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Business, Consumer Services and Housing Agency
Department of Consumer Affairs
Gavin Newsom, Governor

To: Board Members

Subject: Agenda Item III. Discussion and Possible Action Related to Proposed Regulations, Title 16, California Code of Regulations, Repeal of Sections 1708.3, 1708.4, 1735 et seq and 1751 et seq and Addition of Sections 1735 et seq, 1736 et seq, 1737 et seq, and 1738 et seq Related to Compounded Drug Preparations, Hazardous Drugs, and Radiopharmaceuticals, and Review of Comments Received During the 30-Day Comment Period

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Relevant Law:

There are a number of provisions of both state and federal law that govern the practice of pharmacy, including provisions in Pharmacy Law. The rulemaking documents, which have been available to the public, detail many of the provisions. Provided below are some of the provisions with broad applicability.

Section 503A of the federal Food, Drug, and Cosmetic Act (FDCA) describes conditions that must be satisfied for drug products compounded by a licensed pharmacist or licensed physician to be exempt from certain provisions of the FDCA, i.e., sections 505, 502(f)(1), and 501(a)(2)(B). The exemptions concern provisions related to current good manufacturing practices, labeling of drugs with adequate directions for use, and the new drug approval process. A drug product intended for use in humans that is compounded in compliance with section 503A is exempt from these specified requirements; however, all other applicable provisions of the FDCA remain in effect for compounded drugs, even if the conditions of section 503A are met.

Section 503A(b)(1)(A)(i) provides that a drug product may be compounded if the licensed pharmacist or licensed physician compounds the drug product using bulk substances that:

1. Comply with the standards of an applicable United States Pharmacopoeia or National Formulary monograph, if a monograph exists, and the United States Pharmacopoeia chapter on pharmacy compounding;
2. If such a monograph does not exist, are drug substances that are components of drugs approved by the Secretary; or
3. If such a monograph does not exist and the drug substance is not a component of a drug approved by the Secretary, appear on a list

developed by the Secretary through regulations issued by the Secretary under subsection (c) of section 503A.

21 C.F.R. Section 216.23(a) includes the bulk drug substances that can be used to compound drugs products pursuant to section 503A(b)(1)(A)(i)(III).

To gain a full understanding of all of the requirements, pharmacists and others should read section 503A and other applicable provisions of the FDCA. **Note**: A presentation covering the federal requirements was provided during the January 2023 Enforcement and Compounding Committee meeting. Meeting slides are available here and the livestream of the meeting is available here. More recently, a presentation was provided to the Board during the November 6-7, 2024 Board meeting. The slides are available here and the livestream is available here.

Business and Professions Code (BPC) section 4126.8 generally provides that the compounding of drug preparations by a pharmacy for furnishing, distribution, or use in California shall be consistent with the standards established in the pharmacy compounding chapters of the current version of the United States Pharmacopeia-National Formulary. (**Note**: Federal law imposes a similar requirement for compliance with USP.)

BPC section 4127(c) requires the Board to review any formal revisions to General Chapter 797 of the USP, relating to the compounding of sterile preparations, not later than 90 days after the revisions become official, to determine whether amendments are necessary for regulations adopted by the Board.

BPC section 4342 generally provides the Board with the authority to institute any action or actions 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 version of the USP, or that violate any provision of the Sherman Food, Drug, and Cosmetic Law (Health and Safety Code sections 109875 – 111929.4).

Background:

The Board's first regulations relating to compounding became effective in 1986. Over the years, the regulations have been expanded and amended.

The Board's most recent efforts to update its regulations began in 2019, when, in response to proposed changes to the USP, the Board initiated review of its compounding regulations through the Board's Enforcement and Compounding Committee. A series of public meetings were held and proposed language was discussed in a collaborative manner with stakeholders. In response to subsequent appeals to provisions contained within the proposed USP changes, the Board suspended its efforts while appeals were considered by the USP. On

November 5, 2019, in light of the delays with USP, the Committee considered a Draft Policy Statement to provide stakeholders with guidance on the applicability of the Board's compounding regulations and USP compounding chapters while appeals were pending before the USP Committee.

Following finalization of the USP Chapters, the Board, again through the Enforcement and Compounding Committee, resumed its efforts to evaluate, and where necessary update, its compounding regulations. Again, a series of meetings were held with significant participation and comments from stakeholders. Proposed changes include restructuring of the Board's regulations to align with the USP Chapters, elimination and clarification of requirements, and addition of new requirements.

At the April 2023 Board meeting, the Board approved proposed regulation text that would amend the Board's regulations regarding compounded drug preparations to implement, clarify, or make more specific requirements related to the United States Pharmacopeia-National Formulary, Chapter <795> for nonsterile compounding, Chapter <797> for sterile compounding, Chapter <800> related to hazardous drugs – handling in healthcare settings, and Chapter <825> related to radiopharmaceuticals – preparation, compounding, dispensing, and repackaging. Federal law and USP standards are not repeated in the proposed language. Understanding that the USP Chapters became effective on November 1, 2023, and the Board's proposed regulations would not yet be effective, the Board released an updated Policy Statement on September 12, 2023, providing stakeholders with additional guidance.

As required by the Administrative Procedure Act, proposed text that the Board had approved was published and distributed to interested parties for a 45-day comment period on April 19, 2024, which ended on June 3, 2024. Additionally, Board staff held a regulation hearing on June 18, 2024, to accept oral comments. Numerous comments were received.

During the July 31 – August 1, 2024 Board meeting, members considered the comments received and Board staff recommended changes to the text, which were dated 7/19/2024, based on those comments. The Board dedicated a significant amount of time to the discussion and received extensive additional public comment. Ultimately, the Board delegated authority for Members Serpa and Barker to evaluate the information provided at the meeting and, consistent with the Board's discussion and direction, develop further recommended changes to the 7/19/2024 proposed modified text.

During the September 12, 2024 Board meeting, members resumed consideration of the proposed modified text, including additional changes recommended by Members Serpa and Barker, consistent with the Board's discussion and direction. The Board again received significant public comment. Based on the comments

received, the Board determined that additional education was necessary before it proceeded with a determination of the next steps.

Most recently, during the November 6-7, 2024 Board meeting, members resumed consideration of the proposed modified text, which included the additional changes recommended by Members Serpa and Barker. Following extensive discussion and public comment, members voted to:

1. Accept the staff recommended responses and supplemental responses to the initial comments from the 45-day comment period and regulation hearing;
2. Approve the recommended modified regulation text for a 30-day comment period; and
3. Delegate to Members Serpa and Barker the authority to review comments received to the modified text during the 30-day public comment period with staff and to present recommended changes and responses to the Board for consideration at a future Board meeting.

On November 8, 2024, proposed modified text that the Board had approved was published and distributed to interested parties for a 30-day comment period, which ended on December 9, 2024. Comments were received in response to this comment period.

Following the conclusion of the comment period, Members Barker and Serpa worked with staff to identify recommended changes to the proposed modified text.

Summary of Changes

During the meeting, members will have the opportunity to consider the comments received in response to the 30-day comment period as well as changes being recommended to the proposed text based on the comments received during the 30-day comment period. To assist members and interested parties in understanding the scope of the recommended changes, below are summary comments for the various sections of the proposed regulations.

Nonsterile Compounding

- Clarifying that a PIC may also serve as the designated person.
- Clarifying language that a pharmacist shall verify and document the clinically significant difference of a compounded medication.
- Extending provisions for veterinarian office dispensing.
- Providing additional flexibilities for licensed health care facilities to compound "essentially a copy" under specified conditions.
- Incorporating provisions related to the Center for Veterinary Medicine Guidance for Industry #256 – Compounding Animal Drugs from Bulk Drug Substances as specified.

- Establishing specific provisions for a facility that limits compounding to combining a flavoring agent as specified.
- Providing authority for a pharmacist to compound by combining a flavoring agent at the request of the patient or patient's agent without consultation with a prescriber as specified.
- Removing the requirement to include the date and time of compounding on the compounding record as specified.
- Removing provisions related to a written procedure for responding to out-of-range temperature violations as specified.

Sterile Compounding

- Clarifying that a PIC may also serve as the designated person.
- Clarifying language that a pharmacist shall verify and document the clinically significant difference of a compounded medication.
- Updating and extending the period of time for a facility to use immediate use provisions under specified conditions and establishing new provisions related to immediate use provisions for critical access hospitals.
- Extending provisions for veterinarian office dispensing.
- Incorporating provisions related to the Center for Veterinary Medicine Guidance for Industry #256 – Compounding Animal Drugs from Bulk Drug Substances as specified.
- Modifying provisions for use of non-sterile components including removing requirements to perform such compounding in full compliance with USP 797 Category 3 requirements.
- Clarifying requirements related to compounding of an FDA-approved human whole blood or human whole blood derivative product.
- Clarifying garbing, hand hygiene, and aseptic manipulation competencies provisions to allow for use at additional premises.
- Clarifying donning of sterile gloves provisions.
- Removing requirements for dynamic interactions through HVAC systems.
- Updating the title of the reference for CETA CAG-009.
- Modifying labeling requirements for licensed health care facilities related to the rate of infusion as specified.
- Clarifying that SOPs related to compounding using bulk drug substances do not need to require a facility to perform the specified test when such testing is performed by other specified entities.
- Removing reference to USP Chapters 51 and 1207 related to the compounding of allergenic extracts.
- Nonsubstantive changes to the language to address grammatical issues and to improve clarity of the language and to include the titles of

referenced USP Chapters.

Hazardous Drugs (HDs)

- Article will only apply to hazardous drug compounding and in some instances performing the crushing or splitting of tablets or opening capsules of antineoplastic HDs as specified.
- Clarifying provisions related to approval of a facility's list of HDs and clarifying that more than one individual may serve as the designated person.
- Clarifying SOP requirements for considering the use of environmental wipe sample for HD surface residue.
- Clarifying provisions for changing outer gloves and use of disposable preparation mats.
- Relocating labeling requirements for furnishing a compounded antineoplastic HD for administration within a licensed health care facility.

Radiopharmaceuticals

- Removing language related to prohibition for compounding to not take place in an SRPA.
- Updating provisions for preparations with minor deviations.
- Extending the time frame for reporting a complaint to the Board.

Attached to this memo are the following:

1. The recommended second modified text, including the changes recommended by Members Serpa and Barker consistent with delegated authority (dated 1/8/25).
2. Board staff prepared summarized comments with recommendations from the 30-day comment period and hearing.
3. Comments received during the 30-day comment period.
4. The original proposed text (dated 3/24/24) published for the 45-day public comment period.
5. The modified text (dated 8/29/2024) published for the 30-day public comment period.
6. Correspondence from the Reji Varghese, Executive Director, Medical Board of California

Historical information considered during the November 6-7, 2024 Board meeting is available here.

At this Meeting:

During the meeting, members will have the opportunity to review the comments received during the 30-day comment period, staff recommended responses to

comments received, and recommended changes to the modified text.

Possible Motion Language:

1. Accept the Board staff recommended responses to comments received during the 30-day comment period [either "as presented" or "consistent with the Board's discussion"].
2. Approve the recommended third modified text [either "dated 1.8.2025 or "as directed by the Board"] for a 15-day comment period.
3. Additionally, should additional comments be received during the comment period, delegate to Members Serpa and Barker authority to review the comments with staff to offer recommendations to the Board for consideration at a future meeting.