

Board of Pharmacy Proposed Language

To Amend Section 1735.1 of 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.

To Amend Section 1735.2 of 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 United States Pharmacopeia Standards 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 Product – 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.



COMPOUNDING SELF-ASSESSMENT

The California Code of Regulations section 1735.2 requires the pharmacist-in-charge of each pharmacy licensed under section 4037 or 4029 of the Business and Professions Code that compounds drug products to complete a self-assessment of the pharmacy's compliance with federal and state pharmacy law. **The assessment shall be performed before July 1 of every odd-numbered year.** The pharmacist-in-charge must also complete a self-assessment within 30 days whenever; (1) a new pharmacy permit has been issued, or (2) there is a change in the pharmacist-in-charge; or (3) there is a change in the licensed location of the pharmacy. The primary purpose of the self-assessment is to promote compliance through self-examination and education.

The self-assessment must be completed in entirety and may be completed online, printed and retained in the pharmacy. Do not copy a previous assessment.

Each self-assessment must be kept on file in the pharmacy for three years after it is performed.

Pharmacy Name: _____

Address: _____ Phone: _____

Ownership: Sole Owner Partnership Corporation LLC
 Non-Licensed Owner Other (please specify) _____

Permit #: _____ Exp. Date: _____ Other Permit #: _____ Exp. Date: _____

Licensed Sterile Compounding Permit # _____ Expiration: _____

or Accredited by: _____ From: _____ To: _____

DEA Registration #: _____ Exp. Date: _____ Date of DEA Inventory: _____

Hours: *Daily* _____ *Sat* _____ *Sun.* _____ *24 Hours* _____

PIC: _____ RPH # _____ Exp. Date: _____

Pharmacy Staff (pharmacists, intern pharmacists, pharmacy technicians assigned to compounding duties):
(Please use an additional sheet if necessary)

- 2. _____ RPH # _____ Exp. Date: _____
- 3. _____ RPH # _____ Exp. Date: _____
- 4. _____ RPH # _____ Exp. Date: _____
- 5. _____ RPH # _____ Exp. Date: _____
- 6. _____ RPH # _____ Exp. Date: _____
- 7. _____ INT # _____ Exp. Date: _____
- 8. _____ INT # _____ Exp. Date: _____
- 9. _____ INT # _____ Exp. Date: _____
- 10. _____ TCH # _____ Exp. Date: _____
- 11. _____ TCH # _____ Exp. Date: _____
- 12. _____ TCH # _____ Exp. Date: _____
- 13. _____ TCH # _____ Exp. Date: _____
- 14. _____ TCH # _____ Exp. Date: _____
- 15. _____ TCH # _____ Exp. Date: _____
- 16. _____ TCH # _____ Exp. Date: _____

COMPOUNDING SELF-ASSESSMENT

All references to the California Code of Regulations (CCR) are to Title 16 unless otherwise noted.

Please mark the appropriate box for each question. If "NO", enter an explanation on "CORRECTIVE ACTION OR ACTION PLAN" lines at the end of the section. If more space is needed, you may add additional sheets.

ALL COMPOUNDING Complete Sections 1 through 8.

1. Definitions (CCR 1735 and 1735.1)

Yes No N/A

1.1. The pharmacy compounds prescriptions as defined in CCR 1735.

1.2. The compounding pharmacist understands the definitions of [equipment](#), integrity, potency, quality and strength as defined in CCR 1735.1.

2. Compounded Limitations and Requirements (CCR 1735.2)

The pharmacy does not compound drug product prior to receipt of a valid prescription unless under the following conditions. (CCR 1735.2[a])

Yes No N/A

2.1. The pharmacy prepares and stores a limited quantity of a compounded drug product in advance of receipt of a patient specific prescription solely in such quantity as is necessary to ensure continuity of care of an identified patient population as defined. (CCR 1735.2[b])

2.2. The pharmacy compounds a reasonable quantity of drug product that is furnished to a prescriber for office use upon prescriber order as allowed in CCR 1735.2 (c) that:

2.2.1. Is sufficient for administration or application to patients in the prescriber's office or for distribution of not more than a 72-hour supply, (CCR 1735.2[c][1])

2.2.2. Is reasonable considering the intended use of the compounded medication and the nature of the prescriber's practice, (CCR 1735.2[c][2]) AND

2.2.3. Is an amount, which the pharmacy is capable of compounding in compliance with pharmaceutical standards for integrity, potency, quality and strength for any individual prescriber or for all prescribers taken as a whole. (CCR 1735.2[c][3])

2.3. The pharmacy does not compound medication until it has prepared a written master formula that includes the following elements (CCR 1735.2[d][1-6]):

2.3.1. Active ingredients used.

[2.3.2. Equipment to be used.](#)

[2.3.3. Expiration dating requirements.](#)

~~2.3.2.~~ [4.](#) Inactive ingredients used.

~~2.3.3.~~ [5.](#) Process and/or procedure used to prepare the drug.

~~2.3.4.~~ [6.](#) Quality reviews required at each step in the preparation of the drug.

~~2.3.5.~~ [7.](#) Post-compounding process or procedures if required.

~~□ 2.3.6. Expiration dating requirements.~~

Yes No N/A

2.4. The master formula for a drug product that is not routinely compounded by the pharmacy is recorded on the prescription document itself. (CCR 1735.2 [e])

2.5. All chemicals, bulk drug substances, drug products and other components for compounding are stored and used according to compendia and other applicable requirements to maintain their integrity, potency, quality and labeled strength. (CCR 1735.2 [g])

2.6. Compounded drug products are 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. The "beyond use date" of the compounded drug product does 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 may be used if it is deemed appropriate in the professional judgment of the responsible pharmacist. (CCR 1735.2[h])

CORRECTIVE ACTION OR ACTION PLAN: _____

3. Records of Compounded Drug Products (CCR 1735.3)

Yes No N/A

3.1. A record for each compounded drug product includes the following (CCR 1735.3[a][1-10]):

3.1.1. The master formula record.

3.1.2. The date the drug product was compounded.

3.1.3. The identity of the pharmacy personnel who compounded the drug product.

3.1.4. The identity of the pharmacist reviewing the final drug product.

3.1.5. The quantity of each component used in compounding the drug product.

3.1.6. The manufacturer or supplier, expiration date and lot number of each component.

Exempt from this requirement are sterile drug products compounded on a one-time basis for administration within ~~twenty-four hours~~ seventy-two (72) hours and stored in accordance with United States Pharmacopeia Standards to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

~~□ 3.1.7. The equipment used in compounding the drug product.~~

3.1.~~8.~~ 7. The pharmacy assigned reference or lot number for the compounded drug product.

3.1.~~9.~~ 8. The expiration date of the final compounded drug product.

3.1.~~10.~~ 9. The quantity or amount of drug product compounded.

3.2. The pharmacy maintains records of the proper acquisition, storage, and destruction of chemicals, bulk drug substances, drug products and components used in compounding. (CCR 1735.3 [b])

3.3. Chemicals, bulk drug substances, drug products, and components used to compound drug products are obtained from reliable suppliers. (CCR 1735.3 [c])

Yes No N/A

3.4. The pharmacy acquires and retains any available certificates of purity or analysis for chemicals, bulk drug substances, drug products and components used in compounding. (This is not a requirement for drug products approved by the FDA.) (CCR 1735.3 [c])

3.5. The pharmacy maintains and retains all records required in the pharmacy in a readily retrievable form for at least three years (CCR 1735.3 [d]).

4. **Labeling of Compounded Drug Products (CCR 1735.4)**

Yes No N/A

4.1. The label of the compounded drug product contains the generic name(s) of the principle active ingredient(s). (CCR 1735.4[a])

4.2. The prescription label contains all the information required in B&PC 4076 and is formatted in accordance with CCR 1707.5. (CCR 1735.4[a])

4.3. If requested by the patient, the prescription label is printed in 12-point typeface. (CCR 1707.5[a])

4.4. The pharmacy is exempt from the prescription label requirements in CCR 1707.5. (B&PC 4076.5[d])

Exemption approved by the board from: _____ to: _____

4.5. The container or receipt contains a statement that the drug has been compounded by the pharmacy. (CCR 1735.4[b])

4.6. Drug products compounded into unit-dose containers that are too small or otherwise impractical for full compliance with the requirements of [a] and [b] are 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. (CCR 1735.4[c])

CORRECTIVE ACTION OR ACTION PLAN: _____

5. **Compounding Policies and Procedures (CCR 1735.5)**

Yes No N/A

5.1. The pharmacy maintains a written policy and procedure manual for compounding that establishes the following (CCR 1735.5 [a]):

5.1.1. Procurement procedures.

5.1.2. Methodologies for the formulation and compounding of drugs.

5.1.3. Facilities and equipment cleaning, maintenance and operations.

5.1.4. Other standard operating procedures related to compounding.

5.2. The policy and procedure manual is reviewed on an annual basis by the pharmacist-in-charge and is updated whenever changes in process are implemented. (CCR 1735.5 [b])

Yes No N/A

- 5.3. The policy and procedure manual includes procedures for notifying staff assigned to compounding duties of any changes in process or to the policy and procedure manual. (CCR 1735.5[c][1])
- 5.4. The manual includes 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. (CCR 1735.5[c][2])
- 5.5. The manual includes procedures for maintaining, storing, calibrating, cleaning and disinfecting equipment used in compounding and for training on these procedures. (CCR 1735.5[c][3])
- 5.6. The manual includes documentation on the methodology used to test integrity, potency, quality and labeled strength of compounded drug products. (CCR 1735.5[c][4])
- 5.7. The manual includes documentation of the methodology used to determine appropriate expiration dates for compounded drug products. (CCR 1735.5[c][5])

CORRECTIVE ACTION OR ACTION PLAN: _____

6. Compounding Facilities and Equipment (CCR 1735.6)

Yes No N/A

- 6.1. The pharmacy maintains written documentation regarding the facilities and equipment necessary for safe and accurate compounded drug products to include records of certification of facilities or equipment, if applicable. (CCR 1735.6[a])
- 6.2. All equipment used to compound drug products is stored, used and maintained in accordance with manufacturers' specifications. (CCR 1735.6[b])
- 6.3. All equipment used to compound drug products is calibrated prior to use to ensure accuracy. (CCR 1735.6[c])
- 6.4. Documentation of each calibration is recorded in writing and maintained and retained in the pharmacy. (CCR 1735.6[c])

CORRECTIVE ACTION OR ACTION PLAN: _____

7. Training of Compounding Staff (CCR 1735.7)

Yes No N/A

- 7.1. The pharmacy maintains written documentation sufficient to demonstrate that pharmacy personnel have the skills and training required to properly and accurately perform assigned responsibilities relating to compounding. (CCR 1735.7[a])
- 7.2. The pharmacy develops and maintains an on-going competency evaluation process for pharmacy personnel involved in compounding. (CCR 1735.7[b])

Yes No N/A

7.3. Documentation on any and all such training for pharmacy personnel is maintained. (CCR 1735.7[b])

7.4. Pharmacy personnel assigned to compounding duties demonstrate knowledge about processes and procedures used in compounding prior to compounding any drug product. (CCR 1735.7[c])

CORRECTIVE ACTION OR ACTION PLAN: _____

8. Compounding Quality Assurance (CCR 1735.8)

Yes No N/A

8.1. The pharmacy maintains as part of its written policies and procedures, a written quality assurance plan to monitor and ensure the integrity, potency, quality and labeled strength of compounded drug products. (CCR 1735.8[a])

8.2. The pharmacy's quality assurance plan includes the written procedures and standards for the following:

8.2.1. Verification, monitoring and review of the adequacy of the compounding processes as well as documentation of review of those processes by qualified pharmacy personnel. (CCR 1735.8[b])

8.2.2. Qualitative and quantitative integrity, potency, quality and labeled strength analysis of compounded drug products. (CCR 1735.8[c])

8.2.3. Such reports are retained by the pharmacy and collated with the compounding record and master formula. (CCR 1735.8[c])

8.2.4. Scheduled action in the event any compounded drug product is ever discovered to be below minimum standards for integrity, potency, quality or labeled strength. (CCR 1735.8[d])

(Continued on Next Page)

COMPOUNDING STERILE INJECTABLE DRUGS

Does the pharmacy compound sterile injectable drugs? Yes No

If yes, complete Sections 9 through 19.

9. FOR PHARMACIES THAT COMPOUND STERILE INJECTABLE DRUGS: Permit or Accreditation

Yes No N/A

The pharmacy has a board issued Licensed Sterile Compounding permit or has current accreditation from the Joint Commission on Accreditation of Healthcare Organizations, or other board approved accreditation agency. (B&PC 4127.1[a] and 4127.1[d])

LSC # _____ OR

Name of accreditation agency _____

10. Compounding Drug for Other Pharmacy for Parenteral Therapy (B&PC 4123)

Yes No N/A

10.1. The pharmacy contracts to compound a drug for parenteral therapy, pursuant to a prescription, for delivery to another pharmacy.

- 10.1.1. The contractual arrangement is reported to the board within 30 days of commencing that compounding.

11. Sterile Injectable Compounding: Compounding Area (CCR 1751)

Yes No N/A

11.1. If the pharmacy compounds sterile injectable drugs from a nonsterile source, the pharmacy has a designated area or cleanroom for the preparation of sterile products that has one the following:

- 11.1.1. An ISO class 5 laminar airflow hood within an ISO class 7 cleanroom. A positive air pressure differential in the cleanroom that is relative to adjacent areas; (B&PC 4127.7[a])
- 11.1.2. An ISO class 5 cleanroom (B&PC 4127.7[b])
- 11.1.3. A barrier isolator that provides an ISO class 5 environment for compounding. (B&PC 4127.7[c])

11.2. The cleanroom walls, ceiling and floors are made of non-porous, cleanable surfaces and the room is well ventilated (CCR 1751)

- 11.2.1. The laminar airflow hoods and clean room are certified annually; (CCR 1751)
- 11.2.2. Supplies are stored in a manner, which maintains integrity of an aseptic environment; (CCR 1751)
- 11.2.3. A sink with hot and cold running water; (CCR 1751)

- 11.2.4. A refrigerator of sufficient capacity to meet the storage requirements for all material requiring refrigeration. (CCR 1751)

CORRECTIVE ACTION OR ACTION PLAN: _____

12. Sterile Injectable Recordkeeping Requirements. (CCR 1751.1)

Yes No N/A

- 12.1. Pharmacy records are made and kept for sterile injectable products produced for future use (pursuant to section 1735.2), in addition to record requirements of section 1735.3, contain the name, lot number, amount, and date on which the products were provided to a prescriber. (CCR 1751.1[a])

- 12.2. Records for sterile products compounded from one or more non-sterile ingredients are made and kept and contain the following: (CCR 1751.1[b][1-6])
 - 12.2.1. The training and competency evaluation of employees in sterile product procedures;
 - 12.2.2. Refrigerator and freezer temperatures;
 - 12.2.3. Certification of the sterile compounding environment;
 - 12.2.4. Other facility quality control logs specific to the pharmacy's policies and procedures (e.g., cleaning logs for facilities and equipment);
 - 12.2.5. Inspection for expired or recalled pharmaceutical products or raw ingredients; and
 - 12.2.6. Preparation records including the master work sheet, the preparation work sheet, and records of end-product evaluation results.

- 12.3. The pharmacy maintains and retains all records required in the pharmacy in a readily retrievable form for at least three years from the date the record was created. (CCR 1751.1[c])

CORRECTIVE ACTION OR ACTION PLAN: _____

13. Sterile Injectable Labeling Requirements (CCR 1751.2)

Yes No N/A

- 13.1. In addition to the labeling information required under Business and Professions Code section 4076 and CCR 1735.4, the pharmacy's compounded sterile injectable product labels contain: (CCR 1751.2[a-d])
 - 13.1.1. Telephone number of the pharmacy, unless dispensed for a hospital in-patient;
 - 13.1.2. Name and concentrations of ingredients contained in the product;
 - 13.1.3. Instructions for storage and handling; and
 - 13.1.4. A special label that states "Chemotherapy—Dispose of Properly" or "[Cytotoxic Product – Dispose of Properly](#)" for all cytotoxic agents.

CORRECTIVE ACTION OR ACTION PLAN: _____

14. Sterile Injectable Policies and Procedures (CCR 1751.3)

Yes No N/A

- 14.1. The pharmacy has a written manual documenting the policies and procedures associated with the preparation and dispensing of sterile injectable products and, in addition to the elements required by section 1735.5, includes: (CCR 1751.2[a][1-7])
 - 14.1.1. Compounding, filling, and labeling of sterile injectable compounds;
 - 14.1.2. Labeling of the sterile injectable product based on the intended route of administration and recommended rate of administration;
 - 14.1.3. Equipment and supplies;
 - 14.1.4. Training of staff in preparation of sterile injectable products;
 - 14.1.5. Training of patient and/or caregiver in the administration of compounded sterile injectable products;
 - 14.1.6. Procedures for the handling and disposal of cytotoxic agents;
 - 14.1.7. Quality assurance program; and
 - 14.1.8. Record keeping requirements.

- 14.2. Ingredients and compounding process for each preparation is determined in writing and reviewed by a pharmacist before compounding begins. (CCR 1751.3[b])

- 14.3. Policies and procedures address the disposal of infectious materials and/or materials containing cytotoxic residues and include cleanup of spills in conformance with local health jurisdictions. (CCR 1751.3 [c])

- 14.4. If compounding sterile injectable products from one or more non-sterile ingredients, the pharmacy has written policies and procedures that comply with the following: (CCR 1751.3[d][1-3])
 - 14.4.1. Policies and procedures are immediately available to all compounding personnel and board inspectors (CCR 1751.3[d][1]); and
 - 14.4.2. All compounding personnel have read the policies and procedures, any additions, revisions, and deletions before compounding. (CCR 1751.3 [d][2])

- 14.5. Policies and procedures address the following: (CCR 1751.3 [d][3] [A-K])
 - 14.5.1. Competency evaluation;
 - 14.5.2. Storage and handling of products and supplies;
 - 14.5.3. Storage and delivery of final products;
 - 14.5.4. Process validation;
 - 14.5.5. Personnel access and movement of materials into and near the controlled area;

- 14.5.6. 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);
- 14.5.7. A 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;
- 14.5.8. Disposal of packaging materials, used syringes, containers, and needles to enhance sanitation and avoid accumulation in the controlled area;
- 14.5.9. For sterile batch compounding, written policies and procedures for the use of master formulas and work sheets and for appropriate documentation;
- 14.5.10. Sterilization; and
- 14.5.11. End-product evaluation and testing.

CORRECTIVE ACTION OR ACTION PLAN: _____

15. Facility & Equipment Standards for Sterile Injectable Compounding (CCR 1751.4)

Yes No N/A

- 15.1. The compounding environment meets criteria specified in the pharmacy's written policies and procedures for safe compounding of sterile injectable drugs. (CCR 1751.4[a])
- 15.2. Only those who are properly attired pursuant to (CCR 1751.5) are allowed in the cleanroom during the preparation of sterile injectable products. (CCR 1751.4[b])
- 15.3. All equipment used in the designated area or cleanroom is made of easily cleaned and disinfected material. (CCR 1751.4[c])
- 15.4. Exterior workbench surfaces and other hard surfaces in the designated area, such as walls, floors, ceilings, shelves, tables, and stools are disinfected weekly and after any unanticipated event that could increase risk of contamination (CCR 1751.4[d])
- 15.5. The preparation of parenteral cytotoxic agents is done in accordance with Section 505.12.1 of Title 24, Chapter 5, of the California Code of Regulations and includes: (CCR 1751.4[e])
 - 15.5.1. A laminar airflow hood, which is certified annually.
 - 15.5.2. Certification records are maintained for at least three years.

CORRECTIVE ACTION OR ACTION PLAN: _____

16. Sterile Injectable Compounding Attire (CCR 1751.5)

Yes No N/A

- 16.1. When preparing cytotoxic agents, gowns and gloves are worn.(CCR 1751.5[a])
- 16.2. When compounding sterile products from one or more non-sterile ingredients and a barrier isolator is not used: (CCR 1751.5[b][1-5])
 - 16.2.1. Cleanroom garb is donned and removed outside the designated area; (CCR 1751.5[b][2])
 - 16.2.2. Individuals in the cleanroom wear a low-shedding coverall, head cover, face mask, and shoe covers; (CCR 1751.5[b][1])
 - 16.2.3. No hand, finger, or wrist jewelry is worn or if the jewelry cannot be removed, it is cleaned and covered with a sterile glove; (CCR 1751.5[b][3])
 - 16.2.4. Head and facial hair is kept out of critical area or covered (CCR 1751.5[b][4]); and
 - 16.2.5. Gloves of low-shedding material are worn. (CCR 1751.5[b][5])

CORRECTIVE ACTION OR ACTION PLAN: _____

17. Training of Sterile Injectable Compounding Staff, Patient, and Caregiver (CCR 1751.6)

Yes No N/A

- 17.1. Consultation is available to the patient and/or primary caregiver concerning proper use of sterile injectable products and related supplies furnished by the pharmacy. (CCR 1751.6[a])
- 17.2. The pharmacist-in-charge ensures that all pharmacy personnel engaging in compounding sterile injectable drug products has training and demonstrated competence in the safe handling of those products, including cytotoxic agents if the pharmacy compounds such agents. (CCR 1751.6[b])
- 17.3. Records of training and demonstrated competence are available for each individual and are retained for three years beyond the employment period. (CCR 1751.6[c])
- 17.4. The pharmacist-in-charge ensures the continuing competence of pharmacy personnel engaged in compounding sterile injectable products. (CCR 1751.6[d])
- 17.5. When compounding sterile products from one or more non-sterile ingredients, the pharmacy complies with the following training requirements: (CCR 1751.6[e])
- 17.6. The pharmacy follows 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 addresses the following: (CCR 1751.6[e][1][A-J])
 - 17.6.1. Aseptic technique;
 - 17.6.2. Pharmaceutical calculations and terminology;
 - 17.6.3. Sterile product compounding documentation;
 - 17.6.4. Quality assurance procedures;

- 17.6.5. Aseptic preparation procedures;
- 17.6.6. Proper gowning and gloving technique;
- 17.6.7. General conduct in the controlled area;
- 17.6.8. Cleaning, sanitizing, and maintaining equipment used in the controlled area;
- 17.6.9. Sterilization techniques; and
- 17.6.10. Container, equipment, and closure system selection.

Yes No N/A

17.7. Each person assigned to the controlled area successfully completes practical skills training in aseptic technique and aseptic area practices. (CCR 1751.6[e][2])

- 17.7.1. checks involving adherence to aseptic area policies and procedures. (CCR 1751.6[e][2])
- 17.7.2. Each person's proficiency and continuing training is reassessed every 12 months. (CCR 1751.6[e][2])
- 17.7.3. Results of these assessments are documented and retained in the pharmacy for three years. (CCR 1751.6[e][2])

CORRECTIVE ACTION OR ACTION PLAN: _____

18. Sterile Injectable Compounding Quality Assurance and Process Validation (CCR 1751.7)

Yes No N/A

18.1. There is a written, documented, ongoing quality assurance program maintained by the pharmacy that monitors personnel performance, equipment, and facilities, and the pharmacist-in-charge assures that the end-product meets the required specifications by periodic sampling. (CCR 1751.7[a])

18.2. The Quality Assurance Program contains at least the following: (CCR 1751.7[a][1-4])

- 18.2.1. Cleaning and sanitization of the parenteral medication preparation area;
- 18.2.2. The storage of compounded sterile injectable products in the pharmacy and periodic documentation of refrigerator temperature;
- 18.2.3. Actions to be taken in the event of a drug recall; and
- 18.2.4. Written justification of the chosen expiration dates for compounded sterile injectable products in accordance with CCR 1735.2[h]).

18.3. Each individual involved in the preparation of sterile injectable products successfully completes a validation process on technique before being allowed to prepare sterile injectable products. (CCR 1751.7[b])

- 18.3.1. The validation process is 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. (CCR 1751.7[b])
- 18.3.2. The validation process is representative of all types of manipulations, products and batch sizes the individual is expected to prepare. (CCR 1751.7[b])

- 18.3.3. The same personnel, procedures, equipment, and materials are involved. (CCR 1751.7[b])
- 18.3.4. Completed medium samples are incubated. (CCR 1751.7[b])
- 18.3.5. If microbial growth is detected, the sterile preparation process is evaluated, corrective action taken, and the validation process is repeated. (CCR 1751.7[b])
- 18.3.6. Personnel competency is revalidated and documented at least every 12 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 aseptic techniques are observed. (CCR 1751.7[b])

Yes No N/A

18.4. Batch produced sterile injectable drug products compounded from one or more non-sterile ingredients are subject to documented end product testing for sterility and pyrogens and are quarantined until the end product testing confirms sterility and acceptable levels of pyrogens. (CCR 1751.7[c])

CORRECTIVE ACTION OR ACTION PLAN: _____

19. Sterile Injectable Compounding Reference Materials (CCR 1751.8)

Yes No N/A

Current and appropriate reference materials regarding the compounding of sterile injectable products are maintained or immediately available to the pharmacy. (CCR 1751.8)

CORRECTIVE ACTION OR ACTION PLAN: _____

(Continued on next page.)

PHARMACIST-IN-CHARGE CERTIFICATION:

I, (Please print) _____, RPH # _____ hereby certify that I have completed the self-assessment of this pharmacy of which I am the pharmacist-in-charge. Any deficiency identified herein will be corrected. I understand that all responses are subject to verification by the Board of Pharmacy. I further state under penalty of perjury of the laws of the State of California that the information I have provided in this self-assessment form is true and correct.

Signature _____ Date _____

ACKNOWLEDGEMENT BY OWNER OR HOSPITAL ADMINISTRATOR:

I, (please print) _____, hereby certify under penalty of perjury of the laws of the State of California that I have read and reviewed this completed self-assessment. I understand that failure to correct any deficiency identified in this self-assessment could result in the revocation of the pharmacy's license issued by the California State Board of Pharmacy.

Signature _____ Date _____

(Pharmacist-in-Charge)

Kevin Brown, Pharm.D.
2001 Madera Vista Lane
Rescue, California 95672
brownk@sutterhealth.org

April 21, 2012

Board of Pharmacy
Attn: Carolyn Klein, Manager, Legislation and Regulation
1625 N. Market Blvd. N219
Sacramento, CA 95834
carolyn_klein@dca.ca.gov

Re: Proposed Regulations - Article 4.5 General Compounding

Dear Ms Klein:

I have worked as an inpatient pharmacist for 30 years. I am now the Director of Pharmacy at Sutter Medical Center, Sacramento.

I am writing to express my concerns about the negative safety impact the compounding regulation has on patient specific IV compounded products in the inpatient setting.

I have read all the Institute of Medicine publications, starting with To Err Is Human, published in 1999. Consistent themes to reduce the risk of error in these publications are simplification and standardization.

The process of making a single IV compounded product for a specific patient in the hospital is complex. After gathering the materials needed, the person compounding follows the multiple steps in the aseptic technique process. Then the pharmacist checks the drug, the concentration, the amount added, the diluent, the final concentration, the labeling, the beyond use date and checks for appropriate auxiliary labels. This complex process is essential for providing the correct and safe product to the patient.

The requirement to add the documentation required in the new regulations adds no value to the specific product that is being produced for a specific patient. It only adds more steps in an already very complicated procedure. Based on all the human factors engineering information, the extensive safe process information, and the application of lean process techniques to healthcare applications, I believe the regulation actually reduces the safety to the patient because of the increased complexity of the process. The regulations add more steps for the pharmacist or technician to complete, therefore increasing the risk of error. This requirement has actually caused errors.

I respectfully request the Board consider the fundamental differences between batching IV compounded products for future use and preparing patient specific sterile products. When batching, documentation of lot numbers does add value for the patient. Please consider making an exemption for patient specific inpatient compounded products from this regulation because it actually increases the possibility of error without providing any additional protection for our patients.

Respectfully,

Kevin Brown, Pharm.D.



UC San Diego
HEALTH SYSTEM

RECEIVED BY CALIF.
BOARD OF PHARMACY
2012 APR 23 AM 10:45

April 20, 2012

Virginia Herold
Executive Officer
California State Board of Pharmacy

Re: Amendment to Sections 1735 and 1751, Title 16
California Code of Regulations

C/o Carolyn Klein
California State Board of Pharmacy
1625 North Market Blvd, N219
Sacramento, CA 95834

Dear Ms. Herold,

The UC San Diego Health System Pharmacy leadership would like to thank you for the opportunity to comment on the proposed compounding regulation. We appreciate the time the Board members, especially Dr. Kadjioka, and the inspectors devoted to working with many licensees review the challenges that occurred with the implementation of the new regulations instituted in 2010.

Because there were some significant concerns that most facilities faced, we focused on those and did not consider some of the smaller issues or interpretations. The recommendations detailed in this letter refer to CCR 1735 and 1751 et seq. regarding sterile injectable compounding. We would like you to consider making a few more wording changes.

1) 1751.5 Sterile Injectable Compounding Attire

(b)(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. "

While low-shedding coveralls may not be standard of practice and may not be cost effective, we propose wording such as a "**low-shedding gown with sleeves that fit snugly around the wrists**" be substituted for or added to the term "low-shedding coveralls".

2) 1751.4 (e) "Pharmacies preparing parenteral cytotoxic agents shall do so in accordance with Section 4-1106(b) of Title 24 of the California Administrative Code, requiring a laminar flow hood"...., our IV specialists suggest that "**biological safety cabinet**" may be a more accurate term to use as not all cabinets used to prepare medication (such as radioisotope hoods) are laminar flow hoods.

Thank you for the opportunity to comment on the pending changes to the regulations.

Sincerely,

Charles E. Daniels, R.Ph.
Chief Pharmacist
University of California San Diego Health System
200 West Arbor Drive, #8765
San Diego, CA 92103

Carolyn Klein
Manager, Legislation and Regulation
Board of Pharmacy
1625 N. Market Blvd. N219
Sacramento, CA 95834
carolyn_klein@dca.ca.gov

April 23, 2012

Re: Rulemaking File on Title 16, California Code of Regulations Beginning with Section 1735.1, et seq.

Dear Ms. Klein:

Kaiser Permanente, California Pharmacy Programs and Services respectfully submits the following comments to the California Board of Pharmacy (Board) regarding its rulemaking proposal for compounding regulation 1735.1, et seq., requirements.

We appreciate the Board's willingness to receive comments throughout the rulemaking processes. We also understand and appreciate the long-history, evolution, time, and work by the Board and its staff that led to the current compounding regulatory language and to the proposed regulation changes. Kaiser Permanente has been engaged throughout the development of California's compounding regulations and will continue to offer support to implement the intent of the regulation changes through assisting with the revision of the associated Question and Answer (Q&A) documents published by the Board and development of other materials as needed.

Kaiser Permanente does support the following recommended regulatory changes:

- Adding a definition of "equipment" for purposes of compounding drug products as follows – those items that must be calibrated, maintained or periodically certified;
- Requiring that the written master formula record specify what equipment is to be used in compounding the drug product;
- Removing equipment as an item necessary to record in the pharmacy record;
- Extending the one-time basis for administration exemption from 24-hours to 72-hours;
- Specifying an alternate label that reads "Cytotoxic Product – Dispose of Properly."

While CSHP supports these regulatory changes, Kaiser Permanente recommends that the reference to the USP standards be clarified by the following addition, shown in **BOLD CAPS**:

Section 1735.3 (a)

*"...(72) hours and stored in accordance with United States Pharmacopeia Standards **FOR "REDISPENSED CSPs"** IN CHAPTER 797, (35th Revision, Effective May 1, 2012) to an inpatient in a health care facility licensed under section 1250 of the Health and Safety."*

Respectfully,
s/s Steven Gray, PharmD, JD
Pharmacy Regulatory Compliance and Professional Affairs Leader,
Kaiser Permanente, California Pharmacy Programs and Services
steve.w.gray@kp.org 562.658.3660

Katy Marconi, Pharm D
RPh 40587
Registered Address on file:
121 S. Avena Avenue
Lodi, CA 95240
Director of Pharmacy and Clinical Quality
Doctors Hospital of Manteca
1205 E. North Street
Manteca, CA 95336

April 20, 2012

The State Board of Pharmacy
Contact: Carolyn Klein
1625 N. Market Blvd., N219
Sacramento, CA 95834

Dear State Board of Pharmacy:

I have had the opportunity to attend the numerous subcommittee meetings where open discussion regarding compounding regulations has occurred. Many of my colleagues in hospital practice were in attendance as well.

This correspondence outlines the continued concerns I have regarding the direction that will be taken with regard to amending portions of sections 1735 and 1751 of Division 17 of Title 16 of the California Code of Regulations (CCR) with regard to compounding.

OBJECTIVE

To ensure public safety with regard to compounded pharmaceuticals provided to the public.

To ensure that the events of 2001 (pharmacy compounded contaminated injectable products lead to the death of 3 and hospitalization of least 30) are not repeated. Please note that the events in 2001 were a product of non-sterile to sterile compounding.

SCOPE OF SERVICES

1. Existing Practice

- a. The profession of pharmacy encompasses many settings. These practice settings include to name a few, retail (community), closed-door, compounding and hospital. The focus of the original rules and regulations in place since the 1980's, governing the practice of pharmacy, has largely been retail. In recent years, the rules and regs have been updated to include practice settings other than retail.
- b. Compounding can be of various types but can be summarized into 2 categories: compounded final product that is non-sterile and compounded final product that is sterile. Non-sterile compounding is generally thought of as applying to oral and topical preparations – traditionally a retail function. Sterile compounding is

generally thought of as applying to injectable preparations – traditionally a hospital or compounding pharmacy function.

- c. When the State Board of Pharmacy determined to take on “compounding” in reaction to the 2001 public health event, it was decided that all forms of compounding would be addressed. It is important to note that of imminent public danger was the practice of compounding from non-sterile to sterile product. In the era of numerous drug shortages, pharmacists are asked to provide pharmaceuticals that can not be commercially obtained. To provide for the patient what often is determined a necessary part of treatment (medications), non-sterile to sterile compounding is attempted. Lastly, there are times when compounding is used as a money-saving strategy. Regardless of the intent, in order to provide safe non-sterile to sterile compounding, the strictest of processes must be employed – adherence to USP 795 and 797. In order to provide sterile to sterile compounding, certain pre-defined processes must be employed – adherence to USP797 guidelines.
- d. It is important to note that non-sterile to sterile compounding is a very different process from sterile to sterile compounding. Typically, you do not see hospital pharmacies attempt non-sterile to sterile compounding. The majority of the attendees at the compounding hearings/forums were hospital pharmacists. The majority of the hospital pharmacist comments were regarding the disruption of hospital work practice and economic hardship, as a result of the pending regulation changes.
- e. It is also important to note that every hospital pharmacy in the State of California undergoes routine inspection. The inspections can be at both a national/federal and state level. On a national level, The Joint Commission (or other like entity) is required to periodically inspect hospitals as per their standards and on behalf of the Centers for Medicare and Medicaid Services (CMS) to determine in addition to the Conditions of Participation, that adherence to USP797 is in place and enforced. On the state level, CDPH can inspect at any time to determine that adherence to USP797 is in place and enforced.
- f. Appropriate action with regard to recalls of medications is a public safety issue. In addition to the many shortages of medications as referenced earlier, many recalls are occurring as well (thus contributing to shortages). The State Board of Pharmacy was involved with the Heparin recalls of 2008. The State Board of Pharmacy noted that recall efforts were not complete and uniform amongst the hospitals. Built into the revised compounding regulations were processes that were directly linked to the recall process. Specifically, the requirement of recording drug name, personnel, manufacturer and lot number (manf/lot). Much of the debate occurred around this area. It was originally stated that if recording of all elements did not occur, the product, if unused, would need to be destroyed if not used within 24 hours. Issues are:
 - i. Hospital pharmacies had never recorded this information in the past and the process of recording was cumbersome and not effective, in that there is no way to easily sort and identify recorded data in the event of a recall.

- ii. Huge amounts of medication would need to be wasted. Hospitals routinely reuse compounded medications that meet all storage requirements and are still potent and capable of reuse. This hospital waste would contribute to the numerous medication shortages currently being experienced in addition to financial hardship.
- iii. In an age of uncertainty of healthcare reimbursement in general, hospitals need to be good stewards of inventory, minimizing all unnecessary waste.

2. Existing Policy/Rules and Regulations

- a. Many requirements have been placed into current law by the State Board of Pharmacy that go above and beyond the recognized compounding standards of USP 797.
- b. There are 6 areas that the State Board of Pharmacy wishes to regulate. They are:
 - i. Quality assurance assessment
 - ii. Labeling of compounds that are cytotoxic or used for chemotherapy
 - iii. Equipment used in compounding
 - iv. Expiration date of components
 - v. Exemption for hospitals from recording lot number, manufacturer (and proposed expiration date of components) from the daily log for one-time administration in 24 hours.
 - vi. In the interest of patient safety, when compounding stock solutions from non-sterile to sterile ingredients, do the stock solutions need to undergo sterility and pyrogen testing?

1. I take issue with items i., iii., iv., v. and vi.

- c. Quality assurance assessment: USP 797 clearly addresses the need for quality management. Specifically, USP 797 requires that the organization routinely inspects prescription orders, labels, compounding documentation, and expended materials to verify that the correct identity and amounts of ingredients, aseptic mixing and sterilization, packaging, labeling and expected physical appearance are consistent with expectations before they are dispensed. In addition, USP 797 requires that there is evidence that packaging maintains physical integrity, sterility, stability and purity.
- d. Labeling of cytotoxic/chemotherapy compounded items – There is no issue with this portion of the pending regulations.
- e. Equipment used in compounding – This is the section that describes the recorded information as referenced above in sections 1. f. i.-iii. USP 797 does not specifically

address and this matter should not be included under compounding standards. If recalls need to be further addressed, it should be in the areas of regulation that correspond directly to the recall process. The recall process should not differ by any means if the product is compounded or manufactured.

- f. Expiration date of the components – This section directly relates to the above section 2 e., in that in addition to requiring manufacturer/lot#, the expiration date of the product to be compounded is to be recorded as well. As stated above in 2 e., If recalls need to be further addressed, it should be in the areas of regulation that correspond directly to the recall process. The recall process should not differ by any means if the product is compounded or manufactured.
 - g. Exemption for hospitals for recording lot number, manufacturer (and proposed expiration date of components) from the log for one-time administration in 24 hours – USP 797 outlines acceptable Beyond use dates (BUDs) assigned to sterile to sterile compounded products. The BUDs are based on evaluated data from the manufacturers or peer-reviewed literature that substantiates the stability and storage conditions for each type of sterile to sterile compounded product. No additional requirements, as suggested by State Board of Pharmacy regulation should be needed.
 - h. In the interests of patient safety, when compounding stock solutions from non-sterile to sterile ingredients, do the stock solutions need to undergo sterility and pyrogen testing – USP 797 details sterility testing and sterilization methods, depyrogenation, bacterial endotoxin testing and filter integrity testing. No additional requirements, as suggested by State Board of Pharmacy regulation should be needed.
3. Linking practice and policy
- a. I respectfully request that hospitals that are engaged in sterile to sterile compounding be permitted to follow USP 797 and nothing more than USP 797.
 - b. I respectfully request that if the State Board of Pharmacy feels the need to ensure patient safety and to avoid tragic occurrences such as the public health event of 2001, that they apply all of the newly revised laws as they pertain only for those entities that are engaged in **non-sterile to sterile** compounding.
 - c. I respectfully request that any attempts to address the recall process should be separated from issues regarding the compounding process, as both are distinct separate entities that require separate actions in order to maintain patient safety.

YOUR RESPONSIBILITIES

Based on the fact that inspections are frequently occurring at both national and state levels, and that there are nationally recognized guidelines already in place that address the safe compounding of pharmaceuticals (USP 797), I feel it would be in the best interest of the State Board of Pharmacy and those that are licensed with the State Board of pharmacy working in the hospital setting to:

1. That when sterile to sterile compounding is being conducted, adherence to USP 797 is in place and there is evidence of it being strictly enforced.
2. That when non-sterile to sterile compounding is being conducted, adherence to USP 795 and USP 797 is in place and there is evidence of it being strictly enforced
3. That when non-sterile to non-sterile compounding is being conducted, adherence to good pharmaceutical practice should be utilized.

CLOSING

I appreciate the opportunity to provide comment on this very important portion of pharmacy regulation – compounding. I hope that my attendance at the many subcommittee meetings, my comments provided at these subcommittee meetings (along with the comments of my hospital colleagues), plus my numerous years of experience as a hospital pharmacist (25 years) would be considered as you determine the law of compounding.

Sincerely,

Katy Marconi, Pharm D
Director of Pharmacy and Clinical Quality

Kent Martyn, Pharm.D
Director of Pharmacy Services, CVMC
1115 S. Sunset Ave
West Covina, CA 91790

The State Board of Pharmacy
Contact: Carolyn Klein
1625 N. Market Blvd, N219
Sacramento, CA 95834

April 23, 2012

Dear State Board of Pharmacy,

I have attended all the recent meetings discussing the compounding regulations and addressed the board several times on those occasions. I truly appreciate the Board's willingness to discuss this issue. I have been a practicing hospital pharmacist for 32 years.

Although I understand the Board's reasons for feeling the additional regulations are needed, it has been proven in recent discussions that much of what was done would not have impact on patient care but will definitely have an impact on labor demands, systems safety, drug costs, and drug shortages.

I believe it has been shown very clearly that:

- 1) Adding lot# requirements will not affect patient care when it comes to recalls. A historical look at recalls has shown this to be the case. In addition, hospitals already have recall mechanisms in place that make a successful recall possible; all the products within the facility are easily at hand up to the point of administration. If there is any question about affected lot #'s, all products can be gathered. This is not the case for the retail compounding setting.
- 2) Current hospital practice and standards are based on USP 797. Nationally, these are considered the highest level of practice in any setting other than pharmaceutical manufacturing.
- 3) Hospitals are regularly surveyed on IV preparation issues by JCAHO, DPH, and CMS. We are also participants in national quality measures by SCIP, Leapfrog, ARRA, NPSG and NSQIP to impact patient safety and outcomes.
- 4) Low and Moderate Risk solutions presently have manufacturer and literature data validating beyond use dating that meets the requirements for safety and effective patient care. There is no need for "artificial" dating to be applied by the Board. Such appears a more "emotional" response than one based on science.
- 5) All of the compounding issues that created patient harm were due to organizations not following current standards or even basic guidelines. **The mentality that did this cannot be regulated. It doesn't take new regulations around record keeping to identify an organization is not following basic principles of sterile compounding at this time. To apply new regulations to all suggests a gross problem throughout all pharmacy.**
- 6) Non-sterile to sterile compounding is a whole different activity than sterile to sterile compounding. Most of the hospital compounding by far is sterile to sterile compounding.
- 7) It was shown from the literature that adding more steps to a process induces errors. In practice I have seen this to be the case over and over again. We want our pharmacists and technicians to focus on the critical issues around IV preparation. Adding steps that interfere with this process creates errors, increases labor demands, and increases costs without proven benefit.

Hospital, retail, and compounding pharmacies have diverged in their functions and their expertise over the last 20 years. They no longer can be compared, except at very general and fundamental levels.

- a) Regulations, standards, and surveys are different. There is a much higher level of activity and expectations of a hospital pharmacy. Hospital pharmacy is responsible for overseeing all medication practices within the hospital setting from prescribing, administration, and monitoring, to ordering, stocking, and distribution. This is a level of activity and responsibility that is much larger than any retail setting and it is surveyed by numerous regulatory entities.
- b) Hospitals are by far, generally making products for immediate use. Occasionally batches of high use sterile to sterile products are prepared. The purpose of these sterile to sterile batch productions is to prepare ahead for the next 24 hours or so. This allows more efficient use of personnel and quicker response to

orders. Most products from a retail compounding pharmacy are not immediate use and often are non-sterile to sterile compounding and can be shipped all over the country.

- c) All the materials produced are kept within the hospital walls and accessible by the pharmacy at any time up to administration to the patient. At a retail compounding pharmacy, once the products leave the pharmacy, access to them is very difficult and there is less control of shipping and storage.
- d) In the hospital setting because the patients are receiving the drugs in house, the hospital can monitor all drug effects and respond as needed. This cannot be said of any retail setting.
- e) When a hospital pharmacy creates IV solutions, it is subsequent to a physician order and it is prepared for use within the house. It is not sold or sent for use outside of the hospital. This is not “manufacturing” when compared to drug company production of non-patient specific compounds that have extended dating and shipped all over the world. Hospital pharmacies are not manufacturers and should not be held to the same level as pharmaceutical manufacturers. This is not at all reasonable and interferes with other safety activities and processes for which we are responsible.
- f) When the CDC did studies in the early 80’s on the causes of bacteremia, IV techniques only accounted for 0.8% of the occurrences and were considered by the CDC not to be a significant contributor. This was at a time when laminar flow hoods were not required and IVs could be made anywhere within the hospital setting. Now, almost all IVs are made in the pharmacy by JCAHO standards and clean rooms are the norm. Again the offenders that caused recent issues were grossly inadequate in their processes.

In summary:

- 1) Sterile to sterile compounds that are patient specific are meant to be used within very short time frames (not more than 24 hrs). These are made in clean rooms that follow USP 797 with aseptic technique, quality control, and following manufacturer’s and literature recommendations. **These should not be subject to additional bookkeeping requirements.**
- 2) If a patient specific, sterile to sterile product is not used, it should be allowed to be relabeled and used for another patient as long as manufacturer and/or literature stability guidelines are followed. This has been the standard across the country for many years. They are low risk products and accessible at any time up to administration in response to a general product recall process.
- 3) Simple, low risk, sterile to sterile compounds that are batched, and not patient specific, are made to meet needs in the very near future (24-72 hrs). These compounds are low risk; manufacturer and/or literature supported, and again are easily retrievable up to administration. Such products have been made for decades without problems. The reason for this activity is to use personnel efficiently to meet immediate future patient needs. These are time frames that are well within product guidelines and USP 797 standards. Again, those instances where problems did occur it was due to people not following the basic tenants of IV production that already exist for hospitals. **These should also not require additional bookkeeping.**
- 4) **Non sterile to sterile** compounding requires the most attention. This is where the greatest risk point is even for those with good technique. These products require an additional level of activity and demonstration that the final product meets appropriate concentration, stability time frame, and passes pyrogen testing. Appropriate bookkeeping noting all the ingredient details is appropriate here. One caution; if you require testing of every product prior to dispensing, it will drastically interfere with patient care. What should happen here is **process validation and not product validation**. Proof that the process you use to make the product has been tested and shown to be safe and effective. Then there should be occasional revalidation of the process.
- 5) Quality assurance and quality control expectations are normal everyday business for a hospital pharmacy. This is part of the expectations of USP 797 and JCAHO and should be a normal expectation for any pharmacy.

With respect to the Board, I truly hope you are hearing the message we have been trying to give. It is not an issue of doing more work. It is an issue that the work requested has been proven to not impact recall safety or affect product safety. In fact, it will induce errors, increase wastage, increase labor costs, with no proven patient benefit. Our efforts in this industry must be evidenced based. I am involved daily with such discussions with my administration and medical staff. I have found it very difficult to defend the current Board expectations.

I thank you for your consideration of this matter

Kristin Niemi, Pharm.D.
6107 Ridge Creek Ct
Elk Grove, California 95758
niemik@sutterhealth.org

April 19, 2012

Board of Pharmacy
Attn: Carolyn Klein, Manager, Legislation and Regulation
1625 N. Market Blvd. N219
Sacramento, CA 95834
carolyn_klein@dca.ca.gov

Re: Proposed Regulations - Article 4.5 General Compounding

Dear Ms Klein:

I have worked as an inpatient pharmacist for over 20 years. Based on my developing interest in the system aspect of medication safety I stepped into the medication safety position at Sutter Medical Center Sacramento 2 years ago.

Today I am writing to express my concerns on the negative safety impact the compounding regulation has on patient specific IV compounded products in the inpatient setting.

I have read all the Institute of Medicine publications, starting with To Err Is Human, published in 1999. The concepts of simplification and standardization are the overriding mantra in every project or process I participate in.

The process of making a single IV compounded product for a specific patient in the hospital is a complex process. It involves gathering the materials needed. The person doing to compounding follows the multiple steps in the aseptic technique process. The pharmacist checking the product checks the drug, the concentration, the amount added, the diluent, the final concentration the labeling, the beyond use dating and checks for appropriate auxiliary labels. This complex process is essential for providing the correct and safe product to the patient.

The requirement to add extra steps of product documentation required in the new regulations adds no value to the specific product that is being produced for a specific patient. It only adds more steps in an already very complicated procedure. Based on all the human factors engineering information, the extensive safe process information, and the application of lean process techniques to healthcare applications, I believe the regulation actually reduces the safety to the patient because of the increased complexity of the process. The regulations add more steps for the pharmacist or technician to complete, therefore adding more places for an error to be made.

I respectfully request the board consider the fundamental differences between outpatient dispensing and inpatient batching, where documentation of lot numbers does add value for the patient. I request you consider making an exemption for patient specific inpatient compounded products from this regulation because it actually increases the possibility of error without adding any value.

Respectfully,

Kris Niemi

April 23, 2012

Carolyn Klein
California State Board of Pharmacy
1625 N Market Blvd Ste N219
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559.353.3000
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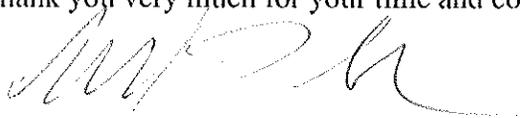
Dear Ms. Klein

I would like to take this opportunity to thank the California State Board of Pharmacy and the Subgroup that took on the task of reviewing Title 16. I support the proposed changes that the Subgroup has come with in order to minimize the unintended consequences of the original proposed changes and interpretation of the changes. I had submitted my concerns several years ago when this was initially proposed. To think about the ramifications of the changes is significant. Utilizing Dr. Shane's data from Cedar-Sinai where it was calculated that it would take about 6 minutes per order to fully comply with the regulations as it should for Children's Hospital Central California would be over 1,800,000 minutes as the organization makes about 321,000 patient specific intravenous admixtures per year. In order for our organization to comply the purchase of a Robotic Intravenous Admixture machine costing over \$1.2 millions in addition to addition staff or hiring over 14 FTEs would be necessary. The redeployment of these limited pharmacy resources either in funds or labor would have unintended consequences. As mentioned previously and pointed out at the presentation by Dr. Shane at one of the work sessions there has not be a bad outcome as a result of the utilization of an outdated medication. Thus the reallocation of a pharmacy's limited resources from known benefits, such as providing clinical services, to potentially beneficial services is not prudent in my estimation.

I fully support the recommendation to make the pharmacist in charge responsible for establishing the quality assurance program for the organization. This makes logical sense in that the pharmacist in charge is also responsible for the organization's quality assurance program

There is one area of concern that the Board should consider. The recommendation to change the expiration of a product from 24 hours to 72 hours falls short of what USP797 recommendations. The Joint Commission and the California Department of Public Health utilizes the USP797 guidelines. Although the Board of Pharmacy does not directly reference USP797 the basic premise is the USP797 guidelines. It was prudent that the Board adopt guidelines that are evidence based and from a panel of experts. In particular is the proposed 72 hour stability versus stability guidelines in the USP797 guidelines. I would recommend that the Board consider utilizing these evidence based federal standards to follow rather than making a regulation which lacks scientific basis.

Thank you very much for your time and consideration in this matter

A handwritten signature in black ink, appearing to read 'RSakai', written in a cursive style.

Richard I. Sakai, PharmD, FASHP, FCSHP

rsakai@childrenscentralcal.org

559.353.5505

Maria D. Serpa, Pharm.D.
6744 Paseo Del Sol
Elk Grove, California 95758
serpam@sutterhealth.org

April 18, 2012

Board of Pharmacy
Attn: Carolyn Klein, Manager, Legislation and Regulation
1625 N. Market Blvd. N219
Sacramento, CA 95834
carolyn_klein@dca.ca.gov

Re: Proposed Regulations - Article 4.5 General Compounding

Dear Ms Klein:

I again am writing about my concerns on the documentation of compounding for **sterile injectable** products. My letters from 2008 and 2009 and letters from the California Society of Health-System Pharmacists are on file. I will not repeat those issues here. Unfortunately, in the Board's attempt to protect patients in "**traditional**" compounding, you have significantly impacted the safety of patients in the acute care setting. **Sterile injectable** compounding should have never been lumped together with the "**traditional**" form of compounding. Previous regulations regarding **sterile injectable** compounding are very specific and detailed from both the United States Pharmacopeia (USP) Convention guidelines at the federal level and previous state BOP regulations.

I appreciate the Board working with the large number of pharmacists that came from throughout the state to the Compounding Sub-Committee hearings. Many of our concerns regarding equipment documentation, quality assurance and auxiliary labeling were addressed. I also agree with the documentation required for batching multiple doses of medications for future use that are NOT patient-specific. This is compounding. But the main concern, the value of documentation for patient-specific sterile injectable doses in acute care settings, which are given almost immediately after preparation, was not addressed. I was disappointed that this main issue was not even considered by the Sub-Committee and presented to the Board for further discussion. Each acute care patient is often on greater than 10-20 doses of sterile injectable medications. Each and every dose now requires onerous documentation and the addition of **thousands of records per day per hospital.** This data was presented to the Sub-Committee and shown to add NO improvement to patient safety or any recall process.

Unfortunately, the additional documentation does have a negative impact on patient safety and the timely receipt of medications, including life-saving drugs. It is common practice for a pharmacy in an acute care facility to prepare emergency medications for the treatment of heart attack, stroke and other life-threatening situations. Currently these STAT medications are prepared in the pharmacy and labeled with adequate information to assure patient safety and recall should a medication be recalled in the next few hours during administration. Additional record keeping for each patient specific single dose compounded does not serve the patient. It only delays medication preparation and delivery and places an additional burden on the pharmacy. There is no value in the additional documentation of patient-specific sterile products that are given

almost immediately. Exempting some sterile products in acute care facilities from some regulations has been done before. The recently updated United States Pharmacopeial Convention (USP) Chapter 797 regulates these processes separately in 2 distinct chapters. USP 797 deals with Pharmaceutical Compounding – Sterile Preparations and USP 795 deals with Pharmaceutical Compounding – Nonsterile Preparations.

I continue to recommend that **sterile injectable** and **non-sterile** compounding return to separate regulations. Previous California regulations, Article 7 Section 1751 (Sterile Injectable Compounding) and Business & Professions Code Section 4127 (Injectable Sterile Drug Products) covered the issues related to **sterile injectable** compounding.

Thank you for your consideration. I ask that the Board continue to address the patient safety needs of **“traditional” non-sterile** compounding and re-think the regulations on **sterile injectable** compounding in the acute care setting.

Respectfully,

Maria D. Serpa, PharmD



CEDARS-SINAI MEDICAL CENTER

April 23, 2012

Carolyn Klein
California State Board of Pharmacy
1625 North Market Blvd, Suite N219
Sacramento, CA 95834

Dear Carolyn:

We appreciate the opportunity to provide comments to the Board of Pharmacy related to the proposed amendments to the California Code of Regulations specifically related to the compounding of drug products.

- 1) In regards to the self-assessment to be completed by July 1 of every odd-numbered year by a pharmacy's PIC, the "Compounding Self-Assessment" Form 17M-39 was updated with proposed changes. Clarification is requested under #3 – "3.1.6. The manufacturer or supplier, expiration date and lot number of each component. Exempt from this requirement are sterile drug products compounded on a one-time basis for administration within seventy-two (72) hours and stored in accordance with United States Pharmacopeia Standards to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code."
 - a) We recommend language to specify "... stored in accordance with USP 797 standards" instead of "...stored in accordance with United States Pharmacopeia Standards."
- 2) In regards to 1735.3(a)6, "The manufacturer, expiration date and lot number of each component."
 - a) In licensed healthcare settings, expired medications cannot be utilized. Therefore, the additional requirement to document expiration date will not enhance patient safety, reduces focus on safe preparation, requires additional time and in most organizations, where the documentation will be performed manually, is subject to transcription error.
- 3) In regards to 1751.2(d), "All cytotoxic agents shall bear a special label which states "Chemotherapy -Dispose of Properly-" or "Cytotoxic Product – Dispose of Properly." "
 - a) We recommend changing verbiage of the cytotoxic label to read "Cytotoxic Agent – Dispose of Properly" as a majority of commercial labels use this verbiage and this would save pharmacy departments having to special order labels that say "Cytotoxic Product – Dispose of Properly."
- 4) "The board conducted a search of Title 21 Code of Federal Regulations (Food and Drugs), as well as the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.) and found no existing federal regulations or statutes that are comparable to the board's proposal. Further, the board conducted a search of the California Code of Regulations and found no existing state regulations that duplicate or address the scope of changes proposed by the board."
 - a) On a federal level, USP regulatory standards are established in the Food, Drug, and Cosmetic Act that provide direction for safely determining the appropriate beyond use dating of compounded products in hospitals or other healthcare facilities.

5) “Business Impact: The board has made an initial determination that the proposed regulatory action would have no significant statewide adverse economic impact directly affecting businesses, including the ability of California businesses to compete with businesses in other states.”

- a) While the extension to 72 hours certainly is an improvement, this timeframe will still result in wastage which has significant patient care and economic consequences, especially during this time of ongoing critical drug shortages (over 240 currently). Adoption of national sterile compounding standards (USP 797), currently surveyed by the CDPH and Joint Commission and which specify 9 day (216 hours) - 14 day (336 hours) dating depending on the level of complexity and stability would enhance our ability to safely preserve drug supplies for our patients. Additionally, wastage of medication has an environmental impact which conflicts with EPA efforts to reduce unnecessary pollution in the water supply.

We appreciate the opportunity to address these issues.

Sincerely,



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April 23, 2012

Carolyn Klein
Manager, Legislation and Regulation
Board of Pharmacy
1625 N. Market Blvd. N219
Sacramento, CA 95834
carolyn_klein@dca.ca.gov

Re: Rulemaking File on Title 16, California Code of Regulations Beginning with Section 1735.1

Dear Ms. Klein:

The California Society of Health-System Pharmacists (CSHP) respectfully submits the following comments to the California Board of Pharmacy (Board) with regard to its rulemaking proposal to update the California compounding regulation requirements.

It is important to recognize that CSHP understands the long-history, evolution, time, and work that led to the current compounding regulatory language. CSHP was always engaged throughout the development of California's compounding regulations. Below are some highlights (which are not completely extensive) of the comments CSHP provided to the Board while various compounding rulemakings took place:

- **June 8, 2007** – CSHP submitted a letter to the Board and provided testimony requesting that sterile and non-sterile compounding regulations be contained in separate regulatory sections as the practices are quite different. This request was made to ensure clarity between these two very different compounding practices and imitate the current compounding requirement standards set forth by the United States Pharmacopeia (USP) 797, which contains sterile and non-sterile compounding information in two different chapters. This request was ignored by the Board.
- **December 20, 2007** – CSHP submitted a letter to the Board and provided public comment requesting an exemption of immediate and one-time use (STAT) compounded drugs from the recordkeeping requirements in proposed Article 4.5, Section 1751.1: Sterile Injectable Recordkeeping Requirements. CSHP's primary concerns were that the additional recordkeeping requirements, with no shown proof to improve patient safety, would delay patient care for individuals in need of immediate and one-time use medications.
- **September 16, 2008** – CSHP submitted a letter to the Board and provided testimony requesting an exemption of immediate and one-time use (STAT) compounded drugs from the recordkeeping and labeling requirements in proposed compounding regulations.
- **March 9, 2009** – CSHP submitted a letter to the Board questioning the necessity of including any inpatient pharmacy compounding operation currently covered by Article 7: Sterile Injectable Compounding under the proposed Article 4.5: Compounding regulations. Further, at the request of CSHP, the Board opened a second 15-day comment period since it exempted some of the record keeping requirements in the proposed section 1735.3(a)(6) for sterile injectable drug products compounded on a one-time basis for administration within 24 hours.
- **July 15, 2009** – The board voted to approve the modified regulations with the exemption request as well as extended the compliance date six months following approval by the Office of Administrative Law and filing from the Secretary of State. Also, the board allowed an additional six months from July 6, 2010 to educate and assist hospital pharmacies with compliance.

CSHP does appreciate the Board's willingness to listen to CSHP and its members' comments throughout the previous rulemaking processes; however, it is important to understand that in no way did CSHP ever believe these regulations were crafted appropriately – taking into consideration the complexity of compounding in the hospital setting and patient safety. As such, it came as little surprise that an overwhelming number of hospital pharmacists took issue to the regulations that went into effect.

As you know, to address hospital pharmacists' concerns with the current regulations, the Board formed the Compounding Regulation Subcommittee, comprised of Chair Randy Kajjoka, PharmD and Board Member Anil "Neil" Badlani, RPh. CSHP commends these members for their work on the subcommittee as they created an environment where hospital pharmacists could freely convey their issues with the regulations that worked counterproductive to patient safety. It is quite evident by the strong showing of hospital pharmacists and CSHP leadership and staff at these subcommittee and full-board meetings that the compounding regulations were in need of revision. Upon hearing numerous presentations by Rita Shane, PharmD, FASHP, FCSHP (PowerPoint attached) and public members, CSHP would like to thank the board for addressing some of the issues brought forth during these meetings.

CSHP does support the following recommended regulatory changes and has one additional recommendation to the Board's proposed language (bold, italics, and underlined):

- Adding a definition of "equipment" for purposes of compounding drug products as follows – those items that must be calibrated, maintained or periodically certified;
- Requiring that the written master formula record specify what equipment is to be used in compounding the drug product;
- Removing equipment as an item necessary to record in the pharmacy record;
- Extending the one-time basis for administration exemption from 24-hours to 72-hours;
- Specifying that sterile injectable drugs must be stored in accordance with United States Pharmacopeia Standards, and adding the following words after Standards: "***for redispensed CSPs in Chapter 797;***" and,
- Specifying an alternate label that reads "Cytotoxic Product – Dispose of Properly."

While CSHP supports these regulatory changes, CSHP does not support the Board's proposal to add the expiration date of each component in the compounded drug product as there is no evidence that suggests that recording this information improves patient safety. Data was presented to both the subcommittee and full-board that added documentation results in NO improvement to patient safety or any recall process. In fact, adding a requirement to record the expiration date of each component in the compounded drug product actually creates more harm to patients than it prevents as it takes additional pharmacists' time away from other activities that improve patient safety. CSHP respectfully requests that this onerous requirement be removed from the regulatory changes.

Founded in 1962, CSHP represents over 4,500 pharmacists, student pharmacists, pharmacy technicians, and associates who serve patients and the public through the promotion of wellness and rational drug therapy. CSHP members practice in a variety of organized healthcare settings, including, but not limited to, hospitals, integrated healthcare systems, medication therapy management clinics, home healthcare and ambulatory care settings.

If you have any questions and/or comments, please do not hesitate to contact me or CSHP Director of Government Affairs Philip Swanger at (916) 447-1033 ext. 108 or philip@cshp.org.

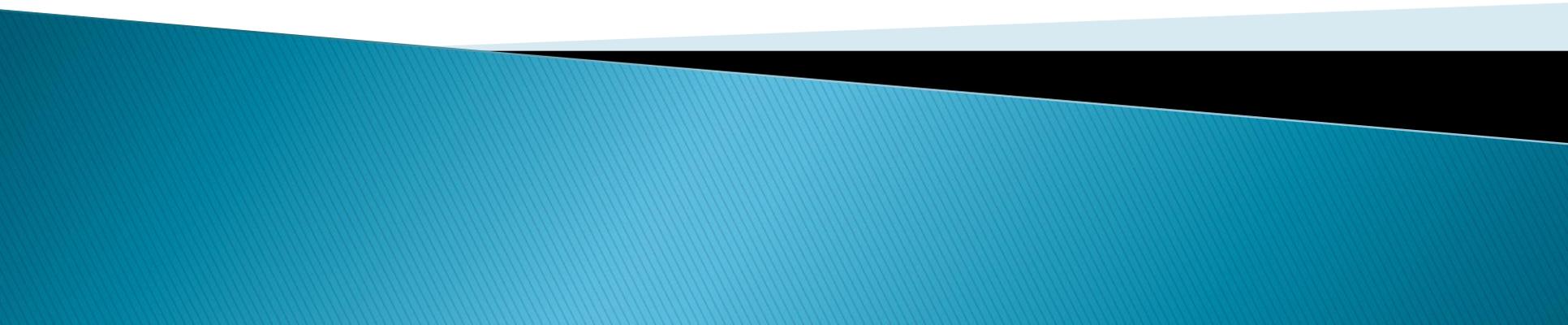
Respectfully,



Dawn Benton
Executive Vice President, CEO

State Board of Pharmacy Sterile Compounding Summary

January 2012



Objectives

- **Ensure safe, timely compounding based on best practices**
 - **Safe management of recalls**
 - **Minimize preventable waste, especially in light of drug shortages**
 - **Minimize distractions**
- 

Hospital Compounded Medications using Sterile Products

Proposed Definitions of Patient-Specific and Non-Patient Specific

▶ **Patient-Specific Compounded Medications**

- Definition: Medications compounded using sterile products for an individual patient based on a physician order (prescription) intended to be administered within 24 hours. (1735.3. (a) (6))
- Interpretation: Medications prepared and not administered due to changes in patients' conditions could be used if sterility and stability standards are met.

▶ **Non-Patient-Specific Compounded Medications**

- Definition: Compounding of sterile medications in anticipation of physicians' orders
- Interpretation: Requires documentation of manufacturer and lot number

Rationale for Exemption of Hospital Patient Specific– Sterile Compounding

- ▶ **Hospital patient–specific sterile compounded medications should not require the recording of mfr and lot numbers because:**
 1. Hospitals use sterile products in compounding (sterile to sterile).
 2. Handwritten documentation for **patient–specific medications delays timely delivery** of critical medications.
 3. Evidence does not support that increased documentation increases safety; however, increasing documentation reduces focus on processes.
- 

Rationale for Exemption of Hospital Patient Specific– Sterile Compounding

4. Harmful events related to sterile compounding **have not been shown to result from drug recalls** but rather from contamination and human errors.
 5. Critical medications **that are on shortage are being discarded** even though considered sterile and stable based on national standards, (antibiotics, heart failure meds, critical care meds, chemotherapy).
 6. Quarantining and removal of all recalled products would ensure **patient safety and timely follow-up and action.**
- 

Time and Motion Evaluation of Compounding and Manual Recording of Mfrs and Lot #s

Compounding IV
with electrolytes
and vitamins

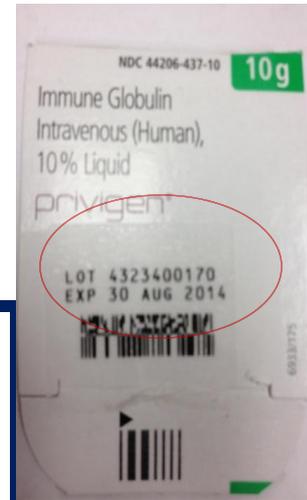
- 5 minutes

Documentation of
manufacturers and
lot numbers

- 3 minutes 51 seconds– represents 77% increase in time
- Each lot # can be 7–10 characters

Pharmacist checking
of documentation of
manufacturers and
lot numbers

- 2 minutes 30 seconds– time to document and pharmacist check of documentation is > than time to compound the medication



6:21
min

Very Few Recalls Involve Sterile Compounded Medications*

2010 Total
Recalls (based on
notifications):
814

Class 1 recalls
involving sterile
compounded
medications: 2

Cisplatin – particulate matter, no
reported patient events

Neoprofen – particulate matter,
no reported patient events

2011 Total Recalls:
775

Class 1 recalls
involving sterile
compounded
medications: 2

Irinotecan – non-sterility (fungus),
no reported patient events

Indomethacin – particulate matter,
no reported patient events

*Source: FDA.gov

Hospital Management of Recalls

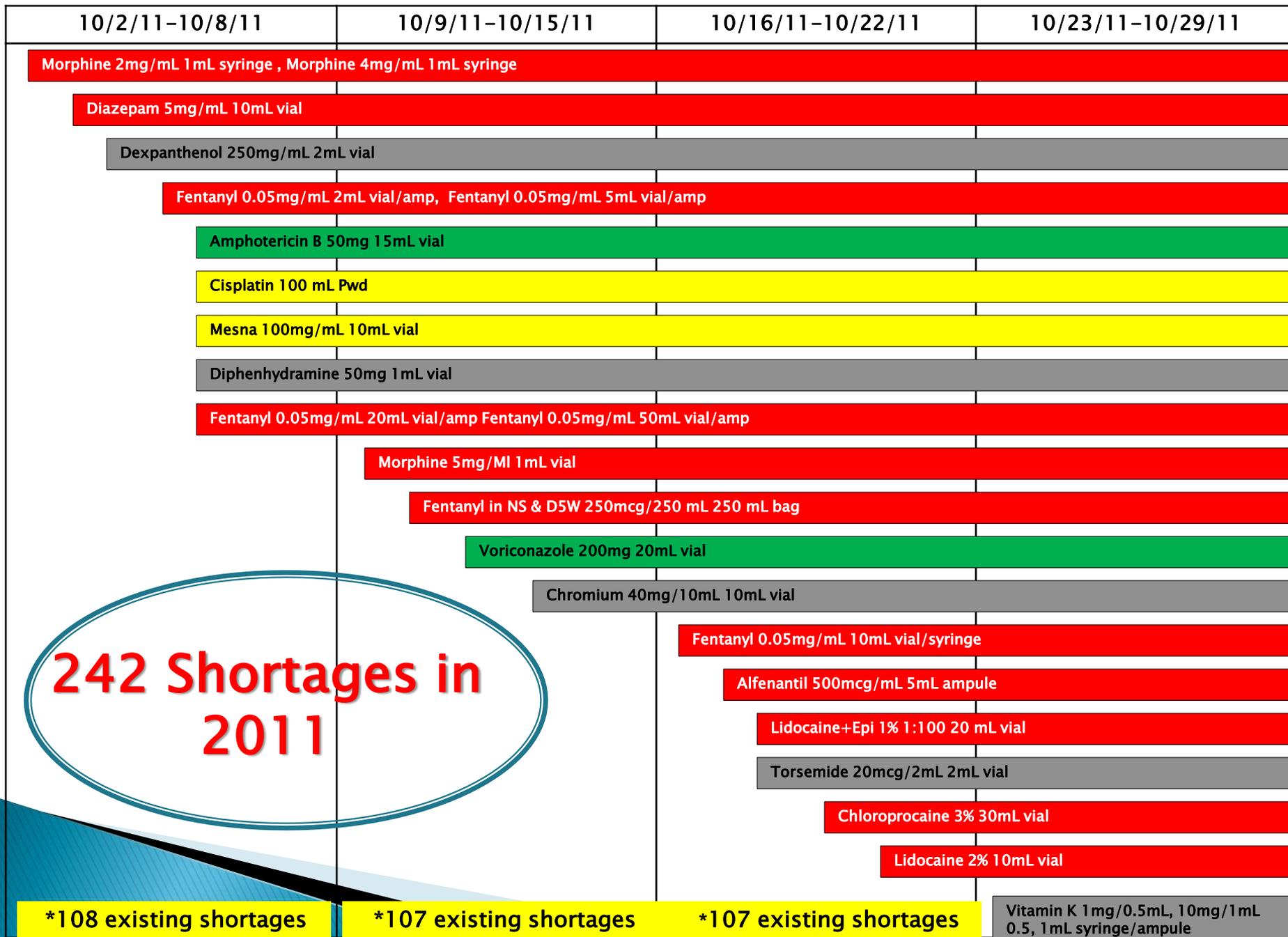
Hospital Recall Survey

- 99% (73 / 74) of hospitals would recall all compounded products not yet administered unless they could verify that they had not received the recalled ingredient
- One hospital is recording mfr and lot #

Recommendation

- Adopt current practice (stated above) to ensure timely removal and quarantining of recalled products

1 Month of Drug Shortages involving Medications used in Sterile Compounding



Distractions Result in Medication Errors

- ▶ USP's MEDMARX medication error-reporting program data found **distractions to be the most common** factor contributing to errors¹
- ▶ Error-producing conditions, such as distractions and interruptions, may predicate an error^{2,3}
- ▶ Sterile compounding occurs in **high-volume, high-demand work environments** where safety may be sacrificed for other priorities⁴
- ▶ **Increased complexity** creates an error-prone medication-use process at the expense of patient safety and quality⁵

1. Santelle JP, Cousins DD, McMeeken J, Hicks R. Medication Errors: Experience of the United States Pharmacopeia (USP) MEDMARX Reporting System. *J Clin Pharmacol* 2003 43: 760.

2. Patient Safety and Quality: An Evidence-Based Handbook for Nurses. Hughes RG, editor. Rockville (MD): Agency for Healthcare Research and Quality (US); 2008 Apr.

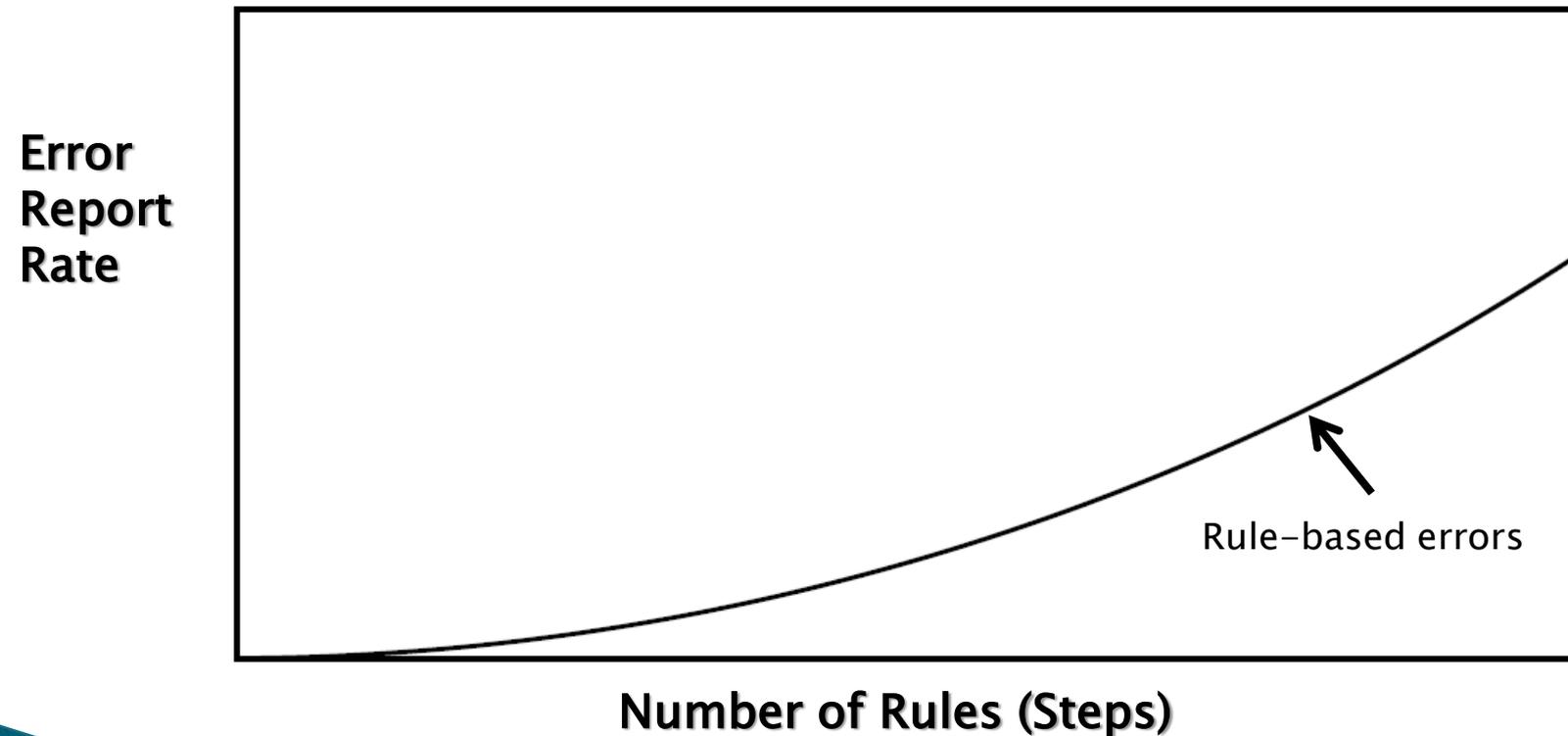
3. Reason J. Human error: models and management. *BMJ* 2000;320(7237):768-770.

4. Proceedings of a summit on preventing patient harm and death from i.v. medication errors. *Am J Health-Syst Pharm.* 2008;65:2367-79.

5. Brennan T, Donnelly K, Somani S. Needs and opportunities for achieving optimal outcomes from the use of medicines in hospitals and health systems. *Am J Health-Syst Pharm.* 2011;68:1086-96.

Mistake-Proofing the Sterile Compounding Area

- ▶ Increasing the number of steps may result in an increase in the number of errors instead of reducing them as intended



Using IV Pharmacists' Specialized Knowledge and Skills to Ensure Safety

Dose, Concentration

Incompatibilities

Route of administration

Osmolarity

Stability

Allergies, Preservatives

Rate of Infusion

IV Pharmacists' Specialized Knowledge of Complex Therapies

High-risk therapies

Chemotherapy
High-alert medications
Patient controlled analgesia (PCA)

High-risk routes

Epidural
Intrathecal
Ophthalmic

High-risk populations

Pediatrics
Dose considerations
Volume considerations
Preservatives
Critical Care

TPNs

Multiple additives
Compatibilities
Use of automated compounders
Order entry

Multiple independent checks performed to ensure safe, accurate compounding

IV Pharmacist's Role in Sterile Compounding Safety

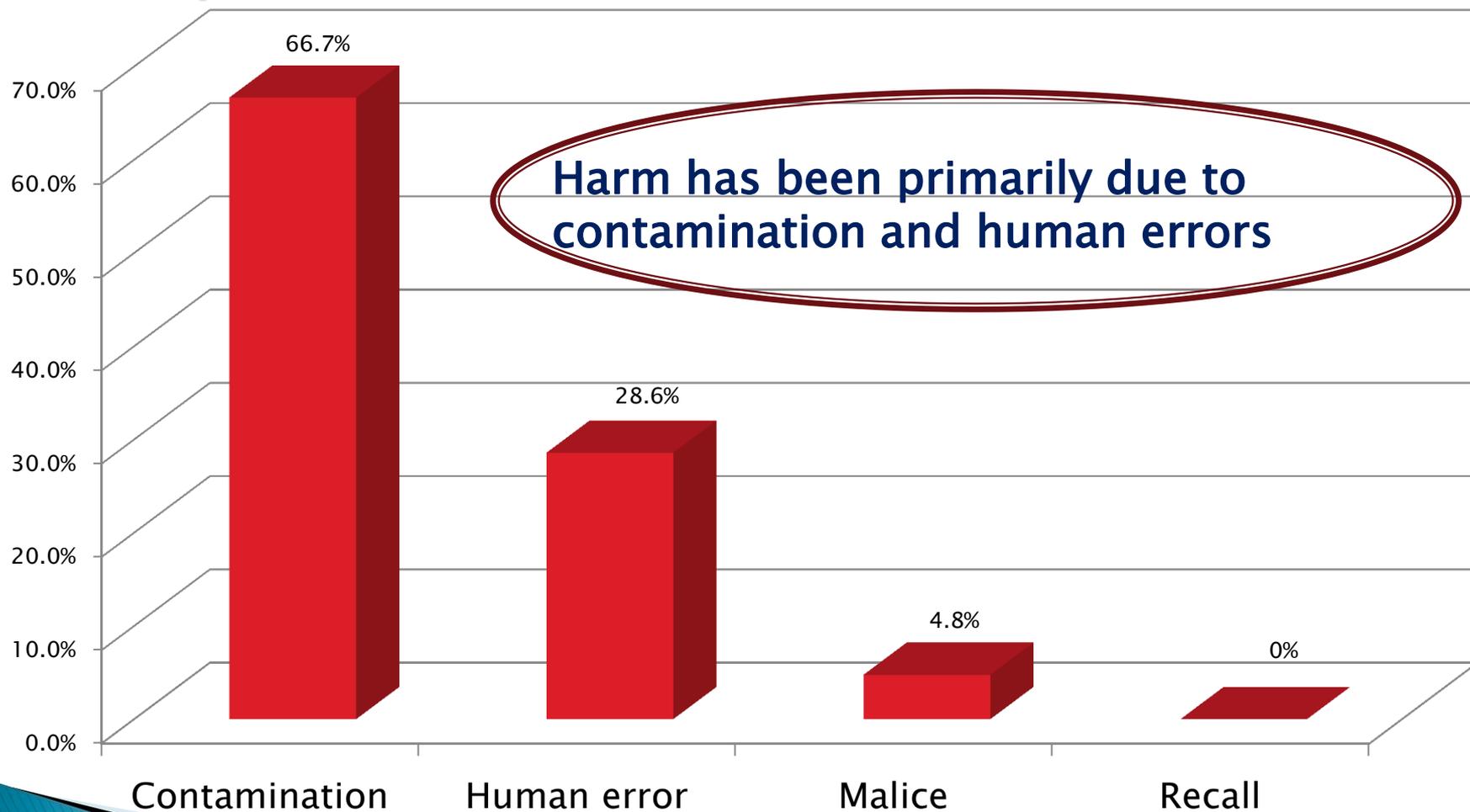
Drug Order	Problem Intercepted	Outcome	Potential Consequence Avoided
Carmustine 450 mg in 300 ml D5W (1.5mg/ml)	Concentration exceeds Maximum concentration: 1 mg/ml	Change drug volume to 500 ml	Avoided infusion related adverse effects from high concentration
Mitoxantrone 17.7 mg ordered daily x 3 days= 53.1 mg total dose	Total dose ordered: 88.5 mg	Order changed	Avoided incorrect dosing regimen
Cytarabine label printed as bag #5	Records indicate that 5 doses were already sent; confirmed with pharmacist that extra dose printed (technology issue)	Extra dose not prepared	Avoided administering an extra dose of chemotherapy
Ondansetron 6.8 mg for pediatric patient	Order placed as undiluted medication; recommended to dilute to 1 mg/ml for administration	Medication diluted	Avoided infusion-related adverse effects from high concentration

IV Pharmacist's Role in Sterile Compounding Safety

Drug Order	Problem Intercepted	Outcome	Potential Consequence Avoided
Alteplase ordered in patient with latex allergy	TPA contains latex that cannot be filtered via 0.22micron filter	Clarified severity of allergy prior to administration of medication	Avoided any potential latex-related ADRs
Sulfamethoxazole-Trimethoprim dose ordered has 2 hr stability based on dilution ratio	Infusion time for medication is 2 hr	Diluted dose in order to ensure stable for infusion	Avoided drug expiration before infusion complete
Methotrexate 91 mg (3.64ml) IM for ectopic pregnancy	Maximum of 2ml is accepted for IM administration	Order changed to 45.5 mg (1.8mL) x 2 doses	Avoided infusion-related adverse effects from large IM volume
TPN order contained excessive amount of calcium and phosphate	Excessive amounts may lead to precipitation	Electrolytes changed so that the product would not exceed threshold	Avoided precipitation and potential thrombotic sequelae

U.S. Publicly Reported Events Associated with Sterile Compounding

Analysis of Causes of Harmful Patient Events



Alabama TPN

- Six hospitals outsourced compounding
- Used Non-Sterile Powder
- 17 patients with bloodstream infections; 9 deaths

USP Pharmacopeial Education

Compounding of 15% Amino Acid Solution



- ❑ Bulk amino acid powders
 - Nonsterile
- ❑ Sterile water in large mixing container
- ❑ 80–100 L batches
- ❑ On occasion, compounded 1–2 days prior to filtration



- Utilized tap water to rinse mixing containers
- Insufficient sampling of amino acid solution (non-sterile) for sterility testing
- Did not follow USP 797

USP 797

- ▶ National standards for sterile compounding to ensure the highest quality
 - ▶ Surveyed by CDPH
 - ▶ Has been adopted by hospital pharmacies
 - ▶ Dating of sterile compounded products is defined by USP based on risk levels which are determined by the level of complexity to prepare compounded products
 - ▶ **Main Goals: Sterility and safety of compounded products**
- 

Sterility and Stability of Sterile Compounded Medications

<u>Sterility:</u> USP 797 National Standards Defines storage until the IV infusion begins <u>Stability:</u> Mfr info, published compendium and literature				CaBOP Supply Mfgr, Lot # & Must be Logged to <u>Reuse</u> Admixtures (Needles, Syringes, Tubing)
<u>Storage until infusion begins</u>	<u>Room Temp</u>	<u>Refrig</u>	<u>Frozen</u>	
Immediate Use	1 hr	1 hr	N/A	
Low Risk \leq 2 adds; BUD < 12 (non-clean room)	12 hrs	12 hrs	12 hrs	
Low Risk \leq 2 adds (IV Clean Room)	48 hrs	14 days	45 days	<u>24 hours</u> No reuse
Medium Risk > 2 adds, chemo, TPN	30 hrs	9 days	45 days	<u>24 hours</u> No reuse
High Risk-non-sterile powder not done	24 hrs	3 days	45 days	<u>24 hours</u> No reuse

Ensuring Sterile Compounding Safety

Recommended Best Practices for Sterile Compounding Safety Based on Ca BOP and Professional Standards*

Training and competency

Demonstrated infection control practices

Observation of sterile compounding processes

Independent double checking processes for complex therapies

Use of standard concentrations whenever possible

Ongoing review of internal and external compounding errors to identify opportunities to improve safety

Use of machine-readable coding to verify medications used in automated IV admixture compounders

Evaluation of outsourced vendors

*Institute of Safe Medication Practices, American Society of Health-Systems Pharmacist, USP 797

Hospital Requirements Related to Expiration Date

- ▶ Prior to dispensing or compounding, medications are checked to ensure that they are not expired
- ▶ Hospitals are required to check **all areas** where medications are stored monthly to ensure the absence of medications that are expired
 - CDPH, CMS Conditions of Participation, The Joint Commission
- ▶ Implications of documenting expiration dates:
 - ↑ time involved in compounding process
 - ↑ distractions
 - ↓ focus on accuracy, safety and sterile preparation

Patient-Centered Sterile Compounding to Prevent Harm



- Safe, timely compounding based on best practices
- Minimizing distractions
- Minimizing preventable waste

Documentation in order to enable retrospective review

Hospital Sterile Compounding Recommendations

1. Exempt **“Hospital Patient–Specific Compounded Medications”** from requiring documentation of mfr and lot number
 - **Definition of “Hospital Patient–Specific Compounded Medications”**: Medications compounded using sterile products for an individual patient based on a physician order (prescription) intended to be given within 24 hours
 - Interpretation: Medications prepared and not administered due to changes in patients’ condition could be used if sterility and stability standards are met
2. Continue to record manufacturer and lot number for medications for **non–patient specific compounding** and non–sterile compounded products
 - **Definition of “Non–Patient–Specific Compounded Medications”**: Compounding of medications in anticipation of physicians’ orders