**California State Board of Pharmacy**
1625 N. Market Blvd, N219, Sacramento, CA 95834
Phone: (916) 574-7900
Fax: (916) 574-8618
www.pharmacy.ca.gov

BUSINESS, CONSUMER SERVICES AND HOUSING AGENCY
DEPARTMENT OF CONSUMER AFFAIRS
GOVERNOR EDMUND G. BROWN JR.

To: Board Members

Subject: Discussion and Consideration of Proposal to Modify Pharmacy Compounding Regulations (Title 16, California Code of Regulations, Sections 1735.1, 1735.2, 1735.6, 1751.1, & 1751.4), Including Review of Public Comments and, Potentially, Modified Text

**Attachment 1**

Background:

At the July 2017 Board Meeting, the board approved proposed text to amend Sections 1735.1, 1735.2, 1735.6, 1751.1, and 1751.4 of Title 16 CCR, related to Compounded Drug Preparations. This proposal formally amends the board's regulations regarding the establishment of compounding beyond use dates as it relates to sterile and non-sterile compounded drug preparations. Additionally, this regulation allows for the use of a double filtration system and further aligns the board's regulations with The United States Pharmacopeia - National Formulary (USP), which is the professional industry standards used across the nation.

USP contains standards developed by a committee of experts that, among other things, help ensure the quality of compounded medications. USP's General Chapters for compounding establish procedures, methods and practices that are utilized by practitioners to help ensure the quality of compounded preparations. The General Chapters for compounding include Chapter 795 (Pharmaceutical Compounding – Nonsterile Compounding), Chapter 797 (Pharmaceutical Compounding – Sterile Preparations) and Chapter 800 (Hazardous Drugs – Handling in Healthcare Settings). Further, the U.S. Federal Food, Drug, and Cosmetics Act designates the USP as the official compendia for drugs marketed in the United States. All drug products within the U.S. market must conform to the standards in USP to avoid possible charges of adulteration and misbranding.

As required by the Administrative Procedure Act, board staff released the proposed text for the 45-day comment period on August 3, 2018, which ended on September 17, 2018 following review by the Department of Consumer Affairs and the Business, Consumer Services, and Housing Agency.

The comments received during the 45-day comment period are included as an attachment. Also included are: board staff prepared recommendations in response to the comments and a proposed modified text.

At this Meeting

The board will have the opportunity to discuss the regulation and determine what course of action it wishes to pursue. Among its options:

1. Amend the regulation to address any concerns raised by stakeholders.
2. Adopt the regulation as noticed by the Board on August 3, 2018.

**The Attachment** contains the following:

1. Approved regulation text as noticed for public comment on August 3, 2018.
2. A copy of each comment received during the 45-day public comment period for board review.
3. A compilation document of the comments received during the 45-day comment period with staff recommendations. This document summarizes the comments received for reference. The board should also review the comments in section two.
4. A staff recommended modified text which addresses concerns raised by a commenter and board staff.

---

**Staff Recommendation:** Adopt the staff recommended modified text, dated September 19, 2018, and notice the language for a 15-day comment period. Additionally, should no negative comments be received, delegate to the executive officer the authority to make technical or non-substantive changes as may be required by the Control agencies to complete the rulemaking file.

---

# Attachment 1

# Approved Regulation Text as noticed on August 3, 2018

**Title 16. Board of Pharmacy**
**Proposed Text**

Proposed changes to the current regulation language are shown by strikethrough for deleted language and underline for added language. Additionally, text in [brackets] indicates language that is not being amended.

Note: The board adopted an emergency regulation affecting regulation section 1735.2 effective December 19, 2017. The strikethrough and underline to the text of that section reflects changes from the board's non-emergency regulation.

**Amend section 1735.1, subdivisions (c) and (f), in Article 4.5 of Division 17 of Title 16 of the California Code of Regulations to read as follows:**

**1735.1. Compounding Definitions.**

[…]

(c) "Biological Safety Cabinet (BSC)" means a ventilated cabinet for compounding sterile drug preparations, having an open front with inward airflow for personnel protection, downward HEPA-filtered laminar airflow for product protection, and HEPA-filtered exhausted air for environmental protection. Where hazardous drugs are prepared, the exhaust air from the biological safety cabinet shall be appropriately removed by properly designed external building ~~ventilation~~ exhausting. This external ~~venting~~ exhaust should be dedicated to one BSC or CACI.

[…]

(f) "Compounding Aseptic Containment Isolator (CACI)" means a unidirectional HEPA-filtered airflow compounding aseptic isolator (CAI) designed to provide worker protection from exposure to undesirable levels of airborne drug throughout the compounding and material transfer processes and to provide an aseptic environment for compounding sterile preparations. Air exchange with the surrounding environment should not occur unless the air is first passed through a microbial retentive filter (HEPA minimum) system capable of containing airborne concentrations of the physical size and state of the drug being compounded. Where hazardous drugs are prepared, the exhaust air from the isolator shall be appropriately removed by properly designed external building ~~ventilation~~ exhaust. This external ~~venting~~ exhaust should be dedicated to one BSC or CACI. Air within the CACI shall not be recirculated nor turbulent.

[…]

Note: Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4029, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.

**Amend section 1735.2, subdivision (i), in Article 4.5 of Division 17 of Title 16 California Code of Regulations to read as follows:**

**1735.2. Compounding Limitations and Requirements; Self-Assessment.**

[…]

(i) Every compounded drug preparation shall be given a beyond use date representing the date or date and time beyond which the compounded drug preparation should not be used, stored, transported or administered, and determined based on the professional judgment of the pharmacist performing or supervising the compounding.

(1) For non-sterile compounded drug preparation(s), the beyond use date shall not exceed any of the following:

(A) the shortest expiration date or beyond use date of any ingredient in the compounded drug preparation,

(B) the chemical stability of any one ingredient in the compounded drug preparation~~;~~,

(C) the chemical stability of the combination of all ingredients in the compounded drug preparation,

(D) ~~180 days~~ for non-aqueous formulations, 180 days or an extended date established by the pharmacist's research, analysis, and documentation,

(E) ~~14 days~~ for water-containing oral formulations, 14 days or an extended date established by the pharmacist's research, analysis, and documentation, and

(F) ~~30 days~~ for water-containing topical/dermal and mucosal liquid and semisolid formulations, 30 days or an extended date established by the pharmacist's research, analysis, and documentation.

(G) A pharmacist, using his or her professional judgment may establish an extended date as provided in (D), (E), and (F), if the pharmacist researches by consulting and applying drug-specific and general stability documentation and literature; analyzes such documentation and literature as well as the other factors set forth in this subdivision, and maintains documentation of the research, analysis and conclusion. The factors the pharmacist must analyze include:

(i) the nature of the drug and its degradation mechanism,

(ii) the dosage form and its components,

(iii) the potential for microbial proliferation in the preparation,

(iv) the container in which it is packaged,

(v) the expected storage conditions, and

(vi) the intended duration of therapy.

Documentation of the pharmacist's research and analysis supporting an extension must be maintained in a readily retrievable format as part of the master formula.

(2) For sterile compounded drug preparations, the beyond use date shall not exceed any of the following:
  (A) The shortest expiration date or beyond use date of any ingredient in the sterile compounded drug product preparation,
  (B) The chemical stability of any one ingredient in the sterile compounded drug preparation,
  (C) The chemical stability of the combination of all ingredients in the sterile compounded drug preparation, and
  (D) The beyond use date assigned for sterility in section 1751.8.

(3) For sterile compounded drug preparations, ~~E~~ extension of a beyond use date is only allowable when supported by the following:
  (A) Method Suitability Test,
  (B) Container Closure Integrity Test, and
  (C) Stability Studies

(4) In addition to the requirements of paragraph three (3), the drugs or compounded drug preparations tested and studied shall be identical in ingredients, specific and essential compounding steps, quality reviews, and packaging as the finished drug or compounded drug preparation.

(5) Shorter dating than set forth in this subsection may be used if it is deemed appropriate in the professional judgment of the responsible pharmacist.

[…]

Note: Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4029, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.

**Amend section 1735.6, subdivision (e), in Article 4.5 of Division 17 of Title 16 of the California Code of Regulations to read as follows:**

**1735.6. Compounding Facilities and Equipment.**

[…]

(e) Hazardous drug compounding shall be completed in an externally ~~vented~~ exhausted physically separate room with the following requirements:

(1) Minimum of 30 air changes per hour except that 12 air changes per hour are acceptable for segregated compounding areas with a BSC or CACI when products

are assigned a BUD of 12 ~~hrs~~ hours or less or when non sterile products are compounded; and
(2) Maintained at a negative pressure of 0.01 to 0.03 inches of water column relative to all adjacent spaces (rooms, above ceiling, and corridors); and
(3) Each ~~PEC~~ BSC in the room shall also be externally ~~vented~~ exhausted except that a BSC used only for nonsterile compounding may use a redundant-HEPA filter in series; and
(4) All surfaces within the room shall be smooth, seamless, impervious, and non-shedding.

[…]

Note: Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4029, 4036, 4037, 4051, 4052 and 4127, Business and Professions Code.

**Amend section 1751.1, subdivision (a)(5), in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:**

**1751.1. Sterile Compounding Recordkeeping Requirements.**

(a) In addition to the records required by section 1735.3, any pharmacy engaged in any compounding of sterile drug preparations shall maintain the following records, which must be readily retrievable, within the pharmacy:
[…]
(5) Biannual ~~V~~ video of smoke studies in all ISO Class 5 certified spaces.
[…]

[…]

Note: Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4029, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.

**Amend section 1751.4, subdivision (k), in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:**

**1751.4. Facility and Equipment Standards for Sterile Compounding.**

[…]

(k) The sterile compounding area in the pharmacy shall have a comfortable and well-lighted working environment, which includes a room temperature of 20~~-24~~ degrees Celsius (68~~-75~~ degrees Fahrenheit) or cooler to maintain comfortable conditions for compounding personnel when attired in the required compounding garb.

[…]

Note: Authority Cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4029, 4036, 4037, 4051, 4052 and 4127, Business and Professions Code; and Section 18944, Health and Safety Code.

# Comments received during the 45-day comment period

## Martinez, Lori@DCA

**From:** Ayk D. <gohayk@gmail.com>
**Sent:** Friday, August 3, 2018 1:30 PM
**To:** Martinez, Lori@DCA
**Subject:** comments 1735 1751

Hello Lori,

I run a sterile and non-sterile compounding pharmacy in Glendale, CA.
The BUD restrictions set forth by CA BOP are basically there to prevent us, the compounding pharmacies from being able to perform our duty to help patients in need. They are very restrictive to our profession and do not allow me to be able to help patients properly. I am not sure where the CA BOP has received the data on the BUD's, but EVERY time we send a sample for testing it surpasses the BUD by 200-300% at least. There are numerous published formulas that have documented BUD, but we cannot use them..how is this normal? For me to do a study on all the compounds I make to establish a usable BUD, I would go out of business. I seems that in some sense that was the purpose of these guidelines; however, I do not want to believe that. Please update the BUD guidelines to allow published BUD in literature to be used as reference when we compound.
The BUD of a sterile preparation of 3 days is absurd..I have to send it for a 2 week turnaround test, so by the time the sample is cleared to be dispensed, it is long expired.. please consider that

Thank you

Ayk Dzhragatspanyan, PharmD

--

Dr Ike D, PharmD



---

## Martinez, Lori@DCA

**From:** Corbin C Bennett <Corbin.Bennett@kp.org>
**Sent:** Friday, September 14, 2018 4:42 PM
**To:** Martinez, Lori@DCA
**Subject:** Comments on Proposed Text 1735 and 1751

Good Afternoon,

A recommendation:

Recommend adding "CACI" after BSC in section 1735.6 (e)(3):

(3) Each ~~PEC~~ BSC in the room shall also be externally ~~vented~~ exhausted except that a BSC used only for nonsterile compounding may use a redundant HEPA filter in series; and

**Corbin Bennett, PharmD, MPH**
**Senior Director of Oncology and Outpatient Infusion Pharmacy Services**
**National Pharmacy Programs and Services | Kaiser Permanente**
Office 559.448.3472 (Tie 454) | Cell: 559.307.1009 |

## Martinez, Lori@DCA

**From:** Han-Yoo, Sarah <Sarah.Han-Yoo@kindred.com>
**Sent:** Tuesday, August 7, 2018 4:19 PM
**To:** Martinez, Lori@DCA
**Subject:** Notice of Proposed Action to amend the text of Title 16 CCR 1751.4

To whom it may concern,
I would like to make a comment regarding the temperature requirement change for the sterile compounding area.

**1751.4. Facility and Equipment Standards for Sterile Compounding.**

[...]

(k) The sterile compounding area in the pharmacy shall have a comfortable and well-lighted working environment, which includes a room temperature of 20~~-24~~ degrees Celsius (68~~-75~~ degrees Fahrenheit) or cooler to maintain comfortable conditions fo compounding personnel when attired in the required compounding garb.

Making the sterile compounding area cooler than 68 Fahrenheit may not be practical since the compounding area's temperature is controlled the same as other area in the hospital. Making entire hospital cooler than 68 Fahrenheit can be too cold for patients. Also, we cannot use a portable air conditioner or fan to make the air cooler in the sterile compounding area only since we should void activities that are extraneous to sterile compounding.
Please re-consider the change. Thank you.

Sarah Han-Yoo, Pharm D, BCPS
Director of Pharmacy
Kindred Rancho
10841 White Oak Avenue
Rancho Cucamonga, CA 91730
909-581-6408

## Martinez, Lori@DCA

**From:** Costantino, Dale <dcostantino@maderahospital.org>
**Sent:** Thursday, August 30, 2018 2:58 PM
**To:** Martinez, Lori@DCA
**Cc:** Chan, Nicole
**Subject:** comments for changing 1751.4

Hello,

I would like to comment on the proposed changes to 1751.4 k. Current law requires a segregated compounding area (SCA) temperature to be less than or equal to 7S degrees Fahrenheit. The proposed change would require sterile compounding areas, including a SCA, to be less than or equal to 68 degrees Fahrenheit. Although, this is a good change to provide comfortable conditions for compounding personnel, this may not be achievable for SCA in some California hospitals due to facility limitations.

Please consider a longer adoption period or a temporary waiver process that can be granted to allow hospitals time to make appropriate changes to accomplish this goal.

Thank You,

Dale

Dale Costantino Pharm.D.
Pharmacy Director
Madera Community Hospital

Office: 559-675-5543
Fax: 559-675-5582

## Martinez, Lori@DCA

**From:** Tou, Michael P <Michael.Tou@providence.org>
**Sent:** Monday, September 17, 2018 10:31 AM
**To:** Martinez, Lori@DCA
**Subject:** Providence St. Joseph Health - Comments on compounded drug preparations regulations
**Attachments:** Providence St. Joseph Health_Compounded Drug Preparations_091718.pdf

**Importance:** High

Good morning,

On behalf of Providence St. Joseph Health and our pharmacy directors, I am submitting comments in response to the Notice of Proposed Rulemaking for Title 16 of the California Code of Regulations, Sections 1735.1 1735.2, 1735.6, 1751.1, 1751.4.

Thank you for the opportunity to comment on the proposed regulations. We hope the Board will consider our recommendations.

Best regards,

Michael

**Michael Tou, MPA** | Director, Government Relations – California
Providence St. Joseph Health
20555 Earl Street | Torrance, CA 90503
Work: (310) 793-8093 | Mobile: (818) 512-4837 | Email: michael.tou@providence.org

Providence St. Joseph Health

**Providence St. Joseph Health**
20555 Earl Street
Torrance, CA 90503

Providence St. Joseph Health

September 17, 2018

California Board of Pharmacy
Attn: Ms. Lori Martinez
1625 N. Market Blvd., N219
Sacramento, CA 95834

**SUBJECT:** **Compounded Drug Preparations, Notice of Proposed Action, Title 16 of the California Code of Regulations, Sections 1735.1, 1735.2, 1735.6, 1751.1, 1751.4. Comment Period: August 3, 2018 to September 17, 2018.**

Dear Ms. Martinez:

Providence St. Joseph Health appreciates the opportunity to submit comments on the proposed compounded drug preparations regulations. The proposed modifications could have significant impacts on the operation of our hospital pharmacies when compounding sterile preparations. We urge the Board to adopt the recommendations highlighted by PSJH in the draft rule.

**Proposed Change to Amend Title 16 CCR Section 1751.4 Facility and Equipment Standards for Sterile Compounding**

The Board of Pharmacy is proposing to remove the higher temperature range (up to 24 degrees Celsius and 75 degrees Fahrenheit, respectively), reducing the maximum temperature for the room where the sterile compounding occurs to 20 degrees C (68 degrees F) or colder. The rationale for the temperature change where compounding occurs is to ensure employees remain comfortable working in all required protective compounding garments and equipment in alignment with USP <797> guidelines.

Our hospital pharmacies are working diligently to construct fully compliant cleanrooms in accordance with state regulations, as well as the final standards in USP <797> and USP <800>. Unfortunately, some of our hospital pharmacies will be unable to comply with the proposed amendment to 16 CCRC Section 1751.4, until construction is completed on the pharmacy later in 2019. While we have received a waiver from the Board to safely compound drug products for our patients, this newly reduced temperature requirement would involve costly and disruptive improvements to the cooling system where the pharmacy is located within the hospital. Construction would be required to reduce the temperature in the existing compounding area to 68 degrees F or below.

Furthermore, we are concerned with the conflicts that exist around drug storage requirements and the Board's proposed temperature modifications. Most medications requiring room temperature storage include the FDA labeling for *USP controlled room temperature* defined as the range of 68 to 77 degrees Fahrenheit. Hospital pharmacies are required to store medications per the manufacturer specifications. Reducing the sterile compounding area temperature to 68 degrees F or below would introduce a conflict with the labeled drug storage temperature requirement. Hospital pharmacies would be restricted from storing drugs at the reduced temperature of the

sterile compounding area. This would be an unintended consequence of this proposed regulatory change.

All chemotherapy drugs require negative pressure room storage and our pharmacies are initiating construction on negative pressure sterile compounding areas to comply with the hazardous drug preparation standards. However, we have not designed or received OSHPD approval for a separate negative pressure room for drug storage as part of the construction permits. If drugs cannot be stored in the negative pressure sterile compounding area, this will increase the risk of cross contamination as drugs will have to be brought in each and every time for compounding. For non-hazardous life-saving drugs that require immediate compounding, the ability to store these drugs in the clean room will ensure patient safety and efficiency.

**Providence St. Joseph Health recommends the following actions be considered by the Board:**

- **Modify the proposed amendment to Section 1751.4(k) and revise sterile compounding area temperature requirements to 20 – 22 Celsius (68–72 degrees Fahrenheit) to ensure comfortable working environment for the compounding personnel but also to allow for storage of select drugs in the compounding area.**

- **Delay implementation of the amendment to Section 1751.4(k) or grant a waiver to pharmacies from compliance with the proposed rule in accordance with Title 16 CCR Section 1735.6(f), in order to allow hospital pharmacies to complete construction on fully compliant cleanrooms.**

Thank you for this important opportunity to comment on the proposed regulations. If you have any questions, please contact me at (310) 793-8093 or michael.tou@providence.org.

Sincerely,

Michael Tou
Director, Government Relations

cc: Providence St. Joseph Health Pharmacy Directors (California)
BJ Bartleson, California Hospital Association

## Martinez, Lori@DCA

**From:** Lauren Ruth Eichstadt-Forsythe <leichstadt@ucdavis.edu>
**Sent:** Tuesday, August 28, 2018 4:21 PM
**To:** Martinez, Lori@DCA
**Subject:** Compounded Drug Preparations Comments

Good Afternoon,

With regards to the proposed edits to the compounding regulations, I have a general comment.

The compounding committee recently recommended to the board (and I believe it was adopted by the board), that USP would be incorporated by reference into CA compounding laws to add clarity and remove any confusion regarding whether the board's regulations line up with USP. If that is being done, then this revision seems to contradict that. Currently USP 795 and 797 are undergoing major revisions. These revisions are due to be finalized by next summer and go into effect December 2019. However, the current proposed text for the CA compounding laws, will likely contradict parts of the finalized USP documents. I propose incorporating USP by reference instead of making the currently proposed edits which would eliminate the confusion of what the exact standards are.

Feel free to reach out if you would like any additional information.

Lauren

~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~

Lauren Eichstadt Forsythe, PharmD, DICVP, FSVHP
Staff Pharmacist

UC Davis Veterinary Medical Teaching Hospital
One Shields Avenue
Davis, California 95616
530-752-4858
leichstadt@ucdavis.edu
~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~

# Compilation document of the comments received during the 45-day comment period with staff recommendations

**Regulatory Proposal Regarding Compounded Drug Preparations**
**Staff Analysis of, and Recommended Responses to, Comments Received**
**During 45-Day Comment Period**

## Summarized 45-day Comments regarding Compounded Drug Preparations with board staff recommendations

Board staff notes that The United States Pharmacopeia - National Formulary (USP) is the professional industry standards used across the nation. USP contains standards developed by a committee of experts that among other things, help ensure the quality of compounded medications. USP's General Chapters for compounding establish procedures, methods and practices that are utilized by practitioners to help ensure the quality of compounded preparations. The General Chapters for compounding include Chapter 795 (Pharmaceutical Compounding – Nonsterile Compounding), Chapter 797 (Pharmaceutical Compounding – Sterile Preparations) and Chapter 800 (Hazardous Drugs – Handling in Healthcare Settings). Further, the U.S. Federal Food, Drug, and Cosmetics Act designates the USP as the official compendia for drugs marketed in the United States. All drug products within the U.S. market must conform to the standards in USP to avoid possible charges of adulteration and misbranding.

## 45-Day Public Comment Period

During the 45-day public comment period from August 3, 2018 to September 17, 2018, the board received six written comments. Each comment is included in its entirety within the meeting materials.

## #1 Written Comments from Ayk Dzhragatspanyan, PharmD.

Comment #1.A: Dr. Dzhragatspanyan expressed concern about the inability to use published formulas for beyond use dates with respect to non-sterile preparations. Dr. Dzhragatspanyan indicated that he believes that the regulation is very restrictive and impacts patients. He recommended that the regulations be amended to allow for the use of published literature when compounding for establishing a BUD.

Board Staff Response to Comment #1.A: The board staff recommend that this comment be rejected because his suggestions are already incorporated into the regulation proposal (See proposed text of CCR section 1735.2(i)(1)(G)). The proposal allows for the use of documentation, literature, research, and analysis by the pharmacist when establishing a beyond use date for non-sterile drug preparations. This change is consistent with USP <795>, specifically the provisions established under the heading, "Stability Criteria and Beyond-Use Dating."

Comment #1.B: Dr. Dzhragatspanyan also expressed concern about the 3-day BUD limit for sterile preparations. Dr. Dzhragatspanyan indicated that the sterility testing takes two weeks to complete.

Board Staff Response to Comment #1.B: Board staff recommend that this comment be rejected. The board's current regulations relating to the establishment of a BUD for sterile

preparations are consistent with USP <797> provisions relating to sterile preparations. The primary focus of this regulation proposal relating to BUDs is on nonsterile compounded preparations.

**#2: Written Comments from Corbin Bennett, Pharm.D.**

Comment #2: Dr. Bennett recommended adding "CACI" following the term "BSC" to section 1735.6(e)(3).

Response to Comment #2: The board staff recommend that this comment be accepted and have provided proposed modified text for the board to consider. The use of a CACI was inadvertently left out of the original proposed text when the language was amended from PEC to BSC. The inclusion of a CACI is appropriate within this section because it is also a type of containment device that would appropriately control particulate distribution that might occur during hazardous compounding.

Upon further review of the proposed language and comment received, it was identified that the language may have inadvertently prevented the ability to use other types of containment devices when preparing hazardous nonsterile compounds. Under the provisions of USP Chapter 800, an alternative containment device (referred to therein as a C-PEC) may be used for compounding hazardous nonsterile preparations, and may alternately use a redundant HEPA filter rather than external exhaustion. In recognition of this, the proposed language was further modified to address this issue.

Further, staff recommends that the word "also" be deleted from the existing language of subsection (e)(3), which appears in staff's proposed new subsection (e)(3)(A), so that, if the containment device is itself externally vented, the facility will satisfy main subsection (e) by exhausting the room through the containment device itself. Though an unusual method of exhausting the room, any particulates should be adequately removed to protect the products and the compounding staff.

**#3: Written Comments from Sarah Han-Yoo, Pharm.D.**

Comment #3: Dr. Han-Yoo expressed concern about that the temperature change from 68-75 degrees Fahrenheit (20-24 degrees Celsius) to a maximum of 68 degrees Fahrenheit (20 degrees Celsius) in section 1751.4. Dr. Han-Yoo indicated that 68 degrees Fahrenheit was too cool for hospital patients and portable air conditioners cannot be used within a sterile environment. She recommends the board reconsider the change, inferring that the board to keep existing language.

Response to Comment #3: The board staff recommend that this comment be rejected as some change will be consistent with the temperature recommendations within USP <797>. Further, board compounding experts note that because of the garbing requirements for staff engaging in compounding, individuals may perspire in the higher temperatures permitted by the existing text. Perspiration contains bacteria which can ultimately compromise the sterility of the environment and of the compounded drug preparations. However, in response to a separate

comment received, board staff is recommending that the proposed language be amended to allow for a maximum of 22 degree Celsius to provide some flexibility within the negative pressure room for the storage of specific hazardous drugs.

Regarding the concern expressed Dr. Han-Yoo about the temperature in patient care areas, the board's proposed regulation applies to compounding areas, not patient care rooms.

**#4: Written Comments from Dale Costantino, Pharm.D.**

Comment #4: Dr. Costantino agreed that lowering the temperature requirement within section 1751.4 was beneficial for compounding personnel; however, he expressed concern about the ability to implement the reduced temperature requirement within hospitals. Dr. Costantino requested that the temperature changed be delayed or that the board allow a waiver to hospitals to make the appropriate changes to the facilities.

Response to Comment #4: The board staff recommend that this comment be accepted in part (accept his agreement with raising the maximum temperature) and rejected in part (reject his request to delay adoption of the change). USP <797> specifies that the temperature should typically be 20 degrees C (68 degrees F) or cooler. Based on a separate comment received, board staff is recommending that the proposed language be amended to allow for a maximum of 22 degrees Celsius to provide some flexibility within the negative pressure room to allow for the storage of some hazardous drugs.

With respect to Dr. Constantino's request for a temporary waiver, board staff recommends denying that comment because if the higher temperature poses a risk to compounded sterile products, it should not be allowed to continue. In addition, with board staff's recommended higher temperature, staff believes compliance should be more easily obtained.

**#5: Written Comments from Michael Tou, Pharm.D.**

Comment #5: Dr. Tou expressed concern about that ability to implement the reduced temperature requirement within hospitals. Dr. Tou indicated that some hospitals will require building modifications to comply. Additionally, Dr. Tou expressed concern that certain drugs used in compounded products are required (by other provisions of USP and by manufacturer specifications) to be stored at controlled room temperatures of 68 degrees F to 77 degrees F. He indicated that reducing the temperature of the sterile environment to 68 degrees or below would conflict with drug storage requirements and would prevent the hospital from storing drugs in the compounding area. Dr. Tou requested that (A) the temperature be modified to include a range from 20 – 22 degrees Celsius (68-72 degrees Fahrenheit) to allow for a comfortable working environment for compounding staff and allow for the storage of specific drugs within the compounding area, or (B) that implementation of any modified temperature range be delayed, or that the board grant a waiver to hospitals in order to allow hospitals to make the appropriate physical changes to their facilities.

Response to Comment #5: The board staff recommend that this comment be accepted in part (allow a temperature maximum of 22 degrees Celsius) and rejected in part (not implement the

change, delay adoption of the change, or grant a waiver during construction). USP <797> specifies that the temperature where sterile compounding occurs should typically be 20 degrees C (68 degrees F) or cooler. In response to comment #5(A), board staff is recommending that the proposed language be amended to allow for a maximum of 22 degree Celsius (71.6 degrees Fahrenheit) to provide some flexibility within the negative pressure room for the storage of specific hazard drugs. With respect to Dr. Tou's request (#5(B)) for delayed implementation or a temporary waiver, the board staff recommends rejecting that comment. Board staff recommends denying that comment because the higher temperature poses a risk to compounded sterile products, and therefore should not be allowed to continue. In addition, with board staff's recommended higher temperature of 22 degrees Celsius, compliance should be more easily obtained.

**#6: Written Comments from Lauren Eichstadt-Forsythe, Pharm.D.**

Comment #6: Dr. Eichstadt-Forsythe recommended that the proposed changes not be implemented and instead, recommended that the board incorporate USP by reference to eliminate confusion. Dr. Eichstadt-Forsythe notes that USP is currently being amended and the amendments will not be finalized until December 2019.

Response to Comment #6: The board staff recommend that this comment be rejected. Board staff notes that the board is working toward incorporating USP into California statute; however, the current proposed changes are necessary to address an immediate issue related to BUDs within existing regulation text. In addition, changes to California law and to USP are, at this point, speculative. Board staff notes that delaying these changes for based on speculative changes will impact patient safety within California.

# Staff Recommended Modified Text

**Title 16. Board of Pharmacy**
**Proposed Text**

Changes made to the originally proposed language are shown by ~~double strikethrough~~ for deleted language and double underline for added language.

Proposed changes to the current regulation language are shown by ~~strikethrough~~ for deleted language and underline for added language. Additionally, text in [brackets] indicates language that is not being amended.

Note: The board adopted an emergency regulation affecting regulation section 1735.2 effective December 19, 2017. The strikethrough and underline to the text of that section reflects changes from the board's non-emergency regulation.

**Amend section 1735.1, subdivisions (c) and (f), in Article 4.5 of Division 17 of Title 16 of the California Code of Regulations to read as follows:**

**1735.1. Compounding Definitions.**

[…]

(c) "Biological Safety Cabinet (BSC)" means a ventilated cabinet for compounding sterile drug preparations, having an open front with inward airflow for personnel protection, downward HEPA-filtered laminar airflow for product protection, and HEPA-filtered exhausted air for environmental protection. Where hazardous drugs are prepared, the exhaust air from the biological safety cabinet shall be appropriately removed by properly designed external building ~~ventilation~~ exhausting. This external ~~venting~~ exhaust should be dedicated to one BSC or CACI.

[…]

(f) "Compounding Aseptic Containment Isolator (CACI)" means a unidirectional HEPA-filtered airflow compounding aseptic isolator (CAI) designed to provide worker protection from exposure to undesirable levels of airborne drug throughout the compounding and material transfer processes and to provide an aseptic environment for compounding sterile preparations. Air exchange with the surrounding environment should not occur unless the air is first passed through a microbial retentive filter (HEPA minimum) system capable of containing airborne concentrations of the physical size and state of the drug being compounded. Where hazardous drugs are prepared, the exhaust air from the isolator shall be appropriately removed by properly designed external building ~~ventilation~~ exhaust. This external ~~venting~~ exhaust should be dedicated to one BSC or CACI. Air within the CACI shall not be recirculated nor turbulent.

[…]

Note: Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4029, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.

**Amend section 1735.2, subdivision (i), in Article 4.5 of Division 17 of Title 16 California Code of Regulations to read as follows:**

**1735.2. Compounding Limitations and Requirements; Self-Assessment.**

[…]

(i) Every compounded drug preparation shall be given a beyond use date representing the date or date and time beyond which the compounded drug preparation should not be used, stored, transported or administered, and determined based on the professional judgment of the pharmacist performing or supervising the compounding.

(1) For non-sterile compounded drug preparation(s), the beyond use date shall not exceed any of the following:

(A) the shortest expiration date or beyond use date of any ingredient in the compounded drug preparation,

(B) the chemical stability of any one ingredient in the compounded drug preparation~~;~~,

(C) the chemical stability of the combination of all ingredients in the compounded drug preparation,

(D) ~~180 days~~ for non-aqueous formulations, 180 days or an extended date established by the pharmacist's research, analysis, and documentation,

(E) ~~14 days~~ for water-containing oral formulations, 14 days or an extended date established by the pharmacist's research, analysis, and documentation, and

(F) ~~30 days~~ for water-containing topical/dermal and mucosal liquid and semisolid formulations, 30 days or an extended date established by the pharmacist's research, analysis, and documentation.

(G) A pharmacist, using his or her professional judgment may establish an extended date as provided in (D), (E), and (F), if the pharmacist researches by consulting and applying drug-specific and general stability documentation and literature; analyzes such documentation and literature as well as the other factors set forth in this subdivision, and maintains documentation of the research, analysis and conclusion. The factors the pharmacist must analyze include:

(i) the nature of the drug and its degradation mechanism,

(ii) the dosage form and its components,

(iii) the potential for microbial proliferation in the preparation,

(iv) the container in which it is packaged,
(v) the expected storage conditions, and
(vi) the intended duration of therapy.

Documentation of the pharmacist's research and analysis supporting an extension must be maintained in a readily retrievable format as part of the master formula.

(2) For sterile compounded drug preparations, the beyond use date shall not exceed any of the following:
(A) The shortest expiration date or beyond use date of any ingredient in the sterile compounded drug product preparation,
(B) The chemical stability of any one ingredient in the sterile compounded drug preparation,
(C) The chemical stability of the combination of all ingredients in the sterile compounded drug preparation, and
(D) The beyond use date assigned for sterility in section 1751.8.

(3) For sterile compounded drug preparations, ~~E~~ extension of a beyond use date is only allowable when supported by the following:
(A) Method Suitability Test,
(B) Container Closure Integrity Test, and
(C) Stability Studies

(4) In addition to the requirements of paragraph three (3), the drugs or compounded drug preparations tested and studied shall be identical in ingredients, specific and essential compounding steps, quality reviews, and packaging as the finished drug or compounded drug preparation.

(5) Shorter dating than set forth in this subsection may be used if it is deemed appropriate in the professional judgment of the responsible pharmacist.

[…]

Note: Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4029, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.

**Amend section 1735.6, subdivision (e), in Article 4.5 of Division 17 of Title 16 of the California Code of Regulations to read as follows:**

**1735.6. Compounding Facilities and Equipment.**

[…]

(e) Hazardous drug compounding shall be completed in an externally ~~vented~~ exhausted physically separate room with the following requirements:

(1) Minimum of 30 air changes per hour except that 12 air changes per hour are acceptable for segregated compounding areas with a BSC or CACI when products are assigned a BUD of 12 ~~hrs~~ hours or less or when non sterile products are compounded; and
(2) Maintained at a negative pressure of 0.01 to 0.03 inches of water column relative to all adjacent spaces (rooms, above ceiling, and corridors); and
(3) (A) For sterile compounding, each ~~Each PEC~~ BSC or CACI ~~in the room~~ shall ~~also~~ be externally ~~vented~~ exhausted, ~~except that a BSC used only~~
(B) ~~f~~For nonsterile compounding, a BSC, a CACI, or other containment ventilated enclosure shall be used and shall either ~~may~~ use a redundant-HEPA filter in series or be externally exhausted.~~; and~~ For purposes of this paragraph, a containment ventilated enclosure means a full or partial enclosure that uses ventilation principles to capture, contain, and remove airborne contaminants through high-efficiency particulate air (HEPA) filtration and to prevent their release into the work environment.
(4) All surfaces within the room shall be smooth, seamless, impervious, and non-shedding.

[…]

Note: Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4029, 4036, 4037, 4051, 4052 and 4127, Business and Professions Code.

**Amend section 1751.1, subdivision (a)(5), in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:**

**1751.1. Sterile Compounding Recordkeeping Requirements.**

(a) In addition to the records required by section 1735.3, any pharmacy engaged in any compounding of sterile drug preparations shall maintain the following records, which must be readily retrievable, within the pharmacy:
[…]
(5) Biannual ~~V~~ video of smoke studies in all ISO Class 5 certified spaces.
[…]

[…]

Note: Authority cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4029, 4036, 4037, 4051, 4052, and 4127, Business and Professions Code.

**Amend section 1751.4, subdivision (k), in Article 7 of Division 17 of Title 16 of the California Code of Regulations to read as follows:**

**1751.4. Facility and Equipment Standards for Sterile Compounding.**

[…]

(k) The sterile compounding area in the pharmacy shall have a comfortable and well-lighted working environment, which typically includes a room temperature of 20~~-24~~ degrees Celsius (68~~-75~~ degrees Fahrenheit) or cooler, but shall not exceed a temperature of 22 degrees Celsius (71.6 degrees Fahrenheit), to maintain comfortable conditions for compounding personnel when attired in the required compounding garb.

[…]

Note: Authority Cited: Sections 4005 and 4127, Business and Professions Code. Reference: Sections 4005, 4029, 4036, 4037, 4051, 4052 and 4127, Business and Professions Code; and Section 18944, Health and Safety Code.