proper storage, handling, use, and disposal of CSPs.	**State Law only addresses proper use. Storage, handling, and disposal are not addressed in California State Law.** **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.

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Personnel Cleansing And Garbing	† Personnel shall also be thoroughly competent and highly motivated to perform flawless aseptic manipulations with ingredients, devices, and components of CSPs.	**1751.6 Training of Sterile Injectable Compounding Staff, Patient, and Caregiver** (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. (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. (E) Aseptic preparation procedures. (2) Each person assigned to the controlled area must successfully complete practical skills training in aseptic technique and aseptic area practices. **1751.7. Sterile Injectable Compounding Quality Assurance and Process Validation.** (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.
	† Personnel with rashes, sunburn, weeping sores, conjunctivitis, active respiratory infection, and cosmetics are prohibited from preparing CSPs.	**Not Specifically Addressed**
	† Compounding personnel remove personal outer garments; cosmetics; artificial nails; hand, wrist, and body jewelry that can interfere with the fit of gowns and gloves; and visible body piercing above the neck.	**State Law only addresses garbing requirements for sterile preparations made from one or more nonsterile ingredients and cytotoxic agents.**

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		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.
	† Order of compounding garb and cleansing in ante-area: shoes or shoe covers, head and facial hair covers, face mask, fingernail cleansing, hand and forearm washing and drying; non-shedding gown.	**Not Specifically Addressed**
	† Order of cleansing and gloving in buffer room or area: hand cleansing with a persistently active alcohol-based product with persistent activity, allow hands to dry; don sterile gloves.	**Not Specifically Addressed**
	† Routinely disinfect gloves with sterile 70% IPA after contacting nonsterile objects.	**Not Specifically Addressed**
	† Inspect gloves for holes and replace when breaches are detected.	**Not Specifically Addressed**
	† Personnel repeat proper procedures after they are exposed to direct contact contamination or worse than ISO Class 8 air.	**Not Specifically Addressed**
	† These requirements are exempted only for immediate use CSPs and CAIs for which manufacturers provide written documentation based on validated testing that such personnel practices are not required to maintain sterility in CSPs.	**Not Specifically Addressed**
Personnel Training And Competency Evaluation Of Garbing, Aseptic Work Practices And Cleaning/Disinfection Procedures	† Personnel who prepare CSPs shall be trained conscientiously and skillfully by expert personnel, multi-media instructional sources, and professional publications in the theoretical principles and practical skills of garbing procedures, aseptic work practices, achieving and maintaining ISO Class 5 environmental conditions, and cleaning and disinfection procedures.	**1735.7. Training of Compounding Staff** (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. **1751.3. Sterile Injectable Policies and Procedures.** (a) Any pharmacy engaged in compounding sterile injectable drug products shall

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		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: (4) Training of staff in the preparation of sterile injectable products. (d) Pharmacies compounding sterile injectable products from one or more non-sterile ingredients must have written policies and procedures that comply with the following: (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. **1751.6 Training of Sterile Injectable Compounding Staff, Patient, and Caregiver** (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. (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.

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	† This training shall be completed and documented before any compounding personnel begin to prepare CSPs.	**1735.7. Training of Compounding Staff** (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. **1751.6 Training of Sterile Injectable Compounding Staff, Patient, and Caregiver** (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. (e) Pharmacies that compound sterile products from one or more non-sterile ingredients must comply with the following training requirements: (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. **1751.7. Sterile Injectable Compounding Quality Assurance and Process Validation.** (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.
	† Compounding personnel shall complete didactic training, pass written competence assessments, undergo skill assessment using observational audit tools, and media-fill testing.	**1751.6 Training of Sterile Injectable Compounding Staff, Patient, and Caregiver** (e) Pharmacies that compound sterile products from one or more non-sterile ingredients must comply with the following training requirements: (2) Each person assigned to the controlled area must successfully

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		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. **1751.7. Sterile Injectable Compounding Quality Assurance and Process Validation.** (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.
	† Media-fill testing of aseptic work skills shall be performed initially before beginning to prepare CSPs and at least annually thereafter for low- and medium-risk level compounding; and semiannually for high-risk level compounding.	**1751.6 Training of Sterile Injectable Compounding Staff, Patient, and Caregiver** (e) Pharmacies that compound sterile products from one or more non-sterile ingredients must comply with the following training requirements: (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. **1751.7. Sterile Injectable Compounding Quality Assurance and Process Validation.** (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,

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		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.
	† Compounding personnel who fail written tests, observational audits, or whose media-fill test vials have one or more units showing visible microbial contamination, shall be reinstructed and re-evaluated by expert compounding personnel to ensure correction of all aseptic work practice deficiencies.	**1751.7. Sterile Injectable Compounding Quality Assurance and Process Validation.** (b) … If microbial growth is detected, then the sterile preparation process must be evaluated, corrective action taken, and the validation process repeated.
	† Compounding personnel shall pass all evaluations prior to resuming compounding of sterile preparations.	**1751.6 Training of Sterile Injectable Compounding Staff, Patient, and Caregiver** (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. **1751.7. Sterile Injectable Compounding Quality Assurance and Process Validation.** (b) … If microbial growth is detected, then the sterile preparation process must be evaluated, corrective action taken, and the validation process repeated.
	† Compounding personnel must demonstrate proficiency of proper hand hygiene, garbing, and consistent cleaning procedures in addition to didactic evaluation and aseptic media fill.	**1751.6 Training of Sterile Injectable Compounding Staff, Patient, and Caregiver** (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: (D) Quality assurance 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. (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.

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	† Cleaning and disinfecting procedures performed by other support personnel shall be thoroughly trained in proper hand hygiene, and garbing, cleaning, and disinfection procedures by a qualified aseptic compounding expert. "In the event that cleaning and disinfecting procedures are also performed by other support personnel e.g. institutional environmental services, housekeeping), thorough training of proper hand hygiene, garbing, and cleaning and disinfection procedures shall be done by a qualified aseptic compounding expert. After completion of training, support personnel shall routinely undergo performance evaluation of proper hand hygiene, garbing, and all applicable cleaning and disinfecting procedures conducted by a qualified aseptic compounding expert."	**1751.6 Training of Sterile Injectable Compounding Staff, Patient, and Caregiver** (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: (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.
	† Support personnel shall routinely undergo performance evaluation of proper hand hygiene, garbing, and all applicable cleaning and disinfecting procedures conducted by a qualified aseptic compounding expert.	**1751.6 Training of Sterile Injectable Compounding Staff, Patient, and Caregiver** (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.
Competency Evaluation of Garbing and Aseptic Work Practices	† Compounding personnel shall be evaluated initially prior to beginning compounding CSPs and whenever an aseptic media fill is performed using a Sample Form for Assessing Hand Hygiene and Garbing Related Practices of Compounding Personnel and the personnel glove fingertip sampling procedures	**Not Specifically Addressed**
Aseptic Work Practice Assessment and Evaluation via Personnel Glove Fingertip Sampling	† Monitoring of compounding personnel glove finger tips shall be performed for all CSP risk level compounding.	**Not Specifically Addressed**
	† Glove fingertip sampling shall be used to evaluate the competency of personnel in performing hand hygiene and garbing procedures in addition to educating compounding personnel on proper work practices.	**Not Specifically Addressed**
	† All personnel shall demonstrate competency in proper hand hygiene and garbing procedures in addition to aseptic work practices.	**Not Specifically Addressed**
	† Sterile contact agar plates shall be used to sample the gloved fingertips of compounding personnel after garbing to assess garbing competency and after completing the media-fill preparation.	**Not Specifically Addressed**
	† Gloves shall not be disinfected with sterile 70% IPA immediately prior to sampling.	**Not Specifically Addressed**
Garbing and Gloving Competency Evaluation	† Compounding personnel shall be visually observed during the process of performing hand hygiene and garbing procedures.	**Not Specifically Addressed**

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	† The visual observation shall be documented on a Sample Form for Assessing Hand Hygiene and Garbing Related Practices of Compounding Personnel and maintained to provide a permanent record of and long-term assessment of personnel competency.	**Not Specifically Addressed**
Gloved Fingertip Sampling	† Immediately after the compounder completes the hand hygiene and garbing procedure, the evaluator shall collect a gloved fingertip and thumb sample from both hands of the compounder onto appropriate agar plates by lightly pressing each fingertip into the agar.	**Not Specifically Addressed**
	† The plates shall be incubated for the appropriate incubation period and at the appropriate temperature.	**Not Specifically Addressed**
	† All employees shall successfully complete an initial competency evaluation and gloved fingertip/thumb sampling procedure (0 cfu) no less than three times before initially being allowed to compound CSPs for human use.	**Not Specifically Addressed**
	† After completing the initial gowning and gloving competency evaluation, re-evaluation of all compounding personnel shall occur at least annually for low- and medium-risk level CSPs and semiannually for high-risk level CSPs before being allowed to continue compounding CSPs.	**1751.6 Training of Sterile Injectable Compounding Staff, Patient, and Caregiver** (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.
	† Gloves shall not be disinfected with sterile 70% IPA prior to testing.	**Not Specifically Addressed**
	† The sampled gloves shall be immediately discarded and proper hand hygiene performed after sampling. The nutrient agar plates shall be incubated as stated below.	**Not Specifically Addressed**
	† The cfu action level for gloved hands shall be based on the total number of cfu on both gloves and not per hand.	**Not Specifically Addressed**
	‡ Results should be reported separately as number of cfu per employee per hand (left hand, right hand).	**Not Specifically Addressed**
Incubation Period (For Gloved Fingertip Sampling)	† At the end of the designated sampling period, the agar plates are recovered, covers secured, inverted and incubated at a temperature and for a time period conducive to multiplication of microorganisms. Trypticase soy agar (TSA) with lecithin and polysorbate 80 shall be incubated at 35° ±2° for 2–3 days.	**Not Specifically Addressed**
Aseptic Manipulation Competency Evaluation	† All compounding personnel shall have their aseptic technique and related practice competency evaluated initially during the media-fill test procedure and subsequent annual or semiannual media-fill test procedures on the Sample Form for Assessing Aseptic Technique and Related Practices of Compounding Personnel.	**1751.6 Training of Sterile Injectable Compounding Staff, Patient, and Caregiver** (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.

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		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.
Media-Fill Test Procedure	† The skill of personnel to aseptically prepare CSPs shall be evaluated using sterile fluid bacterial culture media-fill verification.	**1751.7. Sterile Injectable Compounding Quality Assurance and Process Validation.** (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.
	† Media-filled vials shall be incubated within a range of 35°C ±2° for 14 days.	**Not Specifically Addressed**
Surface Cleaning and Disinfection Sampling and Assessment	† Surface sampling shall be performed in all ISO classified areas on a periodic basis and can be accomplished using contact plates and/or swabs and shall be done at the conclusion of compounding	**Not Specifically Addressed**
	† Locations to be sampled shall be defined in a sample plan or on a form.	**Not Specifically Addressed**
Cleaning and Disinfecting Competency Evaluation .	† Compounding personnel and other personnel responsible for cleaning shall be visually observed during the process of performing cleaning and disinfecting procedures during initial personnel training on cleaning procedures, changes in cleaning staff and at the completion of any Media-Fill Test Procedure.	**Not Specifically Addressed**
	† Visual observation shall be documented on a Sample Form for Assessing Cleaning and Disinfection Procedures and maintained to provide a permanent record of, and long-term assessment of, personnel competency	**Not Specifically Addressed**
Surface Collection Methods	† Immediately after sampling a surface with the contact plate, the sampled area shall be thoroughly wiped with a non-shedding wipe soaked in sterile 70% IPA.	**Not Specifically Addressed**
	‡ Results should be reported as cfu per unit of surface area	**Not Specifically Addressed**

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Action Levels, Documentation, and Data Evaluation	† Environmental sampling data shall be collected and reviewed on a routine basis as a means of evaluating the overall control of the compounding environment.	**Not Specifically Addressed**
	† If an activity consistently shows elevated levels of microbial growth, competent microbiology personnel shall be consulted.	**Not Specifically Addressed**
	† An investigation into the source of the contamination shall be conducted.	**Not Specifically Addressed**
	† When gloved fingertip sample results exceeds action levels after proper incubation, a review of hand hygiene and garbing procedures as well as glove and surface disinfection procedures and work practices shall be performed and documented.	**Not Specifically Addressed**
	‡ Any cfu count that exceeds its respective action level should prompt a re-evaluation of the adequacy of personnel work practices, cleaning procedures, operational procedures, and air filtration efficiency within the aseptic compounding location.	**Not Specifically Addressed**

Compounded Sterile Preparations

CSP Microbial Contamination Risk Levels	† Proper training and evaluation of personnel, proper cleansing and garbing of personnel, proper cleaning and disinfecting of compounding work environments, and proper maintenance and monitoring of controlled environmental locations (all of which are detailed in their respective sections).	**State law only addresses compounds made from one or more nonsterile ingredients and sterile compounds that do not meet these criteria.**
	Low-Risk Level CSPs † Aseptic manipulations within an ISO Class 5 environment using three or fewer sterile products and entries into any container. † In absence of passing sterility test, store not more than 48 hours at controlled room temperature, 14 days at cold temperature, and 45 days in solid frozen state at -25°to -10° or colder. † Media-fill test at least annually by compounding personnel.	**1735. Compounding in Licensed Pharmacies** (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.). **1735.2. Compounding Limitations and Requirements; Self-Assessment** (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. **1751. Sterile Injectable Compounding; Compounding Area; Self-Assessment**
	Low-Risk Level CSPs with 12-Hour or Less BUD † Fully comply with all four specific criteria. ‡ Sinks should not be located adjacent to the ISO Class 5 primary engineering control. ‡ Sinks should be separated from the immediate area of the ISO Class 5 primary engineering control device.	
	Medium-Risk Level CSPs † Aseptic manipulations within an ISO Class 5 environment using prolonged and complex mixing and transfer, more than three sterile products and entries into any container, and pooling ingredients from multiple sterile products to prepare multiple CSPs.	

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	† In absence of passing sterility test, store not more than 30 hours at controlled room temperature, 9 days at cold temperature, and 45 days in solid frozen state at -25°to -10° or colder. † Media-fill test at least annually by compounding personnel.	(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. **1751.6 Training of Sterile Injectable Compounding Staff, Patient, and Caregiver** (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. **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: (4) Written justification of the chosen expiration dates for compounded sterile injectable products.
	High-Risk Level CSPs † Confirmed presence of nonsterile ingredients and devices, or confirmed or suspected exposure of sterile ingredients for more than one hour to air quality inferior to ISO Class 5 before final sterilization. † Sterilization method verified to achieve sterility for the quantity and type of containers. † Meet allowable limits for bacterial endotoxins. † Maintain acceptable strength and purity of ingredients and integrity of containers after sterilization. † In absence of passing sterility test, store not more than 24 hours at controlled room temperature, 3 days at cold temperature, and 45 days in solid frozen state at -25°to -10° or colder. Media-fill test at least semiannually by compounding personnel.	

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Determining Beyond-Use Dates	† Use the general criteria in USP <795> in the absence of direct stability-indicating assays or authoritative literature that supports longer durations.	**1735.2. Compounding Limitations and Requirements; Self-Assessment** (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: (6) Expiration dating requirements. (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. **1751.7. Sterile Injectable Compounding Quality Assurance and Process Validation.** (4) Written justification of the chosen expiration dates for compounded sterile injectable products.
Maintaining Sterility, Purity, and Stability of Dispensed and Distributed CSPs	† Written procedures for proper packaging, storage, and transportation conditions to maintain sterility, quality, purity, and strength of CSPs.	**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. (6) Quality assurance program. (d) Pharmacies compounding sterile injectable products from one or more non-sterile ingredients must have written policies and procedures that comply with the following: (3) Policies and procedures must address at least the following: (B) Storage and handling of products and supplies. (C) Storage and delivery of final products. (D) Process validation. (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. **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:

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		(2) The storage of compounded sterile injectable products in the pharmacy and periodic documentation of refrigerator temperature.
Redispensed CSPs	† When sterility, and acceptable purity, strength, and quality can be ensured.	**Not Specifically Addressed**
	† Assignment of sterility storage times and stability beyond-use dates that occur later than those of originally dispensed CSPs must be based on results of sterility testing and quantitative assay of ingredients.	**Not Specifically Addressed**
Packaging And Transporting CSPs	† Packaging maintains physical integrity, sterility, stability, and purity of CSPs.	**Not Specifically Addressed**
	† Modes of transport that maintain appropriate temperatures and prevent damage to CSPs.	**Not Specifically Addressed**
Immediate Use CSPs	† Fully comply with all six specified criteria. The immediate use provision is intended only for those situations where there is a need for emergency or immediate patient administration of a CSP. Such situations may include cardiopulmonary resuscitation, emergency room treatment, preparation of diagnostic agents, or critical therapy where the preparation of the CSP under conditions described for Low-Risk Level CSPs subjects the patient to additional risk due to delays in therapy. Immediate-use CSPs are not intended for storage for anticipated needs or batch compounding. Preparations that are medium-risk level and high-risk level shall not be prepared as immediate-use CSPs. Immediate-use CSPs are exempt from the requirements described for Low-Risk Level CSPs only when all of the following criteria are met:	**Not Specifically Addressed**
	1. The compounding process involves simple transfer of not more than three commercially manufactured packages of sterile nonhazardous products or diagnostic radiopharmaceutical products from the manufacturers' original containers and not more than two entries into any one container or package (e.g., bag, vial) of sterile infusion solution or administration container/device. For example, anti-neoplastics shall not be prepared as immediate-use CSPs because they are hazardous drugs.	**1735.2. Compounding Limitations and Requirements; Self-Assessment** (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: (3) Process and/or procedure used to prepare the drug. (6) Expiration dating requirements. **1751.4. Facility and Equipment Standards for Sterile Injectable Compounding** (e) Pharmacies preparing parenteral cytotoxic agents shall do so in accordance with Section 41106(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. Certification records must be retained for at least three years.
	2. Unless required for the preparation, the compounding procedure is a continuous process not to exceed 1 hour.	**Not Specifically Addressed**
	3. During preparation, aseptic technique is followed and, if not immediately administered, the finished CSP is under continuous supervision to minimize the potential for contact with non-sterile surfaces, introduction of particulate matter or biological fluids, mix-ups with other CSPs, and direct contact of	**1751.6 Training of Sterile Injectable Compounding Staff, Patient, and Caregiver** (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

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	outside surfaces.	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. **1751.7. Sterile Injectable Compounding Quality Assurance and Process Validation.** (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.
	4. Administration begins not later than 1 hour following the start of the preparation of the CSP.	**Not Specifically Addressed**
	5. Unless immediately and completely administered by the person who prepared it or immediate and complete administration is witnessed by the preparer, the CSP shall bear a label listing patient identification information, the names and amounts of all ingredients, the name or initials of the person who prepared the CSP, and the exact 1-hour BUD and time.	**Not Specifically Addressed**

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	6. If administration has not begun within 1 hour following the start of preparing the CSP, the CSP shall be promptly, properly, and safely discarded.	**<u>**Time Constraints are Not Specifically Addressed</u>** **1735.2. Compounding Limitations and Requirements; Self-Assessment** (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: (5) Post-compounding process or procedures required, if any. (6) Expiration dating requirements. (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. **1751.7. Sterile Injectable Compounding Quality Assurance and Process Validation.** The Quality Assurance Program shall include at least the following: (4) Written justification of the chosen expiration dates for compounded sterile injectable products.
Single-Dose and Multiple-Dose Containers	† Beyond-use date 28 days, unless specified otherwise by the manufacturer, for closure sealed multiple-dose containers after initial opening or entry.	**Not Specifically Addressed**
	† Beyond-use time of 6 hours, unless specified otherwise by the manufacturer, for closure sealed single-dose containers in ISO Class 5 or cleaner air after initial opening or entry.	
	† Beyond-use time of 1 hour for closure sealed single-dose containers after being opened or entered in worse than ISO Class 5 air.	
	† Storage of opened single-dose ampuls is not permitted.	
Hazardous Drugs as CSPs	† Appropriate personnel protective equipment. Appropriate personnel protective equipment (PPE) shall be worn when compounding in a BSC or CACI and when using CSTD devices. PPE should include gowns, face masks, eye protection, hair covers, shoe covers or dedicated shoes, double gloving with sterile chemo-type gloves, and compliance with manufacturers' recommendations when using a CACI	**<u>**State Law only addresses with respect to High Risk CSPs</u>** **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.

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		(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.
	† Appropriate primary engineering controls (BSCs and CACIs) are used for concurrent personnel protection and exposure of critical sites.	**4127.7. Compounding Sterile Injectables from Nonsterile Ingredients; Requirements** On and after July 1, 2005, a pharmacy shall compound sterile injectable products from one or more nonsterile ingredients in one of the following environments: (a) An ISO class 5 laminar airflow hood within an ISO class cleanroom. The cleanroom must have a positive air pressure differential relative to adjacent areas. (b) An ISO class 5 cleanroom. (c) A barrier isolator that provides an ISO class 5 environment for compounding. **1751.3. Sterile Injectable Policies and Procedures.** (3) Policies and procedures must address at least the following: (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 clean rooms, and barrier isolator workstations). **1751.4. Facility and Equipment Standards for Sterile Injectable Compounding** (e) Pharmacies preparing parenteral cytotoxic agents shall do so in accordance with Section 41106(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. Certification records must be retained for at least three years. **505.5.1 Pharmacies: Laminar Flow Biological Safety Cabinet.** In all pharmacies preparing parenteral cytotoxic agents, all compounding shall be conducted within a certified Class II Type A or Class II Type B vertical laminar air flow hood with bag in-bag out design. The pharmacy must ensure that contaminated air plenums that are under positive air pressure are leak tight.
	† Hazardous drugs shall be stored separately from other inventory in a manner to prevent contamination and personnel exposure.	**Not Specifically Addressed**
		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: (5) Procedures for handling cytotoxic agents.
	† At least 0.01 inch water column negative pressure and 12 air changes per hour in non-cleanrooms in which CACIs are located.	**Not Specifically Addressed**

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	† Hazardous drugs shall be handled with caution at all times using appropriate chemotherapy gloves during receiving, distribution, stocking, inventorying, preparing for administration, and disposal.	**Not Specifically Addressed** **1751.2. Sterile Injectable Labeling Requirements.** (d) All cytotoxic agents shall bear a special label which states "Chemotherapy - Dispose of Properly." **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: (5) Procedures for handling cytotoxic agents. (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.
	† Hazardous drugs shall be prepared in an ISO Class 5 environment with protective engineering controls in place, and following aseptic practices specified for the appropriate contamination risk levels.	**No Specific Equivalent addressing risk levels** **4127.7. Compounding Sterile Injectables from Nonsterile Ingredients; Requirements** On and after July 1, 2005, a pharmacy shall compound sterile injectable products from one or more nonsterile ingredients in one of the following environments: (a) An ISO class 5 laminar airflow hood within an ISO class cleanroom. The cleanroom must have a positive air pressure differential relative to adjacent areas. (b) An ISO class 5 cleanroom. (c) A barrier isolator that provides an ISO class 5 environment for compounding. **1751.4. Facility and Equipment Standards for Sterile Injectable Compounding** (e) Pharmacies preparing parenteral cytotoxic agents shall do so in accordance with Section 41106(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. Certification records must be retained for at least three years. **1250.4 Compounding Area for Parenteral Solutions.** The pharmacy shall have a designated area for the preparation of sterile products for dispensing which shall: Any pharmacy that compounds sterile injectable products from one or more nonsterile ingredients must compound the medication in one of the following environments: • 5.1 An ISO class laminar airflow hood within an ISO class 7 cleanroom. The

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		cleanroom must have a positive air pressure differential relative to adjacent areas. • 5.2 An ISO class 5 cleanroom. • 5.3 A barrier isolator that provides an ISO class 5 environment for compounding. **Note**: For additional pharmacy mechanical standard requirements, see Chapter 5, California Mechanical Code. **505.5.1 Pharmacies: Laminar Flow Biological Safety Cabinet.** In all pharmacies preparing parenteral cytotoxic agents, all compounding shall be conducted within a certified Class II Type A or Class II Type B vertical laminar air flow hood with bag in-bag out design. The pharmacy must ensure that contaminated air plenums that are under positive air pressure are leak tight.
	† Access to drug preparation areas shall be limited to authorized personnel.	**Not Specifically Addressed** **1751.3. Sterile Injectable Policies and Procedures.** (d) Pharmacies compounding sterile injectable products from one or more non-sterile ingredients must have written policies and procedures that comply with the following: (3) Policies and procedures must address at least the following: (E) Personnel access and movement of materials into and near the controlled area.
	† A pressure indicator shall be installed that can readily monitor room pressurization, which is documented daily.	**Not Specifically Addressed**
	† Annual documentation of full training of personnel regarding storage, handling, and disposal of hazardous drugs.	**Storage and disposal not specifically addressed** **1751.6 Training of Sterile Injectable Compounding Staff, Patient, and Caregiver** (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.
	† When used, a CSTD shall be used in an ISO Class 5 primary engineering control device.	**Not Specifically Addressed**
	† At least 0.01 inch water column negative pressure is required for compounding of hazardous drugs.	**Not Specifically Addressed**
	‡ Negative-pressure buffer area is not required for low-volume compounding operations when CSTD is used in BSC or CACI.	**Not Specifically Addressed**
	† Compounding personnel of reproductive capability shall confirm in writing that they understand the risks of handling hazardous drugs.	**Not Specifically Addressed**
	† Disposal of all hazardous drug wastes shall comply with all applicable federal and state regulations.	**1751.2.(d)** All cytotoxic agents shall bear a special label which states "Chemotherapy - Dispose of Properly." **1751.3. Sterile Injectable Policies and Procedures.** (c) Pharmacies compounding sterile injectable products shall have written policies and procedures for the disposal of infectious materials and/or materials

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		containing cytotoxic residues. The written policies and procedures shall describe the pharmacy protocols for cleanups and spills in conformity with local health jurisdiction standards.
	‡ Total external exhaust of primary engineering controls.	**Not Specifically Addressed**
	‡ Assay of surface wipe samples every 6 months.	**Not Specifically Addressed**
Radiopharmaceuticals as CSPs	† Positron Emission Tomography is according to USP chapter <823>.	**Radiopharmaceuticals as CSPs are Not Specifically Addressed in Sterile Compounding State Regulations.**
	† Appropriate primary engineering controls and radioactivity containment and shielding.	
	† Radiopharmaceuticals compounded from sterile components, in closed sterile containers, with volume of 100 mL or less for a single dose injection or not more than 30 mL taken from a multiple-dose container shall be designated as and conform to the standards for low-risk level CSPs.	
	† Radiopharmaceutical vials, designed for multi-use, compounded with technetium-99m, exposed to ISO Class 5 environment and punctured by needles with no direct contact contamination may be used up to the time indicated by manufacturers recommendations.	
	† Location of primary engineering controls permitted in ISO Class 8 controlled environment.	
	† Technetium-99m/Molybdenum-99 generators used according to manufacturer, state, and federal requirements.	
	† Radiopharmaceuticals prepared as low-risk level CSPs with 12-hour or less BUD shall be prepared in a segregated compounding area.	
	† Materials and garb exposed in patient-care and treatment area shall not cross a line of demarcation into the segregated compounding area.	
	† Technetium-99m/Molybdenum-99 generators must be eluted in ISO Class 8 conditions.	
	† Segregated compounding area will be designated with a line of demarcation	
	‡ Storage and transport of properly shielded vials of radiopharmaceutical CSPs may occur in a limited access ambient environment without a specific ISO class designation.	
Allergen Extracts as CSPs	† Allergen extracts as CSPs are not subject to the personnel, environmental, and storage requirements for all CSP Microbial Contamination Risk Levels when certain criteria are met.	**Not Specifically Addressed**
Patient Monitoring and Adverse Events Reporting	† Written standard procedures describe means for patients to ask questions and report concerns and adverse events with CSPs, and for compounding supervisors to correct and prevent future problems.	**Not Specifically Addressed**

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	‡ Adverse events and defects with CSPs reported to FDA's MedWatch and USP's MEDMARX programs.	**Not Specifically Addressed**
		1735.5. Compounding Policies and Procedures (c) The policy and procedure manual shall include the following: (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. **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: (3) Actions to be taken in the event of a drug recall.
Quality Assurance		
Verification of Compounding Accuracy and Sterility	† Review labels and document correct measurements, aseptic manipulations, and sterilization procedures to confirm correct identity, purity, and strength of ingredients in, and sterility of, CSPs.	**1735.2. Compounding Limitations and Requirements; Self-Assessment** (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. (i) The pharmacist performing or supervising compounding is responsible for the proper preparation, labeling, storage, and delivery of the compounded drug product.
	‡ Assay finished CSPs to confirm correct identity and, or, strength of ingredients.	1735.8. Compounding Quality Assurance (a) Any pharmacy engaged in compounding shall maintain, as part of its written policies and procedures, a written quality assurance plan designed to monitor and ensure the integrity, potency, quality, and labeled strength of compounded drug 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.
	‡ Sterility test finished CSPs.	**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

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		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. (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. **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: (6) Quality assurance program. (d) Pharmacies compounding sterile injectable products from one or more non-sterile ingredients must have written policies and procedures that comply with the following: (3) Policies and procedures must address at least the following: (J) Sterilization. (K) End-product evaluation and testing.
Sterilization Methods	**Sterilization Methods** † Verify that methods achieve sterility while maintaining appropriate strength, purity, quality, and packaging integrity.	**Not Specifically Addressed**
	‡ Prove effectiveness by USP chapter 71, equivalent, or superior sterility testing.	**Not Specifically Addressed**
Sterilization of High-Risk Level CSPs by Filtration	† Nominal 0.2-µm pore size sterile membranes that are chemically and physically compatible with the CSP.	**Not Specifically Addressed**
	† Complete rapidly without filter replacement.	**Not Specifically Addressed**
	† Subject filter to manufacturers recommended integrity test (e.g., bubble point test) after filtering CSPs.	**Not Specifically Addressed**
Sterilization of High-Risk Level CSPs by Steam	† Test to verify the mass of containers to be sterilized will be sterile after the selected exposure duration in the particular autoclave.	**Not Specifically Addressed**
	† Ensure live steam contacts all ingredients and surfaces to be sterilized.	**Not Specifically Addressed**
	† Pass solutions through a 1.2-µm or smaller nominal pore size filter into final containers to remove particulates before sterilization.	**Not Specifically Addressed**
	† Heated filtered air shall be evenly distributed throughout the chamber by a blower device.	**Not Specifically Addressed**
	† Dry heat shall only be used for those materials that cannot be sterilized by steam, when the moisture would either damage or be impermeable to the materials.	**Not Specifically Addressed**

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	† Sufficient space shall be left between materials to allow for good circulation of the hot air.	**Not Specifically Addressed**
	† The description of dry heat sterilization conditions and duration for specific CSPs shall be included in written documentation in the compounding facility. The effectiveness of dry heat sterilization shall be verified using appropriate biological indicators and other confirmation.	**Not Specifically Addressed**
	‡ The oven should be equipped with a system for controlling temperature and exposure period.	**Not Specifically Addressed**
Depyrogenation by Dry Heat	† Dry heat depyrogenation shall be used to render glassware or containers, such as vials free from pyrogens as well as viable microbes.	**Not Specifically Addressed**
	† The description of the dry heat depyrogenation cycle and duration for specific load items shall be included in written documentation in the compounding facility.	**Not Specifically Addressed**
	† The effectiveness of the dry heat depyrogenation cycle shall be verified using endotoxin challenge vials (ECVs).	**Not Specifically Addressed**
	‡ The bacterial endotoxin test should be performed on the ECVs to verify the cycle is capable of achieving a 3 log reduction in endotoxin.	**Not Specifically Addressed**
FINISHED PREPARATION RELEASE CHECKS AND TESTS		
Inspection of Solution Dosage Forms and Review of Compounding Procedures	† Review procedures and documents to ensure sterility, purity, correct identities and amounts of ingredients, and stability.	**1735.2. Compounding Limitations and Requirements; Self-Assessment** (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. (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. (i) The pharmacist performing or supervising compounding is responsible for the proper preparation, labeling, storage, and delivery of the compounded drug product. **1735.8. Compounding Quality Assurance** (a) Any pharmacy engaged in compounding shall maintain, as part of its written policies and procedures, a written quality assurance plan designed to monitor and ensure the integrity, potency, quality, and labeled strength of compounded drug products. (b) The quality assurance plan shall include written procedures for

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		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. **1751.1. Sterile Injectable Recordkeeping Requirements.** (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: (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. **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.
	† Visually inspect for abnormal particulate matter and color, and intact containers and seals.	**1735.8. Compounding Quality Assurance** (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.
Sterility Testing	† High-risk level CSPs prepared in batches of more than 25 identical containers, or exposed longer than 12 hours at 2°C to 8°C and 6 hours at warmer than 8°C before being sterilized.	**Not Specifically Addressed**
Bacterial Endotoxin (Pyrogen) Testing	† High-risk level CSPs, excluding those for inhalation and ophthalmic administration, prepared in batches of more than 25 identical containers, or exposed longer than 12 hours at 2°C to 8°C and 6 hours at warmer than 8° C before being sterilized.	**Not Specifically Addressed**
Identity and Strength	† Written procedures to verify correct identity, quality, amounts, and	**1735.8. Compounding Quality Assurance**

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Verification of Ingredients	purities of ingredients used in CSPs.	(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. **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.
	†Written procedures to ensure labels of CSPs contain correct names and amounts or concentrations of ingredients, total volumes, beyond-use dates, storage conditions, and route(s) of administration.	**1735.8. Compounding Quality Assurance** (a) Any pharmacy engaged in compounding shall maintain, as part of its written policies and procedures, a written quality assurance plan designed to monitor and ensure the integrity, potency, quality, and labeled strength of compounded drug products. (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. **1735.4. Labeling of Compounded Drug Products** (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

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		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. **1735.5. Compounding Policies and Procedures** (c) The policy and procedure manual shall include the following: (4) Documentation of the methodology used to test integrity, potency, quality, and labeled strength of compounded drug products. **1735.8. Compounding Quality Assurance** (a) Any pharmacy engaged in compounding shall maintain, as part of its written policies and procedures, a written quality assurance plan designed to monitor and ensure the integrity, potency, quality, and labeled strength of compounded drug products. **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: (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." **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.
Environmental Quality and Control		
Exposure of Critical Sites	† ISO Class 5 or better air.	**State Law only addresses ISO Class 5 air for parenteral cytotoxic agents and sterile compounds made from one or more non-sterile ingredients.** **4127.7. Compounding Sterile Injectables from Nonsterile Ingredients; Requirements** On and after July 1, 2005, a pharmacy shall compound sterile injectable products from one or more nonsterile ingredients in one of the following environments: (a) An ISO class 5 laminar airflow hood within an ISO class cleanroom. The

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		cleanroom must have a positive air pressure differential relative to adjacent areas. (b) An ISO class 5 cleanroom. (c) A barrier isolator that provides an ISO class 5 environment for compounding. **1250.4 Compounding Area for Parenteral Solutions.** The pharmacy shall have a designated area for the preparation of sterile products for dispensing which shall: 1. In accordance with Federal Standard 209(b), Clean Room and Work Station Requirements, Controlled Environment, as approved by the Commission, Federal Supply Service, General Services Administration meet standards for class 100 HEPA (high efficiency particulate air) filtered air such as laminar air flow hood or clean room. *Class 100 HEPA filtered air is equivalent to ISO 5 5. Any pharmacy that compounds sterile injectable products from one or more nonsterile ingredients must compound the medication in one of the following environments: • 5.1 An ISO class laminar airflow hood within an ISO class 7 cleanroom. The cleanroom must have a positive air pressure differential relative to adjacent areas. • 5.2 An ISO class 5 cleanroom. • 5.3 A barrier isolator that provides an ISO class 5 environment for compounding. **Note**: For additional pharmacy mechanical standard requirements, see Chapter 5, California Mechanical Code. **505.5.1 Pharmacies: Laminar Flow Biological Safety Cabinet.** In all pharmacies preparing parenteral cytotoxic agents, all compounding shall be conducted within a certified Class II Type A or Class II Type B vertical laminar air flow hood with bag in-bag out design. The pharmacy must ensure that contaminated air plenums that are under positive air pressure are leak tight.
	† Preclude direct contact (e.g., touch and secretions) contamination.	**Not Specifically Addressed**

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ISO Class 5 Air Sources, Buffer Areas, and Ante-Areas	† A buffer area is an area that provides at least ISO Class 7 air quality.	**1250.4 Compounding Area for Parenteral Solutions.** The pharmacy shall have a designated area for the preparation of sterile products for dispensing which shall: 2. In accordance with Federal Standard 209(b), Clean Room and Work Station Requirements, Controlled Environment, as approved by the Commission, Federal Supply Service, General Services Administration meet standards for class 100 HEPA (high efficiency particulate air) filtered air such as laminar air flow hood or clean room. *Class 100 HEPA filtered air is equivalent to ISO 5 6. Any pharmacy that compounds sterile injectable products from one or more nonsterile ingredients must compound the medication in one of the following environments: • 5.1 An ISO class laminar airflow hood within an ISO class 7 cleanroom. The cleanroom must have a positive air pressure differential relative to adjacent areas. • 5.2 An ISO class 5 cleanroom. • 5.3 A barrier isolator that provides an ISO class 5 environment for compounding. **Note**: For additional pharmacy mechanical standard requirements, see Chapter 5, California Mechanical Code. **4127.7. Compounding Sterile Injectables from Nonsterile Ingredients; Requirements** On and after July 1, 2005, a pharmacy shall compound sterile injectable products from one or more nonsterile ingredients in one of the following environments: (a) An ISO class 5 laminar airflow hood within an ISO class cleanroom. The cleanroom must have a positive air pressure differential relative to adjacent areas. (b) An ISO class 5 cleanroom. (c) A barrier isolator that provides an ISO class 5 environment for compounding.
	† New representations of facility layouts.	**Not Specifically Addressed**
	† Each compounding facility shall ensure that each source of ISO Class 5 environment for exposure of critical sites and sterilization by filtration is properly located, operated, maintained, monitored, and verified.	**1735.6. Compounding Facilities and Equipment** (a) Any pharmacy engaged in compounding shall maintain written documentation regarding the facilities and equipment necessary for safe and accurate 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. **1751. Sterile Injectable Compounding; Compounding Area; Self-Assessment**

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		(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 compounding sterile injectable drug products 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. (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. (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. **1751.1. Sterile Injectable Recordkeeping Requirements.** (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: (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). (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. **1751.3. Sterile Injectable Policies and Procedures.** (d) Pharmacies compounding sterile injectable products from one or more non-sterile ingredients must have written policies and procedures that comply with the following: (3) Policies and procedures must address at least the following: (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

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		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. **1751.4. Facility and Equipment Standards for Sterile Injectable Compounding** (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 41106(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 Certification records must be retained for at least three years. **505.5 Pharmacies: Compounding Area for Parenteral Solutions.** The pharmacy shall have a designated area for the preparation of sterile products for dispensing which shall: 1. Be ventilated in a manner not interfering with laminar air flow.
	† Placement of devices (e.g., computers and printers) and objects (e.g., carts and cabinets) can be placed in buffer areas and shall be verified by testing or monitoring.	**Placement of Devices are Not Specifically Addressed** **1250.4 Compounding Area for Parenteral Solutions.** The pharmacy shall have a designated area for the preparation of sterile products for dispensing which shall: 3. The pharmacy shall be arranged in such a manner that the laminar-flow hood is located in an area which is exposed to minimal traffic flow, and is separate from any area used for bulk storage of items not related to the compounding of parenteral solution. There shall be sufficient space, well separated from the laminar-flow hood area, for the storage of bulk materials, equipment and waste materials.
Viable and Nonviable Environmental Sampling (ES) Testing	† Environmental sampling shall occur as part a comprehensive quality management program and shall occur minimally when several conditions exist.	**Not Specifically Addressed**
	‡ The ES program should provide information to staff and leadership to demonstrate that the engineering controls are maintaining an environment within the compounding area that consistently maintains acceptably low viable and nonviable particle levels.	**Not Specifically Addressed**
Environmental Nonviable Particle Testing Program	† Certification and testing of primary (LAFWs, BSCs, CAIs and CACIs) and secondary engineering controls (buffer and ante areas) shall be performed by a qualified individual no less than every six months and whenever the device or room is relocated, altered, or major service to the facility is performed. Certification procedures such as those outlined in the CETA Certification Guide for Sterile	**Not Specifically Addressed**

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	Compounding Facilities (CAG-003-2006) shall be used.	
Total Particle Counts	† Certification that each ISO classified area (e.g., ISO Class 5, 7 and 8) is within established guidelines shall be performed no less than every 6 months and whenever the LAFW, BSC, CAI, or CACI is relocated or the physical structure of the buffer room or ante-area has been altered.	**Not Specifically Addressed**
	† Testing shall be performed by qualified operators using current, state-of-the-art electronic equipment with results meeting ISO Class 5,7, or 8 depending on the requirements of the area.	**Not Specifically Addressed**
	† All certification records shall be maintained and reviewed by supervising personnel or other designated employee to ensure that the controlled environments comply with the proper air cleanliness, room pressures, and air changes per hour.	**Not Specifically Addressed**
Environmental Viable Airborne Particle Testing Program—Sampling Plan	† An appropriate environmental sampling plan shall be developed for airborne viable particles based on a risk assessment of compounding activities performed.	**Not Specifically Addressed**
	† Selected sampling sites shall include locations within each ISO Class 5 environment and in the ISO Class 7 and 8 areas, and the segregated compounding areas at greatest risk of contamination (e.g., work areas near the ISO Class 5 environment, counters near doors, pass-through boxes).	**Not Specifically Addressed**
	† The plan shall include sample location, method of collection, frequency of sampling, volume of air sampled, and time of day as related to activity in the compounding area and action levels.	**Not Specifically Addressed**
	‡ It is recommended that compounding personnel refer to USP Chapter *Microbiological Evaluation of Clean Rooms and Other Controlled Environments* ⍰*1116*⍰⍰and the CDC Guidelines for Environmental Infection Control in Healthcare Facilities-2003 for more information.	**Not Specifically Addressed**
Viable Air Sampling	† Evaluation of airborne microorganisms using volumetric collection methods in the controlled air environments shall be performed by properly trained individuals for all compounding risk levels.	**Not Specifically Addressed**
	† Impaction shall be the preferred method of volumetric air sampling.	**Not Specifically Addressed**
	† For low-, medium-, and high-risk level compounding, air sampling shall be performed at locations that are prone to contamination during compounding activities and during other activities like staging, labeling, gowning, and cleaning.	**Not Specifically Addressed**
	† Locations shall include zones of air backwash turbulence within laminar airflow workbench and other areas where air backwash turbulence may enter the compounding area.	**Not Specifically Addressed**
	† For low-risk level CSPs with 12-hour or less BUD, air sampling shall be performed at locations inside the ISO Class 5 environment and other areas that are in close proximity to the ISO class 5 environment, during the certification of the primary engineering control.	**Not Specifically Addressed**
	‡ Consideration should be given to the overall effect the chosen sampling method will have on the unidirectional airflow within a	**Not Specifically Addressed**

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	compounding environment.	
Air Sampling Devices	† The instructions in the manufacturer's user manual for verification and use of electric air samplers that actively collect volumes of air for evaluation shall be followed.	**Not Specifically Addressed**
	† A sufficient volume of air (400–1000 liters) shall be tested at each location in order to maximize sensitivity.	**Not Specifically Addressed**
	‡ It is recommended that compounding personnel also refer to USP Chapter <1116> that can provide more information on the use of volumetric air samplers and volume of air that should be sampled to detect environmental bioburden excursions.	**Not Specifically Addressed**
Air Sampling Frequency and Process	† Air sampling shall be performed at least semiannually (i.e. every 6 months), as part of the re-certification of facilities and equipment for area where primary engineering controls are located.	**Not Specifically Addressed**
	† A sufficient volume of air shall be sampled and the manufacturer's guidelines for use of the electronic air sampling equipment followed.	**Not Specifically Addressed**
	‡ Any facility construction or equipment servicing may require the need to perform air sampling during these events.	**Not Specifically Addressed**
	† The microbial growth media plates used to collect environmental sampling are recovered, covers secured (e.g., taped), inverted, and incubated at a temperature and for a time period conducive to multiplication of microorganisms.	**Not Specifically Addressed**
	† The number of discrete colonies of microorganisms shall be counted and reported as colony-forming units (cfu) and documented on an environmental monitoring form. Counts from air monitoring need to be transformed into cfu/cubic meter of air and evaluated for adverse trends.	**Not Specifically Addressed**
	‡ TSA should be incubated at 35°±2° for 2–3 days.	**Not Specifically Addressed**
	‡ MEA or other suitable fungal media should be incubated at 28°±2° for 5–7	**Not Specifically Addressed**
Pressure Differential Monitoring	† A pressure gauge or velocity meter shall be installed to monitor the pressure differential or airflow between the buffer area and ante area and the ante-area and the general environment outside the compounding area.	**Not Specifically Addressed**
	† The results shall be reviewed and documented on a log at least every work shift (minimum frequency shall be at least daily) or by a continuous recording device.	**Not Specifically Addressed**
	† The pressure between the ISO Class 7 and general pharmacy area shall not be less than 5 Pa (0.02 inch water column (w.c.).	**Not Specifically Addressed**
	† In facilities where low- and medium-risk level CSPs are prepared, differential airflow shall maintain a minimum velocity of 0.2 meter/second (40 fpm) between buffer area and ante-area.	**Not Specifically Addressed**
Growth Media	† A general microbiological growth medium such as Soybean–Casein Digest Medium (also known as trypticase soy broth (TSB) or agar (TSA)) shall be used to support the growth of bacteria.	**Not Specifically Addressed**

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	† Malt extract agar (MEA) or some other media that supports the growth of fungi shall be used in high-risk level compounding environments.	**Not Specifically Addressed**
	† Media used for surface sampling shall be supplemented with additives to neutralize the effects of disinfecting agents (e.g., TSA with lecithin and polysorbate 80).	**Not Specifically Addressed**
Incubation Period (For Environmental Sampling)	**Incubation Period** † The microbial growth media plates used to collect environmental sampling are recovered, covers secured (e.g., taped), inverted, and incubated at a temperature and for a time period conducive to multiplication of microorganisms.	**Not Specifically Addressed**
	† The number of discrete colonies of microorganisms shall be counted and reported as colony-forming units (cfu) and documented on an environmental monitoring form. Counts from air monitoring need to be transformed into cfu/cubic meter of air and evaluated for adverse trends.	**Not Specifically Addressed**
	‡ TSA should be incubated at 35°±2° for 2–3 days.	**Not Specifically Addressed**
	‡ MEA or other suitable fungal media should be incubated at 28°±2° for 5–7 days.	**Not Specifically Addressed**
Action Levels, Documentation and Data Evaluation	† Sampling data shall be collected and reviewed on a periodic basis as a means of evaluating the overall control of the compounding environment.	**Not Specifically Addressed**
	† Competent microbiology personnel shall be consulted if an environmental sampling consistently shows elevated levels of microbial growth.	**Not Specifically Addressed**
	† An investigation into the source of the environmental contamination shall be conducted.	**Not Specifically Addressed**
	‡ Any cfu count that exceeds its respective action level should prompt a re-evaluation of the adequacy of personnel work practices, cleaning procedures, operational procedures, and air filtration efficiency within the aseptic compounding location.	**Not Specifically Addressed**
	‡ Table titled, Recommended Action Levels for Microbial Contamination should only be used as a guideline	**Not Specifically Addressed**
Facility Design and Environmental Controls	† Compounding facilities are physically designed and environmentally controlled to minimize airborne contamination from contacting critical sites.	**1735.6. Compounding Facilities and Equipment** (a) Any pharmacy engaged in compounding shall maintain written documentation regarding the facilities and equipment necessary for safe and accurate 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.

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		1751. Sterile Injectable Compounding; Compounding Area; Self-Assessment (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 compounding sterile injectable drug products 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. (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. (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. **1751.1. Sterile Injectable Recordkeeping Requirements.** (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: (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). (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 **1751.3. Sterile Injectable Policies and Procedures.** (3) Policies and procedures must address at least the following: (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). **1751.4. Facility and Equipment Standards for Sterile Injectable Compounding** (c) All equipment used in the designated area or cleanroom must be made of a material that can be easily cleaned and disinfected.

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		(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. **1250.4 Compounding Area for Parenteral Solutions.** The pharmacy shall have a designated area for the preparation of sterile products for dispensing which shall: 1 In accordance with Federal Standard 209(b), Clean Room and Work Station Requirements, Controlled Environment, as approved by the Commission, Federal Supply Service, General Services Administration meet standards for class 100 HEPA (high efficiency particulate air) filtered air such as laminar air flow hood or clean room. 2 Have non-porous and cleanable surfaces, walls, floors and floor coverings. 3 The pharmacy shall be arranged in such a manner that the laminar-flow hood is located in an area which is exposed to minimal traffic flow, and is separate from any area used for bulk storage of items not related to the compounding of parenteral solution. There shall be sufficient space, well separated from the laminar-flow hood area, for the storage of bulk materials, equipment and waste materials. 5 Any pharmacy that compounds sterile injectable products from one or more nonsterile ingredients must compound the medication in one of the following environments: • An ISO class laminar airflow hood within an ISO class 7 cleanroom. The cleanroom must have a positive air pressure differential relative to adjacent areas. • 5.2 An ISO class 5 cleanroom. • 5.3 A barrier isolator that provides an ISO class 5 environment for compounding. **Note**: For additional pharmacy mechanical standard requirements, see Chapter 5, California Mechanical Code. **505.5 Pharmacies: Compounding Area for Parenteral Solutions.** The pharmacy shall have a designated area for the preparation of sterile products for dispensing which shall: 1. Be ventilated in a manner not interfering with laminar air flow.
	† Compounding facilities shall provide a comfortable and well-lighted working environment, which typically includes a temperature of 20° or cooler to maintain comfortable conditions for compounding personnel when attired in the required aseptic compounding garb.	**Not Specifically Addressed**
	† Primary engineering controls provide unidirectional (i.e., laminar) HEPA air at a velocity sufficient to prevent airborne particles from contacting critical sites.	**1751.3. Sterile Injectable Policies and Procedures.** (d) Pharmacies compounding sterile injectable products from one or more non-sterile ingredients must have written policies and procedures that comply with the following: (3) Policies and procedures must address at least the following: (F) Use and maintenance of environmental control devices used to create the critical area for manipulation of sterile products (e.g., laminar-airflow

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		workstations, biological safety cabinets, class 100 cleanrooms, and barrier isolator workstations). **1250.4 Compounding Area for Parenteral Solutions.** The pharmacy shall have a designated area for the preparation of sterile products for dispensing which shall: 1 In accordance with Federal Standard 209(b), Clean Room and Work Station Requirements, Controlled Environment, as approved by the Commission, Federal Supply Service, General Services Administration meet standards for class 100 HEPA (high efficiency particulate air) filtered air such as laminar air flow hood or clean room. 5 Any pharmacy that compounds sterile injectable products from one or more nonsterile ingredients must compound the medication in one of the following environments: • 5.1 An ISO class laminar airflow hood within an ISO class 7 cleanroom. The cleanroom must have a positive air pressure differential relative to adjacent areas. • 5.2 An ISO class 5 cleanroom. • 5.3 A barrier isolator that provides an ISO class 5 environment for compounding. **Note**: For additional pharmacy mechanical standard requirements, see Chapter 5, California Mechanical Code.
	† In situ air pattern analysis via smoke studies shall be conducted at the critical area to demonstrate unidirectional airflow and sweeping action over and away from the product under dynamic conditions.	**Not Specifically Addressed**
	† Policies and procedures for maintaining and working within the primary engineering control area shall be written and followed. The policies and procedures will be determined by the scope and risk levels of the aseptic compounding activities used during the preparation of the CSPs.	**State Law only addresses sterile compounds made from one or more non-sterile ingredients. Other risk levels are not specifically addressed.** **1751.3. Sterile Injectable Policies and Procedures.** (d) Pharmacies compounding sterile injectable products from one or more non-sterile ingredients must have written policies and procedures that comply with the following: (3) Policies and procedures must address at least the following: (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). **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

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		specifications. The Quality Assurance Program shall include at least the following: (1) Cleaning and sanitization of the parenteral medication preparation area
	† The principles of HEPA-filtered unidirectional airflow in the work environment shall be understood and practiced in the compounding process in order to achieve the desired environmental conditions.	**1250.4 Compounding Area for Parenteral Solutions.** The pharmacy shall have a designated area for the preparation of sterile products for dispensing which shall: 1 In accordance with Federal Standard 209(b), Clean Room and Work Station Requirements, Controlled Environment, as approved by the Commission, Federal Supply Service, General Services Administration meet standards for class 100 HEPA (high efficiency particulate air) filtered air such as laminar air flow hood or clean room. 3 The pharmacy shall be arranged in such a manner that the laminar-flow hood is located in an area which is exposed to minimal traffic flow, and is separate from any area used for bulk storage of items not related to the compounding of parenteral solution. There shall be sufficient space, well separated from the laminar-flow hood area, for the storage of bulk materials, equipment and waste materials.
	† Clean rooms for nonhazardous and nonradioactive CSPs are supplied with HEPA that enters from ceilings with return vents low on walls, and provide not less than 30 air changes per hour.	**Not Specifically Addressed**
	† Buffer areas maintain 0.02- to 0.05-inch water column positive pressure, and do not contain sinks or drains.	**Not Specifically Addressed**
	† Air velocity from buffer rooms or zones to ante-areas is at least 40 feet/minute.	**Not Specifically Addressed**
	† The primary engineering controls shall be placed within a buffer area in such a manner as to avoid conditions that could adversely affect their operation.	**1250.4 Compounding Area for Parenteral Solutions.** The pharmacy shall have a designated area for the preparation of sterile products for dispensing which shall: 1 In accordance with Federal Standard 209(b), Clean Room and Work Station Requirements, Controlled Environment, as approved by the Commission, Federal Supply Service, General Services Administration meet standards for class 100 HEPA (high efficiency particulate air) filtered air such as laminar air flow hood or clean room. 3 The pharmacy shall be arranged in such a manner that the laminar-flow hood is located in an area which is exposed to minimal traffic flow, and is separate from any area used for bulk storage of items not related to the compounding of parenteral solution. There shall be sufficient space, well separated from the laminar-flow hood area, for the storage of bulk materials, equipment and waste materials.
	† The primary engineering controls shall be placed out of the traffic flow and in a manner to avoid disruption from the HVAC system and room cross-drafts.	**State law does not address HVAC system and room cross-drafts** **1250.4 Compounding Area for Parenteral Solutions.** The pharmacy shall have a designated area for the preparation of sterile products for dispensing which shall: 1. In accordance with Federal Standard 209(b), Clean Room and Work Station Requirements, Controlled Environment, as approved by the Commission, Federal Supply Service, General Services Administration meet standards for class 100 HEPA (high efficiency particulate air) filtered air such as laminar air flow hood or clean room.

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		3. The pharmacy shall be arranged in such a manner that the laminar-flow hood is located in an area which is exposed to minimal traffic flow, and is separate from any area used for bulk storage of items not related to the compounding of parenteral solution. There shall be sufficient space, well separated from the laminar-flow hood area, for the storage of bulk materials, equipment and waste materials.
	† HEPA-filtered supply air shall be introduced at the ceiling.	**Not Specifically Addressed**
	† All HEPA filters shall be efficiency tested using the most penetrating particle size and shall be leak tested at the factory and then leak tested again in situ after installation.	**Not Specifically Addressed**
	† Activities and tasks carried out within the buffer area shall be limited to only those necessary when working within a controlled environment.	**1751.3. Sterile Injectable Policies and Procedures.** (3) Policies and procedures must address at least the following: (E) Personnel access and movement of materials into and near the controlled area.
	† Only the furniture, equipment, supplies, and other material required for the compounding activities to be performed shall be brought into the room.	**1751.3. Sterile Injectable Policies and Procedures.** (3) Policies and procedures must address at least the following: (E) Personnel access and movement of materials into and near the controlled area.
	† Surfaces and essential furniture in buffer rooms or zones and clean rooms shall be nonporous, smooth, nonshedding, impermeable, cleanable, and resistant to disinfectants.	**1751.4. Facility and Equipment Standards for Sterile Injectable Compounding** (c) All equipment used in the designated area or cleanroom must be made of a material that can be easily cleaned and disinfected. **1250.4 Compounding Area for Parenteral Solutions.** The pharmacy shall have a designated area for the preparation of sterile products for dispensing which shall: 2 Have non-porous and cleanable surfaces, walls, floors and floor coverings.
	† The surfaces of ceilings, walls, floors, fixtures, shelving, counters, and cabinets in the buffer area shall be smooth, impervious, free from cracks and crevices, and nonshedding, thereby promoting cleanability and minimizing spaces in which microorganisms and other contaminants may accumulate.	**1751.4. Facility and Equipment Standards for Sterile Injectable Compounding** (c) All equipment used in the designated area or cleanroom must be made of a material that can be easily cleaned and disinfected. **1250.4 Compounding Area for Parenteral Solutions.** The pharmacy shall have a designated area for the preparation of sterile products for dispensing which shall: 2. Have non-porous and cleanable surfaces, walls, floors and floor coverings.
	† The surfaces shall be resistant to damage by disinfectant agents.	**1751.4. Facility and Equipment Standards for Sterile Injectable Compounding** (c) All equipment used in the designated area or cleanroom must be made of a material that can be easily cleaned and disinfected. **1250.4 Compounding Area for Parenteral Solutions.** The pharmacy shall have a designated area for the preparation of sterile products for dispensing which shall: 2 Have non-porous and cleanable surfaces, walls, floors and floor coverings.
	† Junctures of ceilings to walls shall be coved or caulked to avoid cracks and crevices where dirt can accumulate.	**Not Specifically Addressed**
	† Ceiling tiles shall be caulked around each perimeter to seal them to the support frame.	**Not Specifically Addressed**
	† The exterior lens surface of ceiling lighting fixtures shall be smooth, mounted flush, and sealed.	**Not Specifically Addressed**

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	† Any other penetrations through the ceiling or walls shall be sealed.	**Not Specifically Addressed**
	† The buffer area shall not contain sources of water (sinks) or floor drains. Work surfaces shall be constructed of smooth, impervious materials, such as stainless steel or molded plastic, so that they are easily cleaned and disinfected.	**Not Specifically Addressed**
	† Carts shall be of stainless steel wire, nonporous plastic, or sheet metal construction with good quality, cleanable casters to promote mobility.	**Not Specifically Addressed**
	† Storage shelving, counters, and cabinets shall be smooth, impervious, free from cracks and crevices, nonshedding, cleanable, and disinfectable.	**1751.4. Facility and Equipment Standards for Sterile Injectable Compounding** (c) All equipment used in the designated area or cleanroom must be made of a material that can be easily cleaned and disinfected. **1250.4 Compounding Area for Parenteral Solutions.** The pharmacy shall have a designated area for the preparation of sterile products for dispensing which shall: 2 Have non-porous and cleanable surfaces, walls, floors and floor coverings.
	† Their number, design, and manner of installation the items above shall promote effective cleaning and disinfection.	**Not Specifically Addressed**
	‡ If ceilings consist of inlaid panels, the panels should be impregnated with a polymer to render them impervious and hydrophobic.	**Not Specifically Addressed**
	‡ Dust-collecting overhangs, such as ceiling utility pipes, or ledges, such as windowsills, should be avoided.	**Not Specifically Addressed**
	‡ Air returns should be mounted low on the wall creating a general top-down dilution of room air with HEPA-filtered make-up air.	**Not Specifically Addressed**
Placement Of Primary Engineering Controls Within ISO Class 7 Buffer Areas	† Primary engineering controls for nonhazardous and nonradioactive CSPs are located in buffer areas, except for CAIs that are proven to maintain ISO Class 5 air when particle counts are sampled 6 to 12 inches upstream of critical site exposure areas during performance of normal inward and outward transfer of materials, and compounding manipulations when such CAIs are located in air quality worse than ISO Class 7.	**Not Specifically Addressed**
	† Presterilization procedures for high-risk level CSPs, such as weighing and mixing, shall be completed in no worse than an ISO Class 8 environment.	**Not Specifically Addressed**
	† Primary engineering controls shall be located out of traffic patterns and away from room air currents that could disrupt the intended airflow patterns.	**1250.4 Compounding Area for Parenteral Solutions.** The pharmacy shall have a designated area for the preparation of sterile products for dispensing which shall: 1 In accordance with Federal Standard 209(b), Clean Room and Work Station Requirements, Controlled Environment, as approved by the Commission, Federal Supply Service, General Services Administration meet standards for class 100 HEPA (high efficiency particulate air) filtered air such as laminar air flow hood or clean room. 3 The pharmacy shall be arranged in such a manner that the laminar-flow hood is located in an area which is exposed to minimal traffic flow, and is separate

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		from any area used for bulk storage of items not related to the compounding of parenteral solution. There shall be sufficient space, well separated from the laminar-flow hood area, for the storage of bulk materials, equipment and waste materials.
	† When isolators are used for sterile compounding, the recovery time to achieve ISO Class 5 air quality shall be documented and internal procedures developed to ensure that adequate recovery time is allowed after material transfer before and during compounding operations.	**Not Specifically Addressed**
	† When compounding activities require the manipulation of a patient's blood-derived or other biological material (e.g., radiolabeling a patients or a donors white blood cells), the manipulations shall be clearly separated from routine material-handling procedures and equipment used in CSP preparation activities, and they shall be controlled by specific standard operating procedures in order to avoid any cross-contamination.	**Not Specifically Addressed**
	† Food, drinks, and items exposed in patient care areas, and unpacking of bulk supplies and personnel cleansing and garbing are prohibited from buffer areas or rooms.	**Not Specifically Addressed**
	† Demarcation designation between buffer areas or rooms and ante-areas.	**Not Specifically Addressed**
	† Antiseptic hand cleansing and sterile gloves in buffer areas or rooms.	**Not Specifically Addressed**
	‡ Packaged compounding supplies and components, such as needles, syringes, tubing sets, and small- and large-volume parenterals, should be uncartoned and wiped down with a disinfectant that does not leave a residue (e.g., sterile 70% IPA) when possible in an ante-area, of ISO Class 8 air quality, before being passed into the buffer areas.	**Not Specifically Addressed**
Cleaning and Disinfecting the Sterile Compounding Areas	† Trained personnel write detailed procedures including cleansers, disinfectants, and non-shedding wipe and mop materials.	**1735.5. Compounding Policies and Procedures** (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. (c) The policy and procedure manual shall include the following: (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. **1751.3. Sterile Injectable Policies and Procedures.** (3) Policies and procedures must address at least the following: (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.
	† Cleaning and disinfecting surfaces in the LAFWs, BSCs, CAIs, and CACIs shall be cleaned and disinfected frequently including at the beginning of	**Not Specifically Addressed**

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	each work shift, before each batch preparation is started, every 30 minutes during continuous compounding periods of individual CSPs, when there are spills, and when surface contamination is known or suspected from procedural breaches.	
	† Trained compounding personnel are responsible for developing, implementing, and practicing the procedures for cleaning and disinfecting the DCAs written in the SOPs.	**1735.5. Compounding Policies and Procedures** (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.
	† Cleaning and disinfecting shall occur before compounding is performed. Items shall be removed from all areas to be cleaned and surfaces shall be cleaned by removing loose material and residue from spills, e.g., water-soluble solid residues are removed with Sterile Water (for Injection or Irrigation) and low-shedding wipes. This shall be followed by wiping with a residue-free disinfecting agent, such as sterile 70% IPA, which is allowed to dry before compounding begins.	**Not Specifically Addressed**
	† Work surfaces in ISO Class 7 and 8 areas and segregated compounding areas are cleaned at least daily.	**Not Specifically Addressed**
	† Dust and debris shall be removed when necessary from storage sites for compounding ingredients and supplies, using a method that does not degrade the ISO Class 7 or 8 air quality.	**Not Specifically Addressed**
	† Floors in ISO Class 7 and 8 areas are cleaned daily when no compounding occurs.	**State law requires weekly disinfection of floors, while USP 797 requires daily.**
		1751.4. Facility and Equipment Standards for Sterile Injectable Compounding (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.
	† IPA (70% isopropyl alcohol) remains on surfaces to be disinfected for at least 30 seconds before such are used to prepare CSPs.	**Not Specifically Addressed**
	† Emptied shelving, walls, and ceilings in ante-areas are cleaned and disinfected at least monthly.	**Difference in disinfecting schedules between USP797 and State Law**
		1751.4. Facility and Equipment Standards for Sterile Injectable Compounding (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.
	† Mopping shall be performed by trained personnel using approved agents and procedures described in the written SOPs.	**Not Specifically Addressed**
	† Cleaning and disinfecting agents, their schedules of use and methods of application shall be in accordance with written SOPs and followed by custodial and/or compounding personnel.	**1735.5. Compounding Policies and Procedures** (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. (c) The policy and procedure manual shall include the following: (3) The procedures for maintaining, storing, calibrating, cleaning, and disinfecting equipment used in compounding, and for training on these procedures

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		as part of the staff training and competency evaluation process. **1751.3. Sterile Injectable Policies and Procedures.** (3) Policies and procedures must address at least the following: (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. **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.
	† All cleaning materials, such as wipers, sponges, and mops, shall be nonshedding, preferably composed of synthetic micro fibers, and dedicated to use in the buffer area, or ante-area, and segregated compounding areas and shall not be removed from these areas except for disposal.	**Not Specifically Addressed**
	† If cleaning materials are reused (e.g., mops), procedures shall be developed (based on manufacturer recommendations) that ensure that the effectiveness of the cleaning device is maintained and repeated use does not add to the bioburden of the area being cleaned.	**Not Specifically Addressed**
	† Supplies and equipment removed from shipping cartons shall be wiped with a suitable disinfecting agent (e.g., sterile 70% IPA) delivered from a spray bottle or other suitable delivery method.	**Not Specifically Addressed**
	† After the disinfectant is sprayed or wiped on a surface to be disinfected, the disinfectant shall be allowed to dry, and during this time the item shall not be used for compounding purposes.	**Not Specifically Addressed**
	† Sterile 70% IPA wetted gauze pads or other particle-generating material shall not be used to disinfect the sterile entry points of packages and devices.	**Not Specifically Addressed**
Standard Operating Procedures		
Suggested Standard Operating Procedures	† All facilities are required to have these, and they must include at least the items enumerated in this section. The Compounding Facility shall have written, properly approved SOPs designed to ensure the quality of the environment in which a CSP is prepared. The following procedures are recommended:	**1735.5. Compounding Policies and Procedures** (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

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		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. **1735.8. Compounding Quality Assurance** (a) Any pharmacy engaged in compounding shall maintain, as part of its written policies and procedures, a written quality assurance plan designed to monitor and ensure the integrity, potency, quality, and labeled strength of compounded drug products. **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

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		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. **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.
	1. Access to the buffer area is restricted to qualified personnel with specific responsibilities or assigned tasks in the compounding area.	**1751.3. Sterile Injectable Policies and Procedures.** (3) Policies and procedures must address at least the following: (E) Personnel access and movement of materials into and near the controlled area.
	2. All cartoned supplies are decontaminated in the area by removing them from shipping cartons and wiping or spraying them with a nonresidue-generating disinfecting agent while	**1751.3. Sterile Injectable Policies and Procedures.** (3) Policies and procedures must address at least the following: (H) Disposal of packaging materials, used syringes, containers, and needles

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	they are being transferred to a clean and properly disinfected cart or other conveyance for introduction into the buffer area. Manufacturer's directions or published data for minimum contact time will be followed/ Individual pouched sterile supplies need not be wiped because the pouches can be removed as these sterile supplies are introduced into the buffer area.	to enhance sanitation and avoid accumulation in the controlled area.
	3. Supplies that are required frequently or otherwise needed close at hand but not necessarily needed for the scheduled operations of the shift are decontaminated and stored on shelving in the ante-area.	**Not Specifically Addressed**
	4. Carts used to bring supplies from the storeroom cannot be rolled beyond the demarcation line in the ante-area, and carts used in the buffer area cannot be rolled outward beyond the demarcation line unless cleaned and disinfected before returning.	**Not Specifically Addressed**
	5. Generally, supplies required for the scheduled operations of the shift are wiped down with an appropriate disinfecting agent and brought in the buffer area, preferably on one or more movable carts. Supplies that are required for back-up for general support of operations may be stored on the designated shelving in the buffer area, but excessive amounts of supplies are to be avoided.	**1250.4 Compounding Area for Parenteral Solutions.** The pharmacy shall have a designated area for the preparation of sterile products for dispensing which shall: 3. The pharmacy shall be arranged in such a manner that the laminar-flow hood is located in an area which is exposed to minimal traffic flow, and is separate from any area used for bulk storage of items not related to the compounding of parenteral solution. There shall be sufficient space, well separated from the laminar-flow hood area, for the storage of bulk materials, equipment and waste materials.
	6. Nonessential objects that shed particles shall not be brought into the buffer area, including pencils, cardboard cartons, paper towels, and cotton items (e.g., gauze pads).	**Not Specifically Addressed**
	7. Essential paper-related products (e.g. paper syringe overwraps, work records contained a protective sleeve) shall be wiped down with an appropriate disinfecting agent prior to being brought into the buffer area.	**State Law Addresses Equipment but Makes No Specific Mention of Essential Paper-related Products.**
	8. Traffic flow in and out of the buffer area shall be minimized.	**1751.3. Sterile Injectable Policies and Procedures.** (3) Policies and procedures must address at least the following: (E) Personnel access and movement of materials into and near the controlled area.
	9. Personnel preparing to enter the buffer area shall remove all personal outer garments, cosmetics "(because they shed flakes and particles), and all hand, wrist, and other visible jewelry or piercings that can interfere with the effectiveness of PPE.	**State Law Only Addresses Garbing Requirements for Sterile Preparations Made from One or More Non-sterile Ingredients and Cytotoxic agents.**
	10. Personnel entering the ante-area shall don attire described in *Personnel Cleansing and Garbing and Personnel Training and Competency Evaluation of Garbing, Aseptic Work Practices and Cleaning/Disinfection Procedures.*	**1751.4. Facility and Equipment Standards for Sterile Injectable Compounding** (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.
	11. Personnel shall then thoroughly wash hands and forearms to	**Not Specifically Addressed**

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	the elbow with soap and water for at least 30 seconds. An air dryer or disposable nonshedding towels are used to dry hands and forearms after washing.	
	12. Personnel entering the buffer area shall perform antiseptic hand cleansing prior to donning sterile gloves using waterless alcohol-based surgical hand scrub with persistent activity.	**Not Specifically Addressed**
	13. Chewing gum, drinks, candy, or food items shall not be brought into the buffer area or ante-area. Materials exposed in patient care and treatment areas shall never be introduced into areas where components and ingredients for CSPs are present.	**Not Specifically Addressed**
	14. At the beginning of each compounding activity session, and whenever liquids are spilled, the surfaces of the direct compounding environment are first cleaned with USP Purified Water to remove water-soluble residues. Immediately thereafter, the same surfaces are disinfected with a nonresidue-generating agent using a nonlinting wipe.	**Not Specifically Addressed**
	15. Primary engineering controls shall be operated continuously during compounding activity. When the blower is turned off and before other personnel enter to perform compounding activities, only one person shall enter the buffer area for the purposes of turning on the blower (for at least 20 minutes) and disinfecting the work surfaces.	**Not Specifically Addressed**
	16. Traffic in the area of the DCA is minimized and controlled.	**1751.3. Sterile Injectable Policies and Procedures.** (3) Policies and procedures must address at least the following: (E) Personnel access and movement of materials into and near the controlled area.
	17. Supplies used in the DCA for the planned procedures are accumulated and then decontaminated by wiping or spraying the outer surface with sterile 70% IPA or removing the outer wrap at the edge of the DCA as the item is introduced into the aseptic work area.	**Not Specifically Addressed**
	18. All supply items are arranged in the DCA so as to reduce clutter and provide maximum efficiency and order for the flow of work.	**Not Specifically Addressed**
	19. After proper introduction into the DCA of supply items required for and limited to the assigned operations, they are so arranged that a clear, uninterrupted path of HEPA-filtered air will bathe all critical sites at all times during the planned procedures. That is, no objects may be placed between the first air from HEPA filters and an exposed critical site.	**Not Specifically Addressed**
	20. All procedures are performed in a manner designed to minimize the risk of touch contamination. Gloves are disinfected with adequate frequency with an approved disinfectant such as sterile 70% IPA.	**Not Specifically Addressed**
	21. All rubber stoppers of vials and bottles and the necks of ampuls are disinfected by wiping with sterile 70% IPA and	**Not Specifically Addressed**

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	waiting for at least 10 seconds before they are used to prepare CSPs.	
	22. After the preparation of every CSP, the contents of the container are thoroughly mixed and then inspected for the presence of particulate matter, evidence of incompatibility, or other defects.	**1735.2. Compounding Limitations and Requirements; Self-Assessment** (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: (4) Quality reviews required at each step in preparation of the drug. (5) Post-compounding process or procedures required, if any. (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. **1735.8. Compounding Quality Assurance** (a) Any pharmacy engaged in compounding shall maintain, as part of its written policies and procedures, a written quality assurance plan designed to monitor and ensure the integrity, potency, quality, and labeled strength of compounded drug 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. **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.
	23. After procedures are completed, used syringes, bottles, vials and other supplies are removed, but with a minimum of exit and reentry into the DCA so as to minimize the risk of introducing contamination into the aseptic workspace.	**State law addresses disposal of equipment and materials but makes no mention of minimum of exit and reentry into the DCA**

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