Board of Pharmacy

Amended Initial Statement of Reasons

To allow interested parties to identify changes to the original Initial Statement of Reasons, deleted language is shown by ~~double strikethrough~~ and added language is shown by double underline.

Subject Matter of Proposed Regulation: Compounded Drug Products

Sections Affected:

- **Repeal** sections 1708.3, 1708.4, 1708.5 of Article 2 of Division 17 of Title 16 of the California Code of Regulations (CCR)[1].
- **Amend** title of Article 4.5 of Division 17 of Title 16 of the CCR, Nonsterile Compounding.
- **Repeal and Replace** sections 1735, 1735.2, 1735.1, 1735.3, 1735.4, 1735.5, 1735.6, 1735.7, and 1735.8 of Article 4.5 of Division 17 of Title 16 of the CCR, regarding Nonsterile Compounding.
- **Add** Sections 1735.9, 1735.10, 1735.11, 1735.12, 1735.13, and 1735.14 of Division 17 of Title 16 of the CCR, regarding Nonsterile Compounding.
- **Add** Article 4.6 to Division 17 of Title 16 of the CCR, Sterile Compounding
- **Add** Sections 1736 through 1736.21 and new titles to Article 4.6 of Division 17 of Title 16 of the CCR, regarding Sterile Compounding.
- **Add** Article 4.7 to Division 17 of Title 16 of the CCR, Hazardous Drugs.
- **Add** sections 1737 through 1737.18 and new titles to Division 17 of Title 16 of the CCR, regarding Hazardous Drugs.
- **Add** Article 4.8 to Division 17 of Title 16 of the CCR, Radiopharmaceutical Preparation, Compounding, Dispensing, and Repackaging.
- **Add** sections 1738 through 1738.14 and new titles to Division 17 of Title 16 of the CCR, regarding Radiopharmaceutical Preparation, Compounding, Dispensing, and Repackaging.
- **Repeal** Article 7 and sections 1751-1751.10 of Article 7 of Division 17 of Title 16 of the CCR.

Public Hearing

The California State Board of Pharmacy (board) will hold a public hearing on June 18, 2024, beginning at 9:00 a.m. in the First Floor Hearing Room of the California Board of Pharmacy, 2720 Gateway Oaks Drive, Sacramento, CA 95833. Additionally, attendees may participate via the WebEx meeting platform.

[1] All regulatory references are to Division 17 of Title 16 of the California Code of Regulations, unless otherwise noted.

To participate via WebEx meeting platform please contact Lori Martinez at PharmacyRulemaking@dca.ca.gov by 4:30 p.m. on June 17, 2024, to request a link to the meeting. The link to the meeting will also be posted on the board's Laws and Regulations webpage no later than 8:00 a.m. the day of the hearing. The hearing will proceed on the date noted above until all testimony is submitted. At the hearing, any person may present oral or written statements or arguments relevant to the proposed action described in the Informative Digest. The board requests, but does not require, that persons who make oral comments at the hearing also submit a written copy of their testimony via email.

Background

The California State Board of Pharmacy (board) is a state agency vested with the authority to regulate the pharmacy industry, including pharmacies and pharmacists. The board's statutory priority is to protect the public (Business and Professions Code (BPC) section 4001.1). Its stated mission is to protect and promote the health and safety of Californians. Pharmacy Law provides for the licensure and regulation of pharmacists and pharmacies in this state by the board. Existing law requires that compounding of drug preparations by a pharmacy be consistent with standards in the current version of the United States Pharmacopeia-National Formulary. (BPC § 4126.8.) This section further authorizes the board to adopt regulations imposing additional standards for compounding drug preparations. Existing law requires the board to adopt regulations establishing standards for compounding sterile drug products in a pharmacy. (BPC § 4127.) (As discussed below, sterile drug products are primarily those that are injectable.) Existing law requires pharmacies to obtain a license from the board, subject to annual renewal, in order to compound sterile drug products. (BPC § 4127.1.) A similar licensing requirement applies to nonresident pharmacies compounding sterile drug products for shipment into California. (BPC § 4127.2.)

As with other areas of pharmacy law, there is a federal overlay for compounding by licensed pharmacists and pharmacies. Violation of federal law could subject licensees to potential enforcement by United States Food and Drug Administration (FDA) or federal Department of Justice, and discipline of their state-issued licenses or permits. Under federal laws, the FDA has the sole authority to approve drugs for use in the United States. It is a violation of federal law for anyone to introduce or deliver for introduction into interstate commerce any new drug unless the FDA has approved an application filed.

Compounding is the long-standing pharmacy practice of mixing, combining, or altering ingredients. Compounding may involve merely altering an existing drug product or creating an entirely new drug product. Compounded human drugs can serve an important role for patients whose clinical needs cannot be met by an FDA-approved drug. For example, compounding is used when a patient is allergic to an ingredient in an FDA-approved drug, or for when children need a lower strength drug than what is

commercially available. Compounded drugs can be preparations such as topical creams, eye drops, capsules or tablets intended for oral ingestion, or injectable solutions. Generally, each time a drug is compounded, it would be a new drug requiring compliance with all United States Food, Drug, and Cosmetic Act (FDCA) requirements, including required approval of an application by the FDA. Compounded drugs, however, may not be FDA approved. While the FDA has a role in approving the ingredients that may be used in compounding human drugs, it is not practical and would effectively prohibit all compounding of human drugs by pharmacists and pharmacies without an exemption under section 503A of the FDCA (21 U.S.C. 353a) from new drug approval and other FDCA requirements (503A exemption).

A 503A exemption provides a state-licensed pharmacist or pharmacy (or state-licensed physician) with an exemption from certain provisions of the FDCA, including section 501(a)(2)(B) (concerning requirements to comply with current good manufacturing practices), section 502(f) (concerning the labeling of drugs with adequate directions for use), and section 505 (concerning the approval of drugs under new drug applications (NDAs) or abbreviated new drug applications (ANDAs))and. Section 503A(b)(1) contains the specific substantive requirements for a state-licensed pharmacist and pharmacy to qualify for the exemption. A Section 503A exemption does not provide relief from any other provision of the FDCA. Non-compliance with all of the requirements of the 503A exemption could result in violations of one or all of these three statutory provisions, or other provisions of the FDCA.

The FDA has put out written guidance discussing the specific requirements (Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act Guidance (fda.gov) (Pharmacy Compounding Guidance)). The FDA also provides other guidance documents applicable to compounding.

Additionally, there are compounding professional standards that are used across the nation known as the United States Pharmacopeia and The National Formulary (USP–NF). USP-NF is a book of public pharmacopeial standards. It contains standards for compounding, including nonsterile, sterile, hazardous, and radiopharmaceutical drug preparations. USP–NF is a combination of two compendia, the United States Pharmacopeia (USP) and the National Formulary (NF). The FDCA designates the USP–NF as the official compendia for drugs marketed in the United States. A drug product in the U.S. market must conform to the standards in USP–NF to avoid possible charges of adulteration and misbranding.

Because the FDA does not review compounded drugs to evaluate their safety, effectiveness, and quality before they are administered to patients, states are the primary regulators of pharmacists and pharmacies engaged in compounding human drugs. Thus, pharmacists and pharmacies engaged in compounding are subject to both federal and state law. Because compounded drugs can pose a higher risk to patients if they are not FDA approved and because compounding pharmacies, unlike manufacturers and outsourcing facilities, are exempt from the requirements of current

good manufacturing practices if they qualify for the Section 503A exemption, California's law is more restrictive than the federal law in several areas.

Drugs administered orally present less dangers to patients from residual contaminants than drugs injected into the human body. Drugs that are ingested orally go through the body's digestive tract and the human body has the ability to filter out and excrete residual impurities. In contrast, drugs injected into a patient's body bypasses the human body's main defense mechanisms to filter out residual impurities. For example, most vitamins and supplements are intended for oral use and are regulated as a food, and not a drug, for this reason. The acceptable levels of contaminants in injectable drug preparations are lower than for topical or oral drugs. An injectable drug preparation compounded from non-sterile ingredients is considered a high-risk preparation due to its route of administration. All injectable preparations must be sterile for this reason.

California has an extensive statutory and regulatory scheme governing compounding by pharmacies. Similar to federal law, section 111550(a) of the California Health and Safety Code prohibits the sale, delivery, or giving away of a new drug that has not has a new drug application approved under Section 505 of the FDCA. Additionally, Business and Professions Code (BPC) section 4126.8 expressly provides that the compounding of drug preparations by a pharmacy for furnishing in this state shall be consistent with "standards established in the pharmacy compounding chapters of the current version of the United States Pharmacopeia-National Formulary...." This section also expressly authorizes the Board to adopt "regulations to impose additional standards for compounding drug preparations." Additionally, BPC Section 4342 provides authority for the board to institute any action provided by law, that in its discretion, is necessary to prevent the sale of pharmaceutical preparations and drugs that do not conform to the standard and tests as to quality and strength provided in the latest addition of USP or that violate any provisions of the Sherman Food, Drug, and Cosmetic Law. Thus, both state and federal law require compounding pharmacies to comply with the USP chapters on compounding in lieu of compliance with current good manufacturing practices that manufacturers and outsourcing facilities must comply with.

On June 1, 2019, USP published revisions to General Chapter <795> for nonsterile compounding and General Chapter <797> for sterile compounding, as well as a new General Chapter <825> for radiopharmaceutical compounding. After publication of the revised and new compounding standards, USP received appeals on certain provisions in <795>, <797>, and <825>. Therefore, USP postponed the official date of the revised <795> and <797>, and the new general chapter <825> until further notice**.** General Chapter <800> for hazardous compounding was not subject to any pending appeals and became official on December 1, 2019; however, during the postponement and pending resolution of the appeals of <795> and <797>, USP indicated that <800> was informational and not compendially applicable. USP encouraged utilization of <800> in the interest of advancing public health. On November 1, 2022, USP published the final revised General Chapters of <795> and <797> and new Chapter <825> with an official effective date of November 1, 2023.

Existing CA Pharmacy Law at BPC Section 4127(c) requires the board to review any formal revision to General Chapter 797 of the USP-NF relating to the compounding of sterile preparations, no later than 90 days after the revisions become official to determine whether amendments are necessary for the regulations adopted by the board. Upon publication, the board began its review of the revised standards and have worked to update its regulations.

This proposal will implement, clarify, or make more specific requirements related to the respective chapters. For ease of reference to the USP chapters, the board's proposed regulations mirror the structure of the respective chapters. This means the numbering format and section titles of the proposed regulations tend to follow the relative USP chapter. The goal of the board's regulations is not to duplicate provisions of federal law or USP language, but to clarify or make more specific the requirements. If no clarification is needed or no additional requirements are necessary for public safety, additional requirements are not being added to the board's proposed text. Requirements that are already laid out in the USP chapters or federal law that are not just suggestions or discretionary recommendations, but must be followed, were not duplicated. In addition, USP requirements identified in existing regulations have been repealed to eliminate the duplication with federal law.

The board proposed additional requirements that strengthen the USP requirements. While the board can strengthen federal requirements, it cannot promulgate a lesser standard in its regulations. Section 503A is quite extensive but one of the specific conditions a licensee must meet to be eligible for the exemptions provided under 503A is that the drug product is compounded in compliance with USP chapters on pharmacy compounding. Further, as a consumer protection agency, the board must promulgate regulations through the lens of its consumer protection priority as the law makes clear whenever the protection of the public is inconsistent with other interests sought to be promoted, the protection of the public shall be paramount (BPC 4001.1).

Problems Addressed

BPC 4127(c) requires the board to review any formal revision to General Chapter 797 of the USP-NF relating to the compounding of sterile preparations, no later than 90 days after the revisions become official. On November 1, 2022, USP published the final revised General Chapters of <795> and <797> and new Chapter <825> with an official effective date of November 1, 2023. As a result of revision of the USP, the board must update its regulations to ensure consistency between the board's regulations and the USP Chapters.

Anticipated Benefits of the Proposed Regulations

USP General Chapters <795> for nonsterile compounding, <797> for sterile compounding, <800> for hazardous drug handling in healthcare settings, and <825> for

radiopharmaceutical preparation, compounding, dispensing, and repackaging establish the minimum national standards for compounding in the United States. This proposal aligns the board's regulations with the revised USP standards and, in some instances where there are patient safety concerns, the proposed regulations build upon the minimum USP standards to ensure protection of all Californians who require the services of a pharmacist or pharmacy to dispense or furnish to them the compounded drug products that meet their needs. Ensuring compliance with national standards is a benefit to public health and safety, worker safety, and the environment.

Due to the extensive proposed regulatory changes that occurred, the board's proposal repeals the existing articles related to compounding. It adds new articles that follow each other for ease of locating and reviewing compounding regulations. It adds section numbers and titles that tend to follow the revised USP chapters for ease of cross-reference. The repeal and replace is being proposed for clarity as the proposed revisions are extensive and the changes are difficult to read and follow when proposed in a strikeout and underline format.

Specific Purpose of Proposed Changes and Rationale

The board's proposal makes the following changes:

Repeal sections 1708.3, 1708.4, 1708.5 of Article 2 of Division 17 of Title 16 of the California Code of Regulations (CCR).

These sections are specific to radioactive drugs, pharmacist handling radioactive drugs, and pharmacy furnishing radioactive drugs, respectively. These sections are being repealed as the board is reorganizing its regulations, so that all compounding regulations are in numerical order within the CCR. Article 2 contains more general sections related to the business of a pharmacy, and other sections related to radioactive drugs were repealed from Article 2 some years ago. The subject matter will be contained in a proposed new Article 4.8, called Radiopharmaceutical- Preparation, Compounding, Dispensing, and Repackaging and sections 1738, et seq. and will be discussed further down in this document. Having all compounding sections in numerical order will increase clarity to the regulated public.

Article 4.5 Nonsterile Compounding

Amend title of Article 4.5

This proposal amends the title of Article 4.5 from "Compounding in Pharmacies" to "Nonsterile Compounding" for clarity so that the public will understand that the article is now specific to compounding of nonsterile drug preparations (CNSPs).

For clarity and ease of cross reference, because the regulations are being amended to comply with the mandate for standards to be consistent with the current version of the USP-NF, the board determined that the sections of the board's regulations should track

the sections of the revised USP Chapters. Such tracking will also assist in the relevant requirements being read together for greater compliance with both. Accordingly, the title of the Article and the section titles correspond to the section titles within the corresponding USP Chapters. As part of this tracking, some subdivisions may not have additional requirements; however, the subdivision is maintained.

Repeal and Replace Section 1735

Current section 1735 is repealed. Current sections 1735(a) and (b) define what is and is not compounding, respectively. Compounding is defined in USP <795>, and the board determined the definition was complete. Licensees must comply with the compounding standards specified in the current version of the USP (BPC 4126.8). Accordingly, including the definitions in board regulations is not necessary.

Section 1735(c) provides that the parameters and requirements in Article 4.5 apply to all compounding practices, and that additional parameters and requirements applicable solely to sterile compounding are stated in the related article. Because introductory paragraphs in all sections of Article 4.5 related to nonsterile compounding and all sections of Article 4.6 related to sterile compounding provide that all definitions and standards apply throughout each respective article, this section is also repealed.

New section 1735 is added and titled "Compounding Definitions." An opening paragraph is added, providing that the definitions within the section and article are in addition to and supplement the definitions provided in USP <795>. This addition reminds licensees that they must also refer to the corresponding USP Chapter.

New subdivision (a) adds a definition for "Approved labeling" to mean the Food and Drug Administration's (FDA) approved labeling in accordance with sections 201.56 and 201.57 of Title 21, Code of Federal Regulations that includes FDA approved information for the diluent, the resultant strength, the container closure system, and storage time. The board determined that this definition is necessary as it is not included in USP <795> and it ensures clarity to the regulated public with respect to the FDA's labeling requirements for nonsterile compounded drug products.

New subdivision (b) adds the definition of "Designated person(s)". USP <795> states that the designated person(s) is (are) responsible and accountable for the performance and operation of the facility and personnel for the preparation of CNSPs, including overseeing a training program to ensure competency of personnel involved in compounding, selecting components, monitoring and observing compounding activities and taking immediate corrective action if deficient practices are observed, ensuring that standard operating procedures (SOPs) are fully implemented, and establishing, monitoring, and documenting procedures for the handling and storage of CNSPs and/or components of CNSPs. The designated person(s) must ensure that follow-up is carried out if problems, deviations, or errors are identified. The Chapter, however, does not identify who this designated person is. As the pharmacist-in-charge (PIC) is statutorily responsible for ensuring the pharmacy's compliance with all state and federal laws and

regulations pertaining to the practice of pharmacy (BPC § 4036.5), which includes compounding, the board determined that it is the PIC who must identify and assign who the designated person (or persons) is (are) to be responsible and accountable for the performance and operation of the facility and personnel as related to the preparation of CNSPs. The designated person is not permitted to exceed the scope of their issued license. Accordingly, when the designated person is not a pharmacist, the PIC must review all practices related to the operations of the facility that require the professional judgment of a pharmacist. As it is the PIC who is held ultimately responsible for the pharmacy's compliance with statutes and regulations, the board determined that it must be the PIC as a licensed professional to use their judgment to assign the designated person(s) responsible and accountable with respect to the CNSP operations.

New subdivision (c) adds the definition of "Diluent" to mean "a liquid with no pharmacological activity used in reconstitution, such as purified water or sterile water." The board determined that this definition is necessary for clarity as it is used in the definition of reconstitution in USP <795> but is not defined there. This definition is one generally accepted in the practice of pharmacy.

New subdivision (d) adds the definition of "Essentially a copy." A definition is in current section 1735.1(k) of the board's regulations. It is retained and moved into this definitions section of the new language as it is not included within USP <795> and is used elsewhere in the proposed regulations. The board, however, amended the existing language slightly to provide additional clarity and consistency by amending "comparable" to the "same" active pharmaceutical ingredients (APIs). This change is necessary to align the definition with the FDA guidance document, which says "the compounded drug product has the same active pharmaceutical ingredient(s) (API) as the commercially available drug product." (This FDA guidance document is available as underlying data of this rulemaking; see item number 9 in the Underlying Data section of this document.) Further, this definition ensures that the pharmacist can use their professional judgment when determining if a compound is essentially a copy. Pharmacists must remain knowledgeable of current practice standards and legal requirements for the profession when exercising their professional judgment.

New subdivision (e) adds the definition of "Integrity" to mean "retention of strength until the beyond use date provided on the label when the preparation is stored and handled according to the label directions." This definition is in current section 1735.1(s) of the board's regulations. It is retained and moved into this definitions section of new language as it is not included in USP <795> and is used elsewhere in the proposed regulations. The board, however, amended the existing language slightly to provide additional clarity by amending "potency" to "strength" as the term "strength" is defined in this section and strength is used throughout the proposed language. "Integrity" and "strength" have particular meanings within the practice of pharmacy and it is therefore important to have definitions for those terms. Additionally, "potency" was amended to "strength" as the term is utilized in USP and the USP compounding committee indicated that the terms "strength" and "potency" are often used interchangeably, with "potency"

being used more by the general public and “strength” being used more by practitioners and within the official compendia.

New subdivision (f) adds the definition of “Quality” to mean “the absence of harmful levels of contaminants, including filth, putrid, or decomposed substances, or the absence of active ingredients other than those listed on the label, or the absence of inactive ingredients other than those listed on the master formulation record as specified in USP Chapter 795.” This definition is in current section 1735.1(ae) of the Board’s regulations. It is retained in the new language and moved into this definitions section of the new language as it is not included in USP <795> and is used elsewhere in the proposed regulations. It ensures clarity for the public with respect to the meaning within this article because the term “quality” has a particular meaning within the practice of pharmacy. Further, the regulations help ensure the quality of the product to the established beyond use date.

New subdivision (g) adds the definition of “Repackaging” to mean “the act of removing a product or preparation from its original primary container and placing it into another primary container, usually of smaller size without further manipulation, when the act is not done pursuant to a prescription.” The board determined that a definition of the term is necessary to ensure clarity as it is not defined in USP <795>, and the term is used within that Chapter and this article, and it has a particular meaning within the practice of pharmacy. This definition is what is generally understood within the practice.

New subdivision (h~~i~~) adds the definition of “Strength” to mean the amount of active ingredient per unit of a compounded drug preparation. This definition is in current section 1735.1(ag) of the board’s regulations. It is retained in the new language and moved into this definitions section of the new language as it is not defined in USP <795>. The board determined that keeping this definition is necessary as it is not defined in USP <795> and it ensures clarity to the public to define a term that has a particular meaning within the practice of pharmacy and is used within this article.

A Note is added for the new definitions section with Authorities cited as Sections 4005, and 4126.8 of Business and Professions Code. Additionally, references are cited as Sections 4005, 4036, 4037, 4051, 4052, 4076, 4081, 4126.8, 4169, 4301 and 4332 of the Business and Profession Code.

Repeal and Replace Section 1735.1

Current section 1735.1 is repealed. The current language at section is 1735.1 specifies the definitions for compounding. Any definitions retained from this current section are now proposed to be in section 1735, and are identified and discussed above. Licensees must comply with the compounding standards specified in the current version of the USP (BPC 4126.8). Accordingly, any definition within the existing regulation text that is not retained within the new proposed text is clearly specified and defined in USP and duplication is not necessary.

New section 1735.1 is added and titled “Introduction and Scope.” An opening paragraph is added to remind the public that CNSPs must comply with USP <795>, in addition to the requirements of this article. As compliance with USP is statutorily required (BPC § 4126.8), the reminder will help ensure all provisions are read together for optimum compliance.

New subdivision (a) adds “Nonsterile compounding is performed by or under the supervision of a licensed pharmacist pursuant to a patient specific prescription, unless otherwise specified in this article.” This addition clarifies that non-patient specific compounding is not generally permitted under this article. This is an existing prohibition in current section 1735.2(a); it has been reworded, however, for ease of reading, and added to this general section on scope due to the reorganization of the nonsterile compounding regulations.

New subdivision (b) adds “Repackaging of a conventionally manufactured drug product is not considered compounding if compliant with USP Chapter 1178, *Good Repackaging Practices*.” This addition provides clarity that compliance with USP Chapter 1178 is required when repackaging for it not to be considered compounding. Complying with Good Repackaging Practices helps to reduce medication errors and maintain the quality of drug products, increasing patient safety. Providing additional context for what is or is not compounding leads to greater overall understanding of and compliance with compounding standards.

New subdivision (c) is added and reads “Reconstitution of a conventionally manufactured drug product that is not done in accordance with the FDA approved directions is considered compounding.” This addition provides clarity that reconstitution is restricted to FDA approved products with approved labeling, as is required under the USP. Any other reconstitution, for example, reconstitution from a compounding kit, is not FDA approved and as such compounding rules and regulations must be followed.

New subdivision (d) is added and reads “Notwithstanding subdivision (a), a limited quantity of CNSP may be prepared and stored in advance of receipt of a patient specific prescription document where, and solely in such quantity, as is necessary to ensure continuity of care of individual patients based on a documented history of prescriptions for those patient populations.” This is existing language at current section 1735.2(b) and has been relocated to this subdivision due to the reorganization of the nonsterile compounding article. The section has also been reworded for grammatical clarity. This existing requirement is being retained with the proposed regulation to ensure continuity of care for individual patients. Without the ability to prepare and store a limited quantity of an CNSP for individual patients based on the documented history, a patient may not have immediate access to their CNSP, which could pose a risk to patient health and welfare.

New subdivision (e) adds “A reasonable quantity of a compounded drug preparation may be furnished to a veterinary office for use by the veterinarian that is sufficient:”

This is existing language at current section 1735.2(c) and has been relocated to this subdivision due to the reorganization of the nonsterile compounding article; however, the proposed language is specific to veterinarians, as compounded preparations for office use by human patients must be obtained from outsourcing facilities registered under section 503B. This addition allows for the compounding of a reasonable quantity of drug preparations for use by veterinarians for animal patients under circumstances outlined in the following subsections.

New subdivision (e)(1) adds "for administration or application to veterinary patients solely in the veterinarian's office." This language reflects existing subsection (c)(3), restricting compounding for use in veterinary offices. Compounding for veterinary offices is allowable under Animal Medicinal Drug Use Clarification Action of 1994 (AMDUCA) and maintaining the language ensures that compounders are aware of the authorization to compound for veterinary office use.

New subdivision (e)(2) adds "for furnishing of not more than 7-day supply, as fairly estimated by the prescriber, and documented on the purchase order or other documentation submitted to the pharmacy prior to furnishing." This is existing language at section 1735.2(c)(3) and has been relocated to this subdivision due to the reorganization of the nonsterile compounding regulations. The board amended existing language to increase the allowable quantity to be compounded from 120-hour supply (5 days) to a 7-day supply of CNSPs to ensure continuity of care over a full 7-day week if the prescriber estimates the treatment is warranted.

New subdivision (f) outlines the conditions under which compounding must not be performed. The opening sentence specifies that "In addition to prohibitions and requirements for compounding established in federal law, no CNSP shall be prepared that: …" This addition is necessary to indicate that federal prohibitions also apply and must be adhered to. The Board notes that BPC section 4301, subdivision (j) establishes that unprofessional conduct includes "[t]he violation of any of the statutes of this state, of any other state, or of the United States regulating controlled substances and dangerous drugs." Further, BPC section 4301, subdivision (o) provides that unprofessional conduct includes violating any provision of applicable federal laws and regulations governing pharmacy. Accordingly, California law requires that licensees comply with federal laws related to compounding and the language reminds licensees of that.

Subdivision (f)(1) provides that one of the prohibitions is that no CNSP shall be prepared that:

(1) Is essentially a copy of one or more commercially available drug products, unless:
    (A) the drug product appears in an American Society of Health-System Pharmacists (ASHP) or FDA Drug Shortages Database that are in short supply at the time of compounding and at the time of dispense, or

(B) the compounding produces a clinically significant difference of the medical need of an identified individual patient, as determined:
(i) by the prescribing practitioner,
(ii) the compounding pharmacist, and
(iii) the dispensing pharmacist(s).
(C) Documentation describing the conditions in (1)(A) & (1)(B) is maintained in a readily retrievable format"

This is primarily the existing language at section 1735.2(d)(3) and has been relocated to this subdivision due to the reorganization of the nonsterile compounding regulations. The language was amended to indicate that the compounding must produce a clinically significant difference for the patient as determined by the prescriber, compounding pharmacist, and dispensing pharmacist. In order to maintain the highest standards for patient safety, the board determined that the compounding must produce a clinically significant difference over a commercially available drug product to be produced. If the preparation is not clinically different, the commercially available drug product must be utilized. Additionally, the prescriber, compounding pharmacist, and dispensing pharmacist must all determine that the product has a clinically significant difference as all are responsible for using their professional judgment with respect to patient safety. The Board notes that all pharmacists have a professional obligation to patient care, which includes the selection of the drug therapy being provided to their patient. The documentation requirements have been amended slightly to be maintained in a readily retrievable format. The three-year record maintenance has been removed as the record maintenance standard is specified in BPC 4081. The FDA Drug Shortage database is maintained on the FDA's website. The website address is: https://www.fda.gov/drugs/drug-safety-and-availability/drug-shortages. The ASHP Drug Shortage list is also maintained on the ASHP website. The website address is: https://www.ashp.org/drug-shortages/current-shortages?loginreturnUrl=SSOCheckOnly. Finally, subdivisions (d)(1) and (d)(2) of the existing text prohibiting the compounding of a drug preparation that is classified by the FDA as demonstrably difficult to compound or is on the FDA list of drugs withdrawn or removed from the market are being repealed as unnecessary, because those prohibitions are contained within Section 503A of the Federal Food, Drug, and Cosmetic Act [503(b)(1)(C) and (b)(3)].

New subdivision (f)(2) adds the prohibition that no CNSP be "made with any component not suitable for use in a CNSP for the intended patient population, unless allowable under Animal Medicinal Drug Use Clarification Action of 1994 (AMDUCA)." The Food, Drug, and Cosmetic Act specifies the bulk drug substances and components that may be utilized for compounding human drug products. In addition, AMDUCA allows for extralabel drug use in animals, which is the use of components not suitable for CNSPs for human patients to be utilized in compounding for animal patients. This language allows for the compounding of certain drug preparations for use by veterinarians for their animal patients and clarifies for compounding pharmacists that the components allowable under AMDUCA can be used to compound drug preparations for animal patients.

New subdivision (g) provides: “Prior to allowing any CNSP to be compounded within a pharmacy, the pharmacist-in-charge shall complete a self-assessment consistent with the requirements established in section 1715.” The requirement to complete the self-assessment is existing language within section 1735.2(k). The proposed language is simplified, however; the specific form has not been identified in this section as the form is referenced in 1715.

New subdivision (h) adds: “In addition to the provisions provided in Section 1707.2, consultation shall be provided to the patient and/or patient’s agent concerning proper use, storage, handling and disposal of the CNSP and related supplies furnished.” The addition of this language ensures that appropriate consultation is being provided as the use, handling, storage, and disposal of compounded drug preparations is different than that of standard tablet or capsule medication. The Board notes that appropriate consultation with a patient includes patient-centered language and that information on proper disposal could, for example, include, "Our pharmacy offers drug take back services. It is recommended that you place unused medications in our drug take back bin."

New subdivision (i) adds to the nonsterile compounding regulations the requirement for CNSPs with human whole blood or human whole blood derivatives to be prepared in compliance with Health and Safety Code (HSC) section 1602.5. As CNSPs can include the use of blood components, adding this language ensures awareness of the relevant requirements in HSC section 1602.5 and provides reference to the section. The Board notes that federal law does not allow for pharmacy compounding of biological products and that the FDA has released guidance in this area. (See item 18 in the Underlying Data section of this document.) It is incumbent on licensed professionals to remain current on guidance documents issued to ensure compliance with provisions established.

Note is added with authority cited as Sections 4005 and 4126.8 of Business and Professions Code. Additionally, references are cited as Sections 4005, 4051, 4052, 4076, 4081, 4105, 4126.8, 4169, 4301, 4306.5 and 4332 of the Business and Profession Code; and; 21 United States Code Sections 355 and Part 530.

Repeal and Replace Section 1735.2

Current section 1735.2 is repealed. Any regulation text retained from that current section is now in section 1735.1 and identified and discussed above. The proposed language in this new section 1735.2 specifies Personnel Training and Evaluation to track section 2 in USP <795>. An opening paragraph is added to remind the public that the processing of nonsterile compound preparations must meet the requirements of the article in addition to and supplement the standards provided in USP <795>. Licensees must comply with the compounding standards specified in the current version of the USP (BPC 4126.8). Accordingly, any subdivision within the existing regulation text that is not retained within the new proposed text is clearly specified in USP and duplication is not necessary.

Subdivision (a) is added and provides: “Training and competency procedures for all personnel who compound or have direct oversight of personnel performing compounding, verifying, and/or handling a CNSP shall address the following topics:

(1) Quality assurance and quality control procedures,
(2) Container closure and equipment selection, and
(3) Component selection and handling.”

The additional training components are necessary to ensure that the personnel performing or overseeing compounding are appropriately trained in all aspects of compounding, including quality assurance, quality control procedures, container closure and component selection and handling. The Chapter is silent on these training topics; the board, however, believes these topics are important for training purposes to ensure appropriate compounding throughout the entire process. The Board notes that while the PIC may determine the appropriate container closure for use, compounding staff must have foundational knowledge to safely use the container closure system selected. Current compounding staff training requirements are specified in section 1735.7 within existing law and are repealed and replaced with these training and competency topics as the requirements, as identified above, are more specific.

New subdivision (b) provides: “A pharmacist responsible for, or directly supervising, the compounding of CNSPs, shall demonstrate proficiency in skills necessary to ensure the integrity, strength, quality, and labeled strength of a CNSP as described in the facility’s SOPs as referenced in section 1735.11.” As the pharmacist is responsible for the oversight of staff performing the processing, to ensure patient safety they must be able to actually demonstrate that they themselves are proficient in the skills needed to monitor the work product of the compounding personnel. Section 1735.11 requires the SOPs to set forth the methods for complying with any requirements in this article; each pharmacy must determine the best way for the pharmacist to demonstrate proficiency.

Subdivision (c) is added and provides: “Compounding personnel or persons with direct oversight over personnel performing compounding, who fail any aspect of ongoing training and evaluation shall not be involved in compounding or oversight of the preparation of a CNSP until after successfully passing training and competency in the deficient area(s) as detailed in the facility’s SOPs.” As the pharmacist is responsible for the oversight of staff performing the processing, they must be able to demonstrate that they are proficient in the skills needed to monitor the work product of the personnel. Accordingly, if they fail any part of the training, or cannot demonstrate proficiency, it follows that they must be prevented from continuing any involvement until they are capable of demonstrating competency. Similarly for compounding personnel, if they fail ongoing training and evaluation, patient safety must take priority to prevent those individuals from any involvement in compounding or the oversight of the preparations until their training and competency can be tested. Again, section 1735.11 requires the SOPs to set forth the methods for complying with any requirements in this article; each pharmacy must determine the best way for training and competency evaluation .

Subdivision (d) is added and provides: “Any person assigned to provide the training specified in this section shall have demonstrated competency in the skills in which the person will provide training or observe and measure competency described in the facility’s SOPs as referenced in section 1735.11. Documentation must be maintained demonstrating compliance.” The requirement is necessary to ensure that the individual assigned to provide the training to personnel has sufficient knowledge and expertise to provide the training. Additionally, documentation must be maintained for review during inspections to ensure appropriate training has been provided in the interest of patient safety. Again, section 1735.11 requires the SOPs to set forth the methods for complying with any requirements in this article; each pharmacy must determine the best way for it to determine who should provide training .

Note is added with authority cited as sections 4005 and 4126.8 of Business and Professions Code. Additionally, references are cited as Sections 4005, 4051, 4052, 4076, 4081, 4126.8, 4301, 4306.5 and 4332 of the Business and Profession Code.

Repeal and Replace Section 1735.3

Current section 1735.3 is repealed. Any requirements retained from the existing regulation on Record Keeping have been relocated to sections 1735.7, Master Formulation and Compounding Records and 1735.14, Documentation, and will be identified in those sections, respectively. Any content not retained in those two sections is specified in the USP and is not necessary. Newly proposed section 1735.3 is added and titled “Personnel Hygiene and Garbing.” An opening paragraph is added to remind the public that the processing of nonsterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <795>.

New subdivision (a) adds the following: “Prior to admitting any personnel into a compounding area, the supervising pharmacist shall evaluate whether compounding personnel is experiencing any of the following: rashes, recent tattoos or oozing sores, conjunctivitis, active respiratory infection or and other medical condition, to determine if such condition could contaminate a CNSP or the environment (“contaminating condition”). After such evaluation and determination, the supervising pharmacist shall not allow personnel with potentially contaminating conditions to enter the compounding area.” This addition is needed for patient safety to prevent contamination of the CNSP. Contamination of a CNSP could occur from these situations from a cough, sneeze, skin flake, or other activity into the CNSP, which would pose a threat to patient safety. Good policy dictates that determining if a contaminating condition exists requires professional judgment and must be done by a pharmacist. The board notes, for example, that an individual with an active respiratory illness can release airborne pathogens into the compounding environment, thus compromising the environment.

New subdivision (b) adds the requirement for a gown and face mask to be used whenever a closed system processing device is required. A closed system processing

device is a device designed to reduce the potential exposure to personnel, or contamination of the facility or CNSPs, and is a term of art related to compounding. Examples include containment ventilated enclosures (CVEs), biological safety cabinets (BSCs), or single-use containment glove bags. As a closed system processing device is used to reduce potential exposure to personnel or contamination of the facility or CNSPs, a gown and face mask must be utilized for added protection of the compounding personnel from exposure and contamination. Further, the use of a gown and face mask reduce the higher risk of exposure to staff and higher risk of contamination to the compounding environment and CNSP.

New subdivision (c) adds "Disposable garb shall not be shared by staff and shall be discarded if soiled and after each shift. All garb removed during a shift must remain in the compounding area." Garb is an established term within the industry and refers to gloves, shoe covers, head or hair covers, facial hair covers, face masks, and gowns. Restricting the sharing of garb and requiring it to remain in the compounding area after it is discarded is necessary to prevent contamination of the areas outside of the compounding area with any materials or components that may have been used during the shift. The USP details the discarding and laundering of garb.

New subdivision (d) requires that gloves be wiped or replaced before beginning a CNSP that contains different components. While this recommendation is included in the Chapter as discretionary, the board determined that wiping or replacing gloves before beginning a CNSP that contains different components be mandatory. Cleaning or replacing gloves before compounding with different components prevents cross contamination between preparations and is a necessary requirement for patient safety.

New subdivision (e) adds the requirement for non-disposable garb to be cleaned with a germicidal cleaning agent and sanitized with 70% isopropyl alcohol before re-use. The board identified 70% isopropyl alcohol as the sanitizing agent as Chapter <795> defines sanitizing agent as 70% isopropyl alcohol. This language is necessary to require the appropriate cleaning of non-disposable garb with both a germicide and sanitizing agent consistent with the Chapter to prevent cross contamination.

New subdivision (f) requires that any garbing accommodations provided by the designated person be documented; the record must include the name of the individual granted the accommodation, date granted and description of the reasons for granting the accommodation. The record must be retained in accordance with Business and Professions Code section 4081. Appropriate garbing is a very important part of safe and clean compounding. The type, use and reuse, and cleaning of both disposable and non-disposable garb is determined in order to protect both personnel and patients. Where a deviation from the required garbing is necessary for an accommodation, complete documentation of that deviation is necessary for tracking both by the pharmacy and by the board. Documentation of this information provides an additional level of consideration for the designated person in explaining the rationale.

Note is added with authority cited as sections 4005 and 4126.8 of Business and Professions Code. Additionally, reference is cited as sections 4005, 4081, 4126.8, 4301, 4306.5, and 4332 of the Business and Profession Code.

Repeal and Replace Section 1735.4

Current section 1735.4 on Labeling of Compounded Drug Preparations is repealed. Newly proposed section 1735.4 is added and titled "Building and Facilities." Any requirements retained from the existing regulation have been relocated to section 1735.9, Labeling, and will be identified there. An opening paragraph is added to remind the public that the processing of nonsterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <795>.

New subdivision (a) adds: "A sink used for compounding or hand hygiene shall not be part of a restroom or water closet." While USP <795> provides a standard for sinks used during compounding, it does not address a sink being located as part of restroom facilities. Due to the possible contamination and sanitation issues, the board determined that it was necessary to provide additional clarity that the sink used for compounding or hand hygiene cannot be in the restroom or water closet. As an example, compounding personnel leaving the restroom might be touching a door knob to exit the restroom, creating the potential to contaminate their hands.

New subdivision (b) adds the requirement for purified water, distilled water, or reverse osmosis water to be used for rinsing equipment and utensils. While Chapter <795> recommends the use of purified water, distilled water, or reverse osmosis water, the board is requiring the use of purified water, distilled water, or reverse osmosis water to ensure cross contamination does not occur from chemical elements within tap water. Further, the quality of water is of significance for patient safety. As an example, tap water may be contaminated with fungus, bacteria, and other elements that could contaminate the equipment used in the preparation of CNSPs.

New subdivision (c) adds the requirement that "No CNSP shall be compounded if it is known, or reasonably should be known, that the compounding environment fails to meet criteria specified in the law or the facility's SOPs." This subdivision is added to clarify that following all the laws and SOPs are required to prevent contamination of preparations; accordingly, compounding cannot occur if the compounding environment does not meet the required parameters. This language is currently in section 1751.4(a) and is being moved here as part of the reorganization of the text.

Note is added with authority cited as sections 4005 and 4126.8 of Business and Professions Code. Additionally, references are cited as Sections 4005, 4126.8, 4169, and 4306.5 of the Business and Profession Code.

Repeal and Replace Section 1735.5

Current section 1735.5 on Compounding Policies and Procedures is repealed. Newly proposed section 1735.5 is added and titled “Cleaning and Sanitizing.” Any requirements retained from the existing regulation have been relocated to section 1735.11, Standard Operating Procedures, and will be identified there. The remaining language is repealed as the requirements are specified within USP and duplication is not necessary. An opening paragraph is added to remind the public that the processing of nonsterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <795>.

New subdivision (a) adds the requirement for the facility to document each occurrence of the cleaning and sanitizing of the compounding area, with the record to include the individual who completed the cleaning and sanitizing, as well as the product name(s) of the cleaning and sanitizing agent(s) used. The cleanliness and sanitation of the compounding area is paramount to maintain safety and quality for personnel and patients. The addition ensures a complete record of the cleaning of the compounding area so follow-up can be done with both personnel and patients should contamination be identified. The board notes that the documentation of the cleaning process as described in the proposed language is consistent with actions necessary to maintain a clean compounding environment. Further, operationalizing the requirements could be quite simple, including a prepared log that already has the items listed. Individuals performing the cleaning could document the date and time, and place a check mark or other indication next to the products used.

New subdivision (b) adds the requirement that any cleaning or sanitizing agents used by the facility to meet the requirements must be used in accordance with manufacturers’ specifications. This provides clarity to the public that it is not just the product selection that is important, but also the proper use of the products according to the specifications set by the manufacturer. This ensures that the products are handled and used appropriately, which will ensure proper cleaning and sanitizing and prevent cross contamination.

Note is added with authority cited as sections 4005 and 4126.8 of Business and Professions Code. Additionally, references are cited as Sections 4005, 4126.8, 4301 and 4332 of the Business and Profession Code.

Repeal and Replace Section 1735.6

Current section 1735.6 on Compounding Facilities and Equipment is repealed. Newly proposed section 1735.6 is added and titled “Equipment and Components.” Any requirements from the existing regulation not retained in this section have been relocated to Article 4.7, Hazardous Compounding and will be identified there. An opening paragraph is added to remind the public that the processing of nonsterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <795>.

New subdivision (a) adds the requirement that any equipment used to compound a CNSP shall be used in accordance with the manufacturer's specifications. This section is retained from existing regulation text in section 1735.6(b); however, the language was amended to remove "stored, maintained, and cleaned" as these would be included within the manufacturer's specifications. This requirement is to ensure that equipment is being utilized properly and for its intended purpose and not for untested or other purposes that could be ineffective, contaminate the compounded preparation, or pose a risk to patient safety.

New subdivision (b) adds the requirement that any component used to compound a CNSP shall be used and stored in accordance with all federal laws and regulations and industry standards including the manufacturers' specifications and requirements. This subdivision serves to remind the public that the use and storage of compounding components must adhere to a host of standards to ensure the integrity of the components and patient safety. Further, storing components inappropriately can compromise the component and thereby create a risk to the safety and efficacy of the CNSP.

Note is added with authority cited as sections 4005 and 4126.8 of Business and Professions Code. Additionally, references are cited as Sections 4005, 4126.8, and 4301 of the Business and Profession Code.

Repeal and Replace Section 1735.7

Current section 1735.7 on Training of Compounding Staff is repealed. Newly proposed section 1735.7 is added and titled "Master Formulation and Compounding Records." Any requirements retained from the existing regulation on Training of Compounding Staff have been relocated to section 1735.2, Personnel Training and Evaluation, and are identified there. An opening paragraph is added to remind the public that the processing of nonsterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <795>.

New subdivision (a) adds the requirement that the "CNSP shall not be compounded until the facility has first prepared a written master formulation record (MFR) in compliance with USP Chapter 795 and identified in that document the following additional elements:" New subdivision (a)(1) adds the requirement for referenced sources to be readily available at the time of compounding and maintained for three years when they are utilized as reference to support the assigned beyond-use date (BUD). New subdivision (a)(2) adds the requirement for the instructions for the storage and handling of the CNSP to be included in the MFR.

The MFR details how each CNSP must be compounded and therefore the record must be created before compounding is done. This subdivision provides clarity to the regulated public that compounding is not permitted until the MFR has been created for each unique formulation. Language providing for a master formula document in existing

section 1735.2(e), now being repealed, is moved with some amendments into this subdivision and the following to track the changes identified within the USP.

Subdivision (a)(1) is added to the Chapter requirements, providing that the source, if any, supporting the assigned beyond-use-date (BUD) be retrievable and maintained for three years from the date the CNSP is dispensed. This requirement is in current section 1735.2(e)(3) (being repealed) and is necessary to ensure that sources can be reviewed for currency prior to compounding, as well as available for board inspector review during inspections. The language has been amended for ease of reading and to specify the length of time the source is to be maintained. The board determined a three-year period after the CNSP is last dispensed is an appropriate minimum time for maintaining any source for consistency, as BPC 4105 requires the retention of records and documentation for three years. Further, while the information may be stored in different locations, when requested by the board, the compounding record must be produced and include all of the required information in a single document. The board must be able to review all the required information together for individual compounded preparations and not be required to sort through unrelated documents that may not have been relied upon.

Subdivision (a)(2) is also added to the Chapter requirements, providing that storage and handling instructions be included in the MFR. This requirement is in current section 1735.2(e)(8) and is retained as following storage and handling instructions is critical for patient safety and to prevent cross contamination.

New subdivision (b) adds the following exception “Where a facility does not routinely compound a particular drug preparation, the master formulation record for that preparation may be recorded on the prescription document itself.” This exception to the requirement in subdivision (a) is in current section 1735.2(f) and is not being amended; the board has determined that an exception for CNSPs that are not routinely compounded by the facility is permissible as a detailed MFR is not necessary when the preparation is not routine to the facility.

New subdivision (c) adds the following “A compounding record (CR) shall be a single document developed in compliance with USP Chapter 795, and include the following additional elements:

(1) The date and time of compounding, which is the time when compounding the CNSP started, and also determines when the assigned BUD starts.
(2) The manufacturer, lot number, and expiration date for each component.
(3) The assigned internal identification number, which shall be unique for each CR.
(4) The total quantity compounded, which shall include the number of units made and the volume or weight of each unit.
(5) The identity of each person performing the compounding, the person who has direct oversight of compounding, and the pharmacist verifying the final drug preparation.”

For completeness, the board specified the five requirements above to ensure that they are included in the compounding record, although the first four items are included within USP Chapter <795> and are existing regulation in section 1735.3(a) being repealed and added here. The board added the fifth requirement, which is the identity of each person performing the compounding, having oversight over the compounding, and the pharmacist who verified the final preparation. The fifth requirement of the identity of each person performing the compounding and the verifying pharmacist are contained in current sections 1735.3(a)(2)(C) and 1735.3(a)(2)(D) (being repealed) and are being added here for the purpose of identifying those involved and responsible in the event a contamination issue is identified, to help ~~research and locate~~ ensure a possible cause of contamination can be researched with the staff involved. The board determined that ~~it~~ the identity of each person having oversight should be included as well, for the same reason. The board notes that while existing law provides flexibility to record the manufacturer under limited circumstances, continuation of the current provision is not appropriate as it hampers the ability of a facility to respond appropriately in the event of a product recall. Further, the board's proposed regulation text is more explicit than the Chapter as the Chapter requires either the recording of the manufacturers or vendor; however, in separate guidance issued by the FDA, the facility needs to have transparency into the supply chain and awareness of the manufacturer (where the manufacturer and vendor are different.) (See Underlying Data item number 19.)

Note is added with authority cited as sections 4005 and 4126.8 of Business and Professions Code. Additionally, references are cited as Sections 4005, 4081, 4105, 4126.8, 4301, and 4332 of the Business and Profession Code.

Repeal and Replace Section 1735.8

Current section 1735.8 on Compounding Quality Assurance is repealed. Newly proposed section 1735.8 is added and titled “Release Inspections and Testing.” Any requirements retained from the existing regulation have been relocated to section 1735.12, Quality Assurance and Quality Control, and will be identified there. An opening paragraph is added to remind the public that the processing of nonsterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <795>.

The new section provides that a pharmacist performing or supervising the nonsterile compounding is responsible for the integrity, strength, quality, and labeled strength of a CNSP until the beyond-use date indicated on the label provided the patient or the patient’s agent follows the label instructions provided on the CNSP for storage and handling after receiving the CNSP. This requirement is in current section 1735.2(g) and is retained to ensure that there is at least one pharmacist who is always responsible for the overall integrity of the product. The language has been amended to be specific to this article on nonsterile compounding and to be consistent with the other amendment of changing the term “potency” to strength” in prior sections.

Note is added with authority cited as sections 4005 and 4126.8 of Business and Professions Code. Additionally, references are cited as Sections 4005, 4076, 4126.8, 4169, 4301 and 4306.5 of the Business and Profession Code.

Add Section 1735.9

Newly proposed section 1735.9 is added and titled "Labeling." An opening paragraph is added to remind the public that the processing of nonsterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <795>.

New subdivisions (a) and (b) adds mandatory labeling requirements for CNSPs as the labeling elements within the Chapter are discretionary and not mandatory.

New subdivisions (a)(1) and (a)(2) are added and read:

(1) Route of intended administration, and
(2) Name of compounding facility and dispensing facility (if different).

New subdivision (b) adds additional labeling requirements for CNSPs that must be included should they apply to the CNSP being compounded, including:

(1) Any special handling instructions,
(2) Any applicable warning statements, and
(3) Name, address, and phone number of the compounding facility if the CNSP is to be sent outside of the facility or healthcare system in which it was compounded.

The board determined that the labeling requirements must be mandatory; adequate labeling is essential for dispensed medication to ensure patient safety. Informing the patient how to use the medication, where it came from, how to handle it, warnings as to it, and contact information provides the patient with basic safety instructions and what facility to contact if questions arise. The board notes that the route of administration is not always understood. As an example, a capsule could be taken orally or vaginally. Absent inclusion of the route of administration, in such an instance, the patient may self-administer the medication incorrectly. Specifying that this information must be included ensures clarity that the labeling requirements are mandated by the board. The requirements in subdivision (a)(1) and (a)(2) are required for all CNSPs, while the requirements in subdivision (b) would only apply as needed, based on the specific CNSP. The labeling requirements are currently in existing section 1735.4 (being repealed); however, current requirements for admixed IV solutions and unit-dose container dispensing have been removed from the labeling requirements within the new section. Admix IV solutions should be compounded in a sterile environment and would not apply to non-sterile labeling. Additionally, labeling for unit-dose containers is defined within USP <797> for sterile compounding. Finally, the current requirements for hazardous labeling have been removed as hazardous compounding is now specified in USP <800> and are not appropriate within this subdivision.

New subdivision (c) adds the requirement for any CNSP dispensed to a patient or readied for dispensing to a patient shall also include on the label the information required by Business and Professions Code section 4076 and section 1707.5. This language is contained in current section 1735.4(b) and is being relocated here without amendment. The board determined that referring to other applicable labeling requirements is important for a complete understanding of the requirements and ensures patient safety.

Note is added with authority cited as sections 4005 and 4126.8 of Business and Professions Code. Additionally, references are cited as Sections 4005, 4076, 4126.8, and 4301 of the Business and Profession Code.

Add Section 1735.10

New section 1735.10 is added and titled "Establishing Beyond-Use Dates." An opening paragraph is added to remind the public that the processing of nonsterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <795>.

New subdivision (a) is added to establish the beyond-use date's (BUDs) expiration as 11:59 p.m. on the assigned date, if no specific time is otherwise established. This time is added to provide clarity on the time of day that the product can no longer be utilized on its expiration date. The board selected 11:59 p.m. because using "midnight" is confusing, as it is unclear whether that refers to the end of one day or the beginning of the next day.

New subdivision (b) adds the following: A CNSP's BUD shall not exceed any of the following:

(1) The chemical and physical stability data of the active pharmaceutical ingredient (API) and any added component in the preparation,
(2) The compatibility and degradation of the container–closure system with the finished preparation (e.g., possible leaching, interactions, and storage conditions),
(3) The shortest remaining expiration date or BUD of any of the starting components.

The board added the requirement for setting the BUD that shall not exceed three possible limitations. While the Chapter provides these same limitations, the Chapter is discretionary and indicates that the items must only be considered in assigning the BUD. For clear implementation of the Chapter and to ensure patient safety, the board has established the limitations as set criteria that the BUD must not exceed. USP Chapter 795, Section 10.2 specifies that when establishing a BUD for a CNSP compounders MUST consider parameters that may affect quality, including compatibility of the container closure system with the finished preparation (e.g. leachables). The Chapter requires this be done. The board's proposed regulation text goes beyond just considering the information, and ensures that the BUD does not go beyond what the

parameters reveal to support the BUD. Any cost incurred for this determination (e.g. leachables) are a function of compliance with the Chapter, not the Board's regulations. The Board's regulations merely ensure that a pharmacist uses the information they obtain through the USP requirements in establishing a BUD that does not exceed the parameters.

New subdivision (c) adds the requirement that if antimicrobial effectiveness testing results provided by a current FDA-registered drug establishment or outsourcing facility or published in current peer-reviewed literature sources are used to assign the BUD, the reference in its entirety (including raw data and testing method suitability) shall be readily retrievable in accordance with BPC 4081 for three years from the last date the CNSP was dispensed. The use of antimicrobial effectiveness testing results from an FDA-registered facility or published in peer-reviewed literature is allowed by Chapter <795>; the record requirements, however, were specified by the board, as patient safety necessitates that the records be readily available for board inspection to confirm that the testing results were appropriately utilized in assigning the BUD.

Note is added with authority cited as sections 4005 and 4126.8 of Business and Professions Code. Additionally, references are cited as Sections 4005, 4081, 4105, 4126.8, 4169, 4301 and 4332 of the Business and Profession Code.

Add Section 1735.11

New section 1735.11 is added and titled "Standard Operating Procedures (SOPs)." An opening paragraph is added to remind the public that the processing of nonsterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <795>.

New subdivision (a) provides that the facility's standard operating procedures (SOPs) for nonsterile compounding must be followed and adds elements that must be included in the SOPs related to nonsterile compounding. Subdivisions (a)(1) and (a)(2) add the following requirements for what must be addressed in the SOPs:

(1) Comply with USP Chapter 1163, Quality Assurance in Pharmaceutical Compounding.
(2) Also describe the following:
    (A) Methods by which the supervising pharmacist will ensure the quality of compounded drug preparations.
    (B) Procedures for handling, compounding, and disposal of infectious materials. The SOPs shall also describe the facility's protocols for cleanups and spills in conformity with local health jurisdictional standards, if applicable.
    (C) The methods a pharmacist will use to determine and approve the ingredients and the compounding process for each preparation before compounding begins.
    (D) The method for complying with any other requirements specifically required to be addressed in the facility's SOPS as described in this article.

(E) The validated processes for storage, shipping containers and transportation of temperature sensitive CNSPs to preserve quality standards for integrity, quality and labeled strength.

The facility's SOPs inform the personnel as to their basic responsibilities in nonsterile compounding. Patient safety demands that minimum uniform processes and procedures be laid out and followed to ensure quality and consistency. First, in (a)(1) the language requires that the SOPs comply with USP Chapter 1163 as a reminder that in addition to board regulations on quality assurance programs, they must also comply with the USP Chapter requirements, per BPC 4126.8. Second, in (a)(2), the language ensures patient safety by requiring that the quality of the preparation, proper disposal of infectious materials and spills, ingredient approval, and the method for complying with any other requirements of the facility's SOPs be addressed. This information is required in the SOPs to ensure procedures are in place prior to the compounding so that all staff are following the same procedures and the SOPs will be readily available if any possible problem arises and will ensure appropriate action can be taken timely should it be needed to ensure patient safety. The SOPs do not establish requirements, but rather ensure that the facility has established procedures in the specified areas. Further, should a pharmacist using professional judgement determine that an additional SOP may be necessary, an SOP must be developed.

New subdivision (b) adds the requirement for the SOPs to be reviewed on an annual basis by the PIC and that the review must be documented by the PIC consistent with the SOPs. The SOPs shall be updated to reflect changes to compounding processes, facility changes or other changes that impact the CNSP. This annual review is necessary to ensure that any procedure changes are updated within the SOPs. Additionally, changes to the SOP must be disseminated to the affected staff prior to implementation to ensure that staff are operating in compliance with the SOPs of the facility and that all staff are following the same operating procedures. Further, should a pharmacist using professional judgement determine that an additional SOP may be necessary, an SOP must be developed.

New subdivision (c) adds notification to the regulated public that a failure to follow the facility's written SOPs constitutes a basis for enforcement action. While failure to follow many of the board's regulations can constitute a basis for an enforcement action, whether a citation or discipline, this language ensures that the facility and staff understand the importance of developing and following their SOPs and that there is a potential consequence for not doing so.

Note is added with authority cited as sections 4005 and 4126.8 of Business and Professions Code. Additionally, references are cited as Sections 4005, 4052, 4081, 4126.8, 4301 and 4332 of the Business and Profession Code.

Add Section 1735.12

New section 1735.12 is added and titled “Quality Assurance and Quality Control.” An opening paragraph is added to remind the public that the processing of nonsterile compound preparation must meet the requirements in the article and are in addition to and supplement the standards provided in USP <795>.

New subdivision (a) adds the requirement that quality assurance program must comply with section 1711, Quality Assurance Programs, and the standards contained in USP Chapter 1163, Quality Assurance in Pharmaceutical Compounding. This is being added as a reminder that quality assurance programs related to nonsterile compounding must comply with the general board regulations on quality assurance programs, as well as the USP Chapter requirements, per BPC 4126.8.

Further, subdivision (a)(1) adds a requirement that the program shall have a written procedure for scheduled action, such as a recall, in the event any compounded drug preparation is discovered to be outside the expected standards for integrity, quality, or labeled strength. The addition of this language ensures that the program has written procedures to follow should a problem with the preparation be identified. Having written procedures in place prior to the discovery of any possible problem with a patient will ensure appropriate action will be taken timely should it be needed to ensure patient safety.

Subdivision (a)(2) adds a requirement that the program shall have a written procedure for responding to out-of-range temperature variations within the medication storage areas where a furnished drug may be returned for furnishing to another patient. The addition of this language ensures that the program has written procedures to follow prior should a temperature issue be identified. Many compounded preparations require that they be stored at particular temperatures to maintain their integrity. Having procedures in place to identify those issues prior to the discovery of any possible problem with a patient will ensure appropriate action will be taken timely should it be needed to ensure patient safety.

New subdivision (b) adds the requirement that the board must be notified in writing within 72 hours of receipt of a complaint with respect to a potential quality problem or the occurrence of an adverse drug event involving a CNSP. Complaints made to a facility of a potential quality problem or of an adverse reaction may be indicative of a violation of laws or regulations. The board must be notified of any complaints made to the facility to determine if additional investigation is needed or if there are patterns with respect to the nature of the complaint. Requiring that the board be notified within 72 hours is a reasonable time to allow the facility to respond to the complaint and soon enough for the board to adequately assess if immediate action need be taken to protect the public.

In addition to notice to the board as required in subdivision (b), new subdivision (c) adds the requirement that complaints related to a potential quality problem with a CNSP and all adverse events to be reviewed by the pharmacist-in-charge within 72

hours of receipt of the complaint or occurrence. Such review shall be documented and dated as defined in the SOPs. As the PIC is ultimately responsible for the operation of the facility, they must be aware of all quality related reports and adverse events and review them to determine if corrective action is needed. Additionally, documenting the review within the SOPs ensures that the review is taking place, serves as a record for the PIC should the same or similar issues appear, and provides compliance information to board inspector during annual inspections.

Note is added with authority cited as sections 4005 and 4126.8 of Business and Professions Code. Additionally, references are cited as Sections 4005, 4081, 4126.8, 4169, 4301 and 4332 of the Business and Profession Code.

Add Section 1735.13

New section 1735.13 is added and titled "CNSP Packaging and Transporting." The language requires that in addition to the standards provided in USP <795>, the facility's SOPs must describe processes for storage and transportation in shipping containers for temperature sensitive CNSPs to preserve quality standards for integrity, quality and labeled strength. Pursuant to section 1735.11(a)(2)(E), the SOPs must include validated processes for storage of, shipping containers for and transportation of temperature sensitive CNSPs to preserve quality standards for integrity, quality and labeled strength. This language ensures that the facility's SOPs with respect to packaging and transporting temperature sensitive CNSPs meet the standards in the Chapter and adequately consider maintaining integrity, quality, and labeled strength during all aspects of storage and transportation that are appropriate for their business practices.

Note is added with authority cited as sections 4005 and 4126.8 of Business and Professions Code. Additionally, references are cited as Sections 4005, 4081, 4126.8, 4169, and 4332 of the Business and Profession Code.

Add Section 1735.14

New section 1735.14 is added and titled "Documentation." An opening paragraph is added to remind the public that the standards provided in USP <795> must be met in addition to those added by the regulations.

These subdivisions are from the content in current section 1735.3(d) (being repealed), and are being moved here (as well as new section 1735.7, as discussed above) for reorganization. New subdivision (a) requires that records maintained as required by USP Chapter 795 or this Article, must be maintained in a readily retrievable form, for at least three years from the date the record was created or relied upon. If only recorded and stored electronically, on magnetic media, or in any other computerized form, the records shall be maintained as specified by Business and Professions Code section 4070. The board determined that three year was the appropriate time frame as three years is the standard retention time for pharmacy related records per BPC 4081. Additionally, for consistency, the language adds the requirement for electronic records to be stored consistent with the existing electronic record requirements.

New subdivision (b) adds a requirement for records created to be created and maintained in a manner to provide an audit trail for revisions and updates of each record document. Prior versions of each record must be maintained in a readily retrievable format and include the changes to the document, identification of individual who made the change, and the date of each change. This requirement ensures a complete "paper" trail for inspection purposes so that board inspectors can identify when the records were edited and by whom. USP Chapter 795, Section 14 specifies that documentation must comply with all laws and regulations of the applicable regulatory jurisdiction. The Chapter continues that "Records must be legible and stored in a manner that prevents their deterioration and/or loss. All required CRs for a particular CNSP (e.g. MFR, CR, and release inspection and testing results) must be readily retrievable for at least two years after preparation or as required by the laws and regulations of the applicable regulatory jurisdiction, whichever is longer." The board already requires records to be maintained for three years (see, e.g., BPC section 4081, 16 CCR section 1735.3(d)). The USP requirements are clear that the records must be maintained to prevent deterioration and/or loss. The board's language allows for flexibility to maintain the records electronically and specifies that when maintained electronically an audit trail of changes must be maintained. The board's proposed regulation text establishing an audit trail meets the requirements of the USP Chapter provision to prevent "loss or deterioration of records." Absent an audit trail, prior versions of a record (e.g., a master formula, etc.) would be lost if maintained in an electronic format without an audit trail. A facility can elect to maintain the paper records consistent with the Chapter which would not require an electronic audit trail. The proposed language is establishing a means for electronic storage of records that meets the requirements of the USP Chapter to provide flexibility for the business operations of compounding pharmacies.

Note is added with authority cited as sections 4005 and 4126.8 of Business and Professions Code. Additionally, references are cited as Sections 4005, 4081, 4105, 4126.8, 4301 and 4332 of the Business and Profession Code.

Repeal Article 7 and sections 1751-1751.10 and Add Article 4.6, titled "Sterile Compounding"

This article and sections are being added to address sterile compounding. The title of the article was selected to track the title of USP Chapter <797>.

Add Section 1736

New section 1736 is added and titled "Sterile Compounding Definitions." An opening paragraph is added to remind the public that the definitions in the section apply throughout the article and are in addition to and supplement the definitions provided in USP Chapter <797>.

New subdivision (a) adds the definition of "Compounding personnel" to mean any person involved with any procedure, activity, or oversight of the compounding process. This definition provides clarity with respect to which personnel are considered

“compounding personnel” and that it extends beyond those performing the actual task of compounding. The board has determined that it is all those personnel who must be accountable to the process in order to ensure patient safety.

New subdivision (b) adds the definition of “Designated compounding area or compounding area” to mean a restricted location within a facility that limits access, where only activities and items related to compounding are present. As sterile compounding must be completed in an area that is maintained as sterilized, it is necessary to ensure that the access to the area is restricted and that only compounding activities are present in the area.

New subdivision (c) adds the definition of “Designated person(s)” to mean one or more individuals assigned by the pharmacist-in-charge to be responsible and accountable for the performance and operation of the facility and personnel as related to the preparation of the compounded sterile preparations (“CSPs” for the purposes of this article). Nothing in this definition allows for the designated person to exceed the scope of their issued license. When the designated person is not a pharmacist, the Pharmacist-in-Charge (PIC) must review all practices related to the operations of the facility that require professional judgement. USP <797> states that the designated person is responsible for implementing a training program and evaluating competency; however, the Chapter fails to clearly identify who this person is. As the pharmacist-in-charge (PIC) is responsible for the operation of the facility, the board determined that the designated person or persons must be assigned by the PIC to be responsible and accountable for the performance and operation of the facility and personnel as related to the preparation of the compounded sterile preparations (CSP). Nothing in this definition allows for the designated person to exceed the scope of their issued license. When the designated person is not a pharmacist, the PIC must review all practices related to the operations of the facility that require professional judgment. As the PIC is held responsible for the operation of the facility, as a licensed professional, they must be the person who can designate the personnel who can operate the facility and use their professional judgment with respect to the operations of the facility as performed by others.

New subdivision (d) adds the definition of “Diluent” to mean “a liquid with no pharmacological activity used in reconstitution, such as purified water or sterile water for injection.” The board determined that this definition is necessary for clarity as it is not included within USP <797> and the term is used to in the definition of “reconstitution” in the Chapter.

New subdivision (e) adds the definition of “Essentially a copy.” This definition is in current section 1735.1(k)) and is retained in the new language as it is not included within USP <797>. The board amended the existing language slightly to provide additional clarity by amending “comparable” to the “same” active pharmaceutical ingredients (APIs). This change is necessary to align the regulation text with the FDA guidance document, which says “the compounded drug product has the same active

pharmaceutical ingredient(s) (API) as the commercially available drug product...”; (See Underlying data item 9).

New subdivision (f) adds the definition of “Integrity” to mean “retention of strength until the beyond use date provided on the label when the preparation is stored and handled according to the label directions.” This definition is in current section 1735.1(s)) and is retained in the new language as it is not included within USP <797>. The board determined that this definition is necessary as it is not included within USP <797> and it ensures clarity with respect to the meaning of the term “integrity” within this article. Additionally, “potency” was amended to “strength” as the term is utilized in USP and the USP compounding committee (underlying data item 15) indicated that the terms “strength” and “potency” are often used interchangeably, with “potency” being used more by the public and “strength” being used more by practitioners and within the official compendia.

New subdivision (g) adds the definition of “Quality” to mean “the absence of harmful levels of contaminants, including filth, putrid, or decomposed substances, or the absence of active ingredients other than those listed on the label, or the absence of inactive ingredients other than those listed on the master formulation record as specified in USP Chapter 797.” This definition is in current section 1735.1(ae)) and is retained in the new language as it is not included within USP <797>. The board determined that this definition is necessary as it is not included within USP <797> and it ensures clarity with respect to the meaning of the term “quality” within this article.

New subdivision (h) adds the definition of “Strength” to mean the amount of active ingredient per unit of a compounded drug preparation. This definition is in current section 1735.1(ag)) and is retained in the new language as it is not included within USP <797>. The board determined that this definition is necessary is it is not included within USP <797> and it ensures clarity with respect to the meaning of the term “strength” within this article.

Note is added with authority cited as sections 4005, 4126.8, and 4127 of Business and Professions Code. Additionally, references are cited as Sections 4005, 4127.1, 4301 and 4332 of the Business and Profession Code.

Add Section 1736.1

New section 1736.1 is added and titled “Introduction and Scope.” An opening paragraph is added to remind the public that CSPs must comply with USP Chapter <797>, in addition to the requirements of this article. As compliance with USP is required by BPC section 4126.8, reminding the regulated public of requirement will help ensure compliance.

New subdivision (a) adds “For the purposes of this article, sterile compounding occurs, by or under the supervision of a licensed pharmacist, pursuant to a patient specific prescription, unless otherwise specified in this article.” This addition clarifies that non-

patient specific compounding is not permitted under this article. This is an existing requirement in the current section 1735.2(a) (being repealed); however, it has been amended and added here, due to the reorganization of all the compounding regulations. The amendment specified “a patient specific prescription, unless otherwise specified in this article” in lieu of “a valid prescription,” which is necessary as non-patient specific compounding is completed by licensed outsourcing facilities and not pharmacies.

New subdivision (b) adds “CSPs for direct and immediate administration as provided in the Chapter shall only be compounded in those limited situations where the failure to administer such CSP could result in loss of life or intense suffering of an identifiable patient. Any such compounding shall be only in such quantity as is necessary to meet the immediate need of the patient. Documentation for each such CSP shall include identification of the CSP, compounded date and time, number of units compounded, the patient’s name and patient’s unique identifier and the circumstance causing the immediate need of the patient. Such documentation may be available in the patient’s medical record and need not be redocumented by the compounding staff if already available.” This is existing language at section 1751.8(e) and has been relocated to this subdivision due to the reorganization of the language. The language adds “CSPs for direct and immediate administration as provided in the Chapter shall only be done in those limited situations” in the first sentence. This addition provides clarity that direct and immediate administration must comply with the USP Chapter. Additionally, the amended language requires the identification of the CSP in the record and clarifies that the record can be records in the patient’s medical record and need not be documented in an additional location. The remaining language from the existing law has been removed from the board’s regulation due to the changes to the Chapter as the Chapter specifies the other requirements. As compliance with the Chapter is required, such duplication is not necessary. This includes removing the current one-hour start time and will instead allow the four-hour start time provided for in the revised USP Chapter. Further, the Board notes that the proposed regulation text makes clear that separate documentation is not required, rather, the patient's medical record documentation will comply with the regulation.

Additionally, the proposed regulation text provides greater flexibility than the current regulations and should result in cost savings to licensees. Any costs associated with compliance would have been incurred under the existing immediate-use provisions. The Board understands that primary engineering controls (PEC) may fail. Compounding in a PEC is a requirement of the Chapter, not a function of the Board’s regulation. The Chapter established provisions for immediate use that allow for compounding outside of a PEC under specified conditions. The Board’s proposed (and current) regulations allow for this process as well. As included in the Board’s current regulation (CCR 1751.8(e)) immediate use is allowed to prevent loss of life or intense suffering. The Board notes that the inclusion of 1736.1(b)(1) will provide impacted facilities flexibility to continue to care for patients in the event of an equipment failure for 24 hours while the facility implements its required “corrective action plan” that is required in response to any out-

of-range results as established in Chapter 797, Section 5. This flexibility is not provided in the Board's current requirements; however, is included to allow for continuity of patient care while the facility implements its required "corrective action plan." The Board notes that there are requirements from other regulators for all hospitals to have emergency plans. The Board anticipates that equipment failure would be included in such plans in compliance with these other regulatory requirements.

New subdivision (c) is added and reads "Notwithstanding subdivision (a), a limited quantity of CSP may be prepared and stored in advance of receipt of a patient specific prescription document where, and solely in such quantity, as is necessary to ensure continuity of care for individual patients based on a documented history of prescriptions for those patient populations." This is existing language at section 1735.2(b) and has been relocated to this subdivision for due to the reorganization of the language. It has been amended slightly to clarify that this is an exception to the patient-specific preparation set out in subdivision (a) and only applies in a limited circumstance.

New subdivision (d) adds "A reasonable quantity of a compounded drug preparation may be furnished to a veterinary office for use by the veterinarian that is sufficient:
(1) for administration or application to veterinary patients solely in the veterinarian's office;
(2) for furnishing of not more than 120-hour supply, as fairly estimated by the prescriber and documented on the purchase order or other documentation submitted to the pharmacy prior to furnishing;
(A) With the exception of a topical ophthalmics where up to a 28-day supply may be furnished to veterinarian's office for individual patient. Such topical ophthalmics shall be complaint with USP 797 section 14.5, Multiple-Dose CSPs."

This addition allows for the compounding of a reasonable quantity of drug preparations to be used by veterinarians for animal patients, as is currently permitted by section 1735.2(c)(3) within specified limitations and is added to the sterile compounding article due to the reorganization of the language. Subdivision (d)(1) limits the compounding of drug preparations to those administered or applied in the prescribing veterinarian's office. Subdivision (d)(2) further limits the compounding allowed to no more than 120-hour supply. These limitations are in language at section 1735.2(c)(3) and further animal patient safety by ensuring the quality and integrity of the preparation, as well as the premises where administered.

Subdivision (d)(2)(A) adds an exception to the above limitations for a 28-day supply of a topical ophthalmics for individual patient furnished to veterinarian's office and compliant with USP <797> section 14.5, Multiple-Dose CSPs. This exception also furthers animal patient safety by ensuring that topical ophthalmics are compliant with USP and provided in an amount allowable under the provisions of federal law.

New subdivision (e) through (e)(1) adds the following: “(e) In addition to prohibitions and requirements for compounding established in federal law, no CSP shall be prepared that:

(1) Is essentially a copy of one or more commercially available drug products, unless:
(A) that drug product appears on an ASHP (American Society of Health-System Pharmacists) or FDA Drug Shortages Database that are in short supply at the time of compounding and at the time of dispense, or
(B) the compounding produces a clinically significant difference of the medical need of an identified individual patient, as determined:
(i) by the prescribing practitioner,
(ii) the compounding pharmacist, and
(iii) the dispensing pharmacist(s).
(C) Documentation describing the conditions in (1)(A) & (1)(B) is maintained in a readily retrievable format.”

This is existing language at section 1735.2 (d)(3) and has been added to this subdivision due to the reorganization of the language (as well as to the article on nonsterile compounding in new section 1735.1(f)). The language adds “In addition to prohibitions and requirements for compounding established in federal law” in the first sentence. This addition is necessary as a reminder that even with compounding for animal patients all federal law prohibitions apply and must be adhered to. The language was amended to indicate that the compounding must produce a clinically significant difference for the patient as determined by the prescriber, compounding pharmacist, and dispensing pharmacist. The board determined that the compounding must produce a clinically significant difference over a commercially available drug product to be produced. If the preparation is not clinically different, the commercially available drug product must be utilized. This is for patient safety to reduce issues, including contamination, that could arise with a compounded preparation as opposed to a commercially available drug product, which undergo FDA premarket review for safety, effectiveness, and quality. Additionally, the prescriber, compounding pharmacist, and dispensing pharmacist must all determine that the product does have a clinically significant difference as all are responsible for using their professional judgment with respect to patient safety. The FDA Drug Shortage database is maintained on the FDA’s website at this link: https://www.fda.gov/drugs/drug-safety-and-availability/drug-shortages. The ASHP Drug Shortage list is also maintained on the ASHP website at this link: https://www.ashp.org/drug-shortages/current-shortages?loginreturnUrl=SSOCheckOnly.

New subdivision (e)(2) adds “Is made with any component not suitable for use in a CSP for the intended patient population, unless allowable under Animal Medicinal Drug Use Clarification Action of 1994 (AMDUCA).” The Food, Drug, and Cosmetic Act specifies the bulk drug substances and components that may be utilized for compounding human drug products. In addition, AMDUCA allows for extralabel drug use in animals, which is the use of components not suitable for CNSPs for human patients to be

utilized for compounding for animal patients. The language added in this section allows for the compounding of certain drug preparations for use by veterinarians for animal patients and provides clarity to compounding pharmacists that these components can be used to compound drug preparations for animal patients.

New subdivision (e)(3) adds to the prohibitions that no CSP can be "made with a non-sterile component for which a conventionally manufactured sterile product is available and appropriate for the intended CSP." The prohibition is added as USP Chapter <797> indicates that conventionally manufactured sterile products should be used when available and appropriate for CSP. For clarity, the board is mandating that a conventionally manufactured sterile products be used if available as it is guaranteed by the manufacturer to be safe and effective up until the date listed on the product, which ensures the safety of these products.

New subdivision (e)(4) adds that no CSP may require "end product sterilization unless sterilization occurs within the same licensed compounding location." This addition provides clarity to the regulated public with respect to the requirements for sterilization. Under the requirement of Section 503A of the Federal Food, Drug, and Cosmetic Act, compounding must be a done by a pharmacy and end product sterilization is part of the compounding process and it is necessary that facilities understand that the sterilization cannot be done outside of the compounding location, as the pharmacy would not be completing all steps of the compounding process.

Additionally, the Board does not anticipate costs associated with the requirements of this section. The Board determined that the regulation of drug manufacturers falls under the jurisdiction of FDA. The Board has also reached this conclusion for several other reasons. First, the proposed text is similar to the conditions in existing law, CCR Section 1735.2(d)(3). Further, federal law establishes the provisions for when compounding (FDCA section 503A) can occur and provides authority to compound "essentially a copy" only under very limited circumstances. Federal law defines "essentially a copy" in FDCA 503A (b)(2). As included in the FDA's guidance document (see document in underlying data), "The restrictions on making drugs that are essentially copies ensure that pharmacists and physicians do not compound drug products under the exemptions for patients who could use a commercially available drug product. Such a practice would create significant public health risk because patients would be unnecessarily exposed to drug products that have not been shown to be safe and effective and that may have been prepared under substandard manufacturing conditions. FDA has investigated serious adverse events in patients who received contaminated compounded drugs when a comparable approved drug, made in a facility subject to CGMP requirements, was available. Restrictions in section 503A prevent compounders from producing drugs without having to comply with monograph standards, or CGMP requirements."

New subdivision (f) adds "Prior to allowing any CSP to be compounded within a pharmacy, the pharmacist-in-charge shall complete a self-assessment consistent with

the requirements established in section 1715." The requirement to complete the self-assessment is existing language within 1735.2(k); the language has been amended slightly, however, to delete the reference to the specific form and simply refer to section 1715, as the form is referenced in 1715.

New subdivision (g) adds "In addition to the provisions in Section 1707.2, consultation shall be provided to the patient and/or patient's agent concerning proper use, storage, handling and disposal of the CSP and related supplies furnished." The addition of this language ensures that appropriate consultation is being provided because the use, handling, storage, and disposal of compounded drug preparations can be different than that of standard tablet or capsule medication.

New subdivision (h) adds the requirement for CSPs with human whole blood or human whole blood derivatives to be prepared in compliance with Health and Safety Code section 1602.5. As CSPs can include the use of blood components, adding this language ensures awareness of the requirements within HSC 1602.5.

Note is added with authority cited as Sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, 4051, 4052, 4126.8, 4123, 4127, 4127.1, and 4127.2, Business and Professions Code.

Add Section 1736.2

New section 1736.2 is added and titled "Personnel Training and Evaluation" to track the title used for section 2 in USP Chapter <797>. An opening paragraph is added to remind the public that the processing of sterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <797>.

New subdivision (a) adds: "Training and competency procedures for all personnel who compound or have direct oversight of compounding personnel shall address the following topics:

(1) Quality assurance and quality control procedures,
(2) Container closure and equipment selection,
(3) Component selection and handling, and
(4) Sterilization techniques, when applicable."

The additional training components are added to ensure that the personnel performing compounding are appropriately trained in all aspects of compounding, including quality assurance, quality control procedures, container closure and equipment, component selection and handling, and sterilization techniques." The Chapter is silent on these training topics; however, the board believes these topics are important for training purposes and safe compounding practices to ensure patient safety. The Board notes that training is critical to sterile compounding and USP 797 has an entire section, Section 2, dedicated to personnel training and evaluation. The Chapter details the core competencies of training that must be completed at least every 12 months. Any costs

incurred for these trainings is a function of compliance with the Chapter, not the Board's proposed regulation. The Board's proposed regulations do require training in four additional areas not specified in the chapter - - quality assurance and quality control; container closure and equipment selection; component selection and handling; and sterilization techniques (only when applicable). As noted, these additional components ensure that personnel are adequately trained in all aspects of compounding including for example quality assurance which ensure an individual has the knowledge to perform a root cause analysis if an issue arises with product quality or a medication error, or an understanding of a particular component selection when making a compounded preparation that could occur in a number of circumstances, including for example under extreme pressure such as for immediate use. The Board notes that current regulations, CCR 1751.6 requiring training in these areas - - 1751.8(e)(1)(J) container, equipment, and closure system selection; 1751.8(e)(1)(D) quality assurance procedures, 1751.8(e)(I) sterilization technique for compounding. Costs related to these training requirements would already be incurred and not new cost associated with these regulations. Further, the Board notes that Section 9.3 of the Chapter requires an SOP on component selection. Having an SOP without completing training on the provisions undermines the value of the SOP. Section 18 of Chapter 797 requires compliance with the training and assessment requirements. The need for proper training is highlighted in a number of areas, including in the USP 797 commentary document (see Underlying Data number 16) which includes "Personnel are the biggest source of contamination, and this frequency of personnel monitoring helps ensure continued, consistent, and proper performance." Elsewhere in the commentary, in response to another comment the USP includes, "The (training) standards are based on a combination of available evidence, expertise of the Compounding Expert Committee, and input from stakeholders, and take into consideration stability and sterility data, the compounding environment, and the financial impact on compounders and patients. Personnel are the main source of contaminants, and a frequency of every 6 months for the garbing competency for compounders helps ensure continued proper hand hygiene and garbing procedures. The text was changed to allow designated person(s) and personnel who oversee compounding personnel to perform the competency every 12 months."

New subdivision (b) adds the following requirement:
"Initial and ongoing aseptic manipulation training and competency documentation shall include the Primary Engineering Control (PEC) type and PEC unique identifier used during the evaluation. Aseptic manipulation competency evaluation and requalification shall be performed using the same procedures, type of equipment, and materials used in aseptic compounding. Aseptic qualifications from one premises may be used for another premises if all of the following conditions are met:

(1) The SOPs required by section 1736.17 related to compounding are identical.
(2) The Secondary Engineering Control (SEC) facility designs are sufficiently similar to accommodate the use of the same SOPs.
(3) The PECs are of the same type and sufficiently similar to accommodate the use of the same SOPs describing use and cleaning."

This subdivision includes the requirements for aseptic manipulation competency to include the PEC type and identifier and the requirement that competency be completed on the PEC type, using similar materials, and processes in which they will be performing during aseptic manipulation. This addition is necessary to ensure that staff on competent on the equipment they are using and with the materials being compounded. This subdivision includes the requirements for aseptic manipulation competency at multiple locations. As some facilities have staff that work at different locations, the addition of this language allows staff to more easily work at different locations, provided that the three requirements are met, with a single training and competency evaluation. Subdivisions (b)(2) and (b)(3) allow for one SOP to be used at multiple locations when the PECs are the same type and similar SEC design. The use of one SOP eliminates the need for duplicative information for each SEC and PEC within the SOPs.

New subdivision (c) adds “Aseptic manipulation ongoing training and competency shall occur each time and for each staff member involved in an occurrence where the quality assurance program required by the SOPs yields an unacceptable result, as defined in the SOPs, that may indicate microbial contamination of CSPs due to poor practices. Aseptic manipulation ongoing training and competency procedures shall be defined in the facility’s SOPs.” This subdivision includes the requirements for aseptic manipulation competency should contamination occur possibly due to poor practices. Because poor practices may be the source of contamination, staff must be retrained to prevent ongoing contamination when there is any unacceptable result.

New subdivision (d) adds “Compounding personnel or persons with direct oversight over compounding personnel, who fail any aspect of the aseptic manipulation ongoing training and competency evaluation shall not be involved in compounding or oversight of the preparation of a CSP until after successfully passing training and competency in the deficient area(s) as detailed in the facility’s SOPs. A person with only direct oversight over personnel who fails any aspect of the aseptic manipulation ongoing training and competency evaluation may continue to provide only direct oversight for no more than 14 days after a failure of any aspect while applicable aseptic manipulation ongoing training and competency evaluation results are pending.” As the pharmacist is responsible for the oversight of staff performing the processing, they must be proficient in the skills needed to monitor the work product of the personnel for patient safety. The board determined that no more than a 14-day period for the person with direct oversight could safely continue providing the oversight only while training and evaluation are still pending to avoid disruption in compounding. Patient safety requires that there be no disruption while the facility has a chance to make other arrangements, if necessary. Additionally, if compounding personnel then fail ongoing training and evaluation, patient safety must take priority and those individuals shall not be involved in compounding or the oversight of the preparations. The 14-day period, however, allows for a transition if necessary.

New subdivision (e) adds “Any person assigned to provide the training specified in this section shall have demonstrated competency in the skills in which the person will provide training or observe and measure competency described in the facility’s SOPs.

Documentation demonstrating compliance must be maintained." The requirement is necessary to ensure that the individual assigned to provide the training to personnel has sufficient knowledge and expertise to provide the training. Additionally, documentation must be maintained for review during board staff inspections to ensure appropriate training has been provided in the interest of patient safety. While the board is requiring that the documentation be maintained, the method for maintaining the documentation can be determined by the facility based on their business practices.

Note is added with authority cited as sections 4005, 4126.8, and 4127 of Business and Professions Code. Additionally, references are cited as Sections 4005, 4052, 4057, 4114, 4115, 4127, 4301, and 4332 of the Business and Professions Code.

Add Section 1736.3

New section 1736.3 is added and titled "Personnel Hygiene and Garbing." An opening paragraph is added to remind the public that the processing of sterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <797>.

New subdivision (a) adds the following: "The pharmacist overseeing compounding shall not allow personnel with potentially contaminating conditions to enter the compounding area." This addition is needed for patient safety to prevent contamination. As the sterile compounding area must maintain its sterility, it is essential that personnel with possibly contaminating conditions must not be permitted into the sterile environment. It must be an overseeing pharmacist with ultimate responsibility to protect the sterile environment.

New subdivision (b) adds the following "The pharmacist overseeing compounding shall not allow personnel to enter the compounding area with visible non-removable piercings, which could increase the risk of contamination of CSP." This addition is needed for patient safety to prevent contamination. As non-removeable piercings pose a contamination risk from accidental flaking of components or skin, they must be covered.

New subdivision (c) adds the following: "Garb shall be donned in an anteroom or immediately outside the segregated compounding area (SCA). Donning and doffing garb shall not occur in the anteroom at the same time unless the facility's SOP define specific processes that must be followed to prevent contamination." The requirement to garb in the ante-area or outside the SCA ensures that garbing remains clean and prevents cross contamination. Additionally, doffing garb should be done in a manner to prevent cross contamination of new, clean garbs.

New subdivision (d) adds: "Restricted access barrier system and pharmaceutical isolator sleeves and gloves shall be changed according to both the manufacturer's recommendations and the facility's SOP." USP Chapter <797> is silent as to any requirement to change restricted access barrier systems, isolated sleeves, and gloves; accordingly, for patient safety, the board is including the requirement. The board determined that, at minimum, the items need to be changed according to the

manufacturer's recommendation or more frequently, if determined by the facility's SOPs based on an assessment that more frequent changes are necessary.

New subdivision (e) requires that any garbing accommodations provided by the designated person be documented; the documentation must include the name of the individual granted the accommodation, date granted and description of the reasons for granting the accommodation. Appropriate garbing is a very important part of safe and clean compounding. The type, use and reuse, and cleaning of both disposable and non-disposable garb is determined in order to protect both personnel and patients. Where a deviation from the required garbing is necessary for an accommodation, complete documentation of that deviation is necessary for tracking both by the pharmacy and by the Board. The record must be retained in accordance with Business and Professions Code section 4081. Documentation of this information provides an additional level of seriousness for the designated person in explaining the rationale.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, 4126.8 and 4127, Business and Professions Code.

Add Section 1736.4

New section 1736.4 is added and titled "Facilities and Engineering Controls." An opening paragraph is added to remind the public that the processing of sterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <797>.

New subdivision (a) adds: "A sink used for compounding or hand hygiene shall not be part of a restroom or water closet." While USP <797> provides a standard for sinks used during sterile compounding, it does not address a sink being located as part of restroom facilities or a water closet. Due to the possible contamination and sanitation issues, the board determined that it is necessary to provide additional clarity that the sink used for compounding or hand hygiene cannot be in the restroom or water closet.

New subdivision (b) adds the following: "If an SCA is used:

(1) Except for walls, the SCA's visible perimeter shall be at least 1 meter from all sides of the PEC or the SCA can be located in a separate room.
(2) Surfaces within the SCA shall be smooth, impervious, free from cracks and crevices, and non-shedding so they can be easily cleaned and disinfected and to minimize spaces in which microorganisms and other contaminants can accumulate."

This requirement tracks the language within USP Chapter <797> with respect to a visible perimeter at least 1 meter from the PEC; however, the board determined that the perimeter of the SCA should not be within 1 meter of all sides of the PEC to ensure appropriate air flow, which is necessary to reduce the risk of possible cross contamination.

New subdivision (c)(1) adds “Designated compounding area(s) shall typically be maintained at a temperature of 20° Celsius or cooler and also provide comfortable conditions for compounding personnel attired in the required garb.” While the Chapter provides these recommendations, the language is permissive. To ensure the quality and integrity of the preparation, the board determined that the maximum temperature must be mandatory. The cool temperature minimizes the risk of microbial proliferation. This requirement is existing law within section 1751.4(k) (being repealed) and is relocated to this section due to the reorganization of the regulation text.

New subdivision (c)(2) adds: “The temperature shall be monitored in each room of the designated compounding area each day that compounding is performed, either manually or by a continuous recording device.” Chapter <797> requires daily monitoring of the temperature within the cleanroom suite but is silent on individual areas such as the SCA. As the SCA shall be continuously maintained at a temperature of 20 degrees Celsius or cooler, the board determined that temperature monitoring of the SCA should also occur for consistency and preparation quality and integrity.

New subdivision (d) adds: “Where a pass-through is installed in a secondary engineering control after [OAL insert effective date], the doors must be interlocking. An existing secondary engineering control that has a pass-through that is not an interlocking device, may continue to be used if the SOPs document that two doors may not be opened at the same time.” This ensures that future pass-throughs must be interlocking following the effective date of the regulation to ensure that the inside and outside doors are never opened simultaneously. A non-interlocking door can be used if existing, provided that the facility has SOPs that state that the doors may not be opened at the same time. This allows for older facilities to maintain their current structure and would not require older facilities to remodel; however, new pass-through doors installed after the effective date of the regulation must be interlocking. The board determined that new construction must meet the higher, safer standard of an interlocking pass-through and is grandfathering in older, existing compounding facilities so that older facilities would not be required to remodel simply to install interlocking pass-through doors. If these older facilities remodel in the future, they would be required to install interlocking pass-through doors as part of that remodel.

New subdivision (e) adds “Except as provided in subsection (d) dynamic interactions between areas and rooms with classified air shall be controlled through a heating, ventilation, and air condition (HVAC) system.” This is necessary to minimize the risk of contamination during compounding of CSPs as an HVAC system design ensures that specified room conditions are maintained through heating, cooling, air filtration, air distribution, airflow rates and air exchange rates.

New subdivision (f) requires that: “No CSP shall be compounded if the compounding environment fails to meet criteria specified in the law or the facility’s SOPs.” This subdivision is added for completeness, to clearly state that compounding cannot occur if the compounding environment does not meet all the required parameters. This

requirement is also existing law at section 1751.4(a) (being repealed) and is relocated here as part of the reorganization.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, and 4126.8, Business and Professions Code.

Add Section 1736.5

New section 1736.5 is added and titled "Certification and Recertification." An opening paragraph is added to remind the public that the processing of sterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <797>.

New subdivision (a) adds the following: "Testing and certification of all ISO classified areas shall be completed by a qualified technician knowledgeable with certification methods and procedures outlined in the Controlled Environment Testing Association (CETA)'s Certification Guide for Sterile Compounding Facilities as specified in this section. Testing shall be performed in accordance with CETA Certification Guide for Sterile Compounding Facilities (CAG-003, Revised 2022), which is hereby incorporated by reference." This is existing law at section 1751.4(f) (being repealed) and is relocated here as part of the reorganization.

New subdivision (b) adds the following: "CETA standard(s) used to perform certification testing in all ISO classified areas shall be recorded on the report issued by the certifying technician in accordance with the Certification Guide for Sterile Compounding Facilities."

Subdivisions (a) and (b) add the requirement that the certification must be done by a qualified technician. The use of a qualified technician for testing and certification is required by the Chapter; however, the Chapter is silent on the qualifications of the technician. These subsections implement the Chapter further by requiring that the technician understand the CETA certifications methods and the standards to ensure that appropriate evaluation of the areas is completed, as inappropriate certification may result in contamination of drug products and be a risk to patient safety. Recording the standards used on the report will demonstrate that the technician was appropriately qualified.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, and 4126.8, Business and Professions Code.

Add Section 1736.6

New section 1736.6 is added and titled "Microbiological Air and Surface Monitoring." An opening paragraph is added to remind the public that the processing of sterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <797>.

New subdivision (a) adds: “At a minimum of every 6 months, air and surface sampling results shall be identified to at least the genus level, regardless of the CFU count to trend for growth of microorganisms. Investigation must be consistent with the deviation and must include evaluation of trends.” The Chapter requires that testing be completed every 6 months; it only requires, however, genus level identification if the CFU count exceeds a specific value. The proposed language strengthens testing by requiring the genus identification regardless of the count, as the appropriate response could vary depending on the microorganism. Highly pathogenic microorganisms (e.g., Gram-negative rods, coagulase positive staphylococcus, molds, yeasts) can be potentially fatal to patients receiving CSPs and must be immediately remedied, regardless of CFU count. As indicated in the ASHP release “Pharmacy Environmental Monitoring (EM) Implementation Toolkit (underlying data number 20) - “A hallmark of a strong EM program is the measurement of progress in order to continuously program compounding conditions, and effectively correct excursions.” This document further provides metrics to consider during tracking efforts and descriptions of the benefits of the trending. The Board notes that the ASHP document recommends monitoring monthly; however, the Board’s proposed regulation text only requires trending every six months. Further as noted in USP Chapter 1161, “Particulate counts as well as microbial counts within controlled environments vary with the sampling locations and the activities being conducted during sampling. Monitoring the environment for nonviable particulates and microorganisms is an important control function because they both are important in achieving product compendial requirements for Foreign and Particulate Matter and Sterility in Injections and Implanted Drug Products.” Also included in Chapter 1161, “Environmental microbial monitoring and analysis of data by qualified personnel can assist in ensuring that a suitable state of control is maintained.” And the Chapter further provides, “Since the advent of comprehensive environmental monitoring programs, their applications in capturing adverse trends or drifts has been emphasized.”

New subdivision (b) adds: “Environmental sampling shall be done in compliance with the most recent edition of the Controlled Environment Testing Association (CETA)’s Certification Application Guide USP <797> Viable Environmental Sampling & Gowning Evaluation (CAG-009, Revised October 2022), which is hereby incorporated by reference.” The proposed language further implements the Chapter for the environmental sampling requirements by specifying compliance with the CETA guidelines. CETA guidelines establish an industry-based minimum set of criteria appropriate for performance evaluation and certification of facility and environmental controls used for compounding sterile preparations. This minimum set of criteria are necessary to ensure consistent and repeatable testing at all facilities.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, and 4126.8, Business and Professions Code.

Add Section 1736.7

New section 1736.7 is added and titled “Cleaning, Disinfecting, and Applying Sporicidal Disinfectants and Sterile 70% IPA.” An opening paragraph is added to remind the public that the processing of sterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <797>.

New subdivision (a) is added and reads: “Any cleaning, disinfection, and sporicidal disinfectants used by the facility to meet the requirements in this article shall be used in accordance with manufacturers' specifications.” This requirement is added to ensure the regulated public understands all agents must be used consistent with each applicable manufacturer’s specifications as board enforcement staff frequently get asked questions on this topic during inspections.

New subdivision (b) is added and reads: “Reusable cleaning supplies, not for use in the PEC, shall not be stored within 1 meter of the PEC.” This prohibition that cleaning supplies cannot be stored near the PEC when they are not for use in the PEC will help prevent cross contamination from the agents.

New subdivision (c) adds the requirement for the facility to document each occurrence of cleaning, disinfecting, and applying of sporicidal disinfectants in the compounding area and include the identity of the person completing the cleaning and disinfecting, as well as the product name(s) of the cleaning, disinfecting, and sporicidal agent(s) used. The addition ensures a complete record of the cleaning in the compounding area to allow follow-up should contamination be identified.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, 4126.8, and 4127, Business and Professions Code.

Add Section 1736.8

New section 1736.8 is added and titled “Introducing Items into the SEC and PEC.” An opening paragraph is added to remind the public that the processing of sterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <797>.

The section adds: “Introducing items into the SEC and PEC shall comply with the SOPs as required in section 1736.17.” This addition provides consistency with respect to introducing items to the SEC and PEC complying with the facility’s SOPs, which ensures all staff are following the same processes, preventing cross contamination and ensure patient safety.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code Additionally, references are cited as Sections 4005, 4126.8, and 4127, Business and Professions Code.

Add Section 1736.9

New section 1736.9 is added and titled “Equipment, Supplies, and Components.” An opening paragraph is added to remind the public that the processing of sterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <797>.

New subdivision (a) requires that all equipment and supplies used to compound a CSP shall be used in accordance with the manufacturer’s specifications and shall be surface compatible. This requirement is to ensure that equipment is being operated properly, equipment and supplies are placed and used on surfaces capable of withstanding them, and they are utilized for their intended purposes and not for untested or other purposes, which could contaminate the compounded preparation and pose a risk to patient safety.

New subdivision (b) adds the following language: “Incubators used by the facility shall be cleaned, maintained, calibrated, and operated in accordance with manufacturers' specifications. For incubators without specific manufacturers' specifications, cleaning shall take place at least every 30 days and calibration shall take place at least every 12 months.” Chapter <797> requires the use of incubators; however, it is silent on calibration and operation. This subdivision is added for specificity regarding the use of incubators. It ensures an understanding that the cleaning, maintenance, and calibration must be done consistent with the manufacturer’s specifications, as board enforcement staff frequently gets questions on this topic during inspections. The board determined that a minimum of every 30 days for cleaning and every 12 months for calibration are required for safe operation. Industry standards for cleaning vary based on use from one to two times month, and standards for calibration vary from 6 months to one year. The board is specifying that cleaning occur once every 30 days and calibration once every 12 months as the minimum based on these standards; however, a facility may need to clean and calibrate more frequently based on the facility’s usage.

New subdivision (c) provides that any component used to compound a CSP shall be used and stored in accordance with all state and federal laws and the manufacturer’s specifications and requirements. This subdivision serves as a reminder to the regulated public with respect to the usage and storage of compounding components to ensure the integrity of the components and patient safety.

New subdivision (d) requires that all API and excipient components used to compound a CSP be manufactured by an FDA-registered facility, accompanied by a Certificate of Analysis (COA) and suitable for use in sterile pharmaceuticals. A COA that includes the compendial name, the grade of the material, and the applicable compendial designations on the COA must be received and evaluated prior to use, unless components are commercially available drug products. When the COA is received from a supplier, it must provide the name and address of the manufacturer. API and excipient components provided without this data shall not be used in a CSP.

The requirement for the COA is added in accordance with the requirements of the FDCA (section 503A(b)(1)(A)(iii) and further elaborated on in the guidance document - Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act, issued by the FDA. The COA must be issued by the manufacturer for each batch of API. Obtaining and retaining this document ensures that the API is coming from an FDA-registered facility, which means the facility has been inspected by the FDA for good manufacturing practices and that the API was manufactured under an appropriate system for managing quality.

New subdivision (e) adds: "When a bulk drug substance or API is used to compound a CSP, it shall comply with a USP drug monograph, be the active substance of an FDA approved drug, or be listed in 21 CFR 216.23, unless authorized by a public health official in an emergency use situation for a patient specific compounded sterile preparation." This subdivision is added to provide clarity that APIs must comply with USP monographs or be on the FDA approved drug list. Additionally, the language provides for a temporary emergency use situation, authorized by a public health official, for a patient specific preparation, which ensures that patients have access to needed compounded medication during a public health emergency and one of the other requirements cannot be met.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, 4126.8, and 4127, Business and Professions Code.

Add Section 1736.10

New section 1736.10 is added and titled "Sterilization and Depyrogenation." An opening paragraph is added to remind the public that the processing of sterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <797>.

New subdivision (a) adds the requirement for dry heat depyrogenation to be done in compliance with USP Chapter 1228.1, Dry Heat Depyrogenation. Dry heat Depyrogenation is required by USP <797>, but that Chapter directly refers to Chapter <1228>. This requirement ensures clarity to the regulated public that they must comply with USP <1228.1>.

New subdivision (b) adds: "Sterilization by filtration shall be done in compliance with USP Chapter 1229.4, Sterilizing Filtration of Liquids. Filter dimensions and the CSP to be sterilized by filtration shall permit the sterilization process to be completed without the need for replacement of the filter during the process." Sterilization by filtration is required by USP <797>, but that Chapter directly refers to Chapter <1229>. This requirement ensures clarity to the regulated public that they must comply with USP <1229.4>.

New subdivision (c) adds the requirement for steam sterilization to be done in compliance with USP Chapter 1229.1. Steam sterilization is required by USP <797>, but

that Chapter directly refers to Chapter <1229>. This requirement ensures clarity to the regulated public that they must comply with USP <1229.1>.

New subdivision (d) adds the requirement for dry heat sterilization to be done in compliance with USP Chapter 1229.8. Dry heat sterilization is required by USP <797>, but that Chapter directly refers to Chapter <1229>. This requirement ensures clarity to the regulated public that they must comply with USP <1229.8>.

New subdivision (e) adds the requirement that no compound of a CSP from nonsterile components shall be prepared when the licensed location cannot also sterilize the CSP as described in this section. As CSPs made from nonsterile components must be sterilized after preparation, if the licensed location is unable to perform the sterilization, they cannot properly prepare the CSP. The prohibition is necessary as the failure to be able to sterilize the preparation is a patient safety issue.

New subdivision (f) adds the requirement that sterilization of supplies and/or container–closure systems shall be done in compliance with USP Chapter <1229>. Chapter <1229> addresses the sterilization of supplies and/or container-closure systems. This requirement ensures clarity that such sterilization must comply with USP <1229>.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, 4126.8, and 4127, Business and Professions Code.

Add Section 1736.11

New section 1736.11 is added and titled “Master Formulation and Compounding Records.” An opening paragraph is added to remind the public that the processing of sterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <797>.

New subdivision (a) requires that a “CSP shall not be compounded until the facility has first prepared a written master formulation record in compliance with USP Chapter 797 and that record includes the following additional elements:” This subdivision is necessary to ensure appropriate compounding practices are established prior to compounding and compounding is not undertaken until the master formulation record (MFR) has been created for each unique formulation. The MFR details how each CSP shall be compounded and, as such, the record must be created before compounding has begun.

New subdivision (a)(1) adds the requirement for sources referenced to support a beyond-use date (BUD) be readily retrievable at the time of compounding and maintained for three years from the date each CSP is dispensed. This subdivision is necessary to ensure that the reference material is maintained for review by compounding personnel to confirm that it is current to support the BUD. Additionally, it

ensures that the reference material is available for board inspector review during board staff inspections to ascertain that the BUD was supported.

New subdivision (a)(2) adds the requirement for the instructions for the storage and handling of the CSP to also be included in the MFR. This ensures that those instructions are documented and maintained. Storage and handling instructions must be followed for patient safety and to prevent cross contamination.

New subdivision (b) adds the following exception: “When a particular drug preparation is not routinely compounded at a facility, the master formulation record for that preparation may be recorded on the prescription document itself. This record shall comply with USP Chapter 797 and this section.” This subdivision provides an exception for CSPs that are not routinely compounded by the facility. The MFR can be documented on the prescription document, as prescription documents must be maintained within pharmacy records, instead of maintaining it according to the facility’s SOPs. .

New subdivision (c) adds the following: “A compounding record (CR) shall be a single document. The document shall satisfy the requirements of USP Chapter 797, and also contain the following:

(1) The date and time of preparation. The time of preparation is the time when compounding the CSP started, which also determines when the assigned BUD starts.
(2) The assigned internal identification number shall be unique for each CR.
(3) The manufacturer, lot number, and expiration date shall be recorded for each component for CSPs.
(4) The total quantity compounded including the number of units made and either the volume or weight of each unit.
(5) The identity of each person performing the compounding, that has direct oversight of compounding, and pharmacist verifying the final drug preparation.
(6) When applicable, endotoxin level calculations and results.”

The board specified the six requirements above to ensure that they are included in the compounding record. The first five items are included within USP Chapter <797> and are tracked here for completeness to include all elements in one location. The board added the sixth requirement, which is the endotoxin level calculations and results. The board added this requirement for recordkeeping to identify the endotoxin level and the calculations completed. This information will be needed for completion of the testing and determination of the results.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, 4081, 4126.8, 4127, and 4169, Business and Professions Code.

Add Section 1736.12

New section 1736.12 is added and titled "Release Inspections and Testing." An opening paragraph is added to remind the public that the processing of sterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <797>.

New subdivision (a) adds: "A pharmacist performing or supervising the sterile compounding is responsible for the integrity, quality, and labeled strength of a CSP until the beyond use date indicated on the label provided the patient or the patient's agent follows the label instructions provided on the CSP for storage and handling after receiving the CSP." This section is existing law within section 1735.2(g) (being repealed) and is necessary to add here to ensure that there is an identifiable person responsible for the CSP, and that that person is the pharmacist performing or supervising the CSP. As the pharmacist performing or supervising the compounding, they must ensure that compounding is be completed in accordance with the facility's SOPs and USP.

New subdivision (b) adds: "A pharmacist performing or supervising sterile compounding is responsible for ensuring validation of an alternative method for sterility testing is done in compliance with USP Chapter 1223, Validation of Alternative Microbiological Methods and shall receive and maintain documentation of the method-suitability for each CSP formulation for which the alternate method is used." Because there are requirements related to processing sterile compound preparations in addition to USP Chapter <797>, this subdivision is added to ensure that the regulated public understands that they must also comply with USP Chapter <1223>.

New subdivision (c) added: "A pharmacist performing or supervising sterile compounding is responsible for ensuring injectable CSPs made from nonsterile components, regardless of Category, are tested to ensure that they do not contain excessive bacterial endotoxins, as established in USP Chapter 85, Bacterial Endotoxins. Results must be reviewed and documented in the compounding record prior to furnishing." While the requirements for sterility testing and receipt of the results is required by the Chapter, the Chapter is silent on where to document the results. It will now be expressly required for the results to be maintained with the compounding record in the event of a recall or complaint.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, 4081, 4126.8, 4127, 4169, and 4332, Business and Professions Code.

Add Section 1736.13

New section 1736.13 is added and titled "Labeling." An opening paragraph is added to remind the public that the processing of sterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <797>.

New subdivision (a) adds mandatory labeling requirements for CSPs as the labeling requirements within the Chapter are identified as being “as applicable” and not clearly mandatory. Labeling is essential for dispensed medication to ensure patient use of the medication as intended; therefore, ensuring that the regulated public has a clear understanding of the labeling requirements is necessary.

(1) Route of intended administration;
(2) The solution utilized, if applicable;
(3) Instructions for administration;
    (A) For an admixed CSP, the rate of infusion, or range of rates of infusion as prescribed, or the duration, when the entire CSP shall be administered.
(4) Name of compounding facility and dispensing facility (if different).

New subdivisions (a)(1) through (a)(4) are added to ensure that the label contains how the preparations should be administered (route and instructions - to ensure the patient uses the medication as directed), the solution utilized (to ensure appropriate storage), and the name of facilities involved (so the patient has contact information in the event the patient has a question or problem). Again, labeling is essential for dispensed medication to ensure patient safety.

New subdivision (b) adds the requirement for any CSP dispensed or ready to be dispensed to a patient to also include on the label the information required by Business and Professions Code section 4076 and section 1707.5. This is existing law within section 1751.2 (being repealed) and is being added here as part of the relocation. Labeling is essential for dispensed medication to ensure patient safety; therefore, ensuring that the regulated public has a clear understanding of the labeling requirements.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, 4076, 4123, 4126.8, and 4127, Business and Professions Code.

Add Section 1736.14

New section 1736.14 is added and titled “Establishing Beyond-Use Dates.” An opening paragraph is added to remind the public that the processing of sterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <797>.

New subdivision (a) adds the following: “A CSP’s beyond-use date (BUD) shall not exceed:

(1) The chemical and physical stability data of the active pharmaceutical ingredient(s) and any added substances in the preparation;
(2) The compatibility of the container–closure system with the finished preparation (e.g., possible leaching, interactions, and storage conditions); and
(3) The shortest remaining expiration date or BUD of any of the starting components.”

The board added the requirement for setting the BUD that shall not exceed three possible limitations. While the Chapter provides the first two limitations, the Chapter does not include the third limitation. To ensure patient safety, the board has established set criteria that the BUD must not exceed the shortest remaining expiration date or BUD of any of the starting components. This ensures that components used to prepare the compounded product do not expire prior to the assigned BUD, which could impact the quality of the product. To ensure all limitations are followed, the Board included the limitations from the Chapter within the subdivision to have all limitations in one location. These requirements are also existing law at section 1735.2(i)(2) (being repealed); however, have been amended to reflect the changes identified within the Chapter.

New subdivision (b) is added to establish the BUD expiration as 11:59 p.m. on the assigned date, if no specific time is otherwise established. This time is added to provide clarity for the time of day that the product can no longer be utilized on its expiration date. The board selected 11:59 p.m. because using “midnight” is confusing, as it is unclear whether that refers to the end of one day or the beginning of the next day.

New subdivision (c) is added to establish the requirement that prior to dispensing a CSP, the pharmacist performing or supervising sterile compounding is responsible for ensuring that sterility and endotoxin testing for BUD determination is performed and has received and reviewed the results. Additionally, the test results must be retained as part of the compounding record. While the requirements for sterility testing and receipt of the results is required by the Chapter, the Chapter is silent on where to document the results. It will now be expressly required for the results to be maintained in the compounding record in the event of a recall or complaint.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005,4076, 4126.8, 4127, 4169, 4306.5, and 4332, Business and Professions Code.

Add Section 1736.15

New section 1736.15 is added and titled “Use of Conventionally Manufactured Products as Components.” An opening paragraph is added to remind the public that the processing of sterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <797>.

New subdivision (a) adds: “A single-dose container entered or punctured outside of an ISO Class 5 area, must be discarded immediately.” This is added to clarify the USP language, which states that opened single-dose containers cannot be stored for any time period. Clarifying the language ensures that these containers are immediately discarded and not reused, furthering public safety. Existing law at section 1751.9(b)(1) (being repealed) allows for use within 1 hour of needle-puncture. As a result of the specification within the Chapter that opened single-dose container cannot be stored for any time period, the board moved the section here but amended it to require that the containers be discarded immediately.

New subdivision (b) adds: “A single-dose container entered or punctured inside of an ISO class 5 area must be discarded within 12 hours.” Existing law at section 1751.9(b)(2) (being repealed) allows for use within 6 hours of needle-puncture. As a result of the specification within the Chapter that single-dose container must be discarded within 12-hours when opened is ISO class 5 areas or better, the board moved and amended the section to require that the containers be discarded within 12-hours to track the language within the Chapter.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, and 4126.8, Business and Professions Code.

Add Section 1736.16

New section 1736.16 is added and titled “Use of CSPs as Components.” An opening paragraph is added to remind the public that the processing of sterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <797>.

New subdivision (a) adds: “A compounded stock solution intended for use in a CSP must comply with all provisions of this article and USP Chapter 797 Category 1, Category 2, or Category 3.” Because the Chapter does not address a CSP as an ingredient of a CSP, this language clarifies that stock solutions that are themselves CSPs must comply with all sterile compounding requirements when that stock solution will in turn be used in a sterile compound preparation. The Board notes that the USP Chapter includes a definition for compounded stock solution.

New subdivision (b) adds: “Nothing in this section shall prohibit the use of a CSP obtained from a California licensed outsourcing facility.” This subdivision is necessary to include the ability for sterile preparations to be obtained from a California licensed outsourcing facility, which, generally speaking, do not prepare patient specific compounds. Outsourcing facilities compound drug products on a larger scale, however, that can safely be used as components in CSPs.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, 4127.2 and 4127.8, Business and Professions Code.

Add Section 1736.17

New section 1736.17 is added and titled “Standard Operating Procedures (SOPs).” An opening paragraph is added to remind the public that the processing of sterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <797>.

New subdivision (a) adds the requirement for the facility's standard operating procedures (SOPs) for sterile compounding to be followed, and must do the following:

(1) Comply with USP Chapter 1163, Quality Assurance in Pharmaceutical Compounding; and
(2) Define the following:
    (A) Methods by which the pharmacist compounding or supervising the compounding will ensure the quality of compounded drug preparations;
    (B) Procedures for handling, compounding, and disposal of infectious materials. The SOPs shall describe the facility protocols for cleanups and spills in conformity with local health jurisdictional standards;
    (C) The methods a pharmacist will use to determine and approve the ingredients and the compounding process for each preparation before compounding begins; and
    (D) The method for complying with all other requirements specifically defined in the SOPS.

Licensees must develop SOPs on their chosen workflow to ensure consistent operation of the facility and staff. For patient safety, a facility must follow its own SOPs. The processes will then be consistent. Additionally, defining the methods to ensure the quality of the preparations, the procedures for handling, compounding, and disposal of infectious materials, including cleanup and spills, the methods for ingredient determination and approval, and any other requirements identified in other sections for the facility's SOPs is necessary. This information is required in the SOPs to ensure procedures are in place prior to the compounding so that staff are all following the same procedures. The SOPs will be readily available if any possible problem arises and will ensure appropriate action can be taken timely should it be needed to ensure patient safety. The Board is not establishing any requirements above what the Chapter requires.

New subdivision (b) adds the following: "The SOPs shall specify steps to be taken if a classified area(s) fails to meet the specified ISO classification, including the investigative and corrective actions, allowable activities, and retesting procedures." To ensure patient safety, having procedures in place prior to the discovery of any possible problem will ensure appropriate action can be taken timely should a failure to meet requirements be identified. Identifying the steps to investigate the cause of the failure and what processing can be completed until that area meets the required classification are necessary to instruct personnel on the best and most complete way to meet the ISO requirements.

New subdivision (c) adds the following: "The SOPs shall specify steps to be taken when the microbiological air and surface monitoring action levels are exceeded including the investigative and corrective actions, allowable activities, and resampling procedures." To ensure patient safety, having procedures in place prior to the discovery of any possible problem will ensure appropriate action can be taken timely should a problem be identified. Identifying the steps to investigate the cause of the failure and what processing can be completed until the microbiological air and surface monitoring

levels are reduced to instruct personnel on the best and most complete way to meet action levels.

New subdivision (d) adds the requirement that the SOPs shall specify the process and products to be used on any equipment and other items entering from an unclassified area into the clean side of the anteroom, entering a PEC, and entering the SCA. These SOPs must define at a minimum what product is to be used, the dwell time required, and how dwell time will be monitored and documented. To ensure patient safety, this information is required in the SOPs to ensure procedures are in place prior to the compounding so that staff are all following the same procedures. The proposed regulation text requires the facility to develop a policy consistent with its business practice, providing flexibility to the facility to determine how to operationalize its SOP.

New subdivision (e) adds the requirement that the SOPs shall specify the frequency and processes for cleaning, maintenance, and calibration of equipment, supplies and components, including when incubation of samples is taking place such that samples are not compromised. All cleaning, maintenance, and calibration shall be documented and dated as defined in the SOPs. To ensure patient safety, this information is required in the SOPs to ensure procedures are in place prior to the compounding so that staff are all following the same procedures.

New subdivision (f) adds the requirement for the SOPs to be reviewed on an annual basis by the PIC and that the review must be documented by the PIC consistent with the SOPs. The SOPs shall be updated to reflect changes to compounding processes, facility changes, and other changes that impact the CSP. This annual review is necessary to ensure that any procedure changes are updated within the SOPs. Additionally, changes to the SOPs must be disseminated to the affected staff prior to implementation to ensure that staff are operating in compliance with the SOPs of the facility and that all staff are following the same operating procedures.

New subdivision (g) adds the requirement that there shall be written procedures for qualification of storage, shipping containers and transportation of temperature sensitive CSPs to preserve quality standards for integrity, quality and labeled strength. To ensure patient safety, this information is required in the SOPs to ensure procedures are in place prior to the compounding so that staff are all following the same procedures.

New subdivision (h) adds notification to the regulated public that a failure to follow the facility's written SOPs shall constitute a basis for an enforcement action. A violation of any the applicable laws or regulations is always a possible basis for an enforcement action. Since the SOPs are required, this language clarifies that a failure to comply with one's own SOPs is also a basis for an enforcement action, helping to ensure that SOPs are followed by the facility and staff.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, 4126.8, 4301, 4306.5, and 4332, Business and Professions Code.

Add Section 1736.18

New section 1736.18 is added and titled “Quality Assurance and Quality Control.” An opening paragraph is added to remind the public that the processing of sterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <797>.

Existing law at Section 1751.3(a)(19) (being repealed) requires a quality assurance program compliant with section 1711, 1735.8, and 1751.7. New subdivision (a) adds the requirement here as part of the reorganization and provides that quality assurance program must comply with section 1711 and the standards contained in USP Chapter 1163, Quality Assurance in Pharmaceutical Compounding. This amendment reminds the public that they must comply with the board regulations on quality assurance programs, as well as the USP Chapter requirements, per BPC 4126.8.

Existing law at Section 1751.7(a)(2) (being repealed) requires written procedures with respect to actions to be taken in the event of a drug recall. Subdivision (a)(1) relocates and amends this requirement that the program shall have a written procedure for scheduled action, such as a recall, in the event any compounded drug preparation is discovered to be outside the expected standards for integrity, quality, or labeled strength. The addition of this language ensures that the program has a written procedure to follow prior should a problem with the preparation be identified. Having procedures in place prior to the discovery of any possible problem will ensure appropriate action can be taken timely should it be needed to ensure patient safety.

Subdivision (a)(2) adds a requirement that the program shall have a written procedure for responding to out-of-range temperature variations within the medication storage areas where a furnished drug may be returned for furnishing to another patient. The addition of this language ensures that the program has a written procedure to follow prior should a temperature issue be identified that could adversely impact the integrity of the preparation. Having procedures in place prior to the discovery of any possible problem will ensure appropriate action can be taken timely should it be needed to ensure patient safety.

New subdivision (b) adds the requirement that recalls and adverse reporting must be completed in compliance with relevant provisions of law. This addition serves as a reminder to the facility that it must comply with various reporting requirements, including state and federal requirements.

New subdivision (c) adds to the requirement that, in addition to subsection (b), all complaints made to the facility related to a potential quality problem with a CSP and all adverse events shall be reviewed by the pharmacist-in-charge within 72 hours of

receipt of the complaint or occurrence. Such review shall be documented and dated as defined in the SOPs. As the PIC is ultimately responsible for the operation of the facility, they must be aware of all quality related reports and adverse events to determine if corrective action is needed. Additionally, documenting the review as defined in the SOPs ensures that the review is taking place, serves as a reminder to the PIC should the same issue keep appearing, and provides compliance information to board staff during inspections.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, 4127.2, and 4127.8, Business and Professions Code.

Add Section 1736.19

New section 1736.19 is added and titled "CSP Handling, Storage, Packaging, Shipping, and Transport." An opening paragraph is added to remind the public that the processing of sterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <797>.

The section adds the requirement that: "Packaging materials shall protect CSPs from damage, leakage, contamination, degradation, and adsorption while also preventing transportation personnel from inadvertent exposure." While ensuring the packaging materials protect CSPs from damage, leakage, contamination, degradation, and adsorption is required by USP <797>, this language clarifies that one of the goals is to prevent inadvertent exposure to transportation personnel. This language ensures that consideration of packaging materials as they protect the CSP as well as the people who handle them.

Note is added with authority cited as sections Authority cited: Sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, and 4126.8, Business and Professions Code.

Add Section 1736.20

New section 1736.20 is added and titled "Documentation." An opening paragraph is added to remind the public that the processing of sterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <797>.

New subdivision (a) adds a requirement that records shall be maintained as required by USP Chapter 797 and the article related to sterile compounding, in a readily retrievable form, for at least three years from the date the record was created or relied upon. If only recorded and stored electronically, on magnetic media, or in any other computerized form, the records shall be maintained as specified by Business and Professions Code section 4070. The board determined that three year was the appropriate time frame as three years is the standard retention time for pharmacy related records per BPC 4081. Additionally, for consistency, the language adds the requirement for electronic records to

be stored consistent with the existing electronic record requirements.

New subdivision (b) adds a requirement that records created to be created and maintained in a manner to provide an audit trail for revisions and updates of each record document. Prior versions of each record must be maintained in a readily retrievable format and include the changes to the document, identification of individual who made the change, and the date of each change. This requirement is added to ensure an audit trail for inspection purposes so that board inspectors can identify when the a record was edited and by whom. USP Chapter 797, Section 20 specifies that documentation must comply with all laws and regulations of the applicable regulation jurisdiction. The Chapter continues that "Records must be legible and store in a manner that prevents their deterioration and/or loss. All required CRs for a particular CNSP (e.g. MFR, CR, and release inspection and testing results) must be readily retrievable for at least two years after preparation or as required by the laws and regulations, whichever is longer." The Board already requires records to be maintained for three years (e.g. BPC 4081, CCR 1735.3 (d). The USP requirements are clear that the records must be maintained to prevent deterioration and/or loss. The Board language allows for flexibility to maintain the records electronically and specifies that when maintained electronically an audit trail of changes must be maintained. The Board's proposed regulation text establishing an audit trail meets the requirements of the USP Chapter provision to prevent "loss or deterioration of records." Absent an audit trail, prior versions of a record (e.g., a master formula, etc.) would be lost if maintained in an electronic format. The Board notes that a facility can elect to maintain the paper records consistent with the Chapter and not require an electronic audit trail. The Board is trying to establish a means for electronic storage of records that meets the requirements of the USP Chapter to provide flexibility for business operations.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, 4081, 4105, 4126.8, 4127, and 4332, Business and Professions Code.

Add Section 1736.21

New section 1736.21 is added and titled "Compounding Allergenic Extracts." An opening paragraph is added to remind the public that the processing of sterile compound preparations must meet the requirements in the article and are in addition to and supplement the standards provided in USP <797>.

New subdivision (a) adds the requirement that allergenic extract compounding shall take place in a dedicated PEC and no other CSPs may be made in this PEC. The requirement is added as the quality and purity of allergenic extracts may be impacted by processing, extraction, and storage conditions, which will be exacerbated by compounding other CSPs. As it is a patient safety issue, the board determined that a dedicated PEC be utilized.

New subdivision (b) adds: “Compounding of allergenic extracts are limited to patient-specific prescriptions and the conditions limited to Category I and Category 2 CSPs as specified in USP 797.” This subdivision is necessary to ensure that allergenic extract Category 3 CSPs are not compounded due to the high risk of contamination, which is a risk to patient safety.

New subdivision (c) adds: “Any compounded stock solution shall comply with the requirements established in USP 51, Antimicrobial Effectiveness Testing and the requirement established in USP Chapter 1207, Sterile Product Packaging – Integrity Evaluation related to container closure. A compounding record is required for any compounded stock solution.” This ensures that stock solutions comply with the compounding requirements of USP Chapters 51 and 1207 due to the risk to patient safety from contamination. Additionally, compounding records are necessary so that the information is available for pharmacy staff to review during inspections.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, and 4126.8, Business and Professions Code.

Add Article 4.7 titled “Hazardous Drugs”
This article and sections are being added to address hazardous drug compounding. The title of the article was selected to track the title of USP Chapter <800>.

1737 Handling of Hazardous Drugs
New section 1737 is added and titled “Handling of Hazardous Drugs.” An opening paragraph is added to remind the public that the definitions in the section apply throughout the article and are in addition to and supplement the definitions provided in USP Chapter <800>. Finally, the section specifies that, in addition to the article 4.7, the licensee must also comply with Articles 4.5 and 4.6, based on the type of preparation being compounding (non-sterile or sterile) because USP Chapter 800 does not include all end-to-end aspects of hazardous drug (HD) compounding. The provisions are incorporated to ensure all board licensees understand the requirements.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, and 4126.8, Business and Professions Code.

1737.1 Introduction and Scope
New section 1737.1 is added and titled “Introduction and Scope.” An opening paragraph is added to remind the public that HDs must comply with USP Chapter <800>, in addition to the requirements of this article. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance.

Additionally, the language specifies that “In addition to providing consultation in compliance with section 1707.2, consultation shall be provided to the patient and/or

patient's agent concerning handling and disposal of an HD or related supplies furnished." This addition is necessary to ensure proper disposal of hazardous drugs and to avoid inadvertent exposure to the patient, patient's agent, or public, which would pose a safety risk.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, and 4126.8, Business and Professions Code.

1737.2 List of Hazardous Drugs

New section 1737.2 is added and titled "List of Hazardous Drugs." An opening paragraph is added to remind the public that HDs must comply with USP Chapter <800>, in addition to the requirements of this article. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance.

New subdivision (a) adds "The facility's list of HDs as required by USP Chapter 800 must be reviewed and approved by the designated person and the pharmacist-in-charge, professional director of a clinic, or designated representative-in-charge, as applicable. Additionally, the identity of designated person(s) is defined as a single individual approved by the pharmacist-in-charge to be responsible and accountable for the performance and operation of the facility and personnel as related to the handling of hazardous drugs. The designated person shall not exceed the scope of their issued license. When the designated person is not a pharmacist, the PIC must review all practices related to the operations of the facility that require the judgment of a pharmacist. Approval shall be documented at least every 12 months." USP <800> states that the designated person is responsible for implementing a training program and evaluating competency. The Chapter, however, does not clearly identify who the designed person or persons is/are. As the pharmacist-in-charge (PIC) is responsible for the operation of the facility, the board determined that the designated person(s) must be assigned by the PIC to be responsible and accountable for the performance and operation of the facility and personnel as related to the preparation of the HDs. The designated person is not permitted to exceed the scope of their issued license. Accordingly, when the designated person is not a pharmacist, the PIC must review all practices related to the operations of the facility that require the professional judgment of a pharmacist. As it is the PIC who is held ultimately responsible for the pharmacy's compliance with statutes and regulations, the board determined that it must be the PIC as a licensed professional to use their judgment to assign the designated person(s) responsible and accountable with respect to the HD operations. This addition ensures the responsible individual understands the requirements of USP and that they perform annual review of the facility's list of HDs.

New subdivision (b) adds: "If an assessment of risk approach is taken as authorized in USP Chapter 800, it shall be approved by the designated person and the pharmacist-in-charge, professional director of a clinic, or designated representative-in-charge, as applicable. This addition is necessary is ensure that the responsible individual

understands the requirements of USP related to risk assessments as not all board licensees may be familiar with the provisions.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, and 4126.8, Business and Professions Code.

1737.3 Types of Exposure

New section 1737.3 is added and titled "Types of Exposure." An opening paragraph is added to remind the public that HDs must comply with USP Chapter <800>, in addition to the requirements of this article. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance.

Additionally, the language specifies that each premises where HDs are handled shall ensure that all employees are aware of the types of HD exposures that may occur as referenced in the USP Chapter 800 and shall be documented in the SOPs and training documents. This addition is necessary as hazardous material exposure risk is an employee safety issue. Employees must be aware of the materials they are handling and the exposure risks to themselves and others. This requirement is in addition to the requirements of Title 8, California Code of Regulations, Division 1, Department of Industrial Relations.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, and 4126.8, Business and Professions Code.

1737.4 Responsibilities of Personnel Handling Hazardous Drugs

New section 1737.4 is added and titled "Responsibilities of Personnel Handling Hazardous Drugs." An opening paragraph is added to remind the public that HDs must comply with USP Chapter <800>, in addition to the requirements of this article. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance.

Additionally, the language specifies that: "The PIC, designated representative-in-charge, or professional director, as applicable, shall be responsible for all activities and decisions made or approved by the designated person." The language is necessary to ensure an understanding that the individual with overall responsibility of the facility is fully aware that they are also responsible for all decisions made or approved by the person(s) assigned as the designated person.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, and 4126.8, Business and Professions Code.

1737.5 Facilities and Engineering Controls

New section 1737.5 is added and titled "Facilities and Engineering Controls." An opening paragraph is added to remind the public that HDs must comply with USP Chapter <800>, in addition to the requirements of this article. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance.

New subdivision (a) adds "When containment primary engineering control (C-PECs) used for nonsterile and sterile HDs are placed in the same room, biannual certification shall document that the room can continuously maintain ISO 7 classification throughout the nonsterile compounding activity. Specific standard operating procedures (SOPs) shall be written to address the maintenance of the ISO 7 classification." This ensures that the room is continuously maintained at the appropriate ISO classification as particles from hazardous compounding can impact ISO classification. Appropriate ISO classification is necessary to avoid contamination of sterile preparations, which would be a threat to patient safety.

New subdivision (b) adds "A biological-safety cabinet as defined in USP Chapter 800 Class II Type A1 shall not be used for sterile compounding of a volatile HD." This addition is necessary to avoid contamination of the C-PEC, which would contaminate sterile preparations and would be a threat to patient safety. The Chapter identifies Class II BSC types A2, B1, or B2 as appropriate; however, it does not mention Class II Type A1. This subdivision ensures that Class II Type A1 are not used for compounding of a volatile HD as they are not suitable for work that will generate a vapor.

New subdivision (c) adds "Where a pass-through is installed in a containment secondary engineering control (C-SEC) the doors must be gasketed and interlocking. A pass-through is not allowed between the C-SEC into an unclassified space." This ensures that pass-throughs are gasketed and interlocking so that the inside and outside doors are never opened simultaneously, which could result in contamination of the area. Additionally, a pass-through is not allowed into an unclassified space because, while it is designed to minimize the passage of gases or vapors, minor transfer may still occur that can impact the sterility of the area. The Board notes that California Code of Regulations, Title 24, prohibits a passthrough between classified and unclassified spaces in the HD environment. Title 24, 1224.19.3.3.2.8 - Pass-throughs: "If a pass-through is used between the buffer and anteroom, both doors should not be capable of being open at the same time, and the doors should be interlocking. A pass-through is not permitted between the hazardous drug buffer room and any unclassified area."

New subdivision (d) adds "Where a pass-through door is installed or replaced in a secondary engineering control after [OAL insert effective date] the pass-through door shall be a HEPA purge type." This ensures that future pass-throughs doors must be HEPA purge type following the effective date of the regulation. A non-HEPA purge type pass-through can be used if it is part of an existing structure. This allows for older facilities to maintain their current structure and would not require older facilities to remodel; however, new pass-through doors installed after the effective date of the

regulation must be HEPA purge type. The board determined that new construction must meet the higher, safer standard of a HEPA purge type as they ensure the air is free of contaminants and is grandfathering in older, existing compounding facilities so that older facilities would not be required to remodel simply to install interlocking pass-through doors. If these older facilities remodel in the future, they would be required to install interlocking pass-through doors as part of that remodel if the pass through is impacted as part of the remodel.

New subdivision (e) adds “Facility room pressure monitoring equipment shall be placed consistent with CETA Guidelines CAG-003:2022. SOPs shall address corrective and remedial actions in the event of pressure differentials and air changes per hour excursions.” This is existing law at section 1751.4(g) (being repealed) and is relocated here as part of the reorganization. This ensures the requirement to comply with CETA Guidelines for room pressure monitoring is maintained and having procedures in place prior to the discovery of any possible problem will ensure appropriate action can be taken timely should it be needed to ensure patient safety.

New subdivision (f) adds “Containment Supplemental Engineering Controls (CSTDs) shall not be used to extend the in-use time, BUD, or expiration of any manufactured product or HD CSP.” This addition is necessary to ensure that CSTDs are not used to extend timelines, BUDs, or expiration dates. According to USP, some CSTDs have been shown to limit the potential of generating aerosols during compounding; however, there is no certainty that all CSTDs will perform adequately. As performance is not guaranteed, the use poses a patient safety risk and is therefore not allowed.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, and 4126.8, Business and Professions Code.

1737.6 Environmental Quality and Control

New section 1737.6 is added and titled “Environmental Quality and Control.” An opening paragraph is added to remind the public that HDs must comply with USP Chapter <800>, in addition to the requirements of this article. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance.

New subdivision (a) adds “The SOPs of a premises where HDs are handled shall address environmental wipe sampling for HD surface residue, its frequency, areas of testing, levels of measurable contamination, and actions when those levels are exceeded.” As there are currently no studies demonstrating the effectiveness of a specific number or size of wipe samples in determining levels of HD contamination, the facility must establish their specific procedures based on their business practices. While there is no standard, the facility must still perform the sampling to check for contamination and take action to clean any contaminated areas. The Board notes that the Board is only requiring an SOP to describe environmental wipe sampling. SOPs must provide site-specific information as the SOP will define what is necessary for the

facility. For example, an SOP related to environmental wipe samples would most likely be different for a hospital versus an oncology infusion pharmacy specializing in compounding chemotherapy agents. The environmental wipe sampling provides the facility with an understanding of exposure risks in the various environments. The facilities SOPs will determine the spaces, frequency, etc.

New subdivision (b) adds the following: “When actionable levels of contamination is found, at minimum the following shall occur as described in the SOPs:

(1) Reevaluate work practices;
(2) Reevaluate the appropriateness of deactivation, decontamination and cleaning agents;
(3) Re-train personnel on deactivation, decontamination and cleaning; and
(4) Re-train personnel on donning and doffing appropriate personal protective equipment (PPE).”

While the Chapter includes these actions as discretionary recommendations, the language makes them mandatory here to ensure that the actionable levels of contamination are examined, addressed, and actions to taken to prevent future possible contamination issues. The Board notes that the facility's SOP will define how and when wipe sampling will be performed. Any cost associated with wipe sampling would be a function of the facility's SOP. i.e. IF the facility's SOPs established a requirement for wipe sampling in the BSC, THEN a cost would be incurred. However, IF the facility’s SOP does not require wipe sampling in the BSC, the facility would not incur those costs.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, and 4126.8, Business and Professions Code.

1737.7 Personal Protective Equipment (PPE)

New section 1737.7 is added and titled “Personal Protective Equipment (PPE).” An opening paragraph is added to remind the public that HDs must comply with USP Chapter <800>, in addition to the requirements of this article. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance. These requirements are in addition to the requirements of Title 8, California Code of Regulations, Division 1, Department of Industrial Relations.

New subdivision (a) adds “Two pairs of gloves that meet the ASTM D-6978 standard shall be worn for handling HD waste, cleaning HD spills, and performing routine cleaning in HD areas.” Existing law at section 1751.4 (being repealed), requires two pairs of gloves that meet the ASTM D-6978 standard, which is being maintained and relocated due to the overall reorganization; however, the language is clarifying that the two pairs of gloves shall be worn when handling HD waste, spills, and routine cleaning. This requirement is in addition to the requirement of USP <800> and relevant chapters. Two pairs of gloves are necessary for safety to prevent exposure to hazardous materials.

New subdivision (b) adds “The outer pair of gloves that meets the ASTM D-6978 standard chemotherapy gloves shall be changed every 30 minutes during compounding unless otherwise recommended by the manufacturer’s documentation. Documentation from the manufacturer shall be readily retrievable. For sterile compounding both pairs of gloves labeled to meet the ASTM D-6978 standard shall be sterile.” While the Chapter recommends this standard, the board makes it mandatory here to ensure sterility because outer gloves may become permeable after time and use.

New subdivision (c) adds “Outer gloves used for HD compounding shall be changed between each different HD preparation. This addition is necessary to ensure that the outer gloves are changed when switching to a different HD drug to prevent inadvertent cross contamination. Additionally, the Board notes that the type of glove required for BSCs is established within the Chapter and not the Board's regulation. Further, the Board notes that its regulation text could require more frequent changing of gloves, depending on business practice to prevent cross-contamination and these costs are identified under Business Impact below. Note: an online search reveals that the cost of a pair of gloves is about $.14/pair. ASHP guidance notes that many studies show that areas where HDs are handled have significant surface contamination and promotes that outer gloves be removed before labeling or removing the preparation from the C-PEC.

New subdivision (d) adds “PPE shall be removed to avoid transferring contamination to skin, the environment, and other surfaces. PPE worn during compounding shall be disposed of in the proper waste container before leaving the C-SEC. SOPs shall detail the donning and doffing of PPE and where it takes place in the C-SEC.” While the Chapter recommends these standards, the board makes it mandatory here to ensure that cross contamination cannot occur. Additionally, as personnel are working with hazardous materials, it is necessary to ensure they understand that PPE must also be treated as hazardous.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, and 4126.8, Business and Professions Code.

1737.8 Hazard Communication Program

New section 1737.8 is added and titled “Hazard Communication Program.” An opening paragraph is added to remind the public that HDs must comply with USP Chapter <800>, in addition to the requirements of this article. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance. These requirements are in addition to the requirements of Title 8, California Code of Regulations, Division 1, Department of Industrial Relations.

Additional language is added to specify that the designated person shall develop the premise’s hazardous communication program and document the program in the SOPs and training documents. The purpose of a Hazard Communication Program is to inform

employees of the hazards associated with chemicals in their workplace to ensure effective training regarding proper labeling, transport, storage, disposal of the HDs, use of Safety Data Sheets, and appropriate labeling of chemicals. A communication program is necessary to ensure worker safety due to the risk of harm from hazardous material. As the designated person maintains the operations of the facility, they must develop the program. The program must be documented in the SOPs to ensure that staff are aware of the program and allow for review by board staff during inspections.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, and 4126.8, Business and Professions Code.

1737.9 Personnel Training

New section 1737.9 is added and titled Personnel Training." An opening paragraph is added to remind the public that HDs must comply with USP Chapter <800>, in addition to the requirements of this article. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance.

New subdivision (a) adds "Any person assigned to provide the training specified in this Article shall have demonstrated competency in the skills in which the person will provide training or observe and measure competency described in the facilities SOPs as referenced in section 1737.17. Documentation must be maintained demonstrating compliance with training requirements and demonstrating competency must be maintained." The requirement is necessary to ensure that the individual assigned to provide the training to personnel has sufficient knowledge and expertise to provide the training. Additionally, documentation must be maintained for review during board staff inspections to ensure appropriate training has been provided in the interest of patient safety.

New subdivision (b) adds "All personnel responsible for handling HD who fail any aspect of training in handling HDs shall not handle HDs until after successfully passing reevaluations in the deficient area(s), as detailed in the facility's SOPs." If personnel fail ongoing training and evaluation, patient safety must take priority and those individuals must not be involved in handling HDs or the oversight of the preparations as it poses a risk to patient safety and employee safety.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, and 4126.8, Business and Professions Code.

1737.10 Receiving

New section 1737.10 is added and titled "Receiving." An opening paragraph is added to remind the public that HDs must comply with USP Chapter <800>, in addition to the requirements of this article. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance.

Additionally, the language adds “All HD APIs and antineoplastic HDs shall be shipped and received from the supplier in segregated impervious plastic and labeled “Hazardous Drugs” on the outside of the delivery container.” While USP Chapter <800> recommends that “HDs should be received from the supplier in impervious plastic to segregate them from other drugs and to allow for safety in the receiving and internal transfer process,” the board determined that it is necessary to avoid contamination in the event of a spill during the shipping and receiving of an API and that the package also be immediately identifiable as a hazardous product to protect those handling the package.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, and 4126.8, Business and Professions Code.

1737.11 Labeling, Packaging, Transport and Disposal

New section 1737.11 is added and titled “Labeling, Packaging, Transport and Disposal.” An opening paragraph is added to remind the public that HDs must comply with USP Chapter <800>, in addition to the requirements of this article. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance.

New subdivision (a) adds “Any compounded HD preparation dispensed to a patient or readied for dispensing to a patient shall also include on the label the information required by Business and Professions Code section 4076 and section 1707.5.” This is existing law within section 1751.2 (being repealed) and is being retained and moved here as part of the reorganization. Accurate and complete labeling is essential for dispensed medication to ensure patient safety; therefore, it is essential to ensure that the public has a clear understanding of the labeling requirements.

New subdivision (b) adds “All HD APIs and antineoplastic HDs shall be transported from the facility in an impervious plastic container and labeled as HD on the outside of the container.” This is added to provide clarity to the regulated public. While USP Chapter <800> recommends that “HDs should be received from the supplier in impervious plastic to segregate them from other drugs and to allow for safety in the receiving and internal transfer process,” this section requires the use of a impervious plastic container to prevent the leech of chemicals from the plastic into or out of the API and additionally requires a label on the outer container for safety of those that may come in contact with the container during transport and handling.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, and 4126.8, Business and Professions Code.

1737.12 Dispensing Final Dosage Form

New section 1737.12 is added and titled "Dispensing Final Dosage Form." An opening paragraph is added to remind the public that HDs must comply with USP Chapter <800>, in addition to the requirements of this article. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance.

Additionally, the language adds "Equipment used in nonsterile HD compounding shall be dedicated for use with HDs and shall be decontaminated after each use." While these recommendations are established in the Chapter as discretionary, the board is requiring the dedicated use and decontaminated to prevent possible cross contamination and to ensure the quality and integrity of the preparation.

Note is added with authority cited as sections 4005, 4126.8, and 4127, Business and Professions Code. Additionally, references are cited as Sections 4005, and 4126.8, Business and Professions Code.

1737.13 Compounding

New section 1737.13 is added and titled "Compounding." An opening paragraph is added to remind the public that HDs must comply with USP Chapter <800>, in addition to the requirements of this article. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance.

New subdivision (a) adds "A disposable preparation mat shall be placed on the work surface of the C-PEC when compounding HD preparations. Where the compounding is a sterile preparation, the preparation mat shall be sterile. The preparation mat shall be changed immediately if a spill occurs, after each HD drug, and at the end of daily compounding activity." While these recommendations are included in the Chapter as discretionary, the board has established them as requirements to reduce the risk of cross contamination as well as to ensure the sterility of the environment. Note: an online search shows that a sterile preparation mat is about $1.08/mat and a nonsterile preparation mat is about $0.74/mat.

New subdivision (b) adds "Only one HD drug may be handled in a C-PEC at one time." This requirement is necessary to reduce the risk of cross contamination and ensures the quality and integrity of the preparation.

Note: Authority cited: Sections 4005, 4126.8, and 4127, Business and Professions Code. Reference: Sections 4005, and 4126.8, Business and Professions Code.

1737.14 Administering

New section 1737.14 is added and titled "Administering." An opening paragraph is added to remind the public that HDs must comply with USP Chapter <800>, in addition to the requirements of this article. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance.

New subdivision (a) adds “When dispensing an HD to a patient or caregiver for administration, the pharmacy shall:

(1) Place the HD in a decontaminated impervious plastic container with an HD label on the outside of the container; and
(2) For an antineoplastic HD, attach and prime all tubing and attach a CSTD when appropriate.”

While USP Chapter <800> provides “HDs should be received from the supplier in impervious plastic to segregate them from other drugs and to allow for safety in the receiving and internal transfer process,” additional requirements are necessary for dispensing HDs to maintain the safety of those that may come in contact with the container during dispensing and administration.

New subdivision (b) adds “When furnishing an antineoplastic HD, a sufficient supply of gloves that meet the ASTM D-6978 standard to allow for appropriate administration, handling, and disposal of HD drugs by the patient or the patient’s agent shall be provided.” The board determined that adding this requirement is necessary to protect the patient, patient’s agent, or anyone assisting the patient with their medication.

Note: Authority cited: Sections 4005, 4126.8, and 4127, Business and Professions Code. Reference: Sections 4005, and 4126.8, Business and Professions Code.

1737.15 Deactivation, Decontamination, Cleaning, and Disinfecting

New section 1737.15 is added and titled “Deactivation, Decontamination, Cleaning, and Disinfecting.” An opening paragraph is added to remind the public that HDs must comply with USP Chapter <800>, in addition to the requirements of this article. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance.

New subdivision (a) adds “Deactivating, decontaminating, cleaning, disinfecting, and sporicidal agents shall be used in accordance with manufacturers' specifications and shall be surface compatible.” This addition ensures that agents used for cleaning, sanitizing, and sterilization must be used consistent with the manufacturers’ specifications. This is necessary to ensure the products are used as intended.

New subdivision (b) adds “Agents used for deactivation, decontamination, cleaning, and disinfecting all areas and equipment involved in HD handling shall be applied through the use of wipes wetted with appropriate solution and shall not be applied or delivered to the wipe by use of a spray bottle to avoid spreading HD residue.” The board determined that this addition is necessary to protect the employee from inadvertent exposure to hazardous material and patients from cross contamination.

New subdivision (c) adds “SOPs shall include procedures for deactivation and decontamination of the HD preparation container closure and shall be approved by the pharmacist-in-charge or professional director of a clinic, as applicable.” The requirement

of SOPs for decontamination and deactivation are included in USP Chapter <800>. The board further determined that the individual responsible for the operation of the facility must approve all practices, i.e., the SOPs, related to the operations of the facility.

Note: Authority cited: Sections 4005, 4126.8, and 4127, Business and Professions Code. Reference: Sections 4005, and 4126.8, Business and Professions Code.

1737.16 Spill Control

New section 1737.16 is added and titled "Spill Control." An opening paragraph is added to remind the public that HDs must comply with USP Chapter <800>, in addition to the requirements of this article. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance.

New subdivision (a) adds "The premises shall maintain a list of properly trained and qualified personnel able to clean up an HD spill. An SOP shall outline how such a qualified person will be available at all times while HDs are handled." The personnel cleaning HD spills require specific training; it is necessary for the facility to maintain a list of who has received the training so it can easily and quickly be referenced should a spill occur. Additionally, due to the specialized nature of the task, a qualified person must be available at all times when HD materials are being handled. Accordingly, the SOPs must document the procedures to ensure that all this occurs.

Note: Authority cited: Sections 4005, 4126.8, and 4127, Business and Professions Code. Reference: Sections 4005, and 4126.8, Business and Professions Code.

1737.17 Documentation and Standard Operating Procedures

New section 1737.17 is added and titled "Documentation and Standard Operating Procedures." An opening paragraph is added to remind the public that HDs must comply with USP Chapter <800>, in addition to the requirements of this article. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance.

New subdivision (a) adds "Any premises engaged in the compounding or handling of HDs shall maintain and follow written SOPs." This ensures that SOPs are established and followed by the facility and staff. For patient and employee safety, following an entity's SOPs is necessary.

New subdivision (b) is added and reads as follows:
"The SOPs for compounding or handling HDs shall include at least the following:

(1) Hazard communication program
(2) Occupational safety program
(3) Designation of HD areas
(4) Receipt
(5) Storage
(6) Compounding, if applicable

(7) Use and maintenance of proper engineering controls (e.g., C-PECs, C-SECs, and CSTDs), if applicable
(8) Hand hygiene and use of PPE based on activity (e.g., receipt, transport, compounding, administration, spill, and disposal), if applicable
(9) Deactivation, decontamination, cleaning, and disinfection
(10) Dispensing, if applicable
(11) Transport
(12) Administering, if applicable
(13) Environmental monitoring (e.g., wipe sampling)
(14) Disposal
(15) Spill control
(16) Medical surveillance"

While these items are included in the Chapter as recommendations, the board is requiring these topics in the SOPs to ensure appropriate training and knowledge of staff. The board has determined that the items must be included to ensure employee protection and patient safety.

New subdivision (c) adds the requirement for the SOPs to be reviewed on an annual basis by the PIC, professional director of a clinic, or the designated representative in charge (DRIC) in coordination with the designated person and that the review must be documented consistent with the SOPs. To ensure safe practices, the SOPs must be updated to reflect changes to compounding processes, facility changes or other changes that impact the CSP. This annual review is necessary to ensure that any procedure changes are regularly reviewed and updated, as necessary, within the SOPs.

New subdivision (d) adds the requirement for the SOPs to be updated when standard operating procedures change. Additionally, changes to the SOP must be disseminated in written format to the staff responsible for handling HDs prior to implementation to ensure that staff are operating in compliance with the SOPs of the facility and that all staff are following the same operating procedures. All notifications of such changes and the changes shall be documented in the SOPs and training documents. Again, to ensure safe practices, the SOPs must be timely updated to reflect changes. Maintaining these documents is necessary for board review to ensure that staff are receiving the appropriate training and education on the SOPs.

New subdivision (e) adds the advisement that a failure to follow the facility's written SOPs constitute a basis for enforcement action. While a violation of any the applicable laws or regulations is always a possible basis for an enforcement action, since the SOPs are required, this language clarifies that a failure to comply with one's own SOPs is also a basis for an enforcement action, helping to ensure that SOPs are followed by the facility and staff.

Note: Authority cited: Sections 4005, 4126.8, and 4127, Business and Professions Code. Reference: Sections 4005, and 4126.8, Business and Professions Code.

Add Article 4.8 Radiopharmaceuticals - Preparation, Compounding, Dispensing, and Repackaging.

An opening paragraph is added to remind the public that the requirements of this article are in addition to the compounding standards in USP Chapter <825>, which is the USP Chapter specific to radiopharmaceuticals. Licensees must comply with the compounding standards specified in the current version of the USP per BPC 4126, which includes Chapter <825>. This article and sections are being added to address compounding of radiopharmaceuticals, which were previously regulated under sections 1708.3, 1708.4, and 1708.5 of this Title and repealed as previously indicated. The title of the article tracks the title of USP Chapter <825>.

Note is added with authority cited as sections 4005, 4008 and 4126.8, Business and Professions Code. Additionally, references are cited as Sections 4005, 4126.8, 4301, and 4306.5,, Business and Professions Code.

Add Section 1738

New section 1738 is added and titled “Definitions.” An opening paragraph is added to remind the public that the definitions within the section and article are in addition to and supplement the standards provided in USP <825>. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance.

New subdivision (a) adds the definition of “Added substances” to mean “ingredients that are necessary to compound a preparation but are not intended or expected to cause a pharmacologic response if administered alone in the amount or concentration contained in a single dose of the compounded preparation. The term is used synonymously with the terms inactive ingredients, excipients, and pharmaceutical ingredients.” The board determined that this definition is necessary as it is not included in USP <825> and it ensures that the public understands the different terminology utilized for inactive ingredients. Defining the different terminology will ensure clarity within the regulations.

New subdivision (b) adds the definition of “Component” to mean “any ingredient used in the compounding of a preparation, including any active ingredient, added substance, or conventionally manufactured product.” The board determined that this definition is necessary as it is not included within USP <825> and it ensures that the public understands the meaning of the term within the board’s regulations.

New subdivision (c) adds the definition of “Designated person” to mean “a pharmacist identified as assigned, responsible, and accountable for the performance and operation of the radiopharmaceutical processing facility and for personnel who prepare, compound, dispense, and repackage radiopharmaceuticals.” This term is defined within this section, specific to this article and is different from the definition in other articles. The board determined that the designated person must be a pharmacist due to the radiation safety

considerations and contamination control required for compounding radiopharmaceuticals.

New subdivision (d) adds the definition of “Processing,” “processed” or “processing activity” to mean “the preparation, compounding, repackaging, or dispensing of a radiopharmaceutical.” The board determined that this definition is necessary as it is not included within USP <825> and is utilized within the Chapter. Defining the different terminology will ensure clarity within the regulations.

Note is added with authority cited as sections 4005, 4008 and 4126.8, Business and Professions Code. Additionally, references are cited as Sections 4005, 4126.8, 4301, and 4306.5, Business and Professions Code.

Add Section 1738.1

New section 1738.1 is added and titled “Introduction.” An opening paragraph is added to remind the public that the standards within the section and article are in addition to and supplement the standards established in USP <825>. As compliance with USP is required by BPC section 4126.8, reminding the public of requirement will help ensure compliance.

New subdivision (a) adds the requirement for “the use of technologies, techniques, material, and procedures not described in USP 825 shall be based upon published peer-reviewed literature or documents and meet FDA approved labeling requirements in accordance with sections 201.56 and 201.57 of title 21, Code of Federal Regulations, showing the technologies, techniques, material, and procedures to be equivalent or superior to those described in USP Chapter 825.” As compounding must be completed in compliance with t the USP, the board determined that any technology, technique, material, or procedure that is utilized by a facility must comply with the USP. However, technologies and techniques may improve or advance prior to the update of the USP; accordingly, the board determined that these advances in techniques could be used should published peer-reviewed literature show that the methods are, at minimum, equal or superior to the methods in USP <825>. Advances in technology and techniques that are equal to or superior would be a benefit to patients.

New subdivision (b) adds the requirement for processing with human whole blood or human whole blood derivatives to be done in compliance with Health and Safety Code (HSC) section 1602.5. As radiopharmaceutical compounding can include the use of a blood component, adding this language ensures that the public is aware of the requirements in HSC 1602.5.

Note is added with authority cited as sections 4005, 4008 and 4126.8, Business and Professions Code. Additionally, references are cited as Sections 4005, 4126.8, 4301, and 4306.5, Business and Professions Code.

Add Section 1738.2

New section 1738.2 is added and titled “Radiation Safety Considerations.” An opening paragraph is added to remind the public that the processing of radiopharmaceuticals must meet the radiation safety requirements in the article and are in addition to and supplement the standards provided in USP <825>. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance.

New subdivision (a) adds “Radiation detectors and measuring devices, and other necessary equipment may be placed inside an ISO Class 5 PEC but must be placed in a manner that minimizes disruptions of airflow.” This subdivision is added to identify the appropriate type of materials, and the placement of devices within the PEC that must minimize disruption of airflow versus the discretionary recommendation in USP <825>. If there is a spill, a disruption of airflow could spread the radioactive material outside the room, which could potentially contaminate outside areas or staff.

New subdivision (b) adds “Disposable absorbent pads shall be changed after each type of radiopharmaceutical processing.” The board determined that, while the Chapter does not specify a requirement to change the pad after each type of radiopharmaceutical processing, the pad must be changed to avoid cross contamination and ensure the quality and integrity of the radiopharmaceutical.

New subdivision (c) adds “Any deviation made to lower radiation exposure to workers shall be evaluated and documented in an SOP by the designated person prior to the deviation occurring. Exceptions to the environmental controls requirements must be documented in the specific radioactive materials license conditions issued by the California Department of Public Health pursuant to section 30190 of Title 17 of the California Code of Regulations, or a specific radioactive materials license issued by another state or the United States Nuclear Regulatory Commission pursuant to pursuant to section 32.72 of title 10 of the Code of Federal Regulations.” A deviation is a change in the step-by-step procedures of the preparation that may result in the same finished radiopharmaceutical, but incorporates improvements in technology or decreased radiation exposure to pharmacy personnel. This requirement is necessary to ensure that the SOP documents the necessity of any deviation. This documentation is then retained as an SOP and available during an inspection by board inspectors.

Note is added with authority cited as sections 4005, 4008, and 4126.8, Business and Professions Code. Additionally, references are cited as Sections 4005, 4126.8, 4301, and 4306.5, Business and Professions Code.

Add Section 1738.3

New section 1738.3 is added and titled “Immediate Use of Sterile Radiopharmaceuticals.” The section specifies that “processing of radiopharmaceuticals for immediate use may only be done in a patient care setting meeting the applicable requirements in this Article.” Additionally, it specifies that “the patient care facility shall maintain all records required in Section 9 of USP Chapter 825 in accordance with

Business and Professions Code section 4081." This section is necessary to ensure immediate use sterile radiopharmaceuticals are only processed in a patient care setting due to the limited BUD and specificity of that immediate use is intended for a single patient, as specified in the Chapter. Additionally, due to the lack of engineering controls with immediate use sterile radiopharmaceuticals, use must be limited. The subdivision also addresses the necessary documentation that must be maintained for patient safety and audit purposes.

Note is added with authority cited as sections 4005, 4008, and 4126.8, Business and Professions Code. Additionally, references are cited as Sections 4005, 4081, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

Add Section 1738.4

New section 1738.4 is added and titled "Personnel Qualifications, Training, and Hygiene." An opening paragraph is added to remind the public that the processing of radiopharmaceuticals must meet the requirements in the article and are in addition to and supplement the standards provided in USP <825>. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance.

New subdivision (a) adds the following "Processing personnel experiencing any of the following: rashes, recent tattoos or oozing sores, conjunctivitis, active respiratory infection or other conditions that could contaminate a sterile radiopharmaceutical or the environment shall not be allowed to enter the compounding area unless approved by the designated person. Any approvals provided by the designated person shall be documented and the record shall include the name of the individual granted approval, the approval date and time, the reason for granting approval, and the identification of the designated person making the decision." This addition is needed to prevent contamination and ensure the quality and integrity of the radiopharmaceutical. If the designated person to approving the individual to enter, they must document their name, the individuals name, the date and time, and reason. Documentation of this information provides an additional level of accountability for the designated person.

New subdivision (b) adds the requirement for the pharmacist with direct oversight over personnel performing radiopharmaceutical processing shall, as defined in the facility's SOPs, demonstrate proficiency in the skills necessary to ensure the integrity, strength, quality, and labeled strength of radiopharmaceuticals. As the pharmacist is responsible for the oversight of staff performing the processing, they must be proficient in the skills needed to monitor the work product of the personnel to ensure the quality and integrity of the radiopharmaceutical.

New subdivision (c) adds the following requirement:
"Aseptic manipulation competency initial training and competency and ongoing training and competency documentation shall include the Primary Engineering Control (PEC's) type and PEC unique identifier used during the evaluation. Aseptic manipulation

competency evaluation and requalification shall be performed using the same procedures, type of equipment, and materials used in aseptic compounding. Aseptic qualifications from one premises may be used for another premises if all of the following conditions are met:

(1) The SOPs related to compounding are identical.
(2) The SEC facility designs are sufficiently similar to accommodate the use of the same SOPs.
(3) The PECs are of the same type and sufficiently similar to accommodate the use of the same SOPs describing use and cleaning."

This subdivision includes the requirements for aseptic manipulation competency at multiple locations. As some facilities have staff that work at different locations, the addition of this language allows staff to more easily work at different locations, provided that the three requirements are met, with a single training and competency evaluation.

New subdivision (d) adds the following "SOPs must clearly define the acceptable use and cleaning for reusable gowns in order to prevent possible contamination of the Sterile Radiopharmaceuticals and designated compounding area. The facility's SOPs must describe the process to be followed should the facility allow for the reuse of garb." The Chapter is silent on the cleaning requirements of reusable gowns. Therefore, to ensure the quality and integrity of the radiopharmaceutical, the language is added that the SOPs must define the use and cleaning of the gowns as appropriate to the facility to prevent contamination.

New subdivision (e) adds the requirement for eyeglasses to be cleaned as part of hand hygiene and garbing, consistent with the standards specified in the SOPs. This requirement ensures eyeglasses are cleaned appropriately, which will prevent cross contamination in a benefit to patient safety by ensuring the quality and integrity of the radiopharmaceutical.

New subdivision (f) adds the following: "Garb shall be donned and removed in an ante-area or immediately outside the segregated radiopharmaceutical processing area (SRPA). Donning and doffing garb shall not occur in the anteroom at the same time unless the SOPs define specific processes that must be followed to prevent contamination." The requirement to garb in the ante-area or outside the SRPA ensures that garbing is clean and prevents cross contamination. Additionally, appropriately doffing garb will prevent cross contamination of new, clean garbs.

Note is added with authority cited as sections 4005, 4008 and 4126.8, Business and Professions Code. Additionally, references are cited as Sections 4005, 4126.8, 4301, and 4306.5, Business and Professions Code.

Add Section 1738.5

New section 1738.5 is added and titled "Facilities and Engineering Controls." An opening paragraph is added to remind the public that the processing of

radiopharmaceuticals must meet the requirements in the article and are in addition to and supplement the standards provided in USP <825>. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance.

New subdivision (a) adds "A sink used for compounding or hand hygiene shall not be part of a restroom or water closet." While USP <825> provides a standard for sinks used during compounding, it does not address a sink being located as part of restroom facilities or water closet. Due to the possible contamination and sanitation issues, the board determined that it was necessary to provide additional clarity that the sink used for compounding or hand hygiene cannot be in the restroom or water closet.

New subdivision (b) adds the requirement for the temperature to be monitored, either manually or by a continuous recording device, in SRPAs and classified areas each day that processing is performed. Although Chapter <825> requires daily monitoring of the temperature within classified areas, it is silent on SRPAs. As SRPAs must be continuously maintained at a temperature of 25 degrees or cooler per USP, the board determined that temperature monitoring of SRPAs should also be done to ensure that the temperature in that area is maintained.

New subdivision (c) adds the requirement for storage and elution of non-direct infusion radionuclide generators to take place in an ISO Class 8 or better area. Chapter <825> states that an SRPA that meets ISO Class 8 specifications can also be used for this type of storage, the board's language specifies that storage and elution of non-direct infusion radionuclide generators can only be done in an ISO Class 8 or better area and prohibits the use of an SRPA that is located outside an ISO Class 8 or better area to prevent accidental cross contamination from transferring supplies and materials from lower quality classified areas to higher quality.

New subdivision (d) adds the requirement "If an SRPA is used:

(1) Except for walls, the SRPA's visible perimeter shall be at least 1 meter from all sides of the PEC or in a separate room.
(2) Surfaces within the SRPA shall be smooth, impervious, free from cracks and crevices, and non-shedding so they can be easily cleaned and disinfected and to minimize spaces in which microorganisms and other contaminants can accumulate.
(3) Compounding shall not take place in the SRPA."

Chapter <825> is clear that an SRPA is only suitable for radiopharmaceutical preparation (with and without minor deviations), dispensing, and repackaging, and not compounding. This requirement specifies the visible perimeter of the SRPA to prevent accidental contamination of other compounded preparations from disrupted airflow, which may adversely impact the air quality in the PEC.

New subdivision (e)(1) adds the requirement for "Testing and certification of all classified areas shall be completed by a competent individual. A competent individual is a

technician who possesses a current accreditation issued by The Controlled Environment Testing Association (CETA), or who is under the direct supervision of an individual who possesses a current accreditation issued by CETA. The facility shall review and maintain a copy of the accreditation documentation in accordance with requirements in section 1738.9."

New subdivision (e)(2) adds the requirement for "Certification shall be completed consistent with the provisions established in the USP Chapter 797, titled "Pharmaceutical Compounding—Sterile Preparations" (USP Chapter 797). CETA standard(s) used to perform certification testing in all classified areas shall be recorded on the certification report as required and specified in USP Chapter 797."

Subdivisions (e)(1) and (e)(2) adds the requirement that the certification must be done by a qualified technician. The use of a qualified technician for testing and certification is required by the Chapter; however, the Chapter is silent on the qualifications of the technician. These subsections implement the Chapter further by requiring that the technician for testing and certification understand the CETA certifications methods and the standards to ensure that appropriate evaluation of the areas is completed as inappropriate certification may result in contamination of drug products and be a risk to patient safety.

New subdivision (f) adds the following: "SOPs shall specify steps to be taken if any classified area fails to meet the specified ISO classification including the investigative and corrective actions, allowable activities, and retesting procedures." The addition of this language ensures that the program has written procedures to follow should a classified area(s) fail to meet the specified ISO classification. To ensure patient safety, having procedures in place prior to the discovery of any possible problem will ensure appropriate action can be taken timely should a problem be identified. Identifying the steps to investigate the cause of the failure and what processing can be completed until that area meets the required classification are necessary for patient safety.

New subdivision (g) adds the following: "All classified spaces and equipment must be recertified when there is any change in the Primary Engineering Control (PEC), or the compounding environment. For purposes of this subsection, a change includes when the PEC is moved, repaired, or replaced, when the facility is modified in a manner that affects airflow or traffic patterns, or when improper aseptic techniques are observed. SOPs must address the conditions under which recertification must also be completed when temporarily moving or permanently relocating a PEC." To ensure patient safety, having procedures in place prior to the need to move, repair, or replace the PEC will ensure appropriate action can be taken timely should it be needed.

New subdivision (h) adds the following: "Activities and tasks carried out within the SRPA and classified areas shall be limited to only those necessary for processing a radiopharmaceutical." The Chapter is silent on prohibited activities t within the SRPA and classified areas, e.g., eating. The added language is necessary to restrict activities

in these areas to those solely necessary for processing of radiopharmaceuticals for patient safety to prevent cross contamination.

New subdivision (i) adds the following: “Food, drinks, and materials exposed in patient care and treatment areas must not enter SRPA or classified areas.” This added language is necessary to avoid any cross-contamination.

New subdivision (j) adds the following: “A dynamic airflow smoke pattern test must be performed initially and at least every 6 months for all classified spaces and equipment. All dynamic airflow smoke pattern tests shall be immediately retrievable during inspection. A copy of the test shall be provided to the Board’s inspector if requested in accordance with the timeframes set forth in Section 4105 of the Business and Professions Code.” Under various provisions of pharmacy law, the board must confirm compliance with compounding operations prior to issuance or renewal. A review of smoke studies may be part of the assessment and must be provided if requested to ensure compliance prior to renewal. The initial smoke study is required prior to compounding to demonstrate a proper environment for safe compounding. Additionally, biannual smoke studies are required by Chapter <825>.

Note is added with authority cited as sections 4005, 4008 and 4126.8, Business and Professions Code. Additionally, references are cited as Sections 4005, 4081, 4105, 4126.8, 4301, 4306.5, and 4332, Business and Professions Code.

Add Section 1738.6

New section 1738.6 is added and titled “Microbiological Air and Surface Monitoring.” An opening paragraph is added to remind the public that the processing of radiopharmaceuticals must meet the requirements in the article and are in addition to and supplement the standards provided in USP <825>. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance.

New subdivision (a) adds the following: “SOPs shall specify steps to be taken for processing radiopharmaceuticals when the microbiological air and surface monitoring action levels are exceeded, including the investigative and corrective actions, allowable activities, and resampling procedures.” This language ensures that the SOPs specify the actions to be taken when action levels have been exceeded. The Chapter is silent on any requirement for the SOPs to detail out the action steps. To ensure patient safety, having procedures in place prior to the discovery of any possible problem will ensure appropriate action can be taken timely should a problem be identified.

New subdivision (b) adds the following: “In addition to the SOPs at a minimum every 6 months, air and surface sampling results shall be identified to at least the genus level, regardless of the colony forming units (CFU) count to trend for growth of microorganisms. Trends of microorganism growth must be identified and evaluated. SOPs shall specify the appropriate action(s) necessary to remedy identified trends.”

The Chapter requires that testing be completed every 6 months; it only requires, however, genus level identification if the CFU count exceeds a specific value. The proposed language strengthens testing by requiring the identification regardless of the count, as the appropriate response could vary depending on the microorganism. As indicated in the ASHP release "Pharmacy Environmental Monitoring (EM) Implementation Toolkit (underlying data number 20) - "A hallmark of a strong EM program is the measurement of progress in order to continuously program compounding conditions, and effectively correct excursions." This document further provides metrics to consider during tracking efforts and descriptions of the benefits of the trending. The Board notes that the ASHP document recommends monitoring monthly; however, the Board's proposed regulation text only requires trending every six months. Further as noted in USP Chapter 1161, "Particulate counts as well as microbial counts within controlled environments vary with the sampling locations and the activities being conducted during sampling. Monitoring the environment for nonviable particulates and microorganisms is an important control function because they both are important in achieving product compendial requirements for Foreign and Particulate Matter and Sterility in Injections and Implanted Drug Products." Also included in Chapter 1161, "Environmental microbial monitoring and analysis of data by qualified personnel can assist in ensuring that a suitable state of control is maintained." And the Chapter further provides, "Since the advent of comprehensive environmental monitoring programs, their applications in capturing adverse trends or drifts has been emphasized."

New subdivision (c) adds the following: "The designated person shall review and identify data trends for all the sampling results. The designated person shall evaluate trends to determine if corrective action is needed. The results of the review shall be documented in the facility's SOPs and readily retrievable during inspection in accordance with the requirements in section 1738.9." The board determined that while the Chapter speaks to trending, it does not provide specific provisions for the review of the data. The proposed language is necessary to require the data review to ensure corrective action is taken as needed to safeguard the quality and integrity of the radiopharmaceutical.

New subdivision (d) adds the following: "Environmental sampling shall be done in compliance with the Controlled Environment Testing Association (CETA)'s Certification Application Guide USP <797> Viable Environmental Sampling & Gowning Evaluation (CAG-009, Revised October 2022), which is hereby incorporated by reference." The proposed language further implements the Chapter's environmental sampling requirements by specifying compliance with the CETA guidelines. CETA guidelines establish an industry-based minimum set of criteria appropriate for performance evaluation and certification of facility and environmental controls used for compounding sterile preparations. This minimum set of criteria are necessary to ensure consistent and repeatable testing at all facilities.

New subdivision (e) adds the following: "Incubators must be calibrated and operated in accordance with the manufacturer's specifications. Temperatures must be monitored

either manually or by a continuous recording device during incubation, and the results must be reviewed and documented as described in the facility's SOPs." Chapter <825> requires the use of incubators; however, it is silent on calibration and operation. This subdivision is added to ensure incubators are used as intended and temperatures are monitored appropriately for radiopharmaceuticals. Documentation of this information provides an additional level of accountability for the designated person and for audit purposes.

Note is added with authority cited as sections 4005, 4008 and 4126.8, Business and Professions Code. Additionally, references are cited as Sections 4005, 4081, 4126.8, 4301, 4306.5, and 4342, Business and Professions Code.

Add Section 1738.7

New section 1738.7 is added and titled "Cleaning and Disinfecting." An opening paragraph is added to remind the public that the processing of radiopharmaceuticals must meet the requirements in the article and are in addition to and supplement the standards provided in USP <825>. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance.

New subdivision (a) is added and reads: "Cleaning, disinfection, and sporicidal agents shall be used in accordance with manufacturers' specifications and shall occur at the minimum frequencies listed in Table 5 of USP Chapter 825. Incubators must be cleaned at least monthly." This requirement is added to ensure that the cleaning agents are used consistent with the manufacturer's specifications as the board frequently gets questions on this topic during inspections.

New subdivision (b) is added and reads: "Reusable cleaning supplies, not for use in the PEC, shall not be stored within 1 meter of the PEC." This language was added for consistency as it is required by USP <797>; however, Chapter <825> is silent on the topic.

Authority cited: Sections 4005, 4008 and 4126.8, Business and Professions Code. Additionally, references are cited as Sections 4005, 4126.8, 4301, and 4306.5,, Business and Professions Code.

Add Section 1738.8

New section 1738.8 is added and titled "Assigning BUD." An opening paragraph is added to remind the public that the processing of radiopharmaceuticals must meet the requirements in the article and are in addition to and supplement the standards provided in USP <825>. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance.

New subdivision (a) adds the requirement that a "radiopharmaceutical's beyond-use date (BUD) shall not exceed the shortest BUD of any of its components." The Chapter discusses the assignment of a BUD, but it does not account for the expiration date of the

ingredients. This addition ensures that the BUD of a radiopharmaceutical does not exceed the expiration date of components used to prepare the preparation to safeguard the quality and integrity of the radiopharmaceutical.

New subdivision (b) adds the requirement that "no radiopharmaceutical CSP shall be administered after the labeled BUD. A dose shall not be sent for a scheduled administration that would occur after the labeled BUD." The Chapter discusses the assignment of a BUD, but does not address administration in relation to the BUD. This language is meant to prevent the administration of a radiopharmaceutical after the assigned BUD. The product cannot be administered after the BUD due to patient safety as the quality and integrity of the radiopharmaceutical could be impacted.

New subdivision (c) adds the following: "Extension of a suggested use-by time of a conventionally manufactured kit shall not exceed the BUDs in Table 7 of USP Chapter 825, for the sterility of the preparation or product."

New subdivision (d) adds the following: "Prior to the extension of a suggested use-by time for a conventionally manufactured kit, the pharmacy must maintain documentation of at least the following:

(1) Factors that necessitate its extension, including a full assessment of patient need for the extension.
(2) Evidence that supports that the extension maintains the appropriate quality and purity (radiochemical purity and radionuclidic purity) as specified in individual monographs, and other applicable parameters as clinically appropriate.

For the purposes of this section, the facility shall have SOPs that cover and are specific to each facility's location and kit."

The addition of subdivisions (c) and (d) ensures that the extension of the use by time does not exceed the maximum provided by USP as not all manufacturer package inserts provide the extension of the use-by time. The board's proposed language allows for an extension by establishing minimum provisions that must be satisfied to extend the use-by time. For certain radiopharmaceuticals transportation time, radionuclide availability, and other factors may necessitate extending manufacturer-stated/suggested use-by time to meet patient needs. Establishing a maximum standard for extending the use by time ensures consistency and protects the quality of the radiopharmaceutical for patient safety. Additionally, the SOPs must be specific to the location and the kit they are utilizing. The term "kit" is a term of art within the industry and is well understood by the regulated public.

Note is added with authority cited as sections 4005, 4008 and 4126.8, Business and Professions Code. Additionally, references are cited as Sections 4005, 4126.8, 4301, and 4306.5, Business and Professions Code.

Add Section 1738.9

New section 1738.9 is added and titled “Documentation.” An opening paragraph is added to remind the public that the processing of radiopharmaceuticals must meet the requirements in the article and are in addition to and supplement the standards provided in USP <825>. As compliance with USP is required by BPC section 4126.8, reminding the public of the requirements will help ensure compliance.

New subdivision (a) adds the requirement that the record of preparation must include a compounding record compliant with section 9.1 of USP Chapter 825. The Chapter has specific record requirements. To ensure compliance, the language reminds the public that the records are required. Additionally, including reminder also reinforces the importance of the records.

New subdivision (b) adds the following: “A record for preparation with minor deviations or a record of compounding shall be a single document. The document shall satisfy the requirements of USP Chapter 825, as well as the following:

(1) The assigned internal identification number shall be unique for each preparation.
(2) The manufacturer, lot number, and expiration date shall be recorded for each component for radiopharmaceutical. Documenting the National Drug Code (NDC) alone does not meet this requirement.
(3) The total quantity compounded shall include the number of units made and either the volume or the weight of each unit.
(4) The identity of each person performing the compounding and pharmacist verifying the final drug preparation.
(5) When applicable, endotoxin level calculations and readings.”

This language establishes the requirement for a compounding record if the facility is making minor deviations from the manufacturer’s approved instructions. If minor deviations are made, the facility needs to document the required information to support the minor deviation or compounding for record keeping purposes.

New subdivision (c) adds a requirement for records required by USP Chapter 825 or this Article to be maintained in a readily retrievable form, for at least three years from the date the record was created or relied upon. If only recorded and stored electronically, on magnetic media, or in any other computerized form, the records shall be maintained as specified by Business and Professions Code sections 4081 and 4105. The board determined that three years was the appropriate time frame as three years is the standard retention time for pharmacy related records per BPC 4081. Additionally, for consistency, the language adds the requirement for electronic records to be stored consistent with the existing electronic record requirements. This section is necessary to ensure that radiopharmaceutical records are maintained and available for board staff inspection.

New subdivision (d) adds a requirement that records shall be created and maintained in a manner to provide an audit trail for revisions and updates of each record document. Prior versions of each record must be maintained in a readily retrievable and easily

readable or rendered in an easily readable format and include the changes to the document, identification of individual who made the change, and the date of each change. This requirement ensures a complete “paper” trail for inspection purposes so that board inspectors can identify when the record was edited and by whom.

Note is added with authority cited as sections 4005, 4008 and 4126.8, Business and Professions Code. Additionally, references are cited as Sections 4005, 4081, 4105, 4126.8, 4301, and 4306.5, Business and Professions Code.

Add Section 1738.10

New section 1738.10 is added and titled “Preparation.” An opening paragraph is added to remind the public that the processing of radiopharmaceuticals must meet the requirements in the article and are in addition to and supplement the standards provided in USP <825>. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance.

New subdivision (a) adds the requirements for processing a nonsterile radiopharmaceutical and that the individual responsible for preparing must:

“(1) Follow manufacturer preparation instructions, unless minor deviations are made pursuant to subsection (c).
(2) Only use an area that is suitably cleaned and is uncluttered.
(3) Have documented processes in its SOPs for activities (e.g., cleaning) between the preparation cycles of different nonsterile products.”

USP <825> applies to other environments beyond just board licensed facilities. The board included these requirements within the text to ensure that licensees are aware that the requirements apply to them. Additionally, the board tracked the language “suitably cleaned and is uncluttered” to ensure consistency with the requirements of USP <825>.

New subdivision (b) adds the requirements for the individual responsible for preparing a sterile radiopharmaceutical (including intravascular devices) to:
“(1) Follow manufacturer preparation instructions, unless minor deviations are made pursuant to subsection (c).
(2) Use at least the minimum environmental standards from section 7 of USP Chapter 825.”

USP <825> applies to other environments beyond board licensed facilities. The board determined that the processing must meet the requirements for patient safety, to safeguard the quality and integrity of radiopharmaceuticals. USP <825> applies to other environments beyond just board licensed facilities. The board included these requirements within the text to ensure that licensees are aware that the requirements apply to them.

New subdivision (c) adds the following language: “When preparing radiopharmaceuticals with minor deviations (“preparation with minor deviations” as defined in USP Chapter 825) an SOP shall at least define the circumstances that necessitated the deviation and all quality control testing requirements and limits. Such circumstances shall, at a minimum, include patient need or facts that support the deviation that maintains the appropriate quality and purity (radiochemical purity and radionuclidic purity) as specified in individual monographs, and other applicable parameters as clinically appropriate in the professional judgment of the pharmacist.” This requirement educates the public about the documentation requirements when deviations from the manufacturers’ approved labeling occur in the specified areas. Including this information within the SOPs will ensure that all staff are educated and following identical processes.

New subdivision (d) adds the requirement for equipment and supplies initially used for processing of blood components (including red blood cells) to be solely dedicated for processing of blood components. Equipment and supplies shall be thoroughly cleaned and disinfected, in accordance with section 1738.7, prior to initiation of the next radiolabeling procedure. This requirement is necessary to avoid cross contamination when working with blood components for patient safety and to safeguard the quality and integrity of the preparations.

New subdivision (e) adds the requirement that when processing blood components all garb must be removed and replaced prior to initiation of the next radiolabeling procedure. This requirement is necessary to avoid cross contamination when working with blood components.

Note is added with authority cited as sections 4005, 4008 and 4126.8, Business and Professions Code. Additionally, references are cited as Sections 4005, 4126.8, 4301, and 4306.5, Business and Professions Code.

Add Section 1738.11

New section 1738.11 is added and titled “Compounding.” An opening paragraph is added to remind the public that the processing of radiopharmaceuticals must meet the requirements in the article and are in addition to and supplement the standards provided in USP <825>. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance.

New subdivision (a) adds the requirement that all compounding of radiopharmaceuticals shall comply with all radioactive materials licensing requirements for appropriate radiation safety considerations issued by the California Department of Public Health pursuant to section 30190 of Title 17 of the California Code of Regulations, any other state licensing agency that issues specific radioactive materials licenses, or the United States Nuclear Regulatory Commission pursuant to section 32.72 of title 10 of the Code of Federal Regulations, and utilize applicable environmental controls. The requirement is added to ensure that the public is aware of the need to follow requirements for

radioactive materials (RAM) licensure by other authorities related to specified areas. These licensure requirements must be adhered to.

New subdivision (b) adds the requirement for all API and excipient components used to compound a radiopharmaceutical to be manufactured by an FDA-registered facility, accompanied by a Certificate of Analysis (COA), and suitable for use in sterile pharmaceuticals. A COA that includes the compendial name, the grade of the material, and the applicable compendial designations on the COA must be received and evaluated prior to use, unless components are commercially available drug products. API and excipient components provided without this data shall not be used in a CSP. When the COA is received from a supplier, it must provide the name and address of the manufacturer. The requirement for the certification of analysis is added in accordance with the requirements of the FDCA (section 503A(b)(1)(A)(iii) and further elaborated on in the guidance document - Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act, issued by the FDA, which must be issued by the manufacturer for each batch of API. Obtaining and retaining this document ensures that the API is coming from an FDA-registered facility, which means the facility has been inspected by the FDA for good manufacturing practices and that the API was manufactured under an appropriate system for managing quality.

New subdivision (c) adds the following: “Except for sterile radiopharmaceuticals made for inhalation or ophthalmic administration, prior to releasing a sterile radiopharmaceutical made from one or more nonsterile component(s), results of bacterial endotoxin testing shall be reviewed and recorded. Results shall be documented in the compounding record specified in Section 9.2 of USP Chapter 825.” This testing is required by Chapter <825>; however, the board is identifying the specific type of testing, whereas the USP Chapter just refers to another Chapter of the USP. Identifying the specific testing provides clarity to the public without the need to review multiple Chapters of the USP.

Note is added with authority cited as sections 4005, 4008 and 4126.8, Business and Professions Code. Additionally, references are cited as Sections 4005, 4126.8, 4301, and 4306.5, Business and Professions Code.

Add Section 1738.12

New section 1738.12 is added and titled “Dispensing.” An opening paragraph is added to remind the public that the processing of radiopharmaceuticals must meet the requirements in the article and are in addition to and supplement the standards provided in USP <825>. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance.

The new section also adds the requirement for all dispensed radiopharmaceutical doses to be labeled with the information required by Business and Professions Code section 4076 and section 1707.5. Additionally, outer shielding labels shall contain the name and contact information of the dispensing pharmacy. Labeling is essential for dispensed

medication to ensure patient safety; therefore, ensuring that the public has a clear understanding of the labeling requirements when dispensing radiopharmaceutical doses is necessary for patient safety.

Note is added with authority cited as sections 4005, 4008 and 4126.8, Business and Professions Code. Additionally, references are cited as Sections 4005, 4126.8, 4301, and 4306.5, Business and Professions Code.

Add Section 1738.13

New section 1738.13 is added and titled “Repackaging.” An opening paragraph is added to remind the public that the processing of radiopharmaceuticals must meet the requirements in the article and are in addition to and supplement the standards provided in USP <825>. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance.

New subdivision (a) adds the requirement for the inner container of a repackaged radiopharmaceutical to be labeled with the following:

(1) Standard radiation symbol
(2) The words “Caution—Radioactive Material”
(3) The radionuclide and chemical form (generic name)
(4) Radioactivity with units at time of calibration and the calibration time

USP Chapter <825> recommends that the inner container be labeled with the four identified items; however, the board determined that the inner container must be labeled to ensure that individuals handling the container are aware of the contents and the potential hazard related to the contents.

New subdivision (b) adds the requirement for the outer shielding of a repackaged radiopharmaceutical to be labeled with the following:

(1) Standard radiation symbol
(2) The words “Caution—Radioactive Material”
(3) The radionuclide and chemical form (generic name)
(4) Radioactivity with units at time of calibration and the calibration time
(5) Volume, or number of units (e.g., capsules), as applicable
(6) Product expiration or BUD (consistent with Table 7 of USP Chapter 825), as applicable
(7) Special storage and handling instructions

USP Chapter <825> recommends that the outer shielding be labeled with the seven identified items; however, the board determined that the outer shielding must be labeled to ensure that individuals handling the container are aware of the contents and the potential hazard related to the contents.

Note is added with authority cited as sections 4005, 4008 and 4126.8, Business and Professions Code. Additionally, references are cited as Sections 4005, 4126.8, 4301, and 4306.5, Business and Professions Code.

Add Section 1738.14

New section 1738.14 is added and titled “Quality Assurance and Quality Control.” An opening paragraph is added to remind the public that the processing of radiopharmaceuticals must meet the requirements in the article and are in addition to and supplement the standards provided in USP <825>. As compliance with USP is required by BPC section 4126.8, reminding the public of requirements will help ensure compliance.

New subdivision (a) adds the requirement that the quality assurance program must comply with section 1711 and the standards contained in USP Chapter 1163, Quality Assurance in Pharmaceutical Compounding. This is being added as a reminder that quality assurance programs related to radiopharmaceuticals must comply with the board regulations on quality assurance programs, as well as the USP Chapter requirements, per BPC 4126.8.

Further, subdivision (a) adds a requirement that the program shall include a written procedure for any action(s) taken, in the event any radiopharmaceutical processing is discovered to be outside the expected standards for integrity, quality, and purity, such as a recall. The addition of this language ensures that the program has written procedures to follow should a problem with the preparation be identified. Having written procedures in place prior to the discovery of any possible problem with a patient will ensure appropriate action will be taken timely should it be needed to ensure patient safety.

New subdivision (b) adds the requirement that the board must be notified in writing within 72 hours of a complaint involving a radiopharmaceutical. The board must be notified of any complaints made to the facility to determine if additional investigation is needed or if there are patterns with respect to the nature of the complaint. Complaints made to a facility of a potential quality problem or of an adverse reaction may be indicative of a violation of laws or regulations. Additionally, the subdivision adds the reminder that recalls and adverse event reporting must be reported to the board and other agencies in compliance with relevant provisions of law. This addition serves as a reminder to the facility that must comply with various reporting requirements. Requiring that the board be notified within 72 hours is a reasonable time to allow the facility to respond to the complaint and soon enough for the board to adequately assess if immediate action need be taken to protect the public.

In addition to notice to the board as required in subdivision (b), new subdivision (c) adds that complaints related to a potential quality problem with a radiopharmaceutical and all reported adverse events to be reviewed by the pharmacist-in-charge within 72 hours of receipt of the complaint or occurrence. Such review shall be documented and

dated as defined in the SOPs. As the PIC is ultimately responsible for the operation of the facility, they must be aware of and review all quality related reports and adverse events to determine if corrective action is needed. Additionally, documenting the review within the SOPs ensures that the review is taking place, serves as a record to the PIC should the same or similar issues appear, and provides compliance information to board inspector during annual inspections.

New subdivision (d) adds the requirement that the SOPs shall specify the steps to be taken if any classified area fails to meet the specified ISO classification, including the investigative and corrective actions, allowable activities, and retesting procedures. The addition of this language ensures that the program has written procedures to follow prior should a classified area(s) fail to meet the specified ISO classification. To ensure patient safety, having procedures in place prior to the discovery of any possible problem will ensure appropriate action can be taken timely should a problem be identified. Identifying the steps to investigate the cause of the failure and what processing can be completed until that area meets the required classification are necessary for patient safety.

New subdivision (e) adds the requirement for the SOPs to be reviewed on an annual basis by the PIC, consistent with the SOPs. The SOPs shall be updated to reflect changes to compounding processes, facility changes or other changes that impact the CSP. Additionally, changes to the SOP must be disseminated to the affected staff prior to implementation to ensure that staff are operating in compliance with the SOPs of the facility and that all staff are following the same operating procedures.

New subdivision (f) adds notification to the public that a failure to follow the facility's written SOPs constitutes a basis for an enforcement action. While a violation of any the applicable laws or regulations is always a possible basis for an enforcement action. Since the SOPs are required, this language clarifies that a failure to comply with one's own SOPs is also a basis for an enforcement action, helping to ensure that SOPs are followed by the facility and staff.

Note is added with authority cited as sections 4005, 4008 and 4126.8, Business and Professions Code. Additionally, references are cited as Sections 4005, 4126.8, 4126.9, 4127.1, 4301, and 4306.5, Business and Professions Code.

Repeal Article 7 and Sections 1751-1751.10

Current Article 7 and Sections 1751-1751.10 are repealed. This article and the corresponding sections previously provided the regulation text for sterile compounding. Sterile compounding is now specified in Sections 1736-1736.21 of Article 4.5.

Underlying Data

1. Relevant Meeting Materials from the Board of Pharmacy meeting held September 12, 2023 – Agenda Item VIII, Minutes Pages 1, 2-12).

2. Relevant Meeting Materials from the Board of Pharmacy meeting held April 19-20, 2023 – Agenda Item XIV (Enforcement and Compounding Committee Meeting Materials Pages 1-5 and Attachments 1 and 2, Minutes Pages 1, 24-37).
3. Relevant Meeting Materials and Minutes from Board of Pharmacy Enforcement and Compounding Committee Meeting held April 13, 2023 (Meeting Materials Pages 1-4 and Attachments 2 – 5, Minutes Pages 1-29).
4. Relevant Meeting Materials and Minutes from Board of Pharmacy Enforcement and Compounding Committee Meeting held March 23, 2023 (Meeting Materials Pages 1-3 and Attachments 2 and 3, Minutes Pages 1-52).
5. Relevant Meeting Materials and Minutes from Board of Pharmacy Enforcement and Compounding Committee Meeting Held February 15, 2023 (Meeting Materials Pages 1-2 and Attachments 1 and 2, Minutes Pages 1-37).
6. Relevant Meeting Materials and Minutes from Board of Pharmacy Enforcement and Compounding Committee Meeting Held January 23, 2023 – (Meeting Materials Pages 1, 6-7 and Attachments 3 and 4, Minutes Pages 1, 7-41).
7. Food, Drug, and Cosmetic Act – Title 21 United States Code Chapter 9, Subchapter V – Drugs and Devices, Part A
8. ~~Food, Drug and Cosmetic Act~~ FDA Guidance Document, *Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act* (Revised June 2016)
9. ~~Food Drug and Cosmetic Act~~ FDA Guidance Document, *Compounded Drug Products That Are Essentially Copies of a Commercially Available Drug Product Under Section 503A of the Federal Food, Drug, and Cosmetic Act* (January 2018)
10. Chapter 795 of the United States Pharmacopeia - National Formulary (Effective November 1, 2023).
11. Chapter 797 of the United States Pharmacopeia - National Formulary (Effective November 1, 2023).
12. Chapter 800 of the United States Pharmacopeia - National Formulary (Effective July 1, 2020).
13. Chapter 825 of the United States Pharmacopeia - National Formulary (Effective December 1, 2020).
14. Chapter 1163 of the Unites States Pharmacopeia – National Formulary (Effective December 1, 2020).
15. CETA Certification Guide for Sterile Compounding Facilities (CAG-003, Revised October 2022).
16. United States Pharmacopeia 795, 797, 800, and 825 FAQs and Commentary
17. Animal Medicinal Drug Use Clarification Action of 1994 (Title 21 Code of Federal Regulations, Part 530
18. Guidance for Industry, Mixing, Diluting, or Repackaging Biological Products Outside the Scope of an Approved Biologics License Application (January 2018) https://www.fda.gov/media/90986/download
19. FDA to Compounders: Know Your Bulks and Excipients Suppliers, available at https://www.fda.gov/drugs/human-drug-compounding/fda-compounders-know-your-bulks-and-excipients-suppliers

20. Pharmacy Compounding Advisory Committee (PCAC) Information – Glutathione
    - June 8, 2022 PCAC Meeting: https://www.fda.gov/advisory-committees/advisory-committee-calendar/june-8-2022-meeting-pharmacy-compounding-advisory-committee-meeting-announcement-06082022#event-information
    - Briefing document: https://www.fda.gov/media/158541/download (glutathione information is tab 2)
    - Slide presentations: https://www.fda.gov/media/159042/download
    - PCAC Minutes: https://www.fda.gov/media/149084/download
21. FDA highlights concerns with using dietary ingredient glutathione to compound sterile injectables | FDA https://www.fda.gov/drugs/human-drug-compounding/fda-highlights-concerns-using-dietary-ingredient-glutathione-compound-sterile-injectables
22. FDA warns compounders not to use glutathione from Letco Medical to compound sterile drugs | FDA https://www.fda.gov/drugs/drug-safety-and-availability/fda-warns-compounders-not-use-glutathione-letco-medical-compound-sterile-drugs
23. PCAC Information - Methylcobalamin
    - June 9, 2021 PCAC Meeting: https://www.fda.gov/advisory-committees/updated-agenda-information-june-9-2021-meeting-pharmacy-compounding-advisory-committee-meeting#event-materials
    - Briefing document - https://www.fda.gov/media/149084/download (methylcobalamin information is tab 2)
    - Slide presentation - https://www.fda.gov/media/149084/download
    - PCAC Minutes: https://www.fda.gov/media/151410/download#:~:text=Committee%20Discussion%3A%20A%20majority%20of,to%20the%20503A%20Bulks%20List.
24. FDA Inspection Findings
    - La Vita Pharmacy: https://www.fda.gov/media/137497/download
    - McGuff Compounding Pharmacy: https://www.fda.gov/media/133951/download
    - ACRX Specialty Pharmacy: https://www.fda.gov/media/153655/download
    - Infusion Systems of SW Florida - https://www.fda.gov/media/107273/download
    - Carolina Infusion - https://www.fda.gov/media/163087/download
    - Cantrell Drug - https://www.fda.gov/media/112675/download
25. California Board of Pharmacy Case: McGuff Compounding Pharmacy – https://www.pharmacy.ca.gov/enforcement/fy2122/ac217176

Business Impact

The board has made the initial determination that the proposed regulations will not have a significant statewide adverse economic impact directly affecting businesses including the inability of California businesses to compete with businesses in other States.

This initial determination is based on the absence of testimony to that effect during the public discussion and development of the proposed regulation. Additionally, the proposal aligned the board's regulation with the national minimum standard. While the board does, in some instances, establish a higher standard, the board determined that this standard will not have a significant adverse impact.

The board indicates some facilities may need to install an interlocking pass-through door, which would result in one-time costs ranging from $5,000 to $10,000. However, the board does not have an estimate of the number of facilities that may require the door and therefore does not have a total cost estimate at this time.

Additionally, the board anticipates minimal ongoing costs ranging from approximately $5,700 to $15,000 per year related to administrative and maintenance workload and supplies and up to $150,000 over a ten-year period.

Economic Impact Assessment:

The board has determined that:

(1) this proposal will not create jobs within California;
(2) this proposal will not eliminate jobs within California;
(3) this proposal will not create new businesses within California;
(4) this proposal will not eliminate existing businesses within California;
(5) this proposal will not expand businesses currently doing business in the State of California.

This proposal will not create or eliminate jobs and/or businesses within California. Additionally, this proposal will not expand businesses because this regulatory proposal is intended to provide clarity to members of the board's regulated public on the requirements specific to compounded drug products. While national standards apply to all compounding, this proposed set of compounding regulations addresses areas where the board is requiring standards that go above the minimal established by USP guidelines. The higher standards do not impact the creation or elimination of jobs or businesses within the state.

This regulatory proposal benefits the health and welfare of California residents because the proposed regulations increase the safety standards for all Californians relying on compounded and sterile compounded drug products.

This regulatory proposal benefits worker safety because the proposed regulations will increase the incentive for innovation in products, materials, or processes as those

involved in the sterile compounding industry seek ways to improve products and materials as well as processes required for compounding and sterile compounding.

The regulatory proposal does not impact the state's environment. The proposal impacts the safety standards on all businesses performing compounding and sterile compounding; however, those safety standards should not impact the state's environment.

Fiscal Impact Assessment:

The proposed regulation does not result in a fiscal impact to the state. The board currently ensures compliance with its regulation through its robust inspection program, involving both routine and investigatory inspections.

The regulations do not result in costs or savings in federal funding to the state.

Specific Technologies or Equipment

This regulation does not mandate the use of specific technologies or equipment.

Consideration of Alternatives

No reasonable alternative to the regulatory proposal would be either more effective in carrying out the purpose for which the action is proposed or would be as effective or less burdensome to affected private persons and equally effective in achieving the purposes of the regulation in a manner that ensures full compliance with the law being implemented or made specific.

- Option 1: The board considered not implementing the proposed regulations. The board opted not to pursue this option as the current regulations of the CCR would be inconsistent with the current national standards set by USP. Not implementing this proposal would cause confusion and discrepancy throughout the industry.

- Option 2: The board considered not establishing additional regulatory standards beyond the minimum national standards set by USP. The board opted not pursue this option because BPC 4126.8 gives the board authority to adopt regulations to impose additional standards above the minimum national standards set by USP and adopting these additional regulatory standards beyond the minimum national standards set by USP provides clarification to the board's regulated public and benefits the health and welfare of California residents.

Description of reasonable alternatives to the regulation that would lessen any adverse impact on small businesses

No such alternatives have been proposed, however, the board welcomes comments from the public.