

Board of Pharmacy

Final Statement of Reasons

Hearing Date: October 29, 2008

Subject Matter of Proposed Regulation: Compounding and Sterile Injectable Compounding

Updated Information

The Initial Statement of Reasons (ISOR) is included in this rulemaking file. The information contained therein is updated as follows:

The ISOR referenced on page 1 two section numbers to be repealed: 16 CCR 1761.1 and 16 CCR 1761.2. Each number had a transposition error and is correctly referenced below. Despite the transposition errors, the correct section numbers were referenced elsewhere throughout the ISOR.

Sections Affected: Repeal sections
16 CCR 1716.1
16 CCR 1716.2

Non-Substantive Changes

With the express authority of the Board to make non-substantive changes, the Executive Officer made the following non-substantive corrections to the specific text which are reflected in the Order of Adoption.

- In amended section 1751 (pg 9) and in amended section 1751.01 (pg 12) each referenced in the footnote “Authority cited: . . . Section 18944(a), Health and Safety Code.” There is no subdivision (a) of this Health and Safety Code section; thus, the reference was changed in each footnote to accurately read “Section 18944, Health and Safety Code.”
- In proposed section 1735(b), on the second line, a comma was omitted between the words “rectal topical” and the language was corrected to read “direction(s) for oral, rectal, topical, or injectable administration,....”
- In proposed section 1735.2(g), on the second line, a typographical error was corrected to reflect the word “compendia” (not “compendial”).

Local Mandate:

None

Business Impact:

The board has determined that this regulation will not have a significant adverse economic impact on businesses.

This determination was based on the absence of testimony indicating adverse economic impact regarding this rulemaking proposal during the regulation hearing held by the board and during the three comment periods.

Consideration of Alternatives:

No reasonable alternative to the regulation would be either more effective in carrying out the purpose for which the action is proposed or would be as effective and less burdensome to the affected persons than the proposed regulation.

Objections or Recommendations / Responses

The board received many comments to its proposal during the 45-day and two 15-day comment periods. Each comment / recommendation is summarized and is followed by the board's response. For ease of reading and for each comment period, an index is provided of those who commented.

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Comments from Clara E. Evans, Director, Public Policy & Fiscal Advocacy, Catholic Healthcare West (CHW)

Comment #1

CHW stated that they support the regulation proposal to strengthen regulations for pharmacies that compound medications, but have serious concerns regarding the new labeling requirements and pharmacy record requirements on certain compounded IV medications, particularly for pharmacies in acute care facilities dispensing one-time and immediate-use (STAT) medications. CHW is concerned that the added documentation requirements will delay preparation and delivery, placing patients at risk for no additional patient safety benefit.

Board Response

The board appreciates CHW's general support for the regulation proposal; however, it disagrees with the conclusion that the documentation requirements found in section 1753.3 will delay preparation and delivery of medications. In an acute care setting, the regulation proposal allows for one-time preparations to be documented in the pharmacy's copy of the patient's chart order. This chart order can serve as the master formula. Further, the records required in section 1735.3 do not need to be completed in advance of the administration of the compounded drug, thus ensuring that the patient receives STAT medicines timely.

Several of the record keeping requirements for sterile products are already required in current regulation. This proposal does expand on the requirements and now also includes the identity of the person who compounded the drug, the identity of the pharmacist reviewing the final drug product, the quantity of each component, the equipment used in compounding the drug product as well as a pharmacy assigned reference number. The board included the requirements for the identity of the person who compounded the drug as well as the pharmacists who reviewed the final drug product to allow a nonpharmacist to compound the medication, as allowed in other areas of pharmacy law, and to require that a pharmacist complete a review. This check is an essential consumer protection component. Further, the equipment used is necessary to allow for a quality assurance review to be complete should a problem occur with such compounded medications. An internal pharmacy reference number is necessary to allow for a recall of a product if necessary--another essential consumer protection component.

Comment #2

CHW sees the value of documenting pharmacy reference numbers or lot numbers on the label of each dispensed IV as well as providing additional information in the pharmacy log when such labeling and recordkeeping requirements are primarily intended to be used in the event of a medication recall. However, CHW suggests that this information is not useful when the medication dispensed on a one-time, immediate-use basis. CHW urges the board to exempt

one-time, immediate-use sterile products from the manufacturer or supplier and lot number for each component requirement, equipment used in compounding the drug products, the pharmacy assigned reference or lot number for the compounded drug product as well as the expiration date of the final compounded drug product requirements.

Board Response

The board appreciates CHW's understanding of the necessity of the labeling requirements. The intent of the regulation proposal is to improve patient safety. Following the 45-day comment period, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within two hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

Based on comments received during the first 15-day comment period, the board again modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Comment #3

CHW is concerned the minimum 3-year record retention policy is unrealistic considering the hundreds or thousands of products compounded daily, whether STAT or non-urgent. CHW requests this timeframe be reevaluated and take into account common record retention policies.

Board Response

The 3-year time frame required in this proposal is consistent with current pharmacy law that specifies that all records must be maintained for three years from the date of dispensing (see Business and Professions Code section 4105(c)).

Comments from Steve Sloan

Comment #4

The proposed regulations do not take into consideration emergency situations where the additional logging and labeling requirements will be burdensome and cause delays in therapy. The requirements do not improve patient safety because the dose is

administered immediately after compounding. Please make an exception for emergency use.

Board Response

The intent of the regulation proposal is to improve patient safety. Following the 45-day comment period, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within two hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

Based on comments received during the first 15-day comment period, the board again modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Comments from Stephan Flascha

Comment #5

I am really concerned about the documentation requirements in Compounding in an IV room in a major hospital. Please consider this requirement as undoable.

Board Response

Mr. Flascha's comment is a bit vague. In general, however, the documentation is necessary to ensure the integrity, potency, quality and strength of the compounded drug product(s) prepared and delivered to patients. However, should Mr. Flascha's comments be specific to requesting an exemption from one-time immediate use compounded medications, in an acute care setting, the regulation proposal allows for one-time preparations to be documented in the pharmacy's copy of the patient's chart order. This chart order can serve as the master formula. Further, the records required in section 1735.3 do not need to be completed in advance of the administration of the compounded drug, thus ensuring that the patient receives STAT medicines timely.

Comments from Suzanne Baertsch

Comment #6

“I work in a hospital where we compound hundreds of IVs daily in a sterile environment. The additional time it would take for all this record keeping would mean we would have to cut back in other areas which will make it worse for overall patient care. I am especially concerned about first dose antibiotics or cardiovascular drips.”

Board Response

The board rejects this comment. Several of the record keeping requirements for sterile products are already required in current regulation. This proposal does expand on the requirements, and now also includes the identity of the person who compounded the drug, the identity of the pharmacist reviewing the final drug product, the quantity of each component, the equipment used in compounding the drug product as well as a pharmacy assigned reference number. The board included the requirements for the identity of the person who compounded the drug as well as the pharmacists who reviewed the final drug product to allow a nonpharmacist to compound the medication, as allowed in other areas of pharmacy law, and to require that a pharmacist complete a review. This check is an essential consumer protection component. Further, the documentation of the equipment used is necessary to allow for a quality assurance review to be completed should a problem occur with such compounded medications. An internal pharmacy reference number is necessary to allow for a recall of a product if necessary, another essential consumer protection component.

Comment #7

I understand it is valuable to be able to trace back how something is made, but remember, this still does not prevent an error. It only allows you to see what the error is.

Board Response

The board appreciates Ms. Baertsch’s understanding of the necessity of these requirements, but disagrees that these requirements do not prevent errors. In the case of a recall, the specified recordkeeping requirements would allow for patient identification and for a systematic review to be accomplished. Ultimately, patient safety could be improved by system changes made as a result of that review and – ultimately – could prevent future errors.

Comments received from Deborah A. Hass, PharmD, BCOP, Stanford/Oncology Clinical Pharmacist, Stanford Hospitals and Clinics

Comment #8

I agree with the CSHP in asking for an exemption of logging and pharmacy lot number assignment/labeling for those “immediate use” products as defined by USP. These products are needed urgently and there is a potential of delay with the additional record keeping requirements with no benefit to the patient. Any future recall of product would be moot as the IV would be already administered as an immediate-use. This means every STAT alteplase, epinephrine, diltiazem or other like-saving medication prepared by a pharmacist during cardiac resuscitation, in the emergency department, in the operating rooms or in other critical care areas would be delayed in a few minutes longer to assure logging, assignment, and labeling of the IV bag with the pharmacy lot number.

Board Response

The intent of the regulation proposal is to improve patient safety. Following the 45-day comment period, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within two hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

Based on comments received during the first 15-day comment period, the board again modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Comment #9

For all products, whether STAT or non-urgent, extensive recordkeeping would be required for each product prepared and maintained for a minimum of 3 years. Considering the thousands of records daily that would be generated here at Stanford to meet the requirement, the proposed method for recordkeeping and maintaining records for 3 years is unrealistic.

Board Response

Several of the record keeping requirements for sterile products are already required in current regulation. This proposal does expand on the requirements,

and now also includes the identity of the person who compounded the drug, the identity of the pharmacist reviewing the final drug product, the quantity of each component, the equipment used in compounding the drug product as well as a pharmacy assigned reference number. The board included the requirements for the identity of the person who compounded the drug as well as the pharmacists who reviewed the final drug product to allow a nonpharmacist to compound the medication, as allowed in other areas of pharmacy law, and to require that a pharmacist complete a review. This check is an essential consumer protection component. Further, the documentation of the equipment used is necessary to allow for a quality assurance review to be completed should a problem occur with such compounded medications. An internal pharmacy reference number is necessary to allow for a recall of a product if necessary, another essential consumer protection component.

Further, the 3-year time frame required in this proposal is consistent with current pharmacy law that specifies that all records must be maintained for three years from the date of dispensing (see Business and Professions Code section 4105(c)).

Comments from Rob Chopyk, Clinical Pharmacist, Community Hospital of the Monterey Peninsula

Comment #10

I ask for an exemption of the logging and pharmacy lot number assignment/labeling for those “immediate use” products as defined by USP. These products are needed urgently and there is a potential of delay with the additional record keeping requirements with no benefit to the patient. Any future recall of product would be moot as the IV would have already been administered as an immediate-use.

Board Response

The intent of the regulation proposal is to improve patient safety. Following the 45-day comment period, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within two hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

Based on comments received during the first 15-day comment period, the board again modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration

within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

The board recognizes that U.S. Pharmacopoeia (USP) General Chapter 797 (effective January 1, 2004) provides *best practices* for compounding sterile products, but USP 797 is not incorporated by reference into the board's statutes or regulations. As such, USP 797 does not control the board's enforcement of its own regulations regarding pharmacy compounding.

Additionally, upon recall of a product, a systematic review could not be accomplished without the appropriate documentation and recordkeeping required of compounded products. Without adequate documentation, necessary or systematic changes may not be realized and made to prevent future errors, a key patient safety issue.

Comment #11

It is unreasonable to think that every STAT alteplase, epinephrine, diltiazem or other like-saving medication prepared by a pharmacist during cardiac resuscitation, in the emergency department, in the operating rooms or in other critical care areas would be delayed in a few minutes longer to assure logging, assignment, and labeling of the IV bag with the pharmacy lot number.

Board Response

It would appear that Pharmacist Chopyk's comment is in support of the board's proposal and that it is unreasonable that identified products would be delayed because of the proposals requirements.

However, should Dr. Chopyk's comment assert that the proposed regulations *would* delay the administration of compounded drug products in a critical care setting, the board disagrees with the conclusion that the documentation requirements found in section 1753.3 will delay preparation and delivery of medications. In an acute care setting, the regulation proposal allows for one-time preparations to be documented in the pharmacy's copy of the patient's chart order. This chart order can serve as the master formula. Further, the records required in section 1735.3 do not need to be completed in advance of the administration of the compounded drug, thus ensuring that the patient receives STAT medicines timely.

Documentation is necessary to ensure the integrity, potency, quality and strength of the compounded drug product(s) prepared and delivered to patients.

Comment #12

For all products, whether STAT or non-urgent, extensive recordkeeping would be required for each product prepared and maintained for a minimum of 3 years. Considering the hundreds (or in some larger hospitals, thousands) of records daily that would be generated to meet the requirement, the proposed method for recordkeeping and maintaining records for 3 years is unrealistic and wasteful.

Board Response

This regulation does not specify a method for recordkeeping, rather just specifies what records must be kept and for how long. The 3-year time frame required in this proposal is consistent with current pharmacy law that specifies that all records must be maintained for three years (see Business and Professions Code section 4105(c)).

Comments from Robert Fukano, PharmD, Intensive Care Unit/Critical Care Unit Clinical Pharmacist, Community Hospital of the Monterey Peninsula

Comment #13

I have some serious concerns pertaining to the proposed changes for medication regulations, specifically with IV medications preparation and the urgent needs of some of these medications. I would ask for an exemption of logging and pharmacy lot number assignment/labeling for those “immediate use” products as defined by USP. These products are needed urgently and there is not potential of delay with the additional record keeping requirements with no benefit to the patient. Any future recall of product would be moot as the IV would be already administered as an immediate-use.

Board Response

The intent of the regulation proposal is to improve patient safety. Following the 45-day comment period, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within two hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

Based on comments received during the first 15-day comment period, the board again modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board recognizes that U.S. Pharmacopoeia (USP) General Chapter 797 (effective January 1, 2004) provides *best practices* for compounding sterile products, but USP 797 is not incorporated by reference into the board's statutes or regulations. As such, USP 797 does not control the board's enforcement of its own regulations regarding pharmacy compounding.

Additionally, upon recall of a product, a systematic review could not be accomplished without the appropriate documentation and recordkeeping required of compounded products. Without adequate documentation, necessary or systematic changes may not be realized and made to prevent future errors, a key patient safety issue.

Comment #14

It is unreasonable to think that every STAT alteplase, epinephrine, diltiazem or other life-saving medication prepared by a pharmacist during cardiac resuscitation, in the emergency department, in the operating rooms or in other critical care areas would be delayed a few minutes longer to assure logging, assignment, and labeling of the IV bag with a pharmacy lot number.

Board Response

It would appear that Dr. Fukano's comment is in support of the board's proposal and that it is unreasonable that identified products would be delayed because of the proposals requirements.

However, should Dr. Fukano's comment assert that the proposed regulations *would* delay the administration of compounded drug products in a critical care setting, the board disagrees with the conclusion that the documentation requirements found in section 1753.3 will delay preparation and delivery of medications. In an acute care setting, the regulation proposal allows for one-time preparations to be documented in the pharmacy's copy of the patient's chart order. This chart order can serve as the master formula. Further, the records required in section 1735.3 do not need to be completed in advance of the administration of the compounded drug, thus ensuring that the patient receives STAT medicines timely.

Documentation is necessary to ensure the integrity, potency, quality and strength of the compounded drug product(s) prepared and delivered to patients.

Comment #15

There are dozens of hospitals in California without 24-hour pharmacy services in which nurses are compounding and mixing intravenous products without the aid of any sterile preparation area or laminar flow hood/biological safety cabinet. Why the separation of record-keeping of pharmacy-prepared versus nurse-prepared or physician-prepared (thinking of anesthesiologists who prepare medication in the operating room)?

Board Response

The board believes that nurses and physicians performing reconstitution and administration are covered in B&PC 4127.1(e). Documentation of those activities is maintained in the patient's record. Nurses and physicians that compound medications outside of the hospital pharmacy are outside of the board's jurisdiction.

Comment #16

In addition, for all products, whether STAT or non-urgent, extensive recordkeeping would be required for each product prepared and maintained for a minimum of 3 years. Considering the hundreds (or in some larger hospitals) thousands) of records daily that would be generated to meet the requirement, the proposed method for recordkeeping and maintaining records for 3 years is unrealistic and wasteful.

Board Response

This proposal does not specified a method for recordkeeping, rather just specifies what records must be kept and for how long. The 3-year time frame required in this proposal is consistent with current pharmacy law that specifies that all records must be maintained for three years (see Business and Professions Code section 4105(c)).

Comments received from Joanne Hayashi, PharmD, Clinical Pharmacist at the Community Hospital of the Monterey Peninsula

Comment #17

I have some serious concerns pertaining to the proposed changes for medication compounding regulations, specifically with IV medications preparation and the urgent needs of some of these medications. I would ask for an exemption of logging and pharmacy lot number assignment/labeling for those "immediate use" products as defined by USP. These products are needed urgently and there is a potential of delay with the additional record keeping requirements with no benefit to the patient. Any future recall of product would be moot as the IV would be already administered as an immediate-use.

Board Response

The intent of the regulation proposal is to improve patient safety. Following the 45-day comment period, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within two hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

Based on comments received during the first 15-day comment period, the board again modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

The board recognizes that U.S. Pharmacopoeia (USP) General Chapter 797 (effective January 1, 2004) provides *best practices* for compounding sterile products, but USP 797 is not incorporated by reference into the board's statutes or regulations. As such, USP 797 does not control the board's enforcement of its own regulations regarding pharmacy compounding.

Additionally, upon recall of a product, a systematic review could not be accomplished without the appropriate documentation and recordkeeping required of compounded products. Without adequate documentation, necessary or systematic changes may not be realized and made to prevent future errors, a key patient safety issue.

Comment #18

It is unreasonable to think that every STAT alteplase, epinephrine, diltiazem or other life-saving medication prepared by a pharmacist during cardiac resuscitation, in an emergency department, in the operating rooms or in other critical care areas would be delayed a few minutes longer to assure logging, assignment, and labeling of the IV bag with a pharmacy log number.

Board Response

It would appear that Dr. Hayashi's comment is in support of the board's proposal and that it is unreasonable that identified products would be delayed because of the proposals requirements.

However, should Dr. Hayashi's comment assert that the proposed regulations *would* delay the administration of compounded drug products in a critical care setting, the board disagrees with the conclusion that the documentation requirements found in section 1753.3 will delay preparation and delivery of medications. In an acute care setting, the regulation proposal allows for one-time preparations to be documented in the pharmacy's copy of the patient's chart order. This chart order can serve as the master formula. Further, the records required in section 1735.3 do not need to be completed in advance of

the administration of the compounded drug, thus ensuring that the patient receives STAT medicines timely.

Documentation is necessary to ensure the integrity, potency, quality and strength of the compounded drug product(s) prepared and delivered to patients.

Comment #19

In addition, for all products, whether STAT or non-urgent, extensive recordkeeping would be required for each product prepared and maintained for a minimum of 3 years. Considering the hundreds (on in some larger hospitals, thousands) of records daily that would be generated, to meet the requirement, the proposed method for recordkeeping and maintaining records for 3 years is unrealistic and wasteful. It may also compromise patient safety since the focus will be shifted from the real task at hand – safe, aseptic compounding of CSPs to the task of recordkeeping.

Board Response

Several of the record keeping requirements for sterile products are already required in current regulation. This proposal does expand on the requirements, and now also includes the identity of the person who compounded the drug, the identity of the pharmacist reviewing the final drug product, the quantity of each component, the equipment used in compounding the drug product as well as a pharmacy assigned reference number. The board included the requirements for the identity of the person who compounded the drug as well as the pharmacists who reviewed the final drug product to allow a nonpharmacist to compound the medication, as allowed in other areas of pharmacy law, and to require that a pharmacist complete a review. This check is an essential consumer protection component. Further, the documentation of the equipment used is necessary to allow for a quality assurance review to be completed should a problem occur with such compounded medications. An internal pharmacy reference number is necessary to allow for a recall of a product if necessary, another essential consumer protection component.

This regulation does not specify a method for recordkeeping, rather it specifies what records must be kept and for how long. The 3-year time frame required in this proposal is consistent with current pharmacy law that specifies that all records must be maintained for three years (see Business and Professions Code section 4105(c)).

Comments received from Dawn Benton, Executive Vice President, CEO, California Society of Health-System Pharmacists

Comment #20

The California Society of Health-System Pharmacists (CSHP) commends and supports the California Board of Pharmacy (Board) for their previous and current efforts to strengthen the regulations surrounding pharmacies that compound medications.

Board Response

The board appreciates CSHP support with our efforts to strengthen the regulations surrounding pharmacies that compound medications. The intent of the regulation proposal is to improve patient safety.

Comment #21

CSHP has concerns regarding sections of the proposed compounding regulations that pertain to new labeling and pharmacy record requirements with regard to certain compounded IV medications that would inevitably delay treatment to the direst of patients.

Board Response

The intent of the regulation proposal is to improve patient safety. While Ms. Benton’s comments do not address any specific section or subsection of the proposed regulation, the board does address labeling requirements of compounded drug products in §1753.3. Section 1753.3(a)(6) provides that the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code, are exempt from the recordkeeping requirements of that subsection. In an acute care setting, the regulation proposal allows for one-time preparations of compounded drug products to be documented in the pharmacy’s copy of the patient’s chart order. This chart order can serve as the master formula.

Comment #22

CSHP members are concerned that the added documentation requirements for both the label and pharmacy log will delay the preparation and delivery of these one-time and immediate-use medications; therefore placing the patient at risk without any additional benefit to patient safety and care.

Board Response

The board disagrees that the documentation requirements found in section 1753.3 will delay preparation and delivery of medications and place patients at risk. Several of the record keeping requirements for sterile products are already required in current regulation. This proposal does expand on the requirements, and now also includes the identity of the person who compounded the drug, the identity of the pharmacist reviewing the final drug product, the quantity of each component, the equipment used in compounding the drug product as well as a pharmacy assigned reference number. The board included the requirements for the identity of the person who compounded the drug as well as the pharmacists

who reviewed the final drug product to allow a nonpharmacist to compound the medication, as allowed in other areas of pharmacy law, and to require that a pharmacist complete a review. This check is an essential consumer protection component. Further, the documentation of the equipment used is necessary to allow for a quality assurance review to be completed should a problem occur with such compounded medications. An internal pharmacy reference number is necessary to allow for a recall of a product if necessary, another essential consumer protection component.

Comment #23

CSHP fails to see the advantage in delaying treatment for patients with critical conditions to record the pharmacy reference lot number on the label of each dispensed IV and the additional information in the pharmacy log when such labeling and recordkeeping requirements are primarily intended to be used in the event of a medication recall. CSHP believes that such information would be obsolete in situations where patients are in need of one-time and immediate-use compounded products as any future recall of these products would be moot as the IV would already be administered to the patient.

Board Response

The board's response to CSHP's previous comment (Comment #22) addresses Ms. Benton's comment regarding those recordkeeping requirements for those products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

In the case of a recall, the specified recordkeeping requirements would allow for patient identification and for a systematic review to be accomplished. Ultimately, patient safety could be improved by system changes made as a result of that review and – ultimately – could prevent future errors.

Comments from Mona Ghomeshi, PharmD, Mercy San Juan Medical Center

Comment #24

Dr. Ghomeshi stated her opposition to the proposed regulations relating to compounding. She was concerned that delays in patient care will occur due to logging medication prepared in emergent situations, such as cardiac arrest.

Board Response

The board disagrees that the proposed regulations will cause delays in patient care. To the contrary, the intent of the regulation proposal is to improve patient safety.

In an acute care setting, the regulation proposal allows for one-time preparations to be documented in the pharmacy's copy of the patient's chart

order. This chart order can serve as the master formula. Further, the record keeping requirements in section 1735.3 do not need to be completed in advance of the administration of the compounded drug, thus ensuring that the patient receives STAT medicines timely.

Comment #25

Dr. Ghomeshi asked the board to exempt acute care hospitals from the proposed record keeping requirements the pharmacy reference number or the lot number on the label for those compounded drug products prepared for one-time or immediate-use IV medications.

Board Response

Following the 45-day comment period, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within two hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

Based on comments received during the first 15-day comment period, the board again modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Joint comments from Heidi Barsuglia, California Retailers Association (CRA), and Mary Staples, National Association of Chain Drug Stores (NACDS)

Comment #26

Ms. Barsuglia and Ms. Staples acknowledged the board’s decision to exclude flavor enhancements of commercially available oral medications from the definition of “compounding.” They also expressed appreciation to the board for their decision not requiring establishment of a professional relationship between a pharmacist and (both) a prescriber and a patient prior to compounding a drug.

Board Response

The board accepts and appreciates the comments of the California Retailers Association and the National Association of Chain Drug Stores.

Comment #27

CRA and NACDS oppose compounding regulations preventing pharmacies from engaging in “non-sterile basic” compounding. They referred to the Pharmacy Compounding Accreditation Board definition of “non-sterile basic” compounding which involved preparation of a formulation containing two or more non-sterile commercially available products employing basic pharmacy training skill sets. They asked the board to reconsider whether pharmacies which engage in non-sterile basic compounding are required to meet the same requirements (including complete self-assessment) as more complex types of compounding.

Board Response

The board rejects this comment. 1735 specifies what does and does not constitute compounding. The Pharmacy Compounding Accreditation Board’s definition of compounding is not incorporated by reference into the board’s statutes or regulations. As such, that definition does not control the board’s enforcement of its own regulations regarding pharmacy compounding.

Comment #28

Ms. Barsuglia and Ms. Staples acknowledged the board’s determination that allows pharmacies to record the master formula on the prescription document for preparations that pharmacies do not routinely compound. However, they asked the board to reconsider whether pharmacies that only engage in non-sterile basic compounding should have to comply with requirements for a compounding policy and procedure manual, documentation of the facilities and equipment necessary for compounding, documentation of pharmacy staff training and on-going competency evaluation, and a written quality assurance plan. The CRA and NACDS position is that these additional requirements are unnecessary and will act as a hindrance to pharmacies that provide only non-sterile basic compounding services to patients.

Board Response

The board disagrees that record keeping requirements are not necessary for those that engage in non-sterile basic compounding. If a pharmacy ‘compounds’ drug products as defined in 1735, that pharmacy is subject to the provisions of Title 16, Article 4.5 (general compounding) or Article 7 (sterile compounding), and is required to comply with those requirements as defined by those Articles.

The intent of the regulations is to improve patient safety. Even for those products that are not designated ‘sterile’ it is an essential consumer protection component to ensure that products compounded by or under the direction of a pharmacist are in compliance with pharmacy law and regulations, to ensure patient safety.

The documentation is necessary to ensure the integrity, potency, quality and strength of the compounded drug product(s) prepared and delivered to patients – both sterile and non-sterile.

Comments from Geralyn Trujillo, MPP, Director, State Government Affairs, American Society of Health-System Pharmacists (ASHP)

Comment #29

Ms. Trujillo stated opposition to proposed regulation changes to California Code of Regulations Article 4.5, Compounding. On behalf of ASHP, Ms. Trujillo asked the board to consider the professional judgment of pharmacies and the policies of the institutions they practice in during situations demanding flexibility to decide what is best for patients. She referenced label requirements shown in Chapter 797 of the United States Pharmacopoeia (USP), Guidebook to Pharmaceutical Compounding – Sterile Preparations:

“...unless immediately and completed administered...the [compounded sterile preparation (CSP)] shall bear a label listing patient identification information, the names and amounts of all ingredients, the name or initials of the person who prepared the CSP, and the exact 1-hour beyond-use date (BUD) and time.”

Board Response

The board rejects this comment. The board recognizes that U.S. Pharmacopoeia (USP) General Chapter 797 (effective January 1, 2004) provides *best practices* for compounding sterile products, but USP 797 is not incorporated by reference into the board’s statutes or regulations. As such, USP 797 does not control the board’s enforcement of its own regulations regarding pharmacy compounding. The intent of the regulation is to ensure patient safety. The policies and procedures of health facilities are not under the jurisdiction of the board. The board is acting within its consumer protection mandate to appropriately regulate the practice of pharmacy.

Comment #30

Ms. Trujillo referenced ASHP practice guidelines for labeling requirements that exclude compounding of sterile preparations for emergency treatments from its scope, a vital distinction they believe is necessary. She states:

“...ASHP guidelines *do not* apply to the manufacture of sterile pharmaceuticals as define in state and federal laws and regulations, *nor* do they apply to the preparation of medications by pharmacists, nurses, or physicians in emergency situations for *immediate* administrations to patients (e.g., cardiopulmonary resuscitation)...It is recognized that, in certain emergency situations, a pharmacist may be requested to compound products under conditions that do not meet these guidelines. In such situations, it is incumbent upon the pharmacist to employ professional judgment in weighing the potential patient risks and benefits associated with the compounding procedure in question.”

ASHP requests that the board to reconsider the regulatory language affecting labeling during emergency situations that could negatively impact patient care and introduce delays in medication delivery.

Board Response

ASHP practice guidelines are not incorporated by reference into the board's statutes or regulations. As such, these guidelines do not control the board's enforcement of its own regulations regarding pharmacy compounding, and the board is acting within its consumer protection mandate to appropriately regulate the practice of pharmacy.

The intent of the regulation proposal is to improve patient safety. Following the 45-day comment period, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within two hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

Based on comments received during the first 15-day comment period, the board again modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Comment #31

Ms. Trujillo stated that there is confusion as to whether the proposed documentation requirement applies to every product that is prepared, including those for an individual patient, or if the requirement will apply solely to those products prepared in batch for a yet-to-be-determined patient. ASHP asked the board to consider the potential implications of the added documentation, which could delay preparation and delivery of one-time and immediate-use medications to patients.

Board Response

Section 1735 of Article 4.5 defines compounding and further specifies in subdivision (d) of §1735 that Article 4.5 applies to all compounding practices. Further, Article 7 specifies that the provisions of Article 4.5 are applicable to all compounding and provides additional parameters and requirements that are applicable solely to sterile injectable compounding. Section 1735.2(b) provides for the advance preparation of compounded drug products in advance of receipt of a patient-specific prescription. Finally, the regulations do not require that recordkeeping requirements be completed in advance of the administration of the compounded drug product; therefore, the

regulations do not delay the preparation and delivery of one-time and immediate-use medications to patients.

Comments from Reid Toda, MS, RPh

Comment #32

Dr. Toda asked the board to clarify how the proposed compounding regulations will affect pharmacies where a nurse reconstitutes and administers a medication on the [nursing] floor.

Board Response

This comment is outside of the scope of the proposed regulation. Article 4.5 Section 1735(b) provides that compounding does not include reconstitution of a drug pursuant to a manufacturer's direction(s) for oral, rectal, topical, or injectable administration, nor does it include tablet splitting or the addition of flavoring agent(s) to enhance palatability.

The board believes that nurses and physicians performing reconstitution and administration are covered in B&PC 4127.1(e). Documentation of those activities is maintained in the patient's record. Nurses and physicians that compound medications outside of the hospital pharmacy are outside of the board's jurisdiction.

Comments from Michael W. Sanders, PharmD, President, North Coast Society of Health-System Pharmacists

Comment #33

Health systems pharmacies, especially in hospitals, must prepare numerous 'stat' and 'now' compounded IV and other products for acutely ill patients. Without exempting immediate or one time use compounded products from Section 1735.1, Compounding Definitions, the board is placing unreasonable and unnecessary recordkeeping and labeling requirements on already overburdened health care systems in California.

Board Response

The intent of the regulation proposal is to improve patient safety. Following the 45-day comment period, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within two hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

Based on comments received during the first 15-day comment period, the board again modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements

specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Several of the record keeping requirements for sterile products are already required in current regulation. This proposal does expand on the requirements, and now also includes the identity of the person who compounded the drug, the identity of the pharmacist reviewing the final drug product, the quantity of each component, the equipment used in compounding the drug product as well as a pharmacy assigned reference number. The board included the requirements for the identity of the person who compounded the drug as well as the pharmacists who reviewed the final drug product to allow a nonpharmacist to compound the medication, as allowed in other areas of pharmacy law, and to require that a pharmacist complete a review. This check is an essential consumer protection component. Further, the documentation of the equipment used is necessary to allow for a quality assurance review to be completed should a problem occur with such compounded medications. An internal pharmacy reference number is necessary to allow for a recall of a product if necessary, another essential consumer protection component.

Comments received from Lynn Hendrick, PharmD, Clinical Pharmacist at the Community Hospital of the Monterey Peninsula

Comment #34

I have some serious concerns pertaining to the proposed changes for medication compounding regulations, specifically with IV medications preparation and the urgent needs of some of these medications. I would ask for an exemption of logging and pharmacy lot number assignment/labeling for those “immediate use” products as defined by USP. These products are needed urgently and there is a potential of delay with the additional record keeping requirements with no benefit to the patient. Any future recall of product would be moot as the IV would be already administered as an immediate use.

Board Response

The board disagrees with the conclusion that the documentation requirements found in section 1753.3 will delay preparation and delivery of medications. The intent of the regulation proposal is to improve patient safety. Following the 45 day comment period, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot

number of each component, for those sterile products compounded on a one-time basis for administration within two hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

Based on comments received during the first 15-day comment period, the board again modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

The board recognizes that U.S. Pharmacopoeia (USP) General Chapter 797 (effective January 1, 2004) provides *best practices* for compounding sterile products, but USP 797 is not incorporated by reference into the board's statutes or regulations. As such, USP 797 does not control the board's enforcement of its own regulations regarding pharmacy compounding.

Additionally, upon recall of a product, a systematic review could not be accomplished without the appropriate documentation and recordkeeping required of compounded products. Without adequate documentation, necessary or systematic changes may not be realized and made to prevent future errors, a key patient safety issue.

Comment #35

It is unreasonable to think that every STAT alteplase, epinephrine, diltiazem or other life-saving medication prepared by a pharmacist during cardiac resuscitation, in the emergency department, in the operating rooms or in other critical care areas would be delayed a few minutes longer to assure logging, assignment, and labeling of the IV bag with a pharmacy lot number.

Board Response

In an acute care setting, the regulation proposal allows for one-time preparations to be documented in the pharmacy's copy of the patient's chart order. This chart order can serve as the master formula. Further, the records required in section 1735.3 do not need to be completed in advance of the administration of the compounded drug, thus ensuring that the patient receives STAT medicines timely.

Comment #36

In addition, for all products, whether STAT or non-urgent, extensive recordkeeping would be required for each product prepared and maintained for a minimum of 3 years. Considering the hundreds (or in some larger hospitals thousands) of records daily that would be generated to meet the requirement, the proposed method for recordkeeping and maintaining records for 3 years is unrealistic and wasteful.

Board Response

Several of the record keeping requirements for sterile products are already required in current regulation. This proposal does expand on the requirements, and now also includes the identity of the person who compounded the drug, the identity of the pharmacist reviewing the final drug product, the quantity of each component, the equipment used in compounding the drug product as well as a pharmacy assigned reference number. The board included the requirements for the identity of the person who compounded the drug as well as the pharmacists who reviewed the final drug product to allow a nonpharmacist to compound the medication, as allowed in other areas of pharmacy law, and to require that a pharmacist complete a review. This check is an essential consumer protection component. Further, the documentation of the equipment used is necessary to allow for a quality assurance review to be completed should a problem occur with such compounded medications. An internal pharmacy reference number is necessary to allow for a recall of a product if necessary, another essential consumer protection component.

This regulation does not specify a method for recordkeeping, rather it specifies what records must be kept and for how long. The 3-year time frame required in this proposal is consistent with current pharmacy law that specifies that all records must be maintained for three years (see Business and Professions Code section 4105(c)).

Comments received from Man Yi, RPh, Clinical Pharmacist at the Community Hospital of the Monterey Peninsula**Comment #37**

I have some serious concerns pertaining to the proposed changes for medication compounding regulations, specifically with IV medications preparation and the urgent needs of some of these medications. I would ask for an exemption of logging and pharmacy lot number assignment/labeling for those “immediate use” products as defined by USP. These products are needed urgently and there is a potential of delay with the additional record keeping requirements with no benefit to the patient. Any future recall of product would be moot as the IV would be already administered as an immediate use.

Board Response

The board disagrees with the conclusion that the documentation requirements found in section 1753.3 will delay preparation and delivery of medications. The intent of the regulation proposal is to improve patient safety. Following the 45 day comment period, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within two hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

Based on comments received during the first 15-day comment period, the board again modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

The board recognizes that U.S. Pharmacopoeia (USP) General Chapter 797 (effective January 1, 2004) provides *best practices* for compounding sterile products, but USP 797 is not incorporated by reference into the board's statutes or regulations. As such, USP 797 does not control the board's enforcement of its own regulations regarding pharmacy compounding.

Additionally, upon recall of a product, a systematic review could not be accomplished without the appropriate documentation and recordkeeping required of compounded products. Without adequate documentation, necessary or systematic changes may not be realized and made to prevent future errors, a key patient safety issue.

Comment #38

It is unreasonable to think that every STAT alteplase, epinephrine, diltiazem or other life-saving medication prepared by a pharmacist during cardiac resuscitation, in the emergency department, in the operating rooms or in other critical care areas would be delayed a few minutes longer to assure logging, assignment, and labeling of the IV bag with a pharmacy lot number.

Board Response

In an acute care setting, the regulation proposal allows for one-time preparations to be documented in the pharmacy's copy of the patient's chart

order. This chart order can serve as the master formula. Further, the records required in section 1735.3 do not need to be completed in advance of the administration of the compounded drug, thus ensuring that the patient receives STAT medicines timely.

Comment #39

In addition, for all products, whether STAT or non-urgent, extensive recordkeeping would be required for each product prepared and maintained for a minimum of 3 years. Considering the hundreds (or in some larger hospitals thousands) of records daily that would be generated to meet the requirement, the proposed method for recordkeeping and maintaining records for 3 years is unrealistic and wasteful.

Board Response

Several of the record keeping requirements for sterile products are already required in current regulation. This proposal does expand on the requirements, and now also includes the identity of the person who compounded the drug, the identity of the pharmacist reviewing the final drug product, the quantity of each component, the equipment used in compounding the drug product as well as a pharmacy assigned reference number. The board included the requirements for the identity of the person who compounded the drug as well as the pharmacists who reviewed the final drug product to allow a nonpharmacist to compound the medication, as allowed in other areas of pharmacy law, and to require that a pharmacist complete a review. This check is an essential consumer protection component. Further, the documentation of the equipment used is necessary to allow for a quality assurance review to be completed should a problem occur with such compounded medications. An internal pharmacy reference number is necessary to allow for a recall of a product if necessary, another essential consumer protection component.

This regulation does not specify a method for recordkeeping, rather it specifies what records must be kept and for how long. The 3-year time frame required in this proposal is consistent with current pharmacy law that specifies that all records must be maintained for three years (see Business and Professions Code section 4105(c)).

Comments from Alex Berger, Staff Pharmacists, O'Connor Hospital, San Jose

Comment #40

We do not have time for more documentation, when IV medication is needed STAT. STAT means medication is needed now, or the patient will die. This regulation should exempt IVs for immediate/STAT administration.

Board Response

The board agrees with Mr. Berger's comment that the delivery of medications to patients should not be delayed.

In an acute care setting, the regulation allows for one-time preparations to be documented in the pharmacy's copy of the patient's chart order. This chart order can serve as the master formula. Further, the record keeping requirements required in section 1735.3 do not need to be completed in advance of the administration of the compounded drug, thus ensuring that the patient receives STAT medicines timely.

Also, the board exempts from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes this language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Comments from Kimberly Jones, PharmD, Clinical Pharmacist at the Community Hospital of the Monterey Peninsula

Comment #41

I have some serious concerns pertaining to the proposed changes for medication compounding regulations, specifically with IV medications preparation and the urgent needs of some of these medications. I would ask for an exemption of logging and pharmacy lot number assignment/labeling for those "immediate use" products as defined by USP. These products are needed urgently and there is a potential of delay with the additional record keeping requirements with no benefit to the patient. Any future recall of product would be moot as the IV would be already administered as an immediate use.

Board Response

The board disagrees with the conclusion that the documentation requirements found in section 1753.3 will delay preparation and delivery of medications. The intent of the regulation proposal is to improve patient safety. Following the 45 day comment period, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within two hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

Based on comments received during the first 15-day comment period, the board again modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

The board recognizes that U.S. Pharmacopoeia (USP) General Chapter 797 (effective January 1, 2004) provides *best practices* for compounding sterile products, but USP 797 is not incorporated by reference into the board's statutes or regulations. As such, USP 797 does not control the board's enforcement of its own regulations regarding pharmacy compounding.

Additionally, upon recall of a product, a systematic review could not be accomplished without the appropriate documentation and recordkeeping required of compounded products. Without adequate documentation, necessary or systematic changes may not be realized and made to prevent future errors, a key patient safety issue.

Comment #42

It is unreasonable to think that every STAT alteplase, epinephrine, diltiazem or other life-saving medication prepared by a pharmacist during cardiac resuscitation, in the emergency department, in the operating rooms or in other critical care areas would be delayed a few minutes longer to assure logging, assignment, and labeling of the IV bag with a pharmacy lot number.

Board Response

In an acute care setting, the regulation proposal allows for one-time preparations to be documented in the pharmacy's copy of the patient's chart order. This chart order can serve as the master formula. Further, the records required in section 1735.3 do not need to be completed in advance of the administration of the compounded drug, thus ensuring that the patient receives STAT medicines timely.

Comment #43

In addition, for all products, whether STAT or non-urgent, extensive recordkeeping would be required for each product prepared and maintained for a minimum of 3 years. Considering the hundreds (or in some larger hospitals thousands) of records daily that would be generated to meet the requirement, the proposed method for recordkeeping and maintaining records for 3 years is unrealistic and wasteful.

Board Response

Several of the record keeping requirements for sterile products are already required in current regulation. This proposal does expand on the requirements, and now also includes the identity of the person who compounded the drug, the identity of the pharmacist reviewing the final drug product, the quantity of each component, the equipment used in compounding the drug product as well as a pharmacy assigned reference number. The board included the requirements for the identity of the person who compounded the drug as well as the pharmacists who reviewed the final drug product to allow a nonpharmacist to compound the medication, as allowed in other areas of pharmacy law, and to require that a pharmacist complete a review. This check is an essential consumer protection component. Further, the documentation of the equipment used is necessary to allow for a quality assurance review to be completed should a problem occur with such compounded medications. An internal pharmacy reference number is necessary to allow for a recall of a product if necessary, another essential consumer protection component.

This regulation does not specify a method for recordkeeping, rather it specifies what records must be kept and for how long. The 3-year time frame required in this proposal is consistent with current pharmacy law that specifies that all records must be maintained for three years (see Business and Professions Code section 4105(c)).

Comments from Dharma Naidu, PharmD, Pharmacy Supervisor, Community Hospital of the Monterey Peninsula

Comment #44

I have some serious concerns pertaining to the proposed changes for medication compounding regulations, specifically with IV medications preparation and the urgent needs of some of these medications. I would ask for an exemption of logging and pharmacy lot number assignment/labeling for those “immediate use” products as defined by USP. These products are needed urgently and there is a potential of delay with the additional record keeping requirements with no benefit to the patient. Any future recall of product would be moot as the IV would be already administered as an immediate use.

Board Response

The board disagrees with the conclusion that the documentation requirements found in section 1753.3 will delay preparation and delivery of medications. The intent of the regulation proposal is to improve patient safety. Following the 45 day comment period, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot

number of each component, for those sterile products compounded on a one-time basis for administration within two hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

Based on comments received during the first 15-day comment period, the board again modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

The board recognizes that U.S. Pharmacopoeia (USP) General Chapter 797 (effective January 1, 2004) provides *best practices* for compounding sterile products, but USP 797 is not incorporated by reference into the board's statutes or regulations. As such, USP 797 does not control the board's enforcement of its own regulations regarding pharmacy compounding.

Additionally, upon recall of a product, a systematic review could not be accomplished without the appropriate documentation and recordkeeping required of compounded products. Without adequate documentation, necessary or systematic changes may not be realized and made to prevent future errors, a key patient safety issue.

Comment #45

It is unreasonable to think that every STAT alteplase, epinephrine, diltiazem or other life-saving medication prepared by a pharmacist during cardiac resuscitation, in the emergency department, in the operating rooms or in other critical care areas would be delayed a few minutes longer to assure logging, assignment, and labeling of the IV bag with a pharmacy lot number.

Board Response

In an acute care setting, the regulation proposal allows for one-time preparations to be documented in the pharmacy's copy of the patient's chart order. This chart order can serve as the master formula. Further, the records required in section 1735.3 do not need to be completed in advance of the administration of the compounded drug, thus ensuring that the patient receives STAT medicines timely.

Comment #46

In addition, for all products, whether STAT or non-urgent, extensive recordkeeping would be required for each product prepared and maintained for a minimum of 3 years. Considering the hundreds (or in some larger hospitals thousands) of records daily that would be generated to meet the requirement, the proposed method for recordkeeping and maintaining records for 3 years is unrealistic and wasteful.

Board Response

Several of the record keeping requirements for sterile products are already required in current regulation. This proposal does expand on the requirements, and now also includes the identity of the person who compounded the drug, the identity of the pharmacist reviewing the final drug product, the quantity of each component, the equipment used in compounding the drug product as well as a pharmacy assigned reference number. The board included the requirements for the identity of the person who compounded the drug as well as the pharmacists who reviewed the final drug product to allow a nonpharmacist to compound the medication, as allowed in other areas of pharmacy law, and to require that a pharmacist complete a review. This check is an essential consumer protection component. Further, the documentation of the equipment used is necessary to allow for a quality assurance review to be completed should a problem occur with such compounded medications. An internal pharmacy reference number is necessary to allow for a recall of a product if necessary, another essential consumer protection component.

This regulation does not specify a method for recordkeeping, rather it specifies what records must be kept and for how long. The 3-year time frame required in this proposal is consistent with current pharmacy law that specifies that all records must be maintained for three years (see Business and Professions Code section 4105(c)).

Comments from Lois F. Leister, RPh, M.S., M.B.A., Practicing Hospital Pharmacist, Member of CSHP

Comment #47

It is my strong belief, and one I believe is shared by anyone in the hospital pharmacy profession, that IV admixture preparation practice should not be bundled in with compounded prescriptions (topical, oral, injectables compounded from non-sterile product or intended for sale or distribution to a patient or provider).

Board Response

The board appreciates the thoughtful comment submitted by Pharmacist Leister. The board believes that compliance with the regulations as adopted will ensure the integrity, potency, quality and strength of sterile injectable and other compounded drug product(s) prepared and delivered to patients. Likewise, in the event of a recall, the record keeping requirements would allow for patient identification and for a systematic

review to be accomplished. Patient safety could be improved by system changes made as a result of that review and – ultimately – could prevent future errors.

Without such documentation, as specified in the regulations, human error could occur, a patient could receive the wrong strength of an IV admixture, and the hospital staff would have no ability to trace back the problem and make system changes necessary to prevent future errors.

Comment #48

If for every IV admixture prepared the Board would expect to see LOT #, manufacturer, equipment used, personnel identity, pharmacist identity, pharmacy lot number, expiration dating, quality etc., as described in 1735.3, the treatment of acutely ill patients would be as risk. Even in a small rural critical access hospital we often mix over 100 IV admixtures a day. In a larger institution, this number would be 10-20 times higher and the recordkeeping requirements, which the regulations imply, would be overwhelming and create an enormous burden on pharmacy professionals. Furthermore, I believe this extensive recordkeeping would not significantly improve medication or patient safety.

Board Response

The board disagrees with the conclusion that the documentation requirements found in section 1735.3 will delay preparation and delivery of medications to patients. In an acute care setting, the regulation proposal allows for one-time preparations to be documented in the pharmacy's copy of the patient's chart order. This chart order can serve as the master formula. Further, the record keeping requirements in section 1735.3 do not need to be completed in advance of the administration of the compounded drug, thus ensuring that the patient receives STAT medicines timely.

The documentation is necessary to ensure the integrity, potency, quality and strength of the compounded drug product(s) prepared and delivered to patients.

Several of the record keeping requirements for sterile products are already required in current regulation. This proposal does expand on the requirements, and now also includes the identity of the person who compounded the drug, the identity of the pharmacist reviewing the final drug product, the quantity of each component, the equipment used in compounding the drug product as well as a pharmacy assigned reference number. The board included the requirements for the identity of the person who compounded the drug as well as the pharmacists who reviewed the final drug product to allow a nonpharmacist to compound the medication, as allowed in other areas of pharmacy law, and to require that a pharmacist complete a review. This check is an essential consumer protection component. Further, the documentation of the equipment used is necessary to allow for a quality assurance review to be completed should a problem occur

with such compounded medications. An internal pharmacy reference number is necessary to allow for a recall of a product if necessary, another essential consumer protection component.

Based on comments received during the three comment periods, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Comment #49

Please consider the recommendation and consultation of pharmacy professionals with hospital pharmacy practice and how the “sterile compound” regulations pertain to the practice of IV admixture services.

Board Response

In response to Ms. Leister’s general comment, the board has carefully considered the topic of compounding regulations for a number of years and has continually heard public testimony on this proposal.

Comment #50

In addition to the above considerations, please reconsider the language of 1751.5, 1751.6 and 1751.7. It would seem prudent to follow the practice guidelines for USP 797 in the areas such as training, cleaning, garbing and quality assurance as these standards have been reviewed by a group of nationally recognized individuals.

Board Response

The requirements in 1751.5 and 1751.6 are current law and remained unchanged with this regulation with the exception of technical clean-up and renumbering from previous sections. Section 1751.7 now specifies that the quality assurance program as well as written policies and procedures include the requirements specified in section 1738 as well as specify that batch-produced sterile to sterile transfers are subject to period testing.

The board recognizes that U.S. Pharmacopoeia (USP) General Chapter 797 (effective January 1, 2004) provides *best practices* for compounding sterile products, but USP 797 is not incorporated by reference into the board’s statutes or regulations. As such, USP 797 does not control the board’s enforcement of its own regulations regarding pharmacy compounding.

Comments from David Elder, PharmD, Director of Pharmacy Services, Sierra Kings District Hospital

Comment #51

Dr. Elder expressed support for comments provided by CSHP, emphasizing that adequate documentation is already being performed for compounded items. He stressed that compounding skills are already defined, and the proposed regulations would create tedious work that does not protect patients. Dr. Elder asked the board to exempt logging and pharmacy lot number assignment/labeling for those “immediate use” products as defined by USP. He added that future recall of a product would be moot as the IV would have already been administered as immediate use.

Board Response

The intent of the regulation proposal is to improve patient safety. Following the 45-day comment period, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within two hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

Based on comments received during the first 15-day comment period, the board again modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

The board recognizes that U.S. Pharmacopoeia (USP) General Chapter 797 (effective January 1, 2004) provides *best practices* for compounding sterile products, but USP 797 is not incorporated by reference into the board’s statutes or regulations. As such, USP 797 does not control the board’s enforcement of its own regulations regarding pharmacy compounding.

Additionally, upon recall of a product, a systematic review could not be accomplished without the appropriate documentation and recordkeeping required of compounded products. Without adequate documentation, necessary or systematic changes may not be realized and made to prevent future errors, a key patient safety issue.

Comments from Mary Noud-Ikuta, PharmD

Comment #52

Dr. Noud-Ikuta expressed concern that the proposed compounding regulations requiring additional labeling and pharmacy recordkeeping would put patients at risk by delaying treatment. Preparation of compounded medications in an acute care facility include one-time and immediate-use (STAT) medications such as alteplase, epinephrine, or diltiazem. Dr. Noud-Ikuta stated that added documentation requirements for both the label and pharmacy log will delay preparation and delivery of these medications, with no additional benefit to patient safety and care.

The board disagrees with the conclusion that the documentation requirements found in section 1735.3 will delay preparation and delivery of medications to patients. In an acute care setting, the regulation proposal allows for one-time preparations to be documented in the pharmacy's copy of the patient's chart order. This chart order can serve as the master formula. Further, the record keeping requirements in section 1735.3 do not need to be completed in advance of the administration of the compounded drug, thus ensuring that the patient receives STAT medicines timely.

The documentation is necessary to ensure the integrity, potency, quality and strength of the compounded drug product(s) prepared and delivered to patients – a key benefit to patients.

Several of the record keeping requirements for sterile products are already required in current regulation. This proposal does expand on the requirements, and now also includes the identity of the person who compounded the drug, the identity of the pharmacist reviewing the final drug product, the quantity of each component, the equipment used in compounding the drug product as well as a pharmacy assigned reference number. The board included the requirements for the identity of the person who compounded the drug as well as the pharmacists who reviewed the final drug product to allow a nonpharmacist to compound the medication, as allowed in other areas of pharmacy law, and to require that a pharmacist complete a review. This check is an essential consumer protection component. Further, the documentation of the equipment used is necessary to allow for a quality assurance review to be completed should a problem occur with such compounded medications. An internal pharmacy reference number is necessary to allow for a recall of a product if necessary, another essential consumer protection component.

Based on comments received during the three comment periods, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in

§1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Comment #53

Dr. Noud-Ikuta did not recognize any benefits relating to product recalls by requiring the recording of a pharmacy reference number or lot number on the label of a dispensed IV and additional information in the pharmacy log. She stated that in situations where patients are in need of one-time and immediate-use compounded products, any future recall of a product would be moot because the IV would have already been administered to the patient.

Board Response

Board of Pharmacy's priority mandate is to protect the public. This mandate extends to the compounding and labeling of prescription drugs. It is unclear as to what portion of the proposed regulation Dr. Noud-Ikuta is referencing with regard to labeling of a dispensed IV. The board did modify the proposed text of §1753.3(a)(6) to exempt specified labeling requirements from those records of sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

Additionally, upon recall of a product, a systematic review could not be accomplished without the appropriate documentation and recordkeeping required of compounded products. Without adequate documentation, necessary or systematic changes may not be realized and made to prevent future errors, a key patient safety issue.

Comment #54

Dr. Noud-Ikuta referred to Chapter 797 of the United States Pharmacopoeia (USP) and a section related to Immediate-Use Compounded Sterile Products. She asked the board to exempt from additional record keeping requirements the preparation of one-time and immediate-use injectable products in acute care facilities.

Board Response

The board recognizes that U.S. Pharmacopoeia (USP) General Chapter 797 (effective January 1, 2004) provides good *practices* for compounding sterile products, but USP 797 is not incorporated by reference into the board's statutes or regulations. As such, USP 797 does not control the board's enforcement of its own regulations regarding pharmacy compounding.

As previously stated in the board's response to Dr. Noud-Iduta (Comment #53), the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1735.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

Comments from Steve W. Gray, PharmD, J.D., for Kaiser Permanente Pharmacy

Comment #55

Dr. Gray states that the proposed language of 1735.2(c)(1) "appears to limit compounding for a physician's office to a 72-hour supply." He states that for products administered in the office, this is an unreasonably short time. He further states that according to USP <797> risk level 1 CSPs and risk level 2 CSPs may be assigned a beyond use date of up to 14 days and nine (9) days, respectively, when stored under refrigeration. He states this would be a more reasonable length of time.

Dr. Gray recommends a change to the language proposed in 1735.2(c)(1) to read: "(1) is sufficient for administration or application to patients in the prescriber's office, or for ~~distribution~~ dispensing of not more than a 72-hour *supply* to the prescriber's patients, as estimated by the prescriber,"

Board Response

The board recognizes that U.S. Pharmacopoeia (USP) General Chapter 797 (effective January 1, 2004) provides good *practices* for compounding sterile products, but USP 797 is not incorporated by reference into the board's statutes or regulations. As such, USP 797 does not control the board's enforcement of its own regulations regarding pharmacy compounding. The board believes that distribution of a 72-hour supply is "reasonable."

Comment #56

Dr. Gray offers comments on proposed 1735.2(d) and 1735.3(a). He states that the scope of the proposed language "appears to include most compounded sterile preparations (CSPs) in inpatient pharmacies." He adds that inpatient pharmacies typically prepare CSPs to meet the acute needs of patients. He adds that requiring a master formula for small quantities of patient-specific CSPs would cause significant delays in therapy. He states that inpatient pharmacies already have policies and procedures which require the amounts of additives to be calculated and displayed for a pharmacist check. He states the proposed language would be appropriate only when batches of compounded products are prepared which are intended for use in multiple patients.

Dr. Gray recommends a change in the language of proposed 1735.2(d) to read:

“(d) For compounded drug products that are being prepared for use in multiple patients, these products shall not be compounded until the pharmacy has first prepared a written master formula record that includes at least the following elements:”

Board Response

Dr. Gray is accurate that the proposed language of 1735.2(d) and 1735.3(a) (limitations and requirements; records) does apply to compounded sterile preparations in inpatient pharmacies. The master formula requirement found in proposed 1735.2(d) is not new. Current regulation (§1716.1 and §1716.2) specifies the general requirements for compounding, including the requirement to maintain a master formula. Through this regulation proposal, existing §1716.1 and §1716.2 are being repealed, and the requirements placed in proposed §1735.2. Proposed 1735.2(e) provides that “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.” Subsection (e) would appear to address Dr. Gray’s comment relative to small quantities of patient-specific CSPs.

The board does not agree that the proposed language is appropriate only for batches of compounded drug products that are prepared in advance and that are intended for use in multiple patients. As stated in the Initial Statement of Reasons, the purpose for the proposed regulation is to address, among other items in compounding, the strength, efficacy and quality as well as require a quality assurance program for general compounding – even for a single patient-specific compounding prescription order. The board’s proposal provides uniformity in compounding for California consumers. While proposed 1735.2 places limitations on the conditions for compounding, the section also allows for anticipatory compounding under specified conditions.

The board addresses in §1735.5 the criteria for compounding policies and procedures. This proposed section would govern the policies and procedures to which Dr. Gray references (that inpatient pharmacies already have policies and procedures which require the amounts of additives to be calculated and displayed for a pharmacist check).

Comment #57

Dr. Gray states that the proposed language of 1735.2(f) is appropriate in the case of a pharmacist who is compounding a sterile preparation (CSP) for direct dispensing to a patient or their agent, but it is not appropriate if a pharmacist compounds a CSP that is transferred to another pharmacy pursuant to an evergreen agreement. In the latter scenario, Dr. Gray asserts that the compounding pharmacist has no control over the CSP after it has left the pharmacy where the compounding occurred. He further states that if the CSP isn’t stored properly (e.g. storing at room temp instead of under refrigeration), the compounding pharmacist would have no knowledge of this; thus, he or she should not be the responsible party. Dr. Gray concludes by stating the pharmacist-in-charge of the receiving pharmacy should be the responsible party.

Dr. Gray recommends that the proposed language be changed to reflect that the pharmacist performing or supervising compounding is responsible for the integrity, potency, quality, and labeled strength of a compounded product until it is dispensed to the patient (or their agent), to a physician's office, or until it is transferred or distributed to another pharmacy.

Board Response

The language found in §1735.2(f) is applicable to all pharmacies that engage in compounding. Subdivision (a) of that section provides that with certain exceptions, no drug product shall be compounded prior to receipt by a pharmacy of a valid prescription for an individual patient.

In the example provided, the board infers that Dr. Gray would like clarified at what time a receiving pharmacy becomes responsible for a dangerous drug (i.e., compounded sterile preparation).

To respond to Dr. Gray's suggestion, the board refers to other applicable statutes within pharmacy law, as follows:

- §4119.5 of the Business and Professions Code authorizes a pharmacy to transfer a reasonable supply of dangerous drugs to another pharmacy.
- §4052.7 of the Business and Professions Code addresses the repackaging of drugs prior to the dispensing of the drug to a patient. §4052.7(c) specifically states that the repackaging pharmacy and the pharmacy that initially dispensed the drug "shall only be liable for its own actions in providing the drug to the patient or the patient's agent."

The board believes that existing statute, and specifically §4052.7(c), addresses Dr. Gray's concern and that amending 16 CCR §1735.2(f) is not necessary.

Comment #58

Dr. Gray states that proposed 1735.8(c) appears to be directed towards compounding from non-FDA approved ingredients. He states it is inappropriate for compounding sterile products from sterile FDA approved ingredients. He states when preparing sterile products from FDA approved sterile ingredients, a quality assurance plan should only require written standards for visual checks of the final product.

Dr. Gray recommends that the proposed regulation should include a statement that exempts the preparation of products from FDA approved ingredients from subsection (c).

Board Response

Proposed 1735.8(c) does not state that it applies to non-FDA approved ingredients; rather, subsection (c) speaks to the qualitative and quantitative analysis reports for compounded drug products (i.e., the resulting product after compounding). Proposed 1735.8 requires a pharmacy that engages in compounding to maintain a quality assurance plan within its written policies and procedures and what the plan shall include. Subsection (c) specifically requires the quality assurance plan to include written standards for qualitative and quantitative integrity, potency, quality, and labeled strength analysis of compounded drug products (not the individual ingredients in each compounded drug product). It further states that all qualitative and quantitative analysis reports for compounded drug products shall be retained by the pharmacy and collated with the compounding record and master formula.

Comment #59

Dr. Gray states that the proposed language at 1751.3(a)(2) requires that the labels of sterile injectable products display the recommended rate of administration, and that this information on a label can be unhelpful and incorrect. Dr. Gray provides two scenarios and how the proposed regulation might apply. Dr. Gray offers recommended language for paragraph (2) of subdivision (a) to read:

“(2) Labeling of the sterile injectable product based on the intended route of administration. ~~and recommended rate of administration.~~ Facility policies shall state the circumstances whereby it is appropriate to display recommended rates of administration or duration of medication infusions.”

Board Response

Section 1751.3 requires any pharmacy engaged in compounding sterile injectable drug products to maintain a written policy and procedure manual, as specified. One of the elements required to be addressed in that manual is the labeling of the sterile injectable product based on the intended route of administration and recommended rate of administration.

However, the labeling requirements for sterile injectable compounded drug products are specified in section 1751.2. This section does not require that a label of a sterile injectable product display the recommended rate of administration.

Comment #60

Dr. Gray comments on proposed 1751.4(d) related to the cleaning frequency of ceilings, walls, etc., and that the text in subdivision (d) previously applied to sterile preparations compounded from non-sterile ingredients. He states the weekly cleaning frequency as described is excessive and unnecessary for sterile preparations compounded from sterile ingredients. Dr. Gray further states that if the board intends for the title of the section to read “Facility and Equipment Standards for Sterile Injectable Compounding” then the language must change.

Dr. Gray offers recommended language for subdivision (d) to read:

“Exterior workbench surfaces and other hard surfaces in the designated area, such as walls, floors, ceilings, shelves, tables, and stools, must be disinfected ~~weekly~~ monthly and after any unanticipated event that could increase the risk of contamination.”

Board Response

The board intended for the provisions of proposed 1751.7(d) to apply to sterile preparations compounded from sterile ingredients and that the compounding area be disinfected weekly.

Comment #61

Dr. Gray comments on proposed 1751.4(e) related to laminar air flow hoods as the appropriate equipment for preparation of parenteral cytotoxic agents. Dr. Gray states that barrier isolators are recognized by the American Society of Health-Systems Pharmacists and the USP as appropriate equipment as well. He asserts that the use of barrier isolators should be stated in subdivision (e), and he recommends a change in the proposed language as follows:

“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 air flow hood or barrier isolator. The hood or isolator must be certified annually by a qualified technician who is familiar with the methods and procedures for certifying laminar air flow hoods and clean room requirements, in accordance with National Sanitation Foundation Standard 49 for Class II (Laminar Flow) Biohazard Cabinetry, as revised May, 1983 (available from the National Sanitation Foundation, 3475 Plymouth Road, P.O. Box 1468, Ann Arbor, Michigan 48106, phone number (313) 769-8010) or manufacturer’s specifications. Certification records must be retained for at least 3 years. Authority cited: Sections 4005 and 4127, Business and Professions”

Board Response

Section 4-1106(b) of Title 24 of the California Administrative Code is incorporated by reference into the board’s regulations as they apply to California pharmacies and equipment standards for sterile injectable compounding.

Comment #62

Dr. Gray comments on proposed 1751.7(d) stating that the language appears to reintroduce end-product sterility testing for CSPs made from sterile ingredients using aseptic transfers. He states this is of no value and must be deleted.

Dr. Gray states that if the board intended for subdivision (d) to apply to non-sterile to sterile compounding, it should be stated explicitly.

He adds that if the board intended 1751.7(d) to apply to sterile-to-sterile compounding, that existing 1751.7(b) describes the appropriate process very well and should be retained.

Dr. Gray recommends that proposed 1751.7(d) be stricken, and that current regulation 1751.7(b) be inserted.

Board Response

Proposed amendments to 1751.7(d) requires that “batch-produced sterile to sterile transfer shall be subject to periodic testing through process validation for sterility as determined by the pharmacist-in-charge and described in the written policies and procedures.” The board does not agree with Dr. Gray’s statement that periodic testing for sterility as determined by the pharmacist-in-charge and in accordance with a pharmacy’s written policies and procedures is of no value. Subsection (d) does not specify frequency of such periodic testing.

The text of proposed 1751.7(b) (to which Dr. Gray refers) is the requirement that *individuals* involved in the preparation of sterile injectable products must first successfully complete before being allowed to prepare sterile injectable products. This subdivision does specify what the validation process shall include and requires that the same personnel, procedures, equipment and materials must be involved, and other requirements. The text of proposed subdivision (b) does not apply to batch-produced sterile to sterile transfers; it only applies to the validation process an *individual* is required to complete before preparing sterile injectable products.

Comments from Maria D. Serpa, PharmD

Comment #63

Dr. Serpa expressed concern that the proposed compounding regulations would unnecessarily apply to ‘sterile injectable’ products. She acknowledged that the board was charged with the task of strengthening ‘traditional’ compounding practices in order to enhance patient safety. Dr. Serpa asked the board to ensure separation of ‘traditional’ compounding regulations and ‘sterile injectable’ compounding regulations. She referenced United States Pharmacopoeia (USP) Chapter 797 (sterile preparations) and Chapter 795 (nonsterile preparations).

Board Response

The board recognizes that U.S. Pharmacopoeia (USP) General Chapter 797 (effective January 1, 2004) provides good *practices* for compounding sterile products, but USP 797 is not incorporated by reference into the board’s statutes or regulations. As such, USP 797 does not control the board’s enforcement of its own regulations regarding pharmacy compounding.

The Initial Statement of Reasons specified that the regulation proposal would address, among other things, the strength, efficacy and quality in compounding, as well as to require a quality assurance program for general compounding. The ISOR expressly stated that the purpose for proposed amendments is to remove redundancies between requirements for general compounding and sterile

injectable compounding, as well as to ensure consistent sequencing of related requirements in Article 4.5 and Article 7.

Comment #64

Dr. Serpa supported the board's efforts to address patient safety through the proposed 'traditional non-sterile' compounding regulations, stating that those changes are urgently needed. However, she advised against changes affecting regulations for 'sterile injectable' compounding.

Board Response

The board agrees with Dr. Serpa's comments that ensuring patient safety through "traditional non-sterile" compounding regulations is needed. Several of the record keeping requirements for sterile products are already required in current regulation. This proposal does expand on the requirements, and now also includes the identity of the person who compounded the drug, the identity of the pharmacist reviewing the final drug product, the quantity of each component, the equipment used in compounding the drug product as well as a pharmacy assigned reference number. The board included the requirements for the identity of the person who compounded the drug as well as the pharmacists who reviewed the final drug product to allow a nonpharmacist to compound the medication, as allowed in other areas of pharmacy law, and to require that a pharmacist complete a review. This check is an essential consumer protection component. Further, the documentation of the equipment used is necessary to allow for a quality assurance review to be completed should a problem occur with such compounded medications. An internal pharmacy reference number is necessary to allow for a recall of a product if necessary, another essential consumer protection component.

Comments from Robert Batman, PharmD, Kaiser Permanente

Comment #65

Dr. Batman stated that regulations requiring additional record keeping and labeling would be burdensome for acute care hospitals with a large number of compounded IV medications. He advised that typical batch compounding issues encountered in a chronic care setting such as home health or ambulatory care would not apply because acute care settings administer medications immediately after compounding. Dr. Batman asked the board to consider an exemption from record keeping and labeling requirements for acute care facilities, specifically for the compounded IV medication for immediate-use.

Board Response

Several of the record keeping requirements for sterile products are already required in current regulation. This proposal does expand on the requirements, and now also includes the identity of the person who compounded the drug, the identity of the pharmacist reviewing the final drug product, the quantity of each

component, the equipment used in compounding the drug product as well as a pharmacy assigned reference number. The board included the requirements for the identity of the person who compounded the drug as well as the pharmacists who reviewed the final drug product to allow a nonpharmacist to compound the medication, as allowed in other areas of pharmacy law, and to require that a pharmacist complete a review. This check is an essential consumer protection component. Further, the documentation of the equipment used is necessary to allow for a quality assurance review to be completed should a problem occur with such compounded medications. An internal pharmacy reference number is necessary to allow for a recall of a product if necessary, another essential consumer protection component.

Based on comments received during the three comment periods, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Comments from Raffi Svadjian, PharmD, MBA, USC School of Pharmacy

Comment #66

Dr. Svadjian advised that the proposed compounding regulations were provided to the 3rd Year Community Pharmacy Management Elective course at USC. Applicable students were instructed to conduct a survey to determine whether the proposed compounding regulations would affect community pharmacies. Results of the survey revealed that only 2 of the 12 contacted pharmacies had knowledge of the proposed regulatory changes prior to participating in the survey. Pharmacies contacted expressed concern that the proposed regulations would result in some community pharmacies that would halt compounding activities due to cost factors of meeting the new regulatory standards (end product testing, possible purchase of software, etc.).

Board Response

The board appreciates the comments of Dr. Svadjian; however, the survey referred to and the stated results thereof are outside the scope of the proposed regulation. As required by Government Code section 11346 et seq., the board held public discussions of its regulatory proposal before proposed language was noticed to the public on September 5, 2008. The board also posts to its website various agendas, minutes and meeting summaries referencing the topic and discussion of compounding at public meetings. Likewise, and in accordance with Government Code section 11340.85(c) the

board posts on its web site information and available documents regarding proposed regulations and other rulemaking actions. In addition, the board issues “subscriber alerts” to electronically notify those pharmacies and the public who subscribe to the board’s electronic notifications. The board would be happy to add to its mailing list those pharmacies contacted by the USC students, if offer.

Comment #67

Results of the survey conducted by USC School of Pharmacy students referred to a lack of clear definition of end-product testing and quality assurance. Community pharmacists contacted expressed concern that the proposed regulations do not specify the requirements of frequency of end-product testing, record keeping, and which products would need to be tested.

Board Response

These comments do not address any specific text within the regulatory proposal. The results of the survey referenced by Dr. Svadjian are outside of the scope of the regulation proposal.

Comment #68

Results of the survey conducted by USC School of Pharmacy students referred to a lack of distinction between regulations that should be necessary to mix two different products versus complex compounding formulas. Community pharmacies contacted suggested that less oversight should be required in certain instances; for example, when changing a tablet to a liquid dosing form for short-term administration to a patient.

Board Response

The survey referenced is outside of the scope of the regulation proposal. However, the board has adequately described the definitions and requirements of compounding (§1735). In responding to the example offered (changing a tablet to a liquid dosing form), such alteration of the dosage form or delivery of the drug does fall within the definition of “compounding” as provided in proposed section 1735(a). To alter a tablet to a liquid form, a component would have to be added. The patient has a right and a need to know what components or drugs were “compounded” that provided such alteration.

Comments from Kenneth Breslow, MS, R.Ph., FAPhA, PETNET Solutions

Comment #69

Mr. Breslow referred to the lack of statutory distinction in the State of California for operation and licensure of Nuclear Pharmacies (Radiopharmacies). He urged the board to exempt application of any revised sterile compounding regulations to PET drug compounding. Mr. Breslow suggested that the board stipulate the requirement to comply with relevant USP chapters, until such time the board proposes and adopts its own regulations pertinent and applicable to radiopharmaceutical and PET radiopharmaceutical compounding.

Mr. Breslow provided a listing of unique differences between conventional drugs, conventional radiopharmaceuticals, and PET radiopharmaceuticals.

Board Response

Mr. Breslow's comments regarding the operation and licensure of Nuclear Pharmacies is not within the scope of the proposed regulations.

The board recognizes that U.S. Pharmacopoeia (USP) General Chapter 797 (effective January 1, 2004) provides *best practices* for compounding sterile products, but USP 797 is not incorporated by reference into the board's statutes or regulations. As such, USP 797 does not control the board's enforcement of its own regulations regarding pharmacy compounding. Moreover, the suggestion that the board stipulate the requirements to comply with relevant USP chapters, until such time that regulations specific to radiopharmaceutical and PET radiopharmaceutical compounding are adopted is not relevant.

Comments from Ben J. Devine, PharmD, Director of Pharmacy, Sutter Lakeside Hospital

Comment #70

Dr. Devine expressed concern that additional labeling and maintenance of a log serves no purpose in the event of a recall, when an immediate-use compounded medication has already been administered to a patient. He strongly urged the board to reconsider the proposed regulatory change, and grant an exemption for medications compounded for immediate or emergency use.

Board Response

The intent of the regulation proposal is to improve patient safety. Several of the record keeping requirements for sterile products are already required in current regulation. This proposal does expand on the requirements, and now also includes the identity of the person who compounded the drug, the identity of the pharmacist reviewing the final drug product, the quantity of each component, the equipment used in compounding the drug product as well as a pharmacy assigned reference number. The board included the requirements for the identity of the person who compounded the drug as well as the pharmacists who reviewed the final drug product to allow a nonpharmacist to compound the medication, as allowed in other areas of pharmacy law, and to require that a pharmacist complete a review. This check is an essential consumer protection component. Further, the documentation of the equipment used is necessary to allow for a quality assurance review to be completed should a problem occur with such compounded medications. An internal pharmacy reference number is necessary to allow for a recall of a product if necessary, another essential consumer protection component.

Based on comments received during the three comment periods, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Additionally, upon recall of a product, a systematic review could not be accomplished without the appropriate documentation and recordkeeping required of compounded products. Without adequate documentation, necessary or systematic changes may not be realized and made to prevent future errors, a key patient safety issue.

Comments from Gary W. Chan, Clinical Pharmacist, Mercy San Juan Medical Center

Comment #71

Dr. Chan strongly opposed the proposed regulation requiring pharmacist to record in a log each IV that is compounded. He stated that serving as a clinical pharmacist in a hospital requires him to attend codes, rapid responses, and cardiac alerts. Dr. Chan expressed concern that harm will come to patients if the proposed regulation is put in place, particularly in instances where these patients required immediate and one-time (STAT) medications. He asked the board to exempt additional pharmacy record keeping requirements for preparation of one-time and immediate use IV products in acute care hospitals.

Board Response

The intent of the regulation proposal is to improve patient safety. In an acute care setting, the regulation proposal allows for one-time preparations to be documented in the pharmacy's copy of the patient's chart order. The chart order can serve as the master formula. Further, the records required in section 1735.3 do not need to be completed in advance of the administration of the compounded drug, thus ensuring that the patient receives STAT medicines.

Based on comments received during the three comment periods, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Comments from Karen Azama-Kihara, PharmD, Pharmacy Supervisor, Mercy San Juan Medical Center

Comment #72

Dr. Azama-Kihara expressed concern that additional record keeping and log preparation will result in a delay in services to patients during emergency situations, including cardiac arrests. She strongly urged the board to exempt preparation of one-time and immediate use IV products in acute care hospitals. Dr. Azama-Kihara asked the board to exempt one-time and immediate use IV medications from the requirement to record the pharmacy reference number or lot number on the label.

Board Response

The intent of the regulation proposal is to improve patient safety. Several of the record keeping requirements for sterile products are already required in current regulation. This proposal does expand on the requirements, and now also includes the identity of the person who compounded the drug, the identity of the pharmacist reviewing the final drug product, the quantity of each component, the equipment used in compounding the drug product as well as a pharmacy assigned reference number. The board included the requirements for the identity of the person who compounded the drug as well as the pharmacists who reviewed the final drug product to allow a nonpharmacist to compound the medication, as allowed in other areas of pharmacy law, and to require that a pharmacist complete a review. This check is an essential consumer protection component. Further, the documentation of the equipment used is necessary to allow for a quality assurance review to be completed should a problem occur with such compounded medications. An internal pharmacy reference number is necessary to allow for a recall of a product if necessary, another essential consumer protection component.

Based on comments received during the three comment periods, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Comments from Larry W. Schallock

Comment #73

Mr. Schallock stated his support of CSHP's position regarding labeling and record keeping exemptions for one-time and immediate-use medications. He referenced USP Chapter 797 relating to Immediate Use Compounded Sterile Products, which allows exemptions for emergency or immediate use of a compounded product. Mr. Schallock urged the board to grant the exemption in the best interest of patient safety and quality of care.

Board Response

The board recognizes that U.S. Pharmacopoeia (USP) General Chapter 797 (effective January 1, 2004) provides good *practices* for compounding sterile products, but USP 797 is not incorporated by reference into the board's statutes or regulations. As such, USP 797 does not control the board's enforcement of its own regulations regarding pharmacy compounding.

Based on comments received during the three comment periods, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Comments from Gloria Lee Wilder, PharmD, CBHS Pharmacy Director, San Francisco Department of Public Health

Comment #74

Dr. Wilder acknowledged that the underlying reason for the new requirement would be for a pharmacy to be able to trace each unit of IV medication to its specific compounding information. She asked the board to reconsider this requirement, and instead require a pharmacy to trace pedigree (compounding information), rather than prescriptively specifying the method of the 'trace-back.' Dr. Wilder stated that information currently printed on the label included prescription number, patient name, and date/time admixing would allow for this 'trace-back.' She is concerned that adding the pharmacy reference number or lot number would be redundant information for identifying pedigree of a compound product.

Board Response

Several of the record keeping requirements for sterile products are already required in current regulation. This proposal does expand on the requirements, and now also includes the identity of the person who compounded the drug, the

identity of the pharmacist reviewing the final drug product, the quantity of each component, the equipment used in compounding the drug product as well as a pharmacy assigned reference number. The board included the requirements for the identity of the person who compounded the drug as well as the pharmacists who reviewed the final drug product to allow a nonpharmacist to compound the medication, as allowed in other areas of pharmacy law, and to require that a pharmacist complete a review. This check is an essential consumer protection component. Further, the documentation of the equipment used is necessary to allow for a quality assurance review to be completed should a problem occur with such compounded medications. An internal pharmacy reference number is necessary to allow for a recall of a product if necessary, another essential consumer protection component.

The board does not prescriptively specify the method of “trace-back” rather, just information that must be recorded; the method by which this is achieved will be determined by the pharmacy.

Comment #75

Dr. Wilder requested clarification of proposed regulation 1735.2(a) where “the prescriber has approved use of a compounded drug product either orally or in writing....” She asked for clarification from the board as to whether this would be required for all prescriptions compounded in the hospital setting, or would it include prescriptions which can only be dispensed compounded (such as an individualized TPN). Dr. Wilder is concerned that pharmacists would be required to call prescribers to obtain a verbal order, and then add the compounding specifics to the prescription.

Board Response

Proposed regulation §1735.2(a) provides that, except as specified in subsections (b) or (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. Subsection (b) allows a pharmacy to prepare and store a limited quantity of compounded drug product in advance of receipt of a patient-specific prescription where and solely in such quantity 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. Subsection (c) defines “reasonable quantity.” Section 1735.2 applies to all compounded drug products.

Comments from Carolyn Nguyen, PharmD, ED Clinical Pharmacist, Stanford and Clinics Hospital

Comment #76

Dr. Nguyen does not support the proposed labeling and pharmacy record keeping requirements relating to certain compounded IV medications. She stated that the additional requirements will inevitably delay treatment of patients. Dr. Nguyen expressed concern that preparation of emergency compounded medications for patients experiencing heart attack, stroke, and other life-threatening events will be placed at risk by unnecessary labeling and record keeping requirements.

Board Response

The board disagrees with the conclusion that the documentation requirements found in section 1753.3 will place patients at risk. In an acute care setting, the regulation proposal allows for one-time preparations to be documented in the pharmacy's copy of the patient's chart order. This chart order can serve as the master formula. Further, the records required in section 1735.3 do not need to be completed in advance of the administration of the compounded drug, thus ensuring that the patient receives STAT medicines timely.

The documentation is necessary to ensure the integrity, potency, quality and strength of the compounded drug product(s) prepared and delivered to patients.

Comment #77

Dr. Nguyen referred to USP Chapter 797, relating to Immediate-Use Compounded Sterile Products. She advised that Chapter 797 contained a special section related to Immediate-Use Compounded Sterile Products as the provision intended only for those situations where there is a need for emergency or immediate patient administration of a compounded product. Dr. Nguyen asked the board to exempt from additional record keeping requirements the preparation of one-time and immediate-use injectable products in acute care facilities. She suggested that an exemption would benefit patients and ensure that one-time and immediate-use needs are treated in a safe and appropriate timeframe.

Board Response

The board recognizes that U.S. Pharmacopoeia (USP) General Chapter 797 (effective January 1, 2004) provides good *practices* for compounding sterile products, but USP 797 is not incorporated by reference into the board's statutes or regulations. As such, USP 797 does not control the board's enforcement of its own regulations regarding pharmacy compounding.

Based on comments received during the three comment periods, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those

sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Comments from Margaret C. Bradshaw, R.Ph., Mendocino Coast District Hospital

Comment #78

Ms. Bradshaw questioned the feasibility of having only one set of regulations governing both general compounding and sterile compounding. She also expressed concern about ability to regulate all types of compounding without making specific regulations accounting for specific needs encountered in practice sites. Ms. Bradshaw stated that not recognizing inherent differences in services or populations served results in regulations that are incomplete, ambiguous, and unduly burdensome. She asked the board provide pharmacy practitioners with a clear, unambiguous statement of the regulations.

Board Response

As stated in the Initial Statement of Reasons, the regulations remove duplication between Article 4.5 and Article 7 and reorganizes Article 7 to make it consistent with Article 4.5.

Additionally, the regulations address, among other items, the strength, efficacy and quality in compounding, as well as require a quality assurance program for general compounding. Currently, there are no provisions that either define these items for general compounding or set any parameters established in the Pharmacy law (Business and Professions Code §§ 4000 and following) detailing general compounding by a pharmacy.

The regulations also are crafted to remove redundancies between the requirements for general compounding and sterile injectable compounding, as well as to ensure consistent sequencing of related requirements contained in both Articles. The regulations provide uniformity in compounding for California consumers.

Comment #79

Ms. Bradshaw referred to USP Chapter 797, and asked if it is the intent of the board to exempt California pharmacies that compounding sterile preparations from the provisions of USP 797 that differ from the proposed regulations. If not, she suggested that it would serve the board's purpose to protect the public by adopting provisions of USP Chapter 797 as the rules, which govern sterile compounding in California. Ms. Bradshaw stated that current USP Chapter 797 is a direct reflection of the most current discussion in the pharmaceutical community regarding compounded sterile preparations, while the underlying data referred to in the Initial Statement of Reasons was reported in a workgroup that last met in January 2005.

Board Response

The board recognizes that U.S. Pharmacopoeia (USP) General Chapter 797 (effective January 1, 2004) provides good *practices* for compounding sterile products, but USP 797 is not incorporated by reference into the board's statutes or regulations. As such, USP 797 does not control the board's enforcement of its own regulations regarding pharmacy compounding.

Comment #80

Ms. Bradshaw noted specific sections of the proposed regulations that she considers problematic, as stated below. To address each comment thoroughly, a board comment follows each alphabetized item.

80.a. Compounding Definitions – there is a need for definition of additional terms. For example, designated area, critical area, and controlled area are terms used when referring to sterile compounding.

Board response to #80a

The terms referenced in Ms. Bradshaw's comment are not within the scope of the proposed regulations. The board may consider additional definitions in a future rule making.

80.b. Compounding Limitations and Requirements, Section 1735.2(a) – Does the requirement that the prescriber approve use of a compounded drug either orally or in writing apply to chart orders?

Board response to #80b

If a chart order specifies a prescription for a compounded drug product, then that compounded drug product is subject to the provisions of 1735.2(a).

80.c. Compounding Limitations and Requirements, Section 1735.2(h) – Expiration date or beyond use date for compounded sterile preparations depends on both stability and sterility concerns. Determining a beyond use date might also be determined by the nature of the compound.

Board response to #80c

Section 1735.2(h) specifies that a compounded drug product shall be given an expiration date, as specified. This subsection also provides that the pharmacist performing or supervising the compounding may use professional judgment with regard to the expiration date or beyond use date, as specified.

80.d. Compounding Limitations and Requirements, Section 1735.2(i) – The pharmacist performing or supervising compounding may not be the same pharmacist responsible for delivery of a compounded drug product. These activities may be performed by different individuals.

Board response to #80d

As stated in the proposed regulation, the pharmacist that performs or supervises the compounding is responsible for the proper preparation, labeling, storage, and delivery of the compounded drug product. The board acknowledges that every function described in Comment 80d may not be performed by the same individual; however, the pharmacist who performs or supervises the compounding is responsible for that compounded drug product.

80.e. Records of Compounded Drug Products Section 1735.3(a) – Requiring the maintenance of these records for compounded sterile products administered in the hospital inpatient or outpatient setting would be unduly burdensome. These products are used in a short period of time, if not immediately. Except for batch-prepared items, the detailed records this regulation requires would offer little value.

Board response to #80e

The intent of the regulation proposal is to improve patient safety. Several of the record keeping requirements for sterile products are already required in current regulation. This proposal does expand on the requirements, and now also includes the identity of the person who compounded the drug, the identity of the pharmacist reviewing the final drug product, the quantity of each component, the equipment used in compounding the drug product as well as a pharmacy assigned reference number. The board included the requirements for the identity of the person who compounded the drug as well as the pharmacists who reviewed the final drug product to allow a nonpharmacist to compound the medication, as allowed in other areas of pharmacy law, and to require that a pharmacist complete a review. This check is an essential consumer protection component. Further, the documentation of the equipment used is necessary to allow for a quality assurance review to be completed should a problem occur with such compounded medications. An internal pharmacy reference number is necessary to allow for a recall of a product if necessary, another essential consumer protection component.

Based on comments received during the three comment periods, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Adequate recordkeeping of compounded drug products would provide for a meaningful quality assurance review should a problem occur with such compounded medications.

80.f. Records of Compounded Drug Products Section 1735.3(b) – Would this require pharmacies compounding sterile products to maintain records of the acquisition of all sterile medications that are used to prepare sterile products, including IV solutions, and any medication that might be added to an IV solution? Would a hospital pharmacy performing minimal general compounding for an inpatient be required to keep records of items that might not have been purchased with the intent to use those items for compounding?

Board response to #80f

Section 1735 .3(b) provides that a pharmacy shall maintain records of the proper acquisition, storage, and destruction of chemicals, bulk drug substances, drug products, and components used in compounding. If the products referred to in Ms. Bradshaw’s comment are used in compounding as defined in §1735 then – yes – the record keeping requirements provided in §1753.3(b) would apply to those products.

80.g. Labeling of Compounded Drug Products, Section 1735.4 – Does Section 1735.4 refer to outpatient dispensing? Labeling requirements for sterile compounded preparations for administration in a hospital should have certain exemptions.

Board Response to #80g

The provisions of §1735.4 apply to all sterile injectable compounded products. Section 1735.3(a)(g) provides limited exemptions from the labeling requirements of all compounded drug products, including those that are compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under 1250 of the Health and Safety Code.

80.h. Training of Compounding Staff, Section 1735.7 – There is a need for guidelines stating the minimum skills, training, competency or competency assessment. Absent guidelines, the determination of the sufficiency of the training or competency assessment would be left to a board inspector.

Board Response to 80h

The determination of the sufficiency of the training or competency assessment of pharmacy compounding staff is defined in §1735.7. The pharmacist-in-charge

is responsible to ensure that the training of compounding staff pursuant to the criteria found in §1735.7 is met.

80.i. Article 7, Sterile Injectable Compounding – Adoption of USP Chapter 797 would provide necessary regulation of sterile compounding.

Board Response to #80i

The board recognizes that U.S. Pharmacopoeia (USP) General Chapter 797 (effective January 1, 2004) provides good *practices* for compounding sterile products, but USP 797 is not incorporated by reference into the board's statutes or regulations. As such, USP 797 does not control the board's enforcement of its own regulations regarding pharmacy compounding.

80.j. Compounding Area – Definition of a compounding aseptic barrier should be added to Section 1751.

Board Response to #80j

Section 1751.3 provides the provisions that a pharmacy's written policies and procedures shall comply with for those pharmacies that compound sterile injectable products from one or more non-sterile ingredients (see 1751.3(d)(3)(F)), including barrier isolator workstations.

80.k. Sterile Injectable Labeling Requirements, Section 1751.2 (d) – The proposed regulations do not address hazardous drugs, as designated by NIOSH and OSHA.

Board Response to #80k

Those hazardous drugs described by Ms. Bradshaw are not within the scope of the proposed regulations.

80.l. Sterile Injectable Policies and Procedures, Section 1751.3 – Most of the requirements of subsection (d) should apply to all sterile injectable compounding, not just sterile compounding from one or more non-sterile ingredients.

Board Response to #80l

This comment is outside the scope of this regulation change. The text of section 1751.3(d) in its entirety was previously found in section 1751.02. With the exception of re-numbering, the board did not propose any amendments to that subdivision.

80.m. Facility and Equipment Standards for Sterile Injectable Compounding, Section 1751.4(b) – Proper attire required should be specified.

Board Response to #80m

Section 1751.5 defines proper attire, as referenced in §1751.4(b).

80.n. Facility and Equipment Standards for Sterile Injectable Compounding, Section 1751.4(d) – Weekly cleaning schedule specified conflicts with USP Chapter 797 in pharmacies compounding only low and medium risk preparations.

Board Response to #80n

The board recognizes that U.S. Pharmacopoeia (USP) General Chapter 797 (effective January 1, 2004) provides good *practices* for compounding sterile products, but USP 797 is not incorporated by reference into the board's statutes or regulations. As such, USP 797 does not control the board's enforcement of its own regulations regarding pharmacy compounding.

80.o. Facility and Equipment Standards for Sterile Injectable Compounding, Section 1751.4(e) – Use of a compounding aseptic isolator for preparing parenteral cytotoxic agents should be allowed.

Board response to #80o

The board incorporates by reference those facility and equipment requirements found in Title 24 of the California Administrative Code. Section 1751.4 provides that no sterile injectable product shall be compounded if it is known, or reasonably known, that the compounding environment fails to meet criteria specified in the pharmacy's written policies and procedures for the safe compounding of sterile injectable drug products. The pharmacy may incorporate in its policies and procedures the additional requirements as specified by Ms. Bradshaw, in addition to those provided for in that section.

80.p. Sterile Injectable Compounding Attire, Section 1751.5 – Gloves used for sterile compounding should be more than gloves made from low shedding materials. If not sterile gloves, then at least latex or nitrile gloves should be specified. Glove that are ASTM rated for chemotherapy should be specified for personnel preparing cytotoxic agents.

Board Response to #80p

With the exception of re-numbering, as well as a non-substantive change in subdivision (c), the board did not propose amendments to this section.

80.q. Training of Sterile Injectable Compounding Staff – Requirements listed in (e)(1) A-H should be required of all personnel compounding sterile preparations.

Board Response to #80q

Section 1751.6(b) provides that the pharmacist-in-charge shall be responsible to ensure all pharmacy personnel engaging in compounding sterile injectable drug products shall have the training and demonstrated competence in the safe handling and compounding of sterile injectable products, including cytotoxic agents if the pharmacy compounds products with cytotoxic agents. Subsection (e) provides the training requirements of such staff.

Comments from Bryan Carlson, Pharmacy Department, Children's Hospital of Central California**Comment #81**

Mr. Carlson asked the board to consider a 'phase-in' period of 12 months to effect the changes proposed to Section 1716, Requirements for Pharmacies that Compound Medications. He expressed concerns about necessary budget and process changes that will need to occur at Children's Hospital of Central California in order to comply with the regulatory changes proposed.

Board Response

Mr. Carlson's comment is not within the scope of the language provided for comment during the comment period. However, upon adoption of the specific language and at its Board Meeting on July 15, 2009, the board moved to specify that, should the regulations as adopted be approved by OAL, that an effective date of six months following OAL approval will be specified. In addition, the board stated that it will exercise its enforcement discretion for an additional six months.

Comment #82

Mr. Carlson suggested that if manufacturers would standardize bar coding technology to include lot numbers and expiration dates along with the NDC, this would facilitate the proposed record keeping process.

Board Response

The board thanks Mr. Carlson for his comment, however, the technology utilized by manufacturers is not within the scope of the proposed regulations.

Comment #83

Mr. Carlson asked the board for clarification regarding the term "equipment" referred to in Section 1735.3(a)(7). He asked whether every lot number of every syringe and every needle used in the compounding process would need to be documented and stored. Mr. Carlson expressed concern about the extent of documentation needed, and the difficulty in meeting this requirement.

Board Response

Section 1735.3(a)(7) specifies that for each compounded drug product, pharmacy records shall include the equipment used in compounding the drug product. That section does not specify that lot numbers of needles and syringes are required to be recorded.

The board does not prescriptively specify the method of 'trace-back' rather, it specifies what information must be recorded. The method by which this is achieved will be determined by the pharmacy. The lot number requirement is specific to each component, not equipment used.

Comments from Alan Y. Endo, PharmD, Director of Pharmacy, Presbyterian Intercommunity Hospital

Comment #84

Dr. Endo acknowledged the board's efforts to strengthen compounding regulations, but he expressed concern regarding the proposed labeling and pharmacy record keeping requirements for compounded IV medications in acute care hospitals. Dr. Endo referred to a distinction between prescription compounding and bulk manufacturing. He suggested that manufacturing practices applied to acute care settings can seriously jeopardize a hospital pharmacist's ability to respond to acute needs of patients. He asked the board to accept the recommended changes submitted by CSHP, or create a working group of practicing hospital pharmacists to ensure safe guarding the protection of patients.

Board Response

The intent of the regulation proposal is to improve patient safety. In an acute care setting, the regulation proposal allows for one-time preparations to be documented in the pharmacy's copy of the patient's chart order. This chart order can serve as the master formula. Further, the records required in section 1735.3 do not need to be completed in advance of the administration of the compounded drug, thus ensuring that the patient receives STAT medicines timely.

Based on comments received during the three comment periods, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Further, §1735.2(b) provides that a pharmacy may prepare and store a limited quantity of a compounded drug product in advance of receipt of a patient-specific prescription, as specified. Section 1735.2(c) further defines “reasonable quantity.” The board believes this subsection adequately addresses Dr. Endo’s concern about a hospital pharmacist’s ability to respond to acute needs of patients.

Comments from Ray Miller, PharmD, Director of Pharmacy, St. Francis Memorial Hospital

Comment #85

Dr. Miller asked for clarification from the board as to whether the proposed regulations applied to hospital pharmacies that compound admixtures for immediate use on in-patients. He stated that the proposed self-assessment distributed was titled, “Community Pharmacy & Hospital Outpatient Pharmacy Compounding Self-Assessment” which implies that it is not intended for hospitals that are accredited by TJC.

Board Response

Pharmacy law specifies that all pharmacies, either licensed by the board to compound sterile injectable products, or exempt from licensure because of specified accreditation, must comply with regulations.

Comments from Karen Nishi, Director, Regulatory Affairs, Cardinal Health, San Diego, California

Comment #86

Ms. Nishi states that Cardinal Health commends and supports the Board of Pharmacy for their efforts to improve patient safety by strengthening the regulations surrounding compounding.

Board Response

The board thanks Ms. Nishi for Cardinal Health’s stated support to improve patient safety through compounding regulations.

Comment #87

Ms. Nishi suggests that the term “expiration date” should be changed to “beyond use date” to better track with the language used by the United States Pharmacopoeia (USP) and the Joint Commission on Accreditation of Healthcare Organizations.

Board Response

The term “expiration date” is consistent with existing Pharmacy Law, specifically Business and Professions Code section 4076(a)(9), which references the expiration date of the effectiveness of the drug dispensed.

Comment #88

Ms. Nishi suggests that references to the “Joint Commission on Accreditation of Healthcare Organizations” (JCAHO) should be updated to state “Joint Commission.”

Board Response

Ms. Nishi’s general comment recommending that a term be updated to “Joint Commission” is not directed at any specific proposed text. The proposed text of the regulation does not reference “Joint Commission on Accreditation of Healthcare Organizations” or “Joint Commission.”

Comment #89

Ms. Nishi states that the National Institute for Occupational Safety and Health (NIOSH) and the Joint Commission often refer to “cytotoxic agents” and “chemotherapy” as “hazardous drugs”.

Board Response

While this comment is general in nature and is not directed to any specific proposed text, the terms “cytotoxic” and “chemotherapy” are not new and have been used throughout pharmacy regulations (i.e., 1751 et seq.). Through this proposal, and as explained in the Initial Statement of Reasons, several section numbers were renumbered, or text was moved from one section and to another.

Comment #90

Ms. Nishi states that proposed section 1735.3 does not differentiate between routine scheduled drug products and those injectables prepared for stat or immediate use. She states that while Cardinal Health would agree that information such as the master formula, the date compounded, identifiers of who compounded and checked the product, as well as the quantity of each component are essential. She continues that documenting data elements indicating the supplier, lot number, equipment used, assigned pharmacy reference number and “expiration date” may slow the preparation and delivery of emergency medications. She states that the latest USP Chapter 797 has a special section related to “Immediate Use Compounded Sterile Products” which supports the distinction from a scheduled administration. She states that the board could follow the same path as USP 797 by delineating fewer record keeping requirements for injectables prepared for immediate patient administration.

Board Response

The board disagrees that the documentation requirements found in section 1735.3 will delay preparation and delivery of medications. In an acute care setting, the regulation proposal allows for one-time preparations to be documented in the pharmacy’s copy of the patient’s chart order. This chart order can serve as the master formula. Further, the records required in section 1735.3 do not need to be completed in advance of the administration of the compounded drug, thus ensuring that the patient receives STAT medicines timely.

Several of the record keeping requirements for sterile products are already required in current regulation. This proposal does expand on the requirements and now also includes the identity of the person who compounded the drug, the identity of the pharmacist reviewing the final drug product, the quantity of each component, the equipment used in compounding the drug product as well as a pharmacy assigned reference number. The board included the requirements for the identity of the person who compounded the drug as well as the pharmacists who reviewed the final drug product to allow a nonpharmacist to compound the medication, as allowed in other areas of pharmacy law, and to require that a pharmacist complete a review. This check is an essential consumer protection component. Further, the equipment used is necessary to allow for a quality assurance review to be complete should a problem occur with such compounded medications. An internal pharmacy reference number is necessary to allow for a recall of a product if necessary--another essential consumer protection component.

The board recognizes that U.S. Pharmacopoeia (USP) General Chapter 797 (effective January 1, 2004) provides good *practices* for compounding sterile products, but USP 797 is not incorporated by reference into the board's statutes or regulations. As such, USP 797 does not control the board's enforcement of its own regulations regarding pharmacy compounding.

Based on comments received during the three comment periods, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

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Comment from Ernest M. Aldama, Adapt Consulting, Grants Pass, Oregon

Comment #91

In an undated letter, Mr. Aldama stated that Title 24 section 4-1106(b) is not readily available to all persons and it would be helpful to have the applicable information provided within paragraph 1751(b).

Board Response

This comment as it is outside of the scope of the modified text provided for comment during the 15-day comment period.

Comments received from Dawn Benton, Executive Vice President, CEO, California Society of Health-System Pharmacists

Comment #92

Ms. Benton expressed the California Society of Health-System Pharmacists (CSHP) thanks for changes made to section 1735.3(a)(6) that exempts the manufacturer and lot number of each component if the sterile product is compounded "on a one-time basis for administration within two hours to an inpatient in a health care facility..." She further stated that CSHP believes the exemption will help to prevent delay of medications to patients with immediate and urgent needs, but nonetheless still questions the *necessity* of including any inpatient pharmacy currently covered by Article 7: Sterile Injectable Compounding also under the proposed Article 4.5: Compounding regulations.

Board Response

The board appreciates CSHP's comments that the proposed modified text in §1735.3(a)(6) will help prevent delay of medications to patients with immediate and urgent needs.

However, with regard to the applicability of proposed regulations to those pharmacies currently covered by Article 7, to be subject to Article 4.5 as well, the board refers Ms. Benton to the Initial Statement of Reasons. There are currently no provisions that address the various issues for general compounding, or that set parameters established in the Pharmacy Law (Business & Professions Code §§ 4400 and following) for general compounding. The proposal provides uniformity in compounding for California consumers with the goal of improving patient safety.

Following the first 15-day comment period the board further modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Comment #93

Ms. Benton provided a history of the various letters that CSHP has provided to the board on the topic of compounding regulations. She referenced a September 17, 2008, letter where she states CSHP submitted a letter and provided public comment requesting an exemption of immediate and one-time use (STAT) compounded drugs from the recordkeeping and labeling requirements in proposed compounding regulations. She summarized the board's effort to form a 2-person subcommittee to evaluate the requested exemption. She further stated that,

in January 2009, the recommendation of the board subcommittee was to exempt the need to track manufacturer and lot number for each immediate and one-time use sterile injectable product; although the pharmacy assigned lot number is still required in immediate and one-time use sterile injectable products. She states CSHP hopes this is an oversight of the board and can be corrected by also exempting the pharmacy assigned lot number in urgent situations.

Board Response

At the January 2009 Board Meeting, the board publicly noticed and discussed a proposed amendment to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The pharmacy lot number to which Ms. Benton references is found in §1735.3(a)(8), and no suggested amendment to that subparagraph was recommended or discussed by the board at its January 2009 meeting.

Comment #94

Ms. Benton stated that CSHP members have additional issues with the proposed regulations. Specifically, she referenced concerns with proposed sections 1735.3(d), 1735.3(a)(7), 1735(a)(2), 1735(b), as well as the “Community Pharmacy & Hospital Outpatient Pharmacy Compounding Self-Assessment” form. Ms. Benton requested various exemptions within each section referenced and asked that the board consider these exemptions.

Board Response

The comments offered to the self-assessment form and to sections §1735(b)(1), §1735(a)(2) and §1735(b), §1735.3(a)(7), and §1735.3(d) are not within the scope of the proposed modified text provided for comment during the 15-day comment period.

The board agrees that the pharmacy profession is dedicated to patient safety – that is the stated intent of the regulation proposal. While Ms. Benton’s general comments are not expressly directed to the text of §1735.3(a)(6), the board has thoroughly considered what documentation requirements would balance the needs of pharmacy operations within an acute care setting and that of patient safety. In response, the board again modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

Comments received from William J. Blair, PharmD, MBA, McGuff Compounding Pharmacy Services, Inc.

Comment #95

Dr. Blair provided a copy of proposed regulations to 16 CCR §§1716.1 and 1716.2, §§1735-1735.8, §§1751-1751.8, and the board’s Initial Statement of Reasons. This copy was transmitted in a strike-out and underscore format with no commentary.

Board Response

Comments offered to the proposed text of 16 CCR §§1716.1 and 1716.2, §§1735 through 1735.8 (with the exception of §1735.3(a)(6)), §§1751 through 1751.8, and the Initial Statement of Reasons are outside of the scope of the modified text provided for comment during the first 15-day comment period. With regard to the specific language contained in the notice of modified text (15-day comment period), it appears that Dr. Blair changed the word “manufacturer” to “manufacturer’s” in the sentence: “If the manufacturer’s name is demonstrably unavailable,”

The board believes this comment is nonsubstantive and does not change the meaning of the proposed text. Common usage can reflect that, at times, a noun that the possessive modifies is not expressed but merely understood.

Comments received from Margaret Bradshaw, R.Ph., Albion, California

Comment #96

Ms. Bradshaw stated she is a pharmacist employed in a critical access hospital. She provided various patient-pharmacy scenarios for her pharmacy which she states is not staffed 24 hours a day. She added that some pharmacies are closed on weekends. Ms. Bradshaw states that in her scenarios, there would be no greater benefit from the required recordkeeping, as it relates to exemption of sterile products compounded on a one-time basis for administration within two hours than for a 24-hour period.

Board Response

Based on the comments of Ms. Bradshaw and others received during the 15-day comment period, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Comment #97

Ms. Bradshaw states that the volumes of records that will result from the board's record keeping requirements will tax already scarce personnel resources. She adds that small hospitals are negatively impacted because [they] cannot afford to invest in proprietary premixed products that would be more widely available at larger institutions with bigger drug budgets. She adds that even if [they] could afford to purchase products, the volumes would be so small that they could not meet minimum quantities without generating waste from products that expire before they are used. She "rejects the implication that we cannot provide safe products for our patients without the added requirements for the voluminous records that will result from maintaining batch records for individualized compounded sterile products.

Board Response

Several of the record keeping requirements for sterile products are already required in current regulation. This proposal does expand on the requirements, and now also includes the identity of the person who compounded the drug, the identity of the pharmacist reviewing the final drug product, the quantity of each component, the equipment used in compounding the drug product as well as a pharmacy assigned reference number. The board included the requirements for the identity of the person who compounded the drug as well as the pharmacist who reviewed the final drug product. First, the regulations were updated to allow a nonpharmacist to compound the medication as allowed in other areas of pharmacy law, and to require that a pharmacist complete a review. This check is an essential consumer protection component. Second, the equipment used is necessary to allow for a quality assurance review to be complete should a problem occur with such compounded medications.

The intent of the regulation proposal is to improve patient safety. Compounding cannot be done for commercially available products, except as specified. Standards are necessary to ensure the quality, potency, integrity and strength of a compounded product.

Likewise, in an acute care setting, the regulation proposal allows for one-time preparations to be documented in the pharmacy's copy of the patient's chart order. This chart order can serve as the master formula. Further, the records required in section 1735.3 do not need to be completed in advance of the administration of the compounded drug, thus ensuring that the patient receives STAT medicines timely. The regulation does not specify a method for recordkeeping, rather it specifies what records must be kept and for how long. The 3-year time frame required in this proposal is consistent with current pharmacy law that specifies that all records must be maintained for three years (see Business and Professions Code section 4105(c)).

Comment #98

Ms. Bradshaw commented on hospitals that provide compounded sterile products to their outpatient departments on an individual, as needed basis. She referenced those that are

utilized by oncology departments, infusion departments, outpatient surgery department, emergency department and recovery rooms – adding that the patient never takes possession of them, and that they are administered by hospital personnel. She stated that some situations require that STAT medications be given in life or death situations. She stated “the emphasis should be on providing accurate, aseptic products to these patients in a timely manner, not on generating compounding drug records.

Board Response

The board agrees that the preparation and delivery of STAT medications to patients be administered without delay. The intent of the proposed regulation is to improve patient safety. In an acute care setting, the regulation proposal allows for one-time preparations to be documented in the pharmacy’s copy of the patient’s chart order. This chart order can serve as the master formula. Further, the records required in section 1735.3 do not need to be completed in advance of the administration of the compounded drug, thus ensuring that the patient receives STAT medicines timely.

Additionally, and upon recall of a product, the required documentation can be utilized to identify patients to whom the compounded products were administered and to provide a systematic review. Without adequate documentation, necessary or systematic changes may not be realized and made to prevent future errors.

Comment #99

Ms. Bradshaw urged that the exemption to the compounding records requirements should at least extend to outpatients in health care facilities licensed under Section 1250 of the Health and Safety Code.

Board Response

While Ms. Bradshaw’s letter does not explicitly state what her recommendation is, the board has thoroughly considered what documentation requirements provide for patient safety. Patients receiving an IV on site, in an outpatient setting, are not STAT medications.

Based on comments received during the comment periods, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

Patients receiving an IV on site, in an outpatient setting, are not STAT medications and are not subject to the exemption specified in §1735.3(a)(6).

The board believes the text as adopted strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Comments from Kevin R. Brown, PharmD

Comment #100

In response to the 15-day comment period, Dr. Brown provided a general statement that he is concerned about the “sweeping changes” that are proposed to the compounding and documentation of sterile injectable products. He added that current regulations regarding sterile injectable compounding are specific and detailed in both the U.S. Pharmacopoeia (USP) Convention guidelines (federal level) and in current state Board of Pharmacy regulations. He added that additional regulations require assessment of the patient benefits and risks.

Board Response

The broad statement made by Dr. Brown is not entirely within the scope of the 15-day comment period. However, with regarding to Dr. Brown’s comment regarding “documentation of sterile injectable products” the proposed regulations allows for preparations to be documented in the pharmacy’s copy of the patient’s chart order. This chart order can serve as the master formula. Further, the records required in section 1753.3 do not need to be completed in advance of the administration of the compounded drug, thus ensuring that the patient receives STAT medicines timely.

The board recognizes that U.S. Pharmacopoeia (USP) General Chapter 797 (effective January 1, 2004) provides *best practices* for compounding sterile products, but USP 797 is not incorporated by reference into the board’s statutes or regulations. As such, USP 797 does not control the board’s enforcement of its own regulations regarding pharmacy compounding.

Several of the record keeping requirements for sterile products are already required in current regulation. This proposal does expand on the requirements, and now also includes the identity of the person who compounded the drug, the identity of the pharmacist reviewing the final drug product, the quantity of each component, the equipment used in compounding the drug product as well as a pharmacy assigned reference number. The board included the requirements for the identity of the person who compounded the drug as well as the pharmacist who reviewed the final drug product. First, the regulations were updated to allow a nonpharmacist to compound the medication as allowed in other areas of pharmacy law, and to require that a pharmacist complete a review. This check is an essential consumer protection component. Second, the equipment used is necessary to allow for a quality assurance review to be complete should a problem occur with such compounded medications. The intent of the regulation proposal is to improve patient safety.

Comment #101

Dr. Brown states that no documentation has been offered to show changing compounding regulations for sterile injectable products will have a beneficial impact to patient care. He further states that current board regulations and the USP provide adequate safeguards and documentation. He states that adding regulations for additional documentation to sterile injectable products that will be administered within 24 hours is labor intensive and provides no benefit or clear value.

Board Response

The board provided a response (Comment #95) to Dr. Brown regarding USP and that it does not control the board's enforcement of its own regulations regarding pharmacy compounding. The board disagrees with the conclusion that the documentation requirements of sterile injectable products will provide no benefit or clear value.

As stated in the Initial Statement of Reasons, documentation is necessary to ensure the integrity, potency, quality and strength of the compounded drug product(s) prepared and delivered to patients.

Likewise, in the case of a recall, the specified recordkeeping requirements would allow for patient identification and for a systematic review to be accomplished. Ultimately, patient safety could be improved by system changes made as a result of that review and – ultimately – could prevent future errors.

Comment #102

Dr. Brown states that in contrast to the proposed regulations, patient care is likely to be jeopardized by the additional documentation. He states that the added workload will take pharmacy staff away from other patient care functions and programs and, as a result, patient care activities with documented patient benefit will be decreased or eliminated. He closes by stating that current regulations assure patient safety and those changes or additional regulations are not needed.

Board Response

The intent of the regulation is to improve patient safety. Several of the record keeping requirements for sterile products are already required in current regulation. This proposal does expand on the requirements and now includes the identity of the person who compounded the drug, the identity of the pharmacist reviewing the final drug product, the quantity of each component, the equipment used in compounding the drug product as well as a pharmacy assigned reference number. The board rejects Dr. Brown's assertion that the record-keeping and labeling requirements would be burdensome or that it would decrease beneficial patient care activities. In an acute care setting, the regulation proposal allows for one-time preparations to be documented in the pharmacy's copy of the patient's chart order. The patient's chart order can serve as

the master formula. Further the records required in section 1735.3 do not need to be completed in advance of the administration of the compounded drug.

Comments from Alan Endo, PharmD, Presbyterian Intercommunity Hospital, Whittier, California

Comment #103

Dr. Endo provided comments to proposed regulation 16 CCR §§ 1735(c), 1735.2(f), 1735.3(c), 1735.4(b), and 1751.7(c).

Board Response

These comments offered are outside of the scope of the modified text provided for comment during the 15-day comment period.

Comments from Steven W. Gray, PharmD, JD, Kaiser Permanente

Comment #104

Dr. Gray attached to an email a comment regarding proposed language at 16 CCR §1751.4(d) and to the board's Initial Statement of Reasons. Dr. Gray stated that a reference consolidating 1751.01 and 1751.1 is incorrect. He also provided proposed language changes to subdivisions (d) and (e), with a note to move an existing item regarding preparing cytotoxic agents to a new item (f).

Board Response

The specific comments are outside of the scope of the modified text provided for comment during the 15-day comment period. However, the board may consider the comments and the proposed language changes in a future rule making.

Comments from Inaya Hazime, PharmD, Director of Pharmacy, Methodist Hospital of Sacramento, Sacramento, California

Comment #105

Dr. Hazime states "I believe your modifications to the text of section 1735.5 in Title 16 Cal.Code Reg. does not improve the care delivered in California's Joint Commission Accredited Hospitals." She adds "the record-keeping required by the changes will add burden and expense to our licensed hospital pharmacies without positively impacting patient care."

Board Response

Changes made to proposed 16 CCR 1735.5 are not within the scope of the modified text provided for comment during the 15-day comment period. The board considered the requirements on §1735.5 during the initial rule making. Such comments are addressed in board responses to comments submitted during the 45-day comment period.

Comment #106

Dr. Hazime states she has no problem with implementing rules as they apply to control compounding in the outpatient setting and adds “to expect that every admixture bag mixed in a hospital pharmacy will follow the same rules is time consuming and not productive to the end of improving patient safety.”

Board Response

Dr. Hazime’s comments do not specifically address the modified text contained in proposed 16 CCR 1735.3(a)(6). The board disagrees with the statement that the regulation does not improve patient safety.

Comments from Andree S. Hest, R.Ph, MScPharm, California Pacific Medical Center**Comment #107**

The comments received from Andree Hest are general in nature as it relates to the entire rule making but makes no specific comment or reference to the modified text provided for comment during the 15-day comment period.

Board Response

The broad comments offered do not specifically address the modified text contained in proposed 16 CCR 1735.3(a)(6). As such, these comments appear to be outside of the scope of the modified text provided during the 15-day comment period. However, the general comments made are similar to those general comments found in Comments 95, 96, 97, to which the board provided general responses.

Comments from Kathleen Lee, PharmD, Clinical Pharmacist, St. Joseph’s Medical Center, Stockton, California**Comment #108**

Dr. Lee provides comments to various sections of proposed 16 CCR §1735, specifically referencing §1735(a), §1735(b), and §1735.3(d). She adds that the scope of the modified text is unclear. She states she believes the intent of the regulation is to define and set quality assurance parameters for compounding in an outpatient setting. She states that the current language in the regulation makes no distinction between inpatient and outpatient pharmacies, and the definition of compounding is broad enough to be interpreted several ways. She states it would be preferred that the language be made specific to hospital outpatient pharmacies and exclude inpatient hospital pharmacies.

Board Response

The comments offered by Dr. Lee do not specifically address the modified text contained in proposed 16 CCR 1735.3(a)(6). As such these comments are outside of the scope of the 15-day comment period.

Comments from Gary Louie, PharmD, California Pacific Medical Center, San Francisco, California

Comment #109

The comments received from Dr. Louie are general in nature as it relates to the entire rule making but makes no specific comment or reference to the modified text provided for comment during the 15-day comment period.

Board Response

The broad comments offered do not specifically address the modified text contained in proposed 16 CCR 1735.3(a)(6). As such, these comments appear to be outside of the scope of the modified text provided during the 15-day comment period. However, the general comments made are similar to those general comments found in Comments 95, 96, 97, to which the board provided general responses.

Comment from Ed Maurino, R.Ph. FCSHP, Pharmacy Manager, Banner Lassen Medical Center, Susanville, California

Comment #110

Mr. Maurino states “Dawn’s letter about the Board of Pharmacy’s proposed record keeping for compounded sterile products is right on track.” (The board infers that Mr. Maurino is referring to the comments offered by Dawn Benton, CSHP. It is unclear if Mr. Maurino is referring to Ms. Benton’s comments offered during the 45-day comment period [Comments 20, 21, 22, 23] or to those made during the 15-day comment period [Comments 87, 88, 89].) He continues by adding that record keeping would be immense, and there would be little, if any, benefit to the patient. He states most hospitals do a very good job compounding sterile IV’s and asks “what percentage of harm comes knowing that California make millions of CSP’s every day?” He asks that the board heed the points made in Ms. Benton’s letter.

Board Response

The board received comments from Dawn Benton, CSHP, which are summarized in the board’s responses to comments 20, 21, 22, and 23 (during the 45-day comment period). Ms. Benton’s comments provided during the 15-day comment period and related board responses are found in comments 87, 88, 89.

Mr. Maurino’s comments are not specific to the modified text contained in proposed §1735.3(a)(6) and, thus, are outside of the scope of the modified text provided during the 15-day comment period.

However, the board disagrees with Mr. Maurino’s comments that record keeping requirements as prescribed by the proposed regulations would be immense and of little benefit to patients.

As stated in the Initial Statement of Reasons, documentation is necessary to ensure the integrity, potency, quality and strength of the compounded drug product(s) prepared and delivered to patients.

Likewise, in the case of a recall, the specified recordkeeping requirements would allow for patient identification and for a systematic review to be accomplished. Patient safety could be improved and changes made as a result of such a review and – ultimately – could prevent future errors.

Comments from Ray Miller, PharmD, Director of Pharmacy, Saint Francis Memorial Hospital, San Francisco, California

Comment #111

Dr. Miller states “I believe your modifications to the text of section 1735.5 in Title 16 Cal.Code Reg. does not improve the care delivered in California’s Joint Commission Accredited Hospitals.” He adds “the record-keeping required by the changes will add burden and expense to our licensed hospital pharmacies without positively impacting patient care.”

Board Response

Changes made to proposed 16 CCR 1735.5 are not within the scope of the modified text provided for comment during the 15-day comment period. The board considered the requirements on §1735.5 during the initial rule making. Such comments are addressed in board responses to comments submitted during the 45-day comment period.

Comment #112

Dr. Miller states he has no problem with implementing rules as they apply to control compounding in the outpatient setting and adds “to expect that every admixture bag mixed in a hospital pharmacy will follow the same rules is time consuming and not productive to the end of improving patient safety.”

Board Response

The broad comments offered by Dr. Miller do not specifically address the modified text contained in proposed 16 CCR 1735.3(a)(6). As such, these comments appear to be outside of the scope of the modified text provided during the 15-day comment period. The board disagrees with the statement that the regulation does not improve patient safety.

Comments from Eduardo Morin, PharmD, Jackson, California

Comment #113

The comments received from Mr. Morin are general in nature as it relates to the entire rule making but makes no specific comment or reference to the modified text provided for comment during the 15-day comment period.

Board Response

The broad comments offered do not specifically address the modified text contained in proposed 16 CCR 1735.3(a)(6). As such, these comments appear to be outside of the scope of the modified text provided during the 15-day comment period. However, the general comments made are similar to those general comments found in Comments 95, 96, 97, to which the board provided general responses.

Comments from Tracey Okabe-Yamamura, PharmD, Mercy San Juan Medical Center, Carmichael, California

Comment #114

Dr. Okabe-Yamamura states “I am supportive of the changes made to the proposed regulation to section 1735.5(a)(6), which now exempts the manufacturer and lot number of each component if the sterile product is compounded “on a one-time basis for administration within two hours to an inpatient in a health care facility....”

Board Response

The board appreciates Dr. Okabe-Yamamura’s support of the modified language. However, based on comments received during the three comment periods, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1735.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Comment #115

Dr. Okabe-Yamamura states her concern regarding the self-assessment form titled “Community Pharmacy & Hospital Outpatient Pharmacy Compounding Self-Assessment” and text found in §1735(b)(1), §1735(a)(2) and §1735(b), §1735.3(a)(7), and §1735.3(d). Dr. Okabe-Yamamura asks that the board consider the exemptions she offers within these sections. She states she believes that the intent of the regulation is for the documentation within the practice of mass compounding in the event of a potential safety recalls; however, within the inpatient hospital setting, the majority of IV admixtures involve small batches that are generally used within 24 hours. She concludes by stating the pharmacy profession is dedicated to patient safety; however, she states the proposed regulations will not add significantly to patient safety while dramatically increasing the workload for hospital inpatients.

Board Response

The comments offered to the self-assessment form and to sections §1735(b)(1), §1735(a)(2) and §1735(b), §1735.3(a)(7), and §1735.3(d) are not within the scope of the proposed text provided during the 15-day comment period.

**Comments from Charles A. Reynolds, PharmD, B.C.P.P., Residency Program Director,
Department of Pharmaceutical Services, UCLA Health System****Comment #116**

Dr. Reynolds states that he believes the proposed regulations will negatively affect the ability of hospital pharmacists to safely care for patients. He stated the proposal impairs hospital practices without any change in patient safety. He adds that the additional documentation burden could actually be detrimental to hospitalized patients as limited staff capabilities are further stretched with another agency’s regulations. He reminded the board of the classic anxiety/performance curve principle – which demonstrates that as stress is increased past a critical point, performance (i.e. safety) decreases.

Board Response

Dr. Reynolds comments are general in nature and do not specifically address the modified text proposed in §1735.3(a)(6). As such, the comments are not within the scope of the modified text provided for comment during the 15-day comment period. The board disagrees with the statement that the regulation does not improve patient safety.

With regard to Dr. Reynold’s comment that additional documentation could be detrimental to hospitalized patients, the board disagrees. The board has thoroughly considered what documentation requirements provide for patient safety and has determined that the exemption to these requirements would be those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code. The board believes the language adopted strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Comment #117

Dr. Reynolds asserts that the proposed regulations would negatively affect the compounding of medication in every hospital's Intravenous Additive Service (IVAS) in the State of California. He adds that in his institution, he predicts the minimum effect would be an increase of 30 technician hours a day to perform the tasks required for the volume of IV preparations they produce and an additional number of unknown pharmacists FTE to adequately supervise their activities. He asserts that this increased cost to health care cannot be justified.

Board Response

Dr. Reynolds comments are general in nature and do not specifically address the modified text proposed in §1735.3(a)(6). As such, the comments are not within the scope of the modified text provided for comment during the 15-day comment period.

Comment #118

Dr. Reynolds comments that most of changes to the compounding regulations directly effect manual labor activities and will greatly increase the time to prepare a compounded IV solution for a patient. He states the recent exemption provided in §1735.3(a)(6) is a first step, but does not address the whole issue.

Board Response

The board appreciates Dr. Reynolds comment that the exemption language addressed in the scope of the 15-day comment period is a good first step. Following the 15-day comment period, the board again modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1735.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code. The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Comment #119

Dr. Reynolds asks that the board “not pass this proposal without a more intensive evaluation of how it will affect hospital practices.” He states “these kinds of massive changes to well established, safe, compounding practices (which by the way have been historically driven not by regulations, but by the professionalism of many) can only increase risk not improve safety.”

Board Response

While Dr. Reynold's comment is not expressly applicable to the scope of the 15-day comment period, the board disagrees with Dr. Reynold's comments that the regulations do not improve patient safety. The board has publicly addressed the proposed

regulations in open forums, and the proposed language was developed through several workgroup meetings, in which industry representatives participated.

Comments from Richard Sakai, PharmD, Director of Pharmacy Services, Children's Hospital Central California, Madera, California

Comment #120

Dr. Sakai stated he is in support of CSHP's comments.

Board Response

The board thanks Dr. Sakai for his comment. CSHP's comments related to the scope within the 15-day comment period can be found at comments 87, 88, and 89, along with the board's response to each comment.

Comment #121

Dr. Sakai asks that the board exempt hospitals from compliance with any regulation the board approves in 'this area' for a period of five years, at which time full compliance is expected. He states this five-year exemption will allow organizations time to properly budget for the development if needed and plan for the resources to fully comply with regulations. He further provides his comments related to possible board actions if hospitals are found to not be in compliance with the regulation after the five-year exemption.

Board Response

Dr. Sakai's comment is s are general in nature and do not specifically address the modified text proposed in §1735.3(a)(6). Typically, regulations take effect 30 days after approval from the Office of Administrative Law. However, the board voted at its July 15, 2009, Board Meeting to adopt the specified language and also indicate that the effective date of the regulations, if approved by the Office of Administrative Law, be effective six months following OAL approval. The Board further indicated that it would exercise its enforcement discretion for an additional six months beyond the effective date.

Comment #122

Dr. Sakai asks that the board exempt the compounding of medications if one follows USP797 guidelines for beyond use dating as a guideline when lot numbers are required. He states that in the OR (operating room), Anesthesiology often prepares medications of critical nature. He states these medications are often necessary in an event something goes wrong. He states that the time frame the board set (inferred, for record keeping) is not within the normal length of time for a complex surgical case. He asserts the board will hold the PIC ultimately responsible for the physician's actions. He states that regulations jointly prepared and/or endorsed by the Board of Registered Nursing and the Board of Medicine can help better control the safe use of medications.

Board Response

Dr. Sakai's comment does not specifically address the modified text proposed in §1735.3(a)(6). However, the board recognizes that U.S. Pharmacopoeia (USP) General Chapter 797 (effective January 1, 2004) provides *best practices* for compounding sterile products, but USP 797 is not incorporated by reference into the board's statutes or regulations. As such, USP 797 does not control the board's enforcement of its own regulations regarding pharmacy compounding.

With regard to those products compounded by medical staff, documentation of such is typically maintained in the patient's record; likewise, nurses and physicians that compound medications are outside of the board's jurisdiction.

Comment #123

Dr. Sakai requested clarification of the definition of compounding. He is concerned that a single manipulation such as taking a partial amount from a larger vial and putting it into a syringe is not compounding; rather, it is unit dosing of medication. In this example, he infers that the current definition of compounding applies, since the dose is not in the original container. He asserts that the simple transfer of a product from a large container to a smaller one should not be considered compounding.

Board Response

Dr. Sakai's comment is not within the scope of the proposed text of the 15-day comment period. The board directs Dr. Sakai to proposed regulation 16 CCR §1735(a) for the definition of compounding.

Comments from Maria D. Serpa, PharmD, Elk Grove, California

Comment #124

Dr. Serpa states "I believe your modifications to the text of section 1735.5 in Title 16 Cal.Code Reg. does not improve the care delivered in California's Joint Commission Accredited Hospitals." She adds "the record-keeping required by the changes will add burden and expense to our licensed hospital pharmacies without positively impacting patient care.

Board Response

Changes made to 16 CCR 1735.5 are not within the scope of the modified text provided for comment during the 15-day comment period. The board considered the requirements on §1735.5 during the initial rule making. Such comments are addressed in board responses to comments submitted during the 45-day comment period. The board disagrees with the statement that the regulations do not positively impact patient care and safety.

Comment #125

Dr. Serpa states she has no problem with implementing rules as they apply to control compounding in the outpatient setting and adds "to expect that every admixture bag mixed in a

hospital pharmacy will follow the same rules is time consuming and not productive to the end of improving patient safety.”

Board Response

Dr. Serpa’s comments are very general and do not apply to the 15-day comment period. The board disagrees with the statement that the regulation is not improving patient safety.

Comments from Rita Shane, PharmD, FASHP, Director, Pharmacy Services, Cedars-Sinai Medical Center, Los Angeles, California

Comment #126

Dr. Shane offered comments to proposed regulation sections §1735.2(d)(4), §1735.2(f), §1735.3(b), §1735.5(c)(4), and §1751.2(c).

Board Response

The sections referenced by Dr. Shane are not within the scope of the modified text proposed in the 15-day comment period.

Comment #127

Dr. Shane stated that in propose §1735.3(a)(6) maintaining records of lot numbers for each component is a significant requirement and would require recording for lot numbers for any IV product that is diluted such as antibiotics that are administered IVPB, complex products such as TPN, IVs with multiple electrolytes, chemotherapy with multiple vials, etc.

Board Response

The intent of the regulation is to improve patient safety. Several of the record keeping requirements for sterile products are already required in current regulation. This proposal does expand on the requirements and now includes the identity of the person who compounded the drug, the identity of the pharmacist reviewing the final drug product, the quantity of each component, the equipment used in compounding the drug product as well as a pharmacy assigned reference number. In an acute care setting, the regulation proposal allows for one-time preparations to be documented in the pharmacy’s copy of the patient’s chart order. The patient’s chart order can serve as the master formula.

Following the three comment periods, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code. The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Comments from Michael Thompson, Ph.D., Director, Healthcare Operations and Technology Services, University of California, Office of the President, Oakland, California

Comment #128

Mr. Thompson comments on two components of the §1716 Revised Notice document, in that the UC Medical Centers' Department of Pharmacies does not agree with the "business impact" statement in the notice which states "no significant, statewide adverse economic impact." Likewise, the UC Medical Centers' Department of Pharmacies disagrees with the statement in the "Impact n Jobs" sub-section of the notice that states "this regulatory proposal will not have a significant impact on the creation of jobs."

Board Response

The text of the "§1716 Revised Notice" is not within the scope of the modified text provided for comment during the 15-day comment period.

Comment #129

Mr. Thompson comments on the revision document of §1716 which describes the "Specific Purpose of the Proposed Changes." He states the UC Medical Centers' Department of Pharmacies respectfully disagrees with text stating the purpose of the changes is to 'address, among other items, the strength, efficacy, and quality in compounding' and further 'there are no provisions that ... define these items for general compounding' in current laws. He states all licensed acute care hospitals in California are required by the FDA to comply with current USP 797 regulations, which mandate appropriate compounding of sterile products. He adds that [USP 797] regulations are widely accepted as the most comprehensive and evidence-based guidance to ensure safe preparation of aseptic products, do not require the documentation elements included in 1753.3(a)(6) and (8). He makes further comments regarding statements found in the notice documents related to "factual basis" to which UC Medical Centers' Department of Pharmacies disagrees. He summated that the proposed regulations could incur a large increase in costs for acute care hospitals and increased labor demands.

Board Response

The comments by Mr. Thompson did not expressly address the proposed language of §1735.3(a)(6) and are not within the scope of the modified text provided for comment during the 15-day comment period. However, the board recognizes that U.S. Pharmacopoeia (USP) General Chapter 797 (effective January 1, 2004) provides good *practices* for compounding sterile products, but USP 797 is not incorporated by reference into the board's statutes or regulations. As such, USP 797 does not control the board's enforcement of its own regulations regarding pharmacy compounding.

Comments from Gerald R. Trindade, PharmD, Director of Pharmacy, Mendocino Coast Hospital

Comment #130

Dr. Trindade expressed concern that the proposed requirements do not differentiate between preparation of sterile intravenous admixtures for hospital inpatients having short expiration dates and those products compounded for extended use in physician's offices or a patient's home. He asked that the board adopt the standards developed by USP 797 to prevent inconsistencies between USP and additional regulations created in Section 1735.3.

Board Response

The comments by Dr. Trindade do not expressly address the proposed language of §1735.3(a)(6) and do not appear to be within the scope of the modified text provided for comment during the 15-day comment period. Additionally, the board recognizes that U.S. Pharmacopoeia (USP) General Chapter 797 (effective January 1, 2004) provides *best practices* for compounding sterile products, but USP 797 is not incorporated by reference into the board's statutes or regulations. As such, USP 797 does not control the board's enforcement of its own regulations regarding pharmacy compounding.

Comment #131

Dr. Trindade stated that the proposed additional record keeping requirements will not prevent adverse events or improve patient safety. He acknowledged, however, that the additional record keeping requirements may help determine the cause of an adverse reaction. Dr. Trindade expressed concern that additional record keeping will increase the cost of IV Admixture Service to hospitals that are already struggling to keep their doors open.

Board Response

The comments by Dr. Trindade do not expressly address the proposed language of §1735.3(a)(6) and do not appear to be within the scope of the modified text provided for comment during the 15-day comment period. The board agrees with Dr. Trindade's statement regarding the value of the record keeping requirements.

Comments from Geralyn Trujillo, MPP, American Society of Health-System Pharmacists, Bethesda, Maryland

Comment #132

Ms. Trujillo states that the American Society of Health-System Pharmacists (ASHP) seeks to preserve patient safety and ensure that pharmacy practice continues to evolve and develop. She states that "the proposed exemption is in the best interest of all parties and support the adoption of such language." However, she stated ASHP is concerned that there is an overall focus on documentation that is impractical for inpatient situations, which may lead to a reduction in patient care and the effective and timely delivery of medication.

Board Response

The board appreciates ASHP's comments and support of the proposed modified text to 16 CCR §1753.3(a)(6). Several of the record keeping requirements for sterile products are already required in current regulation. This proposal does expand on the requirements and now includes the identity of the person who compounded the drug, the identity of the pharmacist reviewing the final drug product, the quantity of each component, the equipment used in compounding the drug product as well as a pharmacy assigned reference number.

Following the three comment periods, the board modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code.

The board believes the resulting language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Comment #133

ASHP asks the board to be mindful of the potential implications of other proposed modifications to the regulations. She states that "we need to balance the value of documentation with a recognition that onerous requirements may lead to delay in care and have a negligible impact on patient safety.

Board Response

The board appreciates ASHP's comments. The board believes the adopted text strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Comment #134

Ms. Trujillo states that documentation is clearly an important step in the delivery of any medication. "Lot numbers are recorded for large batches, a practice that is reasonable. However, recording lot numbers for small or individual compounds that are administered immediately or within 24-hours is a requirement that removes the focus of the pharmacy from patient care and effective delivery to documentation." She states that ASHP would question the value of such language, from both a workforce perspective as well as that of patient safety and delivery of care.

Board Response

This comment does not expressly address the proposed language of §1735.3(a)(6) and does not appear to be within the scope of the modified text provided for comment during the 15-day comment period. Also, this particular comment by Ms. Trujillo appears to be in contrast with ASHP's earlier comment (Comment #127) that ASHP

believes “the proposed exemption is in the best interest of all parties and support the adoption of such language. “ The board agrees that documentation is an important step in the delivery of any medication. The board thoroughly considered what documentation requirements provide for patient safety and has determined that the exemption to these requirements would be those sterile products compounded on a one-time basis for administration within two hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code. The board believes the adopted text strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Comment #135

Ms. Trujillo states that ASHP applauds the board’s intent to modernize the regulations and its recognition to exempt the sterile compounds for immediate use. She adds that ASHP recommends that the board continue to assess how documentation is being currently achieved and to seriously consider the consequences of requiring hospitals to rapidly divert scarce resources into documentation, rather than critical patient care services. She asks that the board, as the process moves forward, consider a phased-in approach, with defined milestones and deadlines, should the board continue to proceed with the current proposed language.

Board Response

The board appreciates ASHP’s comments. Following the adoption of the specific text at its July 15, 2009, Board Meeting, the board indicated that the effective date of the regulations, if approved by the Office of Administrative Law, will be six months following OAL approval. The board further indicated that it would exercise its enforcement discretion for an additional six months beyond the effective date.

Comments from Carl Washburn, PharmD, Pharmacy Director, Dominican Santa Cruz Hospital

Comment #136

Dr. Washburn asked the board to recognize the differences between safe medication practices in hospitals versus retail-focused pharmacies. He stated that the proposed additional record keeping constitutes ‘busy work’ and does not enhance patient safety.

Board Response

The comments by Dr. Washburn did not expressly address the proposed language of §1735.3(a)(6) and are not within the scope of the modified text provided for comment during the 15-day comment period.

Comment #137

Dr. Washburn asked the board to utilize USP 797, stating that additional mandates would add unnecessary cost to an already difficult healthcare environment.

Board Response

The comments by Dr. Washburn did not expressly address the proposed language of §1735.3(a)(6) and are not within the scope of the modified text provided for comment during the 15-day comment period.

The board recognizes that U.S. Pharmacopoeia (USP) General Chapter 797 (effective January 1, 2004) provides *best practices* for compounding sterile products, but USP 797 is not incorporated by reference into the board's statutes or regulations. As such, USP 797 does not control the board's enforcement of its own regulations regarding pharmacy compounding.

Comments from Don Willis, CPhT., Pharmacy Manager, California Pacific Medical Center

Comment #138

Mr. Willis expressed concern about proposed regulations affecting sterile injectable products. He acknowledged that traditional non-sterile compounding practice lacked specific regulations to adequately protect patients, but that the proposed regulations affecting sterile injectable products would not impact patient care. Mr. Willis asked the board to address patient safety by recognizing the distinctions between USP 797 (Sterile Preparations) and USP 795 (Nonsterile Preparations).

Board Response

The comments by Mr. Willis did not expressly address the proposed language of §1735.3(a)(6) and are not within the scope of the modified text provided for comment during the 15-day comment period.

U.S. Pharmacopoeia (USP) General Chapters 795 and 797 are not incorporated by reference into the board's statutes or regulations. As such, these do not control the board's enforcement of its own regulations regarding pharmacy compounding.

Comments from Bill Yee, PharmD, Clinical Information Coordinator, St. Joseph's Medical Center

Comment #139

Dr. Yee supports proposed changes to Section 1735.3(a)(6) exempting the manufacturer and lot number of each component if the sterile product is compounded on a one-time basis for administration within two hours to an inpatient in a health care facility.

Board Response

The board appreciates Dr. Yee's comments. Following the 15-day comment period, the board again modified the recordkeeping requirements of §1735.3—Records of Compounded Drug Products, to exempt from the recordkeeping requirements specified in §1753.3(a)(6) the manufacturer and lot number of

each component, for those sterile products compounded on a one-time basis for administration within twenty-four hours to an inpatient in a health care facility licensed under section 1250 of the Health and Safety Code. The board believes this language strikes a balance between the needs of pharmacy operations in an acute care setting and that of patient safety.

Comment #140

Dr. Yee provided comments to sections 1735.3(d), 1735.3(a)(7), 1735(a)(2), 1735(b), as well as the “Community Pharmacy & Hospital Outpatient Pharmacy Compounding Self-Assessment” form. Mr. Yee requested various exemptions within each section referenced and asked that the board consider these exemptions.

Board Response

The comments offered to the self-assessment form and to sections §1735(b)(1), §1735(a)(2) and §1735(b), §1735.3(a)(7), and §1735.3(d) are not within the scope of the proposed text provided during the 15-day comment period.

(Continued on next page.)

COMMENTS RECEIVED DURING THE SECOND 15-DAY COMMENT PERIOD

From	Comment Number(s)
Sillman, Michael, Marin General Hospital	141-143
Kaplan, D. and O'Brien, Doug. Pharmacy Strategy and Operations, Kaiser	144-149

Comment from Michael Sillman, Marin General Hospital, Greenbrae, CA

Comment #141

Mr. Sillman states that applying the recordkeeping exemption for 1735.3 to just the manufacturer and lot number still leaves an enormous new burden on hospital pharmacies. Mr. Sillman states that a typical hospital pharmacy's policy requires the preparing pharmacy technician and the checking pharmacist to initial the label of the compounded sterile product. He states the purpose of the initials is to assure that all products have been inspected and cleared by a pharmacist for distribution to the nursing units to be immediately given to patients.

Mr. Sillman states that once a product is administered to a patient, the container with the label and initials is discarded and that no on-going record history of the preparing pharmacy technician or the checking pharmacist is kept that can be tracked to a particular dose on a particular day.

Board Response

Mr. Sillman's comment is not entirely within the scope of the modified text proposed in the 2nd 15-day comment period. In meeting its patient protection mandate, the board has determined that the record keeping requirements of compounded drug products as specified in proposed 1735.3 are necessary. This proposal does not dictate how the records are to be made and stored, rather just what information must be retained. Hospitals can implement a business solution that is least "burdensome" to their operations. Record of a product delivered and administered to a patient would be reflected in the patients chart order. In the event of a recall, one would need to be able to identify which compounded drug products were administered, and to whom, as well as who compounded the product. The records required in section 1753.3 do not need to be completed in advance of the administration of the compounded drug. Under the record keeping requirements proposed in 1735.3, compounded drug products administered on a particular day *would* be able to be tracked back to the applicable pharmacy record for a patient.

Comment #142

Mr. Sillman states that he fails to see how such long-term recordkeeping requirements in 1735.3(a) such as the identity of involved pharmacy personnel and expiration date of the product contribute to the public welfare or safety, considering that the product has already been consumed.

Board Response

The general comments offered to proposed sections 1735.3(a) are not specific to the scope of the proposed text provided during the 2nd 15-day comment period.

Comment #143

Mr. Sillman states that maintaining such information on compounded batches in outpatient pharmacies makes sense due to the fact that part of the batch is still left that can be tested for accuracy of preparation. He said this is not the case in hospital practice.

Board Response

The general comments offered to proposed sections 1735.3(a) are not specific to the scope of the proposed text provided during the 2nd 15-day comment period.

Comments dated May 12, 2009, from D. Kaplan and Doug O'Brien, Pharmacy Strategy and Operations**Comment #144**

Messrs. Kaplan and O'Brien comment on compounded sterile preparations (CSPs) in inpatient pharmacies. They state that inpatient pharmacies typically prepare CSPs to meet acute needs of patients. They state that requiring a master formula for small quantities of patient specific CSPs would cause significant delays in therapy. In addition, they state outpatient pharmacies already have policies and procedures which require the amounts of additives to be calculated and displayed for a pharmacist check. They add "This proposed language would be appropriate only when batches of compounded products are prepared which are intended for use in multiple patients."

Board Response

The general comments by Messrs. Kaplan and O'Brien are not specific to the scope of the proposed text provided during the 2nd 15-day comment period.

Comment #145

Messrs. Kaplan and O'Brien state the proposed language change in 1735.3(a)(6) from two hours to 24 hours provides only a minimal relief from the otherwise onerous requirements of 'this paragraph.' They state their concern is that "1735.3 is just not appropriate for compounding in acute care settings."

In the area of their response to §1735.3, they provide recommended new language for subsection (d) as follows:

“(d) For compounded drug products that are being prepared for use in multiple patients, these products shall not be compounded until the pharmacy has first prepared a written master formula record that includes at least the following elements:”

Board Response

The board disagrees with the comment that 1735.3 is “not appropriate for compounding in acute care settings.” Several of the record keeping requirements for sterile products are already required in current regulation. This proposal does expand on the requirements, and now also includes the identity of the person who compounded the drug, the identity of the pharmacist reviewing the final drug product, the quantity of each component, the equipment used in compounding the drug product as well as a pharmacy assigned reference number. The board included the requirements for the identity of the person who compounded the drug as well as the pharmacist who reviewed the final drug product. The regulations were updated to allow a nonpharmacist to compound the medication as allowed in other areas of pharmacy law, and to require that a pharmacist complete a review. This check is an essential consumer protection component. Also, the equipment used is necessary to allow for a quality assurance review to be complete should a problem occur with such compounded medications. The intent of the regulation proposal is to improve patient safety.

The recommended language change provided by Messrs. Kaplan and O’Brien is labeled subdivision (d) and does not appear to be related to the subject matter found in §1735.3(a)(6), but rather related to §1735.2(d). Assuming this is correct, the proposed language is not within the scope of the modified text provided for comment during the 2nd 15-day comment period.

Comment #146

Messrs. Kaplan and O’Brien cite proposed “1735.8(a)(b)(c).” They state the language appears to be directed towards bulk compounding of non-sterile products or batch compounding of sterile products from non-sterile ingredients. They state it is inappropriate for compounding sterile products from sterile ingredients. They further state that when preparing sterile products from sterile ingredients, a quality assurance plan should include written standards for visual checks of the final products. Finally, they make a recommendation that there should be a statement that exempts the preparation of sterile products from sterile ingredients from subsections (a)(b)(c).

Board Response

The comments offered to proposed sections 1735.8(a)(b)(c) are not within the scope of the proposed text provided during the 2nd 15-day comment period.

Comment #147

Messrs. Kaplan and O'Brien cite proposed 1751.3(a)(2) and their concern that the language requires that labels of sterile injectable products display the recommended rate of administration. They state the recommended rate of administration on a products label can be unhelpful and incorrect, and provide several scenarios to support their point. Recommended language is proposed to replace the text of 1751.3(a)(2).

Board Response

The comments offered to proposed section 1751.3(a)(2) are not within the scope of the proposed text provided during the 2nd 15-day comment period. Proposed 1751.3(a)(2) is a current requirement in regulation (currently found in §1751.02(a)(2)).

Comment #148

Messrs. Kaplan and O'Brien state that in the Initial Statement of Reasons section 1751.4(d) was renumbered from CCR 1751.01 and was consolidated with CCR 1751.1, and that consolidating the language was incorrect. The address CCR 1751.01 as it applied to Sterile Injectable Compounding from Non-Sterile Ingredients. They propose that the frequency of surface cleaning correspond to the risk level of sterile compounding being performed. They propose recommended language, which they state they have adapted from USP <797>.

Board Response

The comments offered to proposed 1751.4(d) and to the Initial Statement of Reasons are not within the scope of the proposed text provided during the 2nd 15-day comment period.

Comment #149

Messrs. Kaplan and O'Brien comment on 1751.7(d) with regard to sterility testing. They state this is of no value and must be deleted. They further state that if the Board of Pharmacy intended for subdivision (d) to apply to non-sterile to sterile compounding it should be stated explicitly. They recommend deleting specified proposed language and inserting an excerpt from the current 1751.7(b).

Messrs. Kaplan and O'Brien state that if the Board of Pharmacy intended for subdivision (d) to apply to sterile to sterile compounding, that the existing 1751.7(b) describes the appropriate process very well and should be retained.

Board Response

The comments offered to proposed sections 1751.7(b) and 1751.7(d) are not within the scope of the proposed text provided during the 2nd 15-day comment period.