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

To: Board Members

Subject: Agenda Item XVII. 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, Including Educational Presentations by Board Counsel and Staff on Federal Law and Background Information, and Consideration of Comments Received During the 45-Day Comment Period and Regulation Hearing

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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 provisions related to approval of drugs under new drug applications or abbreviated new drug applications. 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 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.

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 compounded 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, in response to proposed changes to the USP, through the Board's Enforcement and Compounding Committee, the Board initiated review of its compounding regulations. 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 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 of requirements, 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.

More recently, 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.

Summary of Changes

During the meeting, members will have the opportunity to resume discussion on recommended changes to the proposed regulation text. To assist members and interested parties in understanding the scope of the changes, below are summary comments for the various sections.

Nonsterile Compounding

- Clarifying the provisions for compounding when a pharmacist determines a clinical need exists for a patient.
- Clarifying language surrounding requirements for reporting of potential conditions that could result in contamination of the compounding environment.
- Extending the time period to review and report complaints of potential compounding quality issues to the Board.
- Nonsubstantive changes to the language to address grammatical issues and to improve clarity of the language.

Sterile Compounding

- Provide authority for a health care facility licensed pursuant to Health and Safety Code section 1250 to compound "essentially a copy" of a product under specified conditions.
- Clarifying the provisions for compounding when a pharmacist determines a clinical need exists for a patient.
- Extending the period of time for a person who has failed specified ongoing training and competency to continue performing specified functions.
- Removal of requirement for identification to the genus level, regardless of CFU count, to trend for growth of microorganisms.
- Extending the time period to review and report complaints of potential compounding quality issues to the Board.
- Updating the provisions for compounding using a bulk drug substance published in the FDA 503A Category I bulk drug substances list.
- 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

- Article will only apply to hazardous drug compounding and in some instances performing "other manipulations" included in Table 1 of the Chapter of antineoplastic HDs. (e.g. HD/Antineoplastic Tablet splitting or

crushing)
- Consistent changes necessary to implement the changes noted in the above bullet.

Radiopharmaceuticals
- Removal of requirement for identification to the genus level, regardless of CFU count, to trend for growth of microorganisms.
- Nonsubstantive change to clarify requirement related to facility and engineering controls related to compounding of radiopharmaceuticals and to improve clarity of the language.

Attached to this memo are the following:
1. The updated recommended modified text, including the changes recommended by Members Serpa and Barker consistent with delegated authority (dated 8/29/24).
2. The updated recommended modified text with changes highlighted in yellow to illustrate the changes after the July 31-Aug 1 Board meeting.
3. Supplemental Board staff prepared summarized comments with recommendations incorporating the changes reflected in updated recommended modified text (dated 8/31/24).
4. Board staff prepared summarized comments with recommendations from the 45-day comment period and hearing.
5. Board staff recommended modified text (dated 7/17/24) following the 45-day comment period and hearing.
6. Comments received during the 45-day comment period. (Comments from the regulation hearing are available to hear at the following website: https://youtu.be/VDderHcJsEY)
7. The original proposed text (dated 3/24/24) published for the 45-day public comment period.

At this Meeting:
Consistent with the agenda, members will receive presentations providing education and background information. It is anticipated that these presentations will be provided before the Board resumes its discussion. Staff and counsel will also be prepared to offer recommendations for next steps.