Crystal A. Frost, PhD
December 9, 2024

Written Public Comment on Proposed Amendments to Title 16 CCR Sections 1735-1738

Dear Members of the California State Board of Pharmacy,

I am writing this public comment on behalf of Stop the BOP, a nonpartisan patient-led movement advocating for the protection of access to sterile compounded medications that are essential to the lives of hundreds of thousands of Californians and utilized in countless medical communities around the world.

The proposed amendments to Title 16 of the California Code of Regulations, Sections 1735-1738, threaten to dismantle the fragile lifeline that many patients, caregivers, and healthcare providers depend on. Your decision to advance these regulations, which severely restrict access to Category 1 sterile compounded treatments, is not just a regulatory overreach—it is a decision with profound and unjustified human consequences. I implore you to reconsider this path and to align your actions with the foundational mission of this Board: to protect public health.

Impact on Patient Access: A Matter of Life and Death

These compounded treatments are not a luxury or a choice for the patients who rely on them. They are a necessity. They represent the only effective medical interventions for individuals whose conditions cannot be addressed by standard pharmaceuticals. Though too many to list, this includes:

- **Alzheimer's Disease and Dementia:** Studies have repeatedly connected glutathione deficiency to various forms of dementia, particularly Alzheimer's Disease. Boosting glutathione levels has demonstrated improvements in both memory and cognitive function. Additionally, sterile compounded formulations of Nicotinamide Adenine Dinucleotide (NAD) have shown promise in enhancing cognitive function and slowing neurodegeneration in these patients. (Source*: Int. J. Mol. Sci, "Glutathione in the Brain")
- **Lyme Disease and Long COVID Patients:** Chronic illness patients often face systemic inflammation, immune dysfunction, and debilitating fatigue. Neuroinflammation, glutathione deficiency, and NAD deficiency have been connected to both neurological Lyme and Long COVID. (ACS Infectious

Diseases, 2020) Treatments like intravenous glutathione, Methyl B12 shots, and NAD+ provide these patients with critical support and symptom relief. For many with these conditions, Category 1 sterile compounds are the only options to address neurocognitive decline caused by impaired detox pathways and mitochondrial dysfunction. (Source*: LymeDisease.Org, "The Power Trio")

- **Pernicious Anemia and MTHFR Gene Mutation:** Patients with Pernicious Anemia cannot absorb B12 from food and oral supplements. Cyanocobalamin, the synthetic version of B12 approved by the FDA, contains cyanide molecules harmful to those with impaired detoxification pathways and ineffective for those with the MTHFR gene mutation, which makes conversion from cyanocobalamin to methylcobalamin impossible. For patients with MTHFR mutations, methyl B12 shots are often a life-saving necessity. Without access to it, patients risk debilitating and often life-threatening B12 deficiency, including nerve damage and cognitive decline. (Source*: Ann. Hematol, "MTHFR polymorphisms and vitamin B12 deficiency")
- **Firefighters and First Responders:** Occupational exposure to toxins places firefighters and first responders at heightened risk of oxidative stress and chronic illnesses. Many of them rely on compounded nebulized and IV glutathione to maintain their health and continue serving their communities. In a pilot program, just 16 weeks of IV glutathione resulted in a 93% reduction in glyphosate. (Source*: VFF, "Firefighter Detoxification Pilot Program")
- **Autism Spectrum Disorder:** Methylcobalamin injections have been shown to improve speech, social engagement, and adaptive behaviors in some children with autism, providing hope to families who otherwise had no effective options. (Source*: TACA, "Methyl B12 for Autism")

See pages 7-11 for full list of sources, links to research and educational websites

These are not hypothetical cases. These are real lives—real people—who depend on these treatments to survive, to work, to parent, and to live.

Arbitrary and Unjustifiable Regulations

The proposed amendments exceed federal and U.S. Pharmacopeia (USP) standards in dozens of ways, going far beyond what is required to ensure patient safety. They introduce barriers that are unnecessary and unsupported by evidence. Time and time

again, this Board has failed to provide credible evidence of harm associated with the treatments it seeks to restrict.

In contrast, patient advocates and healthcare providers have presented substantial evidence demonstrating the safety and efficacy of these compounds. The Board's decision to ignore this data is indefensible and flies in the face of its duty to act in the best interests of Californians.

Redundant Stability Testing: An Unnecessary and Costly Barrier Rooted in Misinformation

The proposed amendments introduce stringent stability testing requirements for compounded medications, imposing significant financial burdens on compounding pharmacies. These costs will inevitably be passed on to patients, many of whom are already struggling to afford these essential treatments. Custom medications from compounding pharmacies are often the only option for patients with unique health needs, and the added expense from redundant testing threatens to make these treatments inaccessible.

Board Member Maria Serpa has argued that there are "gaps" in the U.S. Pharmacopeia (USP) guidelines and that these additional stability testing requirements are necessary to fill those gaps. This assertion, however, is misleading and unsubstantiated. The USP already provides comprehensive and evidence-based standards for compounding practices in General Chapters <795> and <797>, which cover both nonsterile and sterile preparations. These guidelines include stringent requirements to ensure the safety, strength, and stability of compounded medications and are widely regarded as the gold standard for compounding practices nationwide.

To suggest that USP guidelines are insufficient without providing clear scientific evidence undermines the credibility of the regulatory process. Imposing redundant testing requirements appears to be less about addressing real gaps and more about creating excessive financial and logistical barriers for compounding pharmacies, effectively pricing out vulnerable patients and eliminating access to life-saving treatments. This approach is not only unjustified but harmful.

The additional stability testing requirements mirror the Board's initial attempt to outright eliminate access to these compounds in the first draft of this proposal—an effort broadly opposed by the public and medical community. Such measures

disproportionately harm patients with chronic illnesses, rare conditions, and other complex needs by further driving up costs for medications that are already difficult to afford.

I urge the Board to reject these redundant and punitive requirements. Regulatory decisions must be based on established science, such as the existing USP guidelines, not on baseless claims or misinformation. It is unacceptable to use unproven assertions as a pretext for policies that will devastate the lives of countless patients. Instead, the Board should focus on supporting access to safe, affordable, and effective compounded treatments.

Universal Concerns About Regulatory Process

It is deeply troubling to witness the degree of influence that Board staff appear to have over member decision-making. Your presentations on November 7th, which attempted to support these regulations through fearmongering and misrepresentation of federal law, were led by two individuals with little to no medical or scientific expertise: Executive Officer Anne Sodergren, whose education consists of a Bachelor's Degree in Communications, and a taxpayer-funded lawyer from the Department of Consumer Affairs.

On the contrary, highly credentialed professionals—including doctors, pharmacists, and researchers—have testified in opposition to these regulations. This dynamic not only undermines the credibility of the Board but also raises serious ethical and legal concerns about undue influence. Patients and patient advocates have passionately testified at your board meetings, sharing deeply personal accounts of how these treatments have saved their lives and pleading with this Board to safeguard their access. You claim these restrictions and testing requirements are intended to protect patients, yet not one patient has stepped forward to express gratitude for these measures. Instead, countless individuals have voiced their belief that these actions are not only harmful but appear to be driven by indifference—or worse, a disregard—for the very people you are meant to serve.

The Board must ask itself: How can it justify restricting access to life-saving treatments when the evidence and expert consensus are overwhelmingly against such action? Who is this board answering to if not the people it has sworn to serve and protect?

Premature Enforcement and the Use of Underground Regulations

Crystal A. Frost, PhD
December 9, 2024

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- **Lyme Disease and Long COVID Patients:** Chronic illness patients often face systemic inflammation, immune dysfunction, and debilitating fatigue. Neuroinflammation, glutathione deficiency, and NAD deficiency have been connected to both neurological Lyme and Long COVID. (ACS Infectious

The California State Board of Pharmacy has been enforcing what can only be described as underground regulations—imposing restrictions and requirements on compounding pharmacies that have not been formally approved through the required rulemaking process. This approach not only violates established regulatory protocols but has already caused irreparable harm to the compounding community and the patients who rely on these treatments.

Numerous 503A compounding pharmacies have been forced to shut down due to the Board's premature enforcement of these unapproved regulations. Others have been coerced into converting into 503B outsourcing facilities, a transition that imposes substantial financial and operational burdens, often rendering patient-specific compounded medications inaccessible. These actions are not only unjustified but also catastrophic for the patients who depend on these pharmacies for life-saving treatments.

One of the key justifications the Board has cited for these underground regulations is the arbitrary claim that certain compounded substances lack USP drug monographs or are not of "pharmaceutical grade." However, this reasoning is fundamentally flawed. The FDA does not define or regulate "pharmaceutical grade" as a standard for compounding substances. Instead, the FDA evaluates compounded medications based on whether they are prepared using components that comply with existing USP standards or are listed on the 503A Bulks List. The Board's reliance on non-existent terminology and unsubstantiated assertions demonstrates a lack of understanding of federal guidelines and creates unnecessary confusion for pharmacies and patients alike.

Furthermore, the Board's focus on whether a compound has a USP monograph ignores the broader framework of federal law, which allows for the use of safe and effective substances in compounding even if they do not have USP monographs, provided they are included on the 503A Bulks List. By arbitrarily restricting access to these substances, the Board is not protecting patients but actively harming them by removing critical treatments from the market.

This overreach and reliance on underground regulations reveal a troubling pattern: the Board appears more intent on creating barriers to compounding than on ensuring patient safety. These actions disregard federal standards, undermine due process, and ultimately jeopardize patient access to essential care.

Patient Advocacy and Public Opposition

Stop the BOP, alongside organizations like LymeDisease.org, the Pernicious Anemia Society, the California Naturopathic Doctors Association, and the Center for Lyme Action, has mobilized thousands of patients, families, and advocates to oppose these harmful regulations. This is a grassroots effort with no funding, and yet our petition alone has gathered over eight thousand signatures, representing a united voice against this overreach.

Board members, this is not a fringe issue as board staff would like you to believe. The outcry from patients and providers reflects the widespread and devastating impact these regulations would have if implemented. In a time when politics painfully highlight the deep divisions in our country, it is extraordinarily rare to see such diverse communities—spanning all political backgrounds and walks of life, including chronic illness patients, first responders, parents, and integrative healthcare providers—unite with such urgency and clarity. Yet here we are, standing together and pleading for you to listen.

Your Responsibility and Legacy

I urge you to reflect on the legacy you wish to leave as members of the California State Board of Pharmacy. Do you want to be remembered as the individuals who ignored public outcry and denied patients access to their safe, life-saving treatments, forcing them to suffer needlessly or—in the case of those who have the freedom to do so—move out of California? Or will you take a stand for science, compassion, and patient rights?

The proposed regulations are not a step forward; they are a step backward into unnecessary suffering and injustice. I ask you to pause, reconsider, and reject these amendments. Please do not let regulatory overreach and bureaucratic inertia rob Californians of the treatments that give them a chance to heal, to live, and to thrive.

Respectfully,

Crystal A. Frost, PhD
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CalDerm
The Voice of California Dermatology

December 9, 2024

California State Board of Pharmacy
Attn: Lori Martinez
2720 Gateway Oaks Drive, Suite 100
Sacramento, CA 95834

Sent via email to: PharmacyRulemaking@dca.ca.gov

Re: Title 16 CCR Sections 1735 et seq, 1736 et seq, 1737 et seq, and 1738 et seq Related to Compounded Drug Preparations, Hazardous Drugs and Radiopharmaceuticals

Dear Members of the California State Board of Pharmacy,

On behalf of the approximately 3,000 members of the California Society of Dermatology & Dermatologic Surgery (*hereafter* "CalDerm"), we urge the California State Board of Pharmacy (*hereafter* "Board") to explicitly exempt physicians and surgeons (MDs/DOs) from the proposed regulations governing sterile and nonsterile compounding. The regulation of physician in-office compounding should remain under the purview of the Medical Board of California and Osteopathic Medical Boards of California.

We respectfully request adding the following language below:

1735.1. Introduction and Scope
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(i). The provisions of this article shall not apply to nonsterile compounding by physicians and surgeons licensed under Chapters 5 and 8 of Division 2 of the California Business and Professions Code.

1736.1. Introduction and Scope

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(i). The provisions of this article shall not apply to sterile compounding by physicians and surgeons licensed under chapters 5 and 8 of Division 2 of the California Business and Professions Code.

For example, existing law (BPC 2220.5) is unequivocal that only the Medical Board of California can take action and discipline its licensees. Specifically, subsection (a) states:

> *"The Medical Board of California is the only licensing board that is authorized to investigate or commence disciplinary actions relating to physicians and surgeons who have been issued a certificate pursuant to Section 2050."*

Whenever physicians and surgeons are engaging in compounding (or any other action that their medical license authorizes them to perform) they must always do so consistent with the standard of care. For the purposes of Medical Board of California enforcement program, the standard of care is established by expert testimony in the context of the facts and circumstances of a specific case.

Furthermore, one in four Americans suffers from a skin disease. Dermatologists diagnose and treat more than 3,000 diseases, including skin cancer, psoriasis, immunologic diseases, and many genetic disorders. As dermatologists on the front lines fighting skin cancer and treating numerous skin diseases, we are advocating for our patients to have access to compounded medications, especially in-office preparations.

Buffering lidocaine with epinephrine is prepared in syringes to reduce pain. As physicians, the tenets of our profession are based on the Hippocratic Oath "to first do no harm." The proposed regulations impose onerous requirements that effectively prohibit dermatologists from buffering lidocaine. We would violate this oath by inflicting unnecessary pain and suffering upon our patients.

Thank you in advance for the opportunity to work together to ensure dermatology patients have access to treatment with an in-office prepared product that significantly reduces patient discomfort and causes no harm. Should you have any questions, please do not hesitate to contact CalDerm Legislative Advocate Bryce Docherty at bdocherty@tdgstrategies.com or (916) 769-0573.

Sincerely,

Anna McNay, MD
President, CalDerm

cc: Kimberley Kirchmeyer, Director, Department of Consumer Affairs
The Honorable Joaquin Arambula, MD
The Honorable Jasmeet Bains, MD
The Honorable Akilah Weber, MD
Richard Figueroa, Special Advisor, Office of Governor Gavin Newsom
Bryce Docherty, TDG Strategies

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RESOLUTE

December 9, 2024

Lori Martinez
California State Board of Pharmacy
2720 Gateway Oaks Drive, Suite 100
Sacramento, CA 95833

Re: Proposed Regulations on Compounded Drug Preparations, Hazardous Drugs and Radiopharmaceuticals- ***Comments Submitted on behalf of the Association of Northern California Oncologists and the Medical Oncology Association of Southern California***

Dear Ms. Martinez,

On behalf of my clients, the Association of Northern California Oncologists (ANCO) and the Medical Oncology Association of Southern California(MOASC) I write to you to provide comments on the proposed regulations regarding compounded drug preparation.

Oncologists deliver chemotherapy treatments to their patients in a variety of ways including in-office injections and infusions. Preparing, mixing, diluting and reconstituting medications that have been approved by the US Food and Drug Administration for cancer treatments in the office setting, under the direct supervision of the oncologist, are common activities at community sites of care. We are concerned that the proposed regulations will require a pharmacist to be present during these types of activities, which would be an onerous burden on community sites of care, particularly those in rural settings. ANCO and MOASC are concerned that these proposed regulations, if adopted, would result in cancer patients being forced to obtain their chemotherapy at a hospital or infusion center, which would place new burdens on patients who are already fighting for their lives.

My clients, therefore, propose the Board of Pharmacy amend the proposed regulations, consistent with amendments suggested by the California Medical Association, which would make clear the proposed regulations do not apply to physicians. (Proposed amendments in ***blue italics***.)

> § 1735.1: In addition to the standards in USP Chapter 795 and, Food Drug Cosmetic Act (FDCA) section 503a (21 U.S.C. §353a) the compounding of a CNSP shall meet the

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following requirements of this article. ***This article shall not apply to compounding by or under the direct supervision of a licensed physician and surgeon.***

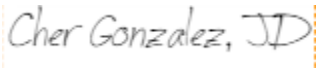
§ 1736.1: In addition to the standards set forth in USP Chapter 797 and Food Drug Cosmetic Act (FDCA) section 503a (21 U.S.C. §353a) the following requirements apply throughout this article. ***This article shall not apply to compounding by or under the direct supervision of a licensed physician and surgeon.***

§ 1737.1: In addition to the requirements in USP Chapter 800 and Food Drug Cosmetic Act (FDCA) section 503a (21 U.S.C. §353a) the following requirements apply to the compounding of Hazardous Drugs. ***This article shall not apply to compounding by or under the direct supervision of a licensed physician and surgeon.***

§ 1738.1: In addition to the standards in the USP Chapter 825, the processing of Radiopharmaceuticals shall meet the requirements of this section. ***This article shall not apply to compounding by or under the direct supervision of a licensed physician and surgeon.***

Thank you for considering these comments. Should you have any questions please feel free to reach me at cher@resolutecompany.com.

Regards,



Cher Gonzalez

Partner, Resolute and Gonzalez Government Consulting

On behalf of the Association of Northern California Oncologists (ANCO) and the Medical Oncology Association of Southern California (MOASC)

REACT19

RESEARCH • EDUCATION • ACTION • THERAPEUTICS

To: California State Board of Pharmacy
Email: Lori Martinez, PharmacyRulemaking@dca.ca.gov
Fax: (916) 574-8618
Re: Title 16 CCR Sections 1735–1738 – Opposition to Proposed Regulations on Sterile Compounded Medications

Date: December 5, 2024

Dear Members of the California Board of Pharmacy,

React19, a 501(c)(3) nonprofit organization, represents over 36,000 individuals suffering from life-altering effects of COVID-19 vaccination. These adverse reactions, often referred to as 'Long Vax,' affect hundreds of thousands globally, causing severe, disabling conditions. Despite extensive documentation and evidence of these injuries, research and development of treatments remain neglected. The proposed regulations further exacerbate these challenges by restricting access to therapies critical for both patient care and advancing medical innovation. These therapies are often their only means of managing symptoms in the absence of FDA-approved treatments.

Why These Regulations Harm Patients

Unnecessary Barriers to Critical Treatments
The proposed regulations impose restrictions that go beyond federal FDA guidelines. The Board's proposal complicates existing federal oversight without evidence of safety risks. Implementing regulations that conflict with and exceed FDA guidelines creates unnecessary barriers to care for patients and burdens for providers. These therapies are often the only treatment options for individuals with complex chronic conditions who cannot rely on mass-manufactured medications.

While the Board proposes severe restrictions on compounded medications, FDA-approved drugs with well-documented risks—ranging from contaminated generics to addictive opioids—continue to receive lenient oversight. Such apparent double standards risk undermining public confidence in regulatory processes and further alienating communities already harmed by an FDA EUA substance.

Disproportionate Impact on Vulnerable Populations
These patients are Californians—not abstractions—who depend on sterile compounded therapies to maintain a semblance of quality of life. By restricting access, the Board risks leaving these individuals without any viable options, forcing them to endure worsened symptoms and diminished independence.

Risks to Medical Innovation
Sterile compounded medications are indispensable for advancing research into neglected conditions like Long Vax. Curtailing access could hinder California's role as a leader in medical innovation and delay breakthroughs desperately needed by millions worldwide.

Undue Influence
These restrictions not only disregard the needs of patients but also raise concerns about the motivations driving them, suggesting undue influence by pharmaceutical interests over patient care. Limiting access to compounded therapies unfairly shifts the burden of risk onto vulnerable populations.

What's at Stake
The Board risks sending the message that their suffering is invisible and their lives expendable. This outcome is unacceptable for a regulatory body charged with protecting public health and safety.

Recommendations
React19 urges the Board to:
1. Withdraw the Proposed Regulations and align policies with evidence-based federal standards under FDA sections 503A and 503B.
2. Engage Stakeholders—including patients, clinicians, and researchers—in developing patient-centered guidelines that reflect real-world needs.
3. Delay Implementation to assess the regulations' unintended consequences on patient care and research.

Legal and Regulatory Context
The compounding practices targeted by these regulations adhere to USP <797> standards, which outline rigorous sterility and safety protocols. These compounded medications comply with federal guidelines under Sections 503A and 503B, which govern the preparation of customized therapies for patient care.

In conclusion, these regulations threaten the health and well-being of vulnerable Californians. React19 urges the Board to reconsider and prioritize policies that protect access to essential treatments while maintaining safety standards.

Thank you for your attention to this critical issue.

Sincerely,

The React19 Board of Directors

California Rheumatology Alliance

Advocacy for Patient Access to Rheumatology Care

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December 9, 2024

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re: Proposed Regulations on Compounded Drug Preparations, Hazardous Drugs and Radiopharmaceuticals

Dear Ms. Martinez,

The California Rheumatology Alliance (CRA) appreciates the opportunity to provide comments on the proposed regulations on compounded drug preparation. Rheumatologists are medical professionals who specialize in diagnosing and treating conditions that cause inflammation in the joints, muscles, ligaments, tendons, and bones. For most rheumatology patients they are receiving treatment for their chronic conditions for years if not decades to help them manage their disease. Our goal is to improve the quality of life of our patients by reducing pain, preserving joint function, and helping them manage their rheumatic conditions.

For many patients, treatments may include receiving injections or infusions in their rheumatologist's office. Many times, the medications are delivered to the rheumatologist's office in a powder form and requires the physician to add saline or dextrose. This is sometimes referred to as buffering, a medication which, is our understanding constitutes compounding.

We are concerned that the proposed regulations will not allow rheumatologists to buffer injection/infusion medications in-office. We are interpreting the proposed regulations to require a pharmacist be present or performing the buffering of the injection/infusion medications. Rheumatology practices would not be able to afford to employ a pharmacist for this one purpose. This would lead to rheumatology practices no longer offering this service for our patients. Patients would then be forced to obtain their injection/infusions at a hospital or infusion center which would not only be less convenient for our patients, but it would be more expensive for the patient and the overall healthcare system.

The mixing of medications by rheumatologists when injecting/infusing is viewed as the standard of care. We believe it is important to note we are not aware of any issues with rheumatologists "compounding" injection/infusion medications.

We would like to propose the Board of Pharmacy adopt the language suggested by the California Medical Association as shown below.

> **§ 1735.1:** In addition to the standards in USP Chapter 795 and, Food Drug Cosmetic Act (FDCA) section 503a (21 U.S.C. §353a) the compounding of a CNSP shall meet the following requirements of this article. **This article shall not apply to compounding by or under the direct supervision of a licensed physician and surgeon.**
>
> **§ 1736.1:** In addition to the standards set forth in USP Chapter 797 and Food Drug Cosmetic Act (FDCA) section 503a (21 U.S.C. §353a) the following requirements apply throughout this article. **This article shall not apply to compounding by or under the direct supervision of a licensed physician and surgeon.**
>
> **§ 1737.1:** In addition to the requirements in USP Chapter 800 and Food Drug Cosmetic Act (FDCA) section 503a (21 U.S.C. §353a) the following requirements apply to the compounding of Hazardous Drugs. **This article shall not apply to compounding by or under the direct supervision of a licensed physician and surgeon.**
>
> **§ 1738.1:** In addition to the standards in the USP Chapter 825, the processing of Radiopharmaceuticals shall meet the requirements of this section. **This article shall not apply to compounding by or under the direct supervision of a licensed physician and surgeon.**

We believe this will be the best approach to maintain a physician's ability to compound in the best interest of the patient. We appreciate your consideration of our requested changes.

Respectfully,

Samy Metyas, MD
President, California Rheumatology Alliance

December 9, 2024

Lori Martinez
Board of Pharmacy
2720 Gateway Oaks Drive, Ste. 100
Sacramento, CA 95833

Submitted via e-mail to Lori.Martinez@dca.ca.gov

SUBJECT: Board of Pharmacy Proposed Modified Regulations: Compounded Drug Preparations

Dear Ms. Martinez,

On behalf of more than 400 hospitals and health systems, the California Hospital Association (CHA) appreciates the opportunity to comment on the Board of Pharmacy's (BoP) proposed modified regulations for compounded drug preparations.

The compounding of drugs is important to patients because it allows for personalized care that addresses individual patient needs, particularly when commercially available medications are not suitable. By providing customized dosages, alternative delivery forms, and formulations that avoid allergens or other sensitivities, compounding can improve medication adherence, treat rare or complex conditions, manage chronic pain, and ensure continuity of care during drug shortages. Ultimately, compounding improves patient outcomes by providing solutions that are not available in standard pharmaceutical offerings, allowing for more effective and targeted treatments.

Compounding in hospitals is critically important because it allows health care providers to offer personalized, flexible, and precise treatments tailored to the unique needs of individual patients. In hospital settings, patients may have complex medical conditions that require specialized medications that are not available in commercially manufactured forms. Compounding enables hospitals to address these needs effectively, ensuring optimal therapeutic outcomes and enhancing patient care.

While CHA agrees regulations are essential in the field of pharmacy, CHA only supports the promulgation of regulations that, based on evidence, are needed to ensure public safety, effective health care delivery, and the integrity of the pharmaceutical profession. CHA does not believe these modified proposed regulations will meaningfully enhance protection of or promote the health and safety of Californians. Furthermore, they are duplicative of federal law, which already requires the compounding of drug preparations to be consistent with extensive and strict standards in the current version of the United States Pharmacopeia (USP)-National Formulary. When states implement their own regulations

on areas already covered by federal law, it leads to regulatory redundancy, which burdens businesses, individuals, and government agencies with unnecessary compliance efforts, legal complexities, and costs.

Additionally, the BoP has failed to produce empirical evidence in both the Initial Statement of Reason *and* the modified statement indicating either systemic challenges or that patients have been placed in harm's way — or that hospital pharmacies are not meeting safety standards that might necessitate additional BoP regulations. We were unable to substantiate hospital pharmacies failing to follow either the BoP's current regulations or the detailed federal USP standards. Regulations lacking a solid evidence base will lead to unnecessary compliance costs for hospitals, and they may lead to confusion and legal disputes between regulators and businesses.

Today, more than half of all California hospitals lose money every day to provide care for patients. This is driven by stagnant reimbursement in the face of ever-increasing expenses for labor, pharmaceuticals, **regulatory mandates**, and more. The cost to deliver care has risen more than 30% in the past five years alone.

Adopting these regulations will divert patient care dollars from hospitals' finite resources, increase compliance confusion and uncertainty, reduce efficiency, and increase the risk of legal penalties. Striking a balance between necessary oversight and the minimizing of confusing and inefficient compliance standards is critical to fostering a sustainable health care system for the needs of current and future patients.

Hospitals, the California Legislature, and the California Department of Health Care Access and Information are working diligently to lower health care costs. Every additional requirement a hospital must fulfill raises costs, which runs counter to this shared goal. These considerations must be balanced when creating new regulations.

There is abundant and effective regulatory guidance provided by the USP, and the BoP's proposed modified regulations would have too many unintended consequences. In lieu of adopting new regulations, we recommend the BoP adopt the federal USP standards as written and delete current outdated state regulations.

CHA appreciates the opportunity to discuss these perspectives. If you have questions, please contact me at slowe@calhospital.org or 916-240-8277.

Sincerely,

Sheree Lowe
Vice President, State Policy

CALIFORNIA MEDICAL ASSOCIATION

December 9, 2024

Lori Martinez
Board of Pharmacy
2720 Gateway Oaks Drive, Suite 100
Sacramento, CA 95833
PharmacyRulemaking@dca.ca.gov

Sent via e-mail

RE: Compounded Drug Preparation Regulations, Modified Text Aug. 29, 2024

Dear Ms. Martinez:

On behalf of its over 50,000 medical student and physician members, the California Medical Association (CMA) submits the following comments on the Board of Pharmacy's proposed Compounded Drug Preparations regulations. The Board proposes to amend, repeal, and replace existing regulations, and to add new regulations, relating to drug compounding.

CMA supports protecting and promoting public health and patient safety. In making these changes, however, the Board has created ambiguities concerning the scope of the regulations that potentially interfere with the practice of medicine by imposing insurmountable barriers to the compounding of drugs by licensed physicians in medical office settings. In-office compounding is conducted in accordance with applicable state and federal law and the standard of care; is common in certain practice settings; and results in better care and patient experience. Applying the pharmacy-centric requirements of these proposed regulations to physician practices would adversely affect patient care.

Accordingly, we request that the Board revise the proposed compounding regulations to clarify that the regulations do not apply to compounding by licensed physicians, consistent with the Board's intended effect.

Applicability of Regulations to Non-Pharmacists and Non-Pharmacy Settings (§§ 1735.1, 1736.1, 1737.1, & 1738.1)

The modified text of the proposed regulations is unclear as to the scope of the regulatory requirements for the various types of compounding described in Articles 4.5, 4.6, 4.7, and 4.8. The proposed text on its face appears to apply to compounding activities by physicians in medical office settings, but the Board and its staff have made statements indicating they do not believe or intend for these requirements to apply outside of pharmacies or to individuals other than licensed pharmacists. This lack of clarity violates the rulemaking standards under the Administrative Procedure Act (APA) (Gov. Code § 11340 *et seq.*; 1 CCR § 10 *et seq.*). CMA urges the Board to modify its proposed text to clarify, at a minimum, that the regulatory

requirements in these proposed regulations do not apply to compounding activities performed by licensed physicians outside of a pharmacy setting.

1. Proposed Regulations Delete Existing Language Defining Scope

The existing compounding regulations in Article 4.5 of Division 17 of Title 16 of the California Code of Regulations (16 CCR § 1735 *et seq*.) expressly carve out compounding that occurs outside of a pharmacy setting. The regulations define "compounding" to mean "activities occurring in a licensed pharmacy, by or under the supervision of a licensed pharmacist, pursuant to a prescription," thereby limiting the standards and restrictions of the regulations to activities occurring in a pharmacy by, or under the supervision of, pharmacists. (16 CCR § 1735(a).)

In contrast, the proposed regulations impose standards on compounding without specifying the type of licensee or setting of care. The proposed regulations eliminate the existing language in Section 1735, and replace it with definitions that apply broadly regardless of the health care setting. The rest of the proposed text does not contain any limitation on the scope of applicability, leaving the proposed regulations silent on the scope of the regulatory requirements.

The absence of such language in the proposed regulations creates confusion and uncertainty among physicians about whether they would now be subject to the requirements and restrictions of the Board's compounding regulations when compounding drug products in a non-pharmacy setting. This uncertainty is evidenced by numerous comments from stakeholders asking the Board to clarify the applicability of its proposed regulations in other health care settings.

2. Language of Proposed Text Conflicts with Board's Description of Its Effect

This lack of clarity results from the plain and ordinary meaning of the proposed text, which, as written, applies broadly to any compounding as described in the proposed regulations,[1] and contradictory statements by the Board and its staff indicating the regulations would not apply outside of pharmacy settings or to individuals who are not licensed pharmacists:

> Staff note its jurisdiction are individuals and businesses within its practice act. Board staff read the comment as suggesting that the Board's proposed regulations would apply to a physician. It may be appropriate for the commenter to confer with those licensing boards to determine compounding requirements.[2]

[1] Proposed § 1735.1 (applying requirements of Article 4.5 to "compounding of a CNSP" [compounded nonsterile preparations]), § 1736.1 (applying Article 4.6 to "sterile compounding"), §§ 1737 & 1737.1 (applying Article 4.7 to "compounding of Hazardous Drugs"), and § 1738.1 (applying Article 4.8 to "processing of Radiopharmaceuticals").
[2] Board of Pharmacy, Sep. 2024 Board Meeting Materials, "Attachment 4 - Initial Staff Prepared Summarized Comments With Recommendations as Presented During July 2024 Board Meeting," "General Comments as Presented During July 2024 Board Meeting" at 1, https://www.pharmacy.ca.gov/meetings/agendas/2024/24_jul_bd_mat_iv_general.pdf; see also *id*. at 6-7 (providing similar responses to comments about applicability to orthopedic surgeons).

The above statement was given in response to stakeholder comments from multiple physician groups seeking changes to the proposed sterile compounding language because of the lack of clarity therein. The Board's response signals the Board's own uncertainty about whether its regulations would apply to physicians, and reinforces the uncertainty among physician groups and practices by suggesting, but not explicitly stating, that the regulations may not apply to physicians as licensees not within the Board's jurisdiction.

While the Board does not have jurisdiction or disciplining authority over physicians and surgeons, the Medical Board may discipline a physician and surgeon for violating any provision of the Medical Practice Act or any other provision of Division 2 of the Business and Professions Code.[3] Furthermore, in a recent letter to the Board of Pharmacy, the Medical Board stated that, while it maintains exclusive jurisdiction to discipline its physician licensees, including for violations of the standard of care for compounding,

> It is certainly possible that whatever regulations that are implemented by the Board of Pharmacy may influence the standard of care for physicians who are compounding, especially since some of the proposed regulations reflect what is already required for physician compounding under federal law, including, but not limited to, Section 503A of the Federal Food, Drug, and Cosmetic Act (BPC section 2225(b) allows MBC to investigate violations of federal law related to the practice of medicine).[4]

3. Nature of Proposed Requirements Only Applicable to Pharmacy Settings

Several of the requirements proposed in the Board of Pharmacy's regulations only work in pharmacy settings, and are not feasible in others such as medical offices. These include, but are not limited to, requiring compounding to be performed or directly supervised by a "licensed pharmacist" (proposed §§ 1735.1(a), 1736.1(a), 1738.1) or otherwise involve a pharmacist-in-charge (§ 1737.2), requiring annual review of standard operating procedures by a pharmacist-in-charge (§§ 1735.11(b)) & 1736.17(h)), requiring patient consults by a pharmacist (§§ 1735.1(g), 1736.1(g), 1737.1(a)), and requiring a pharmacist to supervise the area where compounding is performed (§ 1736.3). In general, the requirements in these proposed regulations are designed around the assumption that a pharmacist is present in the health care setting where compounding is to occur. While this approach may work in pharmacies and hospitals with pharmacy staff, it creates an insurmountable barrier for medical offices that effectively puts compounding out of reach for physician offices.

The Board acknowledges that its jurisdictional authority is limited to pharmacists and pharmacies.[5] Based on the pharmacy-centric nature of the proposed requirements, the

[3] Bus. & Prof. Code § 2220.5(b). Medical Board regulations also authorize the Medical Board to issue a citation or fine to its licensee for a violation of "any other statute or regulation upon which the Board may base a disciplinary action." (16 CCR § 1364.11(a)(47) & (b).)
[4] Letter from Reji Varghese, Executive Director, Medical Board of California, to Anne Sodergren, Executive Officer, California State Board of Pharmacy, dated November 18, 2024.
[5] Amended Initial Statement of Reasons at 2 (Nov. 8, 2024) (citing Bus. & Prof. Code §§ 4126.8 & 4127, among others).

statements in the Amended Initial Statement of Reasons (ISOR), and the Board's statements at recent public meetings, it is apparent that the Board intends these proposed regulations to apply only to its own licensees.[6] We do not believe that the Board intends to expand the scope and application of its compounding regulations to licensees of other healing arts boards, such as physicians and surgeons.

However, the plain language of the proposed regulations contradicts their stated effect as described in the Amended ISOR, and the Board's intentions as described in recent public meetings. This misalignment between the language of the regulation, which applies compounding in any setting by any licensed health care professional, and the Board's description of the effect of the regulation, violates the "clarity" standard of the Administrative Procedure Act. (Gov. Code §§ 11340(b) & 11349.1(a)(3); 1 CCR § 16(a)(2).) The continued confusion by physicians about whether they may continue to perform in-office compounding using current methodologies only underscores the lack of clarity of the proposed regulations. CMA is concerned that the lack of clarity and the cost of the measures needed for medical offices to comply with these requirements (including but not limited to hiring a licensed pharmacist) will lead physicians to cease in-office compounding, to the detriment of their patients.

4. Proposed Text Should Clarify Scope of Applicability

CMA accordingly requests that the Board revise the proposed text to clarify that the requirements do not apply to compounding performed by licensed physicians and surgeons:

> **§ 1735.1:** In addition to the standards in USP Chapter 795 and, Food Drug Cosmetic Act (FDCA) section 503a (21 U.S.C. §353a) the compounding of a CNSP shall meet the following requirements of this article. **This article shall not apply to compounding by or under the direct supervision of a licensed physician and surgeon.**
>
> **§ 1736.1:** In addition to the standards set forth in USP Chapter 797 and Food Drug Cosmetic Act (FDCA) section 503a (21 U.S.C. §353a) the following requirements apply throughout this article. **This article shall not apply to compounding by or under the direct supervision of a licensed physician and surgeon.**
>
> **§ 1737.1:** In addition to the requirements in USP Chapter 800 and Food Drug Cosmetic Act (FDCA) section 503a (21 U.S.C. §353a) the following requirements apply to the compounding of Hazardous Drugs. **This article shall not apply to**

[6] See Amended Initial Statement of Reasons at 7 (Nov. 8, 2024) ("*Licensees* must comply with the compounding standards specified in the current version of the USP (BPC 4126.8)."; "This addition reminds *licensees* that they must also refer to the corresponding USP Chapter." (Emphasis added.))

compounding by or under the direct supervision of a licensed physician and surgeon.

§ 1738.1: In addition to the standards in the USP Chapter 825, the processing of Radiopharmaceuticals shall meet the requirements of this section. **This article shall not apply to compounding by or under the direct supervision of a licensed physician and surgeon.**

The Board's intent or interpretation of its regulatory authority notwithstanding, its regulations must be clear, and should reflect the Board's intended scope of application. (Gov. Code §§ 11340(b) & 11349.1(a)(3); 1 CCR § 16(a)(2).) The current proposed language is unclear, contradicts the Board's stated intent, and fails to conform to the APA's rulemaking standards. The suggested language above would clarify the scope of the proposed regulations so that the text is "written or displayed so that the meaning of regulations will be easily understood by those persons directly affected by them." (Gov. Code § 11349(c).)

Were the Board to adopt these suggested changes, physicians would remain subject to the standards and requirements in state and federal law related to compounding, the practice of medicine (Bus. & Prof. Code § 2225(b), and applicable standards of care (§§ 2234(c) & 2242). The Medical Board and the Osteopathic Medical Board enforce these standards over their respective licensees. The language suggested above does not—and cannot—change physicians' existing obligations under other state and federal statutes and regulations. Nor does it exempt physicians from having to meet the applicable standard of care when compounding drugs.

The suggested language only clarifies that physicians are not subject to the specified articles in the proposed Board of Pharmacy regulations (Articles 4.5, 4.6, 4.7, and 4.8 of Division 17 of Title 16), so that physicians who perform in-office compounding would not be required to comply with the pharmacy-centric standards in these proposed regulations. CMA believes these changes are consistent with the Board's intent and would allow physicians to continue providing patients timely and appropriate care.

Thank you for your consideration. Please feel free to contact me with any questions at (916) 444-5532 or asanchez@cmadocs.org.

Sincerely,

S. Alecia Sanchez
Chief Strategy Officer
California Medical Association

Department of Pharmacy Services

12/6/2024

California State Board of Pharmacy
2720 Gateway Oaks Drive, Suite 100
Sacramento, CA 95833

Attn: Lori Martinez

On behalf Cedars-Sinai Medical Center, we would like to provide comments and recommendations for consideration to the Board of Pharmacy (Board) for proposed amendments to Article 4.5, and additions of Articles 4.6, 4.7, and 4.8. on compounding regulations and hazardous medications. Attached is a summary for the committees review and consideration. We appreciate the opportunity provided by the Board.

Please contact me should you have any questions.
Sincerely,

Rita Shane, PharmD, FASHP, FCSHP
Vice President & Chief Pharmacy Officer
Rita.shane@cshs.org

Vipul Patel, Pharm.D,
Executive Director of Pharmacy
Pharmacist-In-Charge Signature
Vipul.Patel@cshs.org

Institution/Contact Name	**Cedars-Sinai Medical Center** Department of Pharmacy Services 310-423-5611 Rita Shane, PharmD, FASHP, FCSHP, Vice President & Chief Pharmacy Officer; rita.shane@cshs.org Vipul Patel, PharmD, Executive Director, Pharmacy & Oncology Services; Vipul.patel@cshs.org	
Section, Subdivision	**Proposed Language**	**Recommendation / Comment**
Non-Sterile Compounding		
CCR 1735.1 Introduction and Scope. Subsection (e) (1) (A):	**(e) In addition to prohibitions and requirements for compounding established in federal law, 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 dispensing, or	**Rationale:** • The ASHP and FDA drug shortage lists do not always reflect real-time real time drug shortages. As an example, the 2023 Akorn recall was posted after the State Board notification of the company shut down which resulted in multiple drug shortages. (see attached) [1] Health systems have monitoring strategies in place to track these drug shortages real-time from drug manufacturers or wholesalers before these shortage drugs get added to the ASHP and FDA drug shortage lists. • Additionally, wholesalers themselves often run out of supply of critical medications (pre-shortage situations). Inability to procure medications or restrictions to compound in these events would have contribute to heightened risk and safety concerns for patients. With the growing number of medications going on shortage[2] and recent manufacturer bankruptcies (i.e. Akorn, Apotex) it is becoming more challenging for Health-Systems to obtain commercially available products. References:  FDA Akorn recall.pdf 1. 2. Drug Shortages Statistics - ASHP **Recommendation:** Recommend the board to revise language to be consistent with language changes in section 1736.1 subsection (e) (1) (A). ***1735.1 Introduction and Scope. Subsection (f) (1) (A):*** ***(e) In addition to prohibitions and requirements for compounding established in federal law, no CNSP shall be prepared that:*** ***(1) Is essentially a copy of one or more commercially available drug***

		products, unless: *(A) that 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 dispensing, or in a health care facility licensed pursuant to Health and Safety Code Section 1250 where the drug product cannot be obtained from the manufacturer or wholesaler and documentation is maintained, or*
CCR 1735.7 Master Formulation and Compounding Records. subsection (c)(2):	(c)(2) The manufacturer, lot number, and expiration date for each component for the CSP.	**Rationale:** Current language in CCR 1735.3 below has a provision for CSPs compounded in health facilities to prevent delays in care to acutely ill patient, i.e. infections, cancer, critical care, etc. The current language states: (F) The manufacturer, expiration date and lot number of each component. If the manufacturer name is demonstrably unavailable, the name of the supplier may be substituted. If the manufacturer does not supply an expiration date for any component, the records shall include the date of receipt of the component in the pharmacy, and the limitations of section 1735.2, subdivision (l) shall apply. *(i) Exempt from the requirements in this paragraph (1735.3(a)(2)(F)) are sterile preparations compounded in a single lot for administration within seventy-two (72) hours to a patient in a health care facility licensed under section 1250 of the Health and Safety Code and stored in accordance with standards for "Redispensed CSPs" found in Chapter 797 of the United States Pharmacopeia – National Formulary (USP37-NF32) Through 2nd Supplement (37th Revision, Effective December 1, 2014), hereby incorporated by reference.* **Recommendation:** To prevent delays in care to acutely ill patients, recommend the board consider including the same exemption language to the 1735.7 Master Formulation and Compounding Records, subsection (c)(2): *The manufacturer, lot number, and expiration date for each component.* *(i) Exempt from the requirements in this paragraph are non-sterile preparations compounded in a single lot for administration within seventy-two (72) hours to a patient in a health care facility licensed under section 1250 of the Health and Safety Code.*
1735.12. Quality	(c) All complaints made to the facility related	**Rationale:**

Assurance and Quality Control. Subsection (c)	to a potential quality problem with a CNSP and all adverse drug experiences events shall be reviewed by the pharmacist-in charge within 72 hours of receipt of the complaint or occurrence of the adverse drug experience event. Such a review shall be documented and dated as defined in the SOPs.	A requirement of 72 hours may not provide sufficient time for health-systems to investigate and notify the necessary regulatory bodies in cases where it occurs over the holiday weekend. **Recommendation** *(c)All complaints related to a potential quality problem with a CNSP and all adverse events shall be reviewed by the pharmacist-in-charge within 3 business days ~~72 hours~~ of receipt of the complaint or occurrence of the adverse event. Such review shall be documented and dated as defined in the SOPs.*
Sterile Compounding		
CCR 1736.1 Introduction and Scope. Subsection (b) (2):	(2) If the sterile compounding equipment or environment fail(s) to meet any required specification, an immediate use CSP may be compounded without the requirement for there to be loss of life or intense suffering of an identifiable patient. This provision may only be used for 24 hours after such failure(s). All such failures must be documented in accordance with facility's SOP and shall be reported to the BOP within 72 hours.	**Rationale:** • Requiring health-system pharmacies to remedy equipment failures within 24 hours may not be feasible due to a variety of reasons why there could have been equipment failures. Often times, it may take more than 24 hours to remedy. • To use outside facility or vendor to provide compounding preparations would still pose a safety risk as they may not be following the health-systems processes and procedures. • Given the concerns about potential audits, institutions may hesitate to report issues to the Board of Pharmacy. We urge the Board to embrace a 'Just Culture' framework, which emphasizes accountability and learning over punitive measures. • **Recommendation:** To remove the requirement for immediate use compounding under this provision to be used for 24 hours after such failure(s), and requiring such failures must be documented in accordance with facility's SOP and shall be reported to the BOP within 3 business days. ***CCR 1736.1 Introduction and Scope. Subsection (b) (2):*** *(2) If the sterile compounding equipment or environment fail(s) to meet any required specification, an immediate use CSP may be compounded without the requirement for there to be loss of life or intense suffering of an identifiable patient. This provision may only be used for 7 business days after such failure(s). All such failures must be documented in accordance with facility's SOP and shall be available upon inspection. ~~and shall be reported to the BOP within 72 hours.~~*

CCR 1736.2 Personnel Training and Evaluation. Subsection (d)	(d) Compounding personnel or persons with direct supervision and control of compounding personnel who fail any aspect of the aseptic manipulation ongoing training and competency evaluation shall not be involved in compounding 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 supervision and control of 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 30 days after a failure of any aspect while applicable aseptic manipulation ongoing training and competency evaluation results are pending	**Rationale:** Multiple factors can contribute to failure of staff in aseptic technique training and competency evaluation including environmental testing failure, and engineering control failure. Prohibiting compounding personnel from compounding without an evaluation of contributing factors and timeframe would significantly disrupt patient treatment and jeopardize health-systems ability to operate. **Recommendation:** Recommend to the following revisions to section 1736.2 subsection (d) to allow personnel who fail any aspect of aseptic manipulation training to continue to perform in-process checks, final verification and dispensing of CSPs for no more than 30 days. **Proposed Regulation Revision:** *(d) 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 including performing in-process checks, final verification, and dispensing of CSPs for no more than 30 days after a failure of any aspect while applicable aseptic manipulation ongoing training and competency evaluation results are pending*
CCR. 1736.4 Facilities and Engineering Controls Subsection (c)	(1) Designated compounding area(s) shall typically be maintained at a temperature of 20° Celsius or cooler.	**Rationale:** • The USP chapter 797 recommends maintaining a temperature of 20° Celsius or cooler for staff comfort within the classified compounding areas where multiple layers of PPE are worn. • The term "designed compounding area" is defined by CCR. 1736 as a restricted location within a facility that limits access, where only activities and items related to compounding are present. This definition would include both classified compounding areas and segregated compounding areas. • If the language remains as is, 'shall typically' this can lead to severe consequences for many health systems, as many would have to make significant

		changes to their Heating, Ventilation, and Air Conditioning (HVAC) systems to be compliant with this requirement. Additionally, many of these classified compounding rooms and segregated compounding areas maintain room temperature medication which must be stored in temperatures defined in USP Chapter 659 as 20°–25° (68°–77° F). • The manufacturer storage label for medications include a range 20°–25° (68°–77° F). If the temperatures in the compounding areas must be below 20° Celsius, the medications would be exposed to temperature excursion and would not be considered safe to use. • If the requirement remains as written, many institutions will need to build new storage rooms for all medications, including HD medications, and upgrade HVAC systems. This would involve large construction projects, adding significant strain to already overburdened healthcare facilities. **Recommendation:** (1) Designated compounding area(s) ~~shall~~ *should* typically be maintained at a temperature of 20° Celsius or cooler.
CCR 1736.11 Master Formulation and Compounding Records. subsection (c)(2):	(c)(2) The manufacturer, lot number, and expiration date for each component for the CSP.	**Rationale:** Current language in CCR 1735.3 below has a provision for CSPs compounded in health facilities to prevent delays in care to acutely ill patient, i.e. infections, cancer, critical care, etc. The current language states: (F) The manufacturer, expiration date and lot number of each component. If the manufacturer name is demonstrably unavailable, the name of the supplier may be substituted. If the manufacturer does not supply an expiration date for any component, the records shall include the date of receipt of the component in the pharmacy, and the limitations of section 1735.2, subdivision (l) shall apply. *(i) Exempt from the requirements in this paragraph (1735.3(a)(2)(F)) are sterile preparations compounded in a single lot for administration within seventy-two (72) hours to a patient in a health care facility licensed under section 1250 of the Health and Safety Code and stored in accordance with standards for "Redispensed CSPs" found in Chapter 797 of the United States Pharmacopeia – National Formulary (USP37-NF32) Through 2nd Supplement (37th Revision, Effective December 1, 2014), hereby incorporated by reference.* **Recommendation:**

		Add back the language above: 1736.11 Master Formulation and Compounding Records, subsection (c)(3): *(c)(3) The manufacturer, lot number, and expiration date shall be recorded for each component for CSPs.* *(i) Exempt from the requirements in this paragraph are sterile preparations compounded in a single lot for administration within seventy-two (72) hours to a patient in a health care facility licensed under section 1250 of the Health and Safety Code.*
CCR 1736.13 Labeling subsection (a):	(a) A CSP label shall include all of the following: (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 for the entire CSP to be administered.	**Rationale:** Most health-systems utilize electronic health record (EHR) system which accurately provides the patient specific order rate, duration of infusion. Requiring a range of rates on the label could cause confusion and result in medication errors if nurses misinterpret the ranges. Rates are updated on an ongoing basis in response to changes in the patient's condition and the EHR is the source of truth for the current rate. The duration may not be specified at the time the CSP is initiated since duration will be based on the patient's response to therapy, e.g. blood pressure changes, determination of infection source, blood glucose, etc. Therefore, instructions for administration may reference the EHR when rate changes are anticipated. Additionally, due to changes in the patient's condition, the rate documented on the label may change by the time the CSP is hung on the pt **Recommendations:** Recommend updating the regulation to: *(a) A CSP label shall include all of the following and these can also be readily retrievable from the EHR:* *(1) Route of intended administration;* *(2) The solution utilized, if applicable;* *(3) Instructions for administration will include the rate and/or reference the EHR which serves as the source of truth for the rate of drug to be infused based on the patient's condition.* *(~~A) For an admixed CSP, the rate of infusion, or range of rates of infusion as prescribed, or the duration for the entire CSP to be administered~~*
CCR. 1736.17 Standard Operating Procedures (SOPS) subsection (a)(2)(c)	(a)(2)(c) The methods a pharmacist will use to determine and approve the ingredients and the compounding process for each preparation before compounding begins;	**Rationale:** Many health-systems currently utilize IV room workflow system that utilizes barcode scanning to check for correct components before allowing technicians to proceed with compounding. Moreover, with pharmacy recruitment issues, it would become challenging for health-systems to provide manual individual checks for a large

		number of CSPs. **Recommendations:** The methods a pharmacist will use to determine and approve the ingredients and the compounding process for each preparation before compounding begins; *(i) A sterile compounding workflow system may be utilized for verification of correct components used for preparing a CSP.*
CCR. 1736.17 Standard Operating Procedures (SOPS) subsection (d)	(d) 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.	**R Rationale:** Pharmacist/Health-systems have SOPs that define the product used, dwell time (based on manufacturer data), and how staff are monitoring and observations to determine compliance. Requiring documentation for the frequency and quantity of items entering a sterile compounding area in hospital settings or PEC, will add a significant burden to the workload of sterile compounding staff which could increase the risk of causing an error in compounding. **Recommendation:** *d) 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.~~*
CCR. 1736.18 Quality Assurance and Quality Control subsection (c)	(c) 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.	**Rationale:** A requirement of 72 hours may not provide sufficient time for health-systems to investigate and notify the necessary regulatory bodies in cases where it occurs over the holiday weekend. **Recommendation:** *(c) 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 3 business days ~~72 hours~~ of receipt of the complaint or occurrence. Such review shall be documented and dated as defined in the SOPs.*
1736.21 Compounding Allergenic Extracts subsection (c)	(c) Any compounded stock allergy solution shall comply with the requirements established in USP Chapter 51, Antimicrobial Effectiveness Testing and the requirement established in USP Chapter 1207, Sterile Product Packaging – Integrity Evaluation	**Rationale:** • USP 797 states "Because of certain characteristics of allergenic extracts and allergy practice, preparation of allergenic extract prescription sets is not subject to all of the requirements in this chapter that are applicable to other sterile CSPs." Additionally, USP 797 does not require allergenic extracts to conduct antimicrobial effectiveness testing or packaging integrity evaluation

	related to container closure. A compounding record is required for any compounded stock solution.	related to container closure.
		• Organizations such as the American Academy of Allergy, Asthma & Immunology (AAAAI) and the American College of Allergy, Asthma & Immunology (ACAAI) highlight that allergenic extract compounding practices, conducted under general aseptic conditions, have maintained a strong safety record without requiring ISO-classified environments or extensive sterility controls. This long history of safe use has supported continued in-office compounding of allergenic extracts under specific guidelines to ensure patient safety and access to care.
		• Requiring compounded stock solution to be compounded at the time of the appointment, with unused doses discarded, will create the following issues:
		  ○ Increased Waste: unused doses that are discarded after each visit will generate significant pharmaceutical waste, raising environmental and resource utilization concerns.
		  ○ Higher Costs for Patients: The need to compound a new stock solution for every visit will increase operational costs, which will likely be passed on to patients, leading to financial burden.
		  ○ Additional Workload: Compounding single-use stock solutions for each patient will add to the workload of pharmacy staff, placing further strain on health-systems already facing staffing challenges and resource limitations.
		  ▪ These challenges would disrupt workflows and amplify the financial and operational pressures on healthcare institutions and their patients.
		• Allergen extract shortages are common, with nearly all surveyed providers reporting experiences of disruption, mainly involving venom, pollen, and mold extracts. 95% of providers reported patient care was affected, with varying degrees of severity. Interruptions may lead to worsened asthma or allergic reactions in untreated patients.[1]
		
		Reference:
		1. Ezhuthachan ID, Banks TA, Cerise JE, Wong SC, Ponda P. Allergen immunotherapy extract shortages and their effects on clinical care: A work group report of the AAAAI Immunotherapy, Allergen Standardization, and Allergy Diagnostics Committee. J Allergy Clin Immunol Pract. 2022;10(2):444-452. doi:10.1016/j.jaip.2021.10.057
		
		Recommendations:

		(c) ~~Any compounded stock allergy solution shall comply with the requirements established in USP Chapter 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.
Hazardous drugs		
CCR 1737.2 List of Hazardous Drugs subsection (a) and (b) :	(a) 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 (PIC), professional director of a clinic, or designated representative-in-charge, as applicable. The designated person must be 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. (b) 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.	**Rationale:** Often times, the designated person may be the pharmacist-in-charge **Recommendation:** Recommend revising the language to allow the Pharmacist-in-charge or designated person to review and approve the facility's list of HDs annually. ***CCR 1737.2 List of Hazardous Drugs subsections:*** ***(a) The facility's list of HDs as required by USP Chapter 800 must be reviewed and approved by the designated person ~~and~~ or the pharmacist-in-charge (PIC), or professional director of a clinic, or designated representative-in-charge, as applicable. The designated person must be 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.*** *(b) If an assessment of risk approach is taken as authorized in USP Chapter 800, it shall be approved by the designated person ~~and~~ or the pharmacist-in-charge, or professional director of a clinic, or designated representative-in-charge, as applicable.*
CCR 1737.6 Environmental Quality and Control. Subsection (a)	(a) 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.	**Rationale:** • USP 800 only recommends performing environmental wipe sampling for HD surface residue routinely. • Currently, there is currently no standard for acceptable limits for HD surface contamination.[1] • Additionally, requiring additional sampling will add an undue burden to test without any concrete actionable limits.

		Reference 1. Connor et al. Surface wipe sampling for antineoplastic (chemotherapy) and other hazardous drug residue in healthcare settings: Methodology and recommendations. Journal of Occupational and Environmental Hygiene. **Recommendations**: Request the board to consider removing the section or revise language to "should" to be consistent with USP 800 Chapter and to provide guidance on the specific requirement such as action level, frequency what to do when actionable levels have been reached as there is no standards provided. ***CCR 1737.6 Environmental Quality and Control*** *a) The SOPs of a premises where HDs are handled ~~shall~~ should address environmental wipe sampling for HD surface residue, its frequency, areas of testing, levels of measurable contamination, and actions when those levels are exceeded.*
CCR 1737.7. Personal Protective Equipment (PPE), subsection (c).	(c) Outer gloves used for HD compounding shall be changed between each different HD preparation.	**Rationale:** • Many health-systems use closed system transfer device (CSTD) when compounding antineoplastic HDs. The use of CSTD has shown to significantly reduce overall chemical contamination (12.24% vs. 26.39%).[1] • Double-gloving is primarily designed to offer extra protection against hazardous drug compounds, with the outer glove serving as a first line of defense. If the outer glove is repeatedly removed or exposed to rough conditions, it may wear down, possibly increasing the risk of puncturing or compromising the inner glove. This could lead to reduced protection, especially when handling hazardous drug compound.[2,3] • Frequent removal and disposal of outer glove changes creates significant waste.[2] **Reference** 1. Simon N, Vasseur M, Pinturaud M, et al. Effectiveness of a Closed-System Transfer Device in Reducing Surface Contamination in a New Antineoplastic Drug-Compounding Unit: A Prospective, Controlled, Parallel Study. Ahmad A, ed. PLoS One 2016;11:e0159052. Available at: https://dx.plos.org/10.1371/journal.pone.0159052. 2. Kirk H. Double gloving when handling cytotoxic drugs. *Hospital Pharmacy Europe*. Published March 2, 2009. Available from:

		https://hospitalpharmacyeurope.com/news/editors-pick/double-gloving-when-handling-cytotoxic-drugs/ 3. McNeilly L. Double gloving: Myth versus fact. *Infection Control Today*. Published May 5, 2011. Available from: https://www.infectioncontroltoday.com/view/double-gloving-myth-versus-fact **Recommendations**: Revise the proposed language to: *(c) Outer gloves used for HD compounding shall be changed between each different HD preparation if a closed system transfer device (CSTD) is not used.*
Radiopharmaceutical- Preparation, Compounding, Dispensing, and Repackaging		
CCR 1738.5. Facilities and Engineering Controls subsection (e)	(e) Compounding shall not take place in the SRPA.	**Rationale:** Per USP 825, for compounding sterile radiopharmaceuticals, the ISO 5 PEC must be placed in a classified area. However, non-radiopharmaceutical sterile compounds were not applicable for this restriction in USP 825. Prohibiting all compounding at SRPA would have a significant impact in the workload on health-systems that does not have a dedicated classified room for radiopharmaceuticals as they would not be able to prepare any supportive meds that has an SRPA. **Recommendation** *(d) Radiopharmaceutical compounding shall not take place in the SRPA.*
CCR 1738.10. Preparation subsection (c)	(c) 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.	**Rationale:** The proposed language is inconsistent with USP 825 recommendations, will require health-systems to incorporate patient need which may not be pertinent information. **Recommendation:** *(c) 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.*

CCR 1738.14. Quality Assurance and Quality Control subsection (b)	(b) The board shall be notified in writing within 72 hours of the facility's receipt of a complaint, excluding delivery delays, involving a radiopharmaceutical. Recalls and adverse drug experiences as defined in 21 CFR 310.305(b) must be reported to the Board and other agencies in compliance with relevant provisions of law.	**Rationale:** A requirement of 72 hours may not provide sufficient time for health-systems to investigate and notify the necessary regulatory bodies in cases where it occurs over the holiday weekend. Recommend the board to revise language to be consistent with the updated CA BOP revised changes in section 1735.12 Quality Assurance and Quality Control subsection (b). **Recommendation:** (*b) ~~The board shall be notified in writing within 72 hours of a complaint involving a radiopharmaceutical. Recalls and adverse events must be reported to the Board and other agencies in compliance with relevant provisions of law~~. The Board shall be notified in writing within 96 hours of the facility's receipt of a complaint of a potential quality problem or the occurrence of an adverse drug experience as defined in 21 CFR 310.305(b) involving a CNSP*
CCR 1738.14. Quality Assurance and Quality Control subsection (c)	(c) In addition to subsection (b), all complaints made to the facility related to a potential quality problem with a radiopharmaceutical, and all reported adverse drug experiences, as defined in 21 CFR 310.305(b) 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. In the event the PIC is not available within 72 hours the PIC will define in the SOPs the pharmacist who will be required to review	**Rationale:** A requirement of 72 hours may not provide sufficient time for health-systems to investigate and notify the necessary regulatory bodies in cases where it occurs over the holiday weekend. **Recommendation:** *(c) In addition to subsection (b), all complaints related to a potential quality problem with a radiopharmaceutical and all reported adverse events shall be reviewed by the pharmacist-in-charge within 3 business days ~~72 hours~~ of receipt of the complaint or occurrence. Such review shall be documented and dated as defined in the SOPs.*

California Hospital Association

December 9, 2024

Lori Martinez
Board of Pharmacy
2720 Gateway Oaks Drive, Ste. 100
Sacramento, CA 95833

Submitted via e-mail to Lori.Martinez@dca.ca.gov

SUBJECT: Board of Pharmacy Proposed Modified Regulations: Compounded Drug Preparations

Dear Ms. Martinez,

On behalf of more than 400 hospitals and health systems, the California Hospital Association (CHA) appreciates the opportunity to comment on the Board of Pharmacy's (BoP) proposed modified regulations for compounded drug preparations.

The compounding of drugs is important to patients because it allows for personalized care that addresses individual patient needs, particularly when commercially available medications are not suitable. By providing customized dosages, alternative delivery forms, and formulations that avoid allergens or other sensitivities, compounding can improve medication adherence, treat rare or complex conditions, manage chronic pain, and ensure continuity of care during drug shortages. Ultimately, compounding improves patient outcomes by providing solutions that are not available in standard pharmaceutical offerings, allowing for more effective and targeted treatments.

Compounding in hospitals is critically important because it allows health care providers to offer personalized, flexible, and precise treatments tailored to the unique needs of individual patients. In hospital settings, patients may have complex medical conditions that require specialized medications that are not available in commercially manufactured forms. Compounding enables hospitals to address these needs effectively, ensuring optimal therapeutic outcomes and enhancing patient care.

While CHA agrees regulations are essential in the field of pharmacy, CHA only supports the promulgation of regulations that, based on evidence, are needed to ensure public safety, effective health care delivery, and the integrity of the pharmaceutical profession. CHA does not believe these modified proposed regulations will meaningfully enhance protection of or promote the health and safety of Californians. Furthermore, they are duplicative of federal law, which already requires the compounding of drug preparations to be consistent with extensive and strict standards in the current version of the United States Pharmacopeia (USP)-National Formulary. When states implement their own regulations

on areas already covered by federal law, it leads to regulatory redundancy, which burdens businesses, individuals, and government agencies with unnecessary compliance efforts, legal complexities, and costs.

Additionally, the BoP has failed to produce empirical evidence in both the Initial Statement of Reason *and* the modified statement indicating either systemic challenges or that patients have been placed in harm's way — or that hospital pharmacies are not meeting safety standards that might necessitate additional BoP regulations. We were unable to substantiate hospital pharmacies failing to follow either the BoP's current regulations or the detailed federal USP standards. Regulations lacking a solid evidence base will lead to unnecessary compliance costs for hospitals, and they may lead to confusion and legal disputes between regulators and businesses.

Today, more than half of all California hospitals lose money every day to provide care for patients. This is driven by stagnant reimbursement in the face of ever-increasing expenses for labor, pharmaceuticals, **regulatory mandates**, and more. The cost to deliver care has risen more than 30% in the past five years alone.

Adopting these regulations will divert patient care dollars from hospitals' finite resources, increase compliance confusion and uncertainty, reduce efficiency, and increase the risk of legal penalties. Striking a balance between necessary oversight and the minimizing of confusing and inefficient compliance standards is critical to fostering a sustainable health care system for the needs of current and future patients.

Hospitals, the California Legislature, and the California Department of Health Care Access and Information are working diligently to lower health care costs. Every additional requirement a hospital must fulfill raises costs, which runs counter to this shared goal. These considerations must be balanced when creating new regulations.

There is abundant and effective regulatory guidance provided by the USP, and the BoP's proposed modified regulations would have too many unintended consequences. In lieu of adopting new regulations, we recommend the BoP adopt the federal USP standards as written and delete current outdated state regulations.

CHA appreciates the opportunity to discuss these perspectives. If you have questions, please contact me at slowe@calhospital.org or 916-240-8277.

Sincerely,

Sheree Lowe
Vice President, State Policy

CALIFORNIA MEDICAL ASSOCIATION

December 9, 2024

Lori Martinez
Board of Pharmacy
2720 Gateway Oaks Drive, Suite 100
Sacramento, CA 95833
PharmacyRulemaking@dca.ca.gov

Sent via e-mail

RE: Compounded Drug Preparation Regulations, Modified Text Aug. 29, 2024

Dear Ms. Martinez:

On behalf of its over 50,000 medical student and physician members, the California Medical Association (CMA) submits the following comments on the Board of Pharmacy's proposed Compounded Drug Preparations regulations. The Board proposes to amend, repeal, and replace existing regulations, and to add new regulations, relating to drug compounding.

CMA supports protecting and promoting public health and patient safety. In making these changes, however, the Board has created ambiguities concerning the scope of the regulations that potentially interfere with the practice of medicine by imposing insurmountable barriers to the compounding of drugs by licensed physicians in medical office settings. In-office compounding is conducted in accordance with applicable state and federal law and the standard of care; is common in certain practice settings; and results in better care and patient experience. Applying the pharmacy-centric requirements of these proposed regulations to physician practices would adversely affect patient care.

Accordingly, we request that the Board revise the proposed compounding regulations to clarify that the regulations do not apply to compounding by licensed physicians, consistent with the Board's intended effect.

Applicability of Regulations to Non-Pharmacists and Non-Pharmacy Settings (§§ 1735.1, 1736.1, 1737.1, & 1738.1)

The modified text of the proposed regulations is unclear as to the scope of the regulatory requirements for the various types of compounding described in Articles 4.5, 4.6, 4.7, and 4.8. The proposed text on its face appears to apply to compounding activities by physicians in medical office settings, but the Board and its staff have made statements indicating they do not believe or intend for these requirements to apply outside of pharmacies or to individuals other than licensed pharmacists. This lack of clarity violates the rulemaking standards under the Administrative Procedure Act (APA) (Gov. Code § 11340 *et seq.*; 1 CCR § 10 *et seq.*). CMA urges the Board to modify its proposed text to clarify, at a minimum, that the regulatory

requirements in these proposed regulations do not apply to compounding activities performed by licensed physicians outside of a pharmacy setting.

1. Proposed Regulations Delete Existing Language Defining Scope

The existing compounding regulations in Article 4.5 of Division 17 of Title 16 of the California Code of Regulations (16 CCR § 1735 *et seq*.) expressly carve out compounding that occurs outside of a pharmacy setting. The regulations define "compounding" to mean "activities occurring in a licensed pharmacy, by or under the supervision of a licensed pharmacist, pursuant to a prescription," thereby limiting the standards and restrictions of the regulations to activities occurring in a pharmacy by, or under the supervision of, pharmacists. (16 CCR § 1735(a).)

In contrast, the proposed regulations impose standards on compounding without specifying the type of licensee or setting of care. The proposed regulations eliminate the existing language in Section 1735, and replace it with definitions that apply broadly regardless of the health care setting. The rest of the proposed text does not contain any limitation on the scope of applicability, leaving the proposed regulations silent on the scope of the regulatory requirements.

The absence of such language in the proposed regulations creates confusion and uncertainty among physicians about whether they would now be subject to the requirements and restrictions of the Board's compounding regulations when compounding drug products in a non-pharmacy setting. This uncertainty is evidenced by numerous comments from stakeholders asking the Board to clarify the applicability of its proposed regulations in other health care settings.

2. Language of Proposed Text Conflicts with Board's Description of Its Effect

This lack of clarity results from the plain and ordinary meaning of the proposed text, which, as written, applies broadly to any compounding as described in the proposed regulations,[1] and contradictory statements by the Board and its staff indicating the regulations would not apply outside of pharmacy settings or to individuals who are not licensed pharmacists:

> Staff note its jurisdiction are individuals and businesses within its practice act. Board staff read the comment as suggesting that the Board's proposed regulations would apply to a physician. It may be appropriate for the commenter to confer with those licensing boards to determine compounding requirements.[2]

[1] Proposed § 1735.1 (applying requirements of Article 4.5 to "compounding of a CNSP" [compounded nonsterile preparations]), § 1736.1 (applying Article 4.6 to "sterile compounding"), §§ 1737 & 1737.1 (applying Article 4.7 to "compounding of Hazardous Drugs"), and § 1738.1 (applying Article 4.8 to "processing of Radiopharmaceuticals").
[2] Board of Pharmacy, Sep. 2024 Board Meeting Materials, "Attachment 4 - Initial Staff Prepared Summarized Comments With Recommendations as Presented During July 2024 Board Meeting," "General Comments as Presented During July 2024 Board Meeting" at 1, https://www.pharmacy.ca.gov/meetings/agendas/2024/24_jul_bd_mat_iv_general.pdf; see also *id*. at 6-7 (providing similar responses to comments about applicability to orthopedic surgeons).

The above statement was given in response to stakeholder comments from multiple physician groups seeking changes to the proposed sterile compounding language because of the lack of clarity therein. The Board's response signals the Board's own uncertainty about whether its regulations would apply to physicians, and reinforces the uncertainty among physician groups and practices by suggesting, but not explicitly stating, that the regulations may not apply to physicians as licensees not within the Board's jurisdiction.

While the Board does not have jurisdiction or disciplining authority over physicians and surgeons, the Medical Board may discipline a physician and surgeon for violating any provision of the Medical Practice Act or any other provision of Division 2 of the Business and Professions Code.[3] Furthermore, in a recent letter to the Board of Pharmacy, the Medical Board stated that, while it maintains exclusive jurisdiction to discipline its physician licensees, including for violations of the standard of care for compounding,

> It is certainly possible that whatever regulations that are implemented by the Board of Pharmacy may influence the standard of care for physicians who are compounding, especially since some of the proposed regulations reflect what is already required for physician compounding under federal law, including, but not limited to, Section 503A of the Federal Food, Drug, and Cosmetic Act (BPC section 2225(b) allows MBC to investigate violations of federal law related to the practice of medicine).[4]

3. Nature of Proposed Requirements Only Applicable to Pharmacy Settings

Several of the requirements proposed in the Board of Pharmacy's regulations only work in pharmacy settings, and are not feasible in others such as medical offices. These include, but are not limited to, requiring compounding to be performed or directly supervised by a "licensed pharmacist" (proposed §§ 1735.1(a), 1736.1(a), 1738.1) or otherwise involve a pharmacist-in-charge (§ 1737.2), requiring annual review of standard operating procedures by a pharmacist-in-charge (§§ 1735.11(b)) & 1736.17(h)), requiring patient consults by a pharmacist (§§ 1735.1(g), 1736.1(g), 1737.1(a)), and requiring a pharmacist to supervise the area where compounding is performed (§ 1736.3). In general, the requirements in these proposed regulations are designed around the assumption that a pharmacist is present in the health care setting where compounding is to occur. While this approach may work in pharmacies and hospitals with pharmacy staff, it creates an insurmountable barrier for medical offices that effectively puts compounding out of reach for physician offices.

The Board acknowledges that its jurisdictional authority is limited to pharmacists and pharmacies.[5] Based on the pharmacy-centric nature of the proposed requirements, the

[3] Bus. & Prof. Code § 2220.5(b). Medical Board regulations also authorize the Medical Board to issue a citation or fine to its licensee for a violation of "any other statute or regulation upon which the Board may base a disciplinary action." (16 CCR § 1364.11(a)(47) & (b).)
[4] Letter from Reji Varghese, Executive Director, Medical Board of California, to Anne Sodergren, Executive Officer, California State Board of Pharmacy, dated November 18, 2024.
[5] Amended Initial Statement of Reasons at 2 (Nov. 8, 2024) (citing Bus. & Prof. Code §§ 4126.8 & 4127, among others).

statements in the Amended Initial Statement of Reasons (ISOR), and the Board's statements at recent public meetings, it is apparent that the Board intends these proposed regulations to apply only to its own licensees.[6] We do not believe that the Board intends to expand the scope and application of its compounding regulations to licensees of other healing arts boards, such as physicians and surgeons.

However, the plain language of the proposed regulations contradicts their stated effect as described in the Amended ISOR, and the Board's intentions as described in recent public meetings. This misalignment between the language of the regulation, which applies compounding in any setting by any licensed health care professional, and the Board's description of the effect of the regulation, violates the "clarity" standard of the Administrative Procedure Act. (Gov. Code §§ 11340(b) & 11349.1(a)(3); 1 CCR § 16(a)(2).) The continued confusion by physicians about whether they may continue to perform in-office compounding using current methodologies only underscores the lack of clarity of the proposed regulations. CMA is concerned that the lack of clarity and the cost of the measures needed for medical offices to comply with these requirements (including but not limited to hiring a licensed pharmacist) will lead physicians to cease in-office compounding, to the detriment of their patients.

4. Proposed Text Should Clarify Scope of Applicability

CMA accordingly requests that the Board revise the proposed text to clarify that the requirements do not apply to compounding performed by licensed physicians and surgeons:

> **§ 1735.1:** In addition to the standards in USP Chapter 795 and, Food Drug Cosmetic Act (FDCA) section 503a (21 U.S.C. §353a) the compounding of a CNSP shall meet the following requirements of this article. **This article shall not apply to compounding by or under the direct supervision of a licensed physician and surgeon.**
>
> **§ 1736.1:** In addition to the standards set forth in USP Chapter 797 and Food Drug Cosmetic Act (FDCA) section 503a (21 U.S.C. §353a) the following requirements apply throughout this article. **This article shall not apply to compounding by or under the direct supervision of a licensed physician and surgeon.**
>
> **§ 1737.1:** In addition to the requirements in USP Chapter 800 and Food Drug Cosmetic Act (FDCA) section 503a (21 U.S.C. §353a) the following requirements apply to the compounding of Hazardous Drugs. **This article shall not apply to**

[6] See Amended Initial Statement of Reasons at 7 (Nov. 8, 2024) ("*Licensees* must comply with the compounding standards specified in the current version of the USP (BPC 4126.8)."; "This addition reminds *licensees* that they must also refer to the corresponding USP Chapter." (Emphasis added.))

compounding by or under the direct supervision of a licensed physician and surgeon.

§ 1738.1: In addition to the standards in the USP Chapter 825, the processing of Radiopharmaceuticals shall meet the requirements of this section. **This article shall not apply to compounding by or under the direct supervision of a licensed physician and surgeon.**

The Board's intent or interpretation of its regulatory authority notwithstanding, its regulations must be clear, and should reflect the Board's intended scope of application. (Gov. Code §§ 11340(b) & 11349.1(a)(3); 1 CCR § 16(a)(2).) The current proposed language is unclear, contradicts the Board's stated intent, and fails to conform to the APA's rulemaking standards. The suggested language above would clarify the scope of the proposed regulations so that the text is "written or displayed so that the meaning of regulations will be easily understood by those persons directly affected by them." (Gov. Code § 11349(c).)

Were the Board to adopt these suggested changes, physicians would remain subject to the standards and requirements in state and federal law related to compounding, the practice of medicine (Bus. & Prof. Code § 2225(b), and applicable standards of care (§§ 2234(c) & 2242). The Medical Board and the Osteopathic Medical Board enforce these standards over their respective licensees. The language suggested above does not—and cannot—change physicians' existing obligations under other state and federal statutes and regulations. Nor does it exempt physicians from having to meet the applicable standard of care when compounding drugs.

The suggested language only clarifies that physicians are not subject to the specified articles in the proposed Board of Pharmacy regulations (Articles 4.5, 4.6, 4.7, and 4.8 of Division 17 of Title 16), so that physicians who perform in-office compounding would not be required to comply with the pharmacy-centric standards in these proposed regulations. CMA believes these changes are consistent with the Board's intent and would allow physicians to continue providing patients timely and appropriate care.

Thank you for your consideration. Please feel free to contact me with any questions at (916) 444-5532 or asanchez@cmadocs.org.

Sincerely,

S. Alecia Sanchez
Chief Strategy Officer
California Medical Association

CSHP CALIFORNIA SOCIETY OF HEALTH-SYSTEM PHARMACISTS

December 9, 2024

Lori Martinez
2720 Gateway Oaks Drive Ste. 100
Sacramento, CA 95833
Email: PharmacyRulemaking@dca.ca.gov

RE: Compounding Regulations

Ms. Martinez:

On behalf of the California Society of Health-System Pharmacists (CSHP) we are submitting comments to the draft Compounding Regulations requesting changes, amendments, and deletions to the proposed regulations. The comments and recommendations for the Draft Compounding Regulations are attached as a separate document to this cover letter titled "CSHP specific comments on BOP draft compounding regulations_12.09.24".

We wish to bring to the California Board of Pharmacy's attention CSHP's concern regarding the "Business Impact" assessment present in the revised Initial Statement of Reasons (ISOR). The ISOR indicates under "Business Impact": "…proposed regulations will not have a significant statewide adverse economic impact directly affecting businesses" and "the board anticipates minimal ongoing costs ranging from approximately $5,700 to $15,000 per year related to administrative and maintenance workload and supplies…" We believe this is a gross underestimation of the associated costs with the proposed regulations that specifically exceed that of the national standards for compounding.

The Board states their initial determination of cost is based on the absence of testimony to that effect during the public discussion and development of the proposed regulation. The public meetings mandate testimony be limited to a few minutes and attendees tend to focus their input on the specific wording of the proposed regulation and not the cost. Simply because it wasn't stated doesn't mean it's not an issue.

Understandably the Board lacks the internal expertise to accurately reflect the anticipated costs associated with development of policies and procedures, monitoring implementation of those procedures, correctly reporting to the Board as proposed by many of the proposed regulations, cost of monitoring visits by the Board, enhanced testing, implementation of technology to support the deployment of the policies and procedures and hiring of additional staff to support compliance with the proposed regulations.

As such, its incumbent on the Board to actively pursue input from those that can accurately project the economic impact to health systems when proposing new regulatory requirements. The Board should, during public meetings or by other means, actively seek input from experts who can inform the Board's ISOR development as it relates to both "Business Impact" and "Economic Impact Assessment" to ensure it accurately reflects the impact on health care delivery, access, and cost while promoting patient safety.

We request that in the absence of an informed development of the amended ISOR the proposed regulations be suspended to provide the Board an opportunity to re-evaluate their "Business Impact" and "Economic Impact Assessment" and to provide evidence the current regulations fail to address patient safety outcomes.

We are ready to collaborate with the Board of Pharmacy to address these concerns. I can be contacted at 916 447 1033 or ldemartini@cshp.org.

Sincerely,

Loriann De Martini, PharmD, MPH, BCGP
Chief Executive Officer
California Society of Health System Pharmacists

California Society of Health System Pharmacist: December 9, 2024

Section, Subdivision	Proposed Language	Recommendation / Comment
Non-Sterile Compounding		
CCR 1735.1 Introduction and Scope. Subsection (e) (1) (A):	(e) In addition to prohibitions and requirements for compounding established in federal law, 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 dispensing, or (B) The pharmacist determines and documents that the compounding produces a clinically significant difference for the medical need of an identified individual patient,	**Rationale:** We recognize the positive changes made to address concerns expressed for patient safety to section 1736(1)(e). Regarding this section, we once more reiterate our previous concerns: • The ASHP and FDA drug shortage lists do not always reflect real-time drug shortages. As an example, the 2023 Akorn recall was posted after the State Board notification of the company shut down which resulted in multiple drug shortages. (see attached). [1] Health systems have monitoring strategies in place to track these drug shortages real-time from drug manufacturers or wholesalers before these shortage drugs get added to the ASHP and FDA drug shortage lists. • Additionally, wholesalers themselves often run out of supplies of critical medications (pre-shortage situations). Inability to procure medications or restrictions to compound in these events will contribute to heightened risk and safety concerns for patients. With the growing number of medications going on shortage[2] and recent manufacturer bankruptcies (i.e. Akorn, Apotex) it is becoming more challenging for Health-Systems to obtain commercially available products. • This proposed regulation has the potential to dramatically impact public heath by disabling health system pharmacies in their efforts to provide life-saving medications to acutely ill patients during the scenarios above. We ask that the Board to provide avenues for hospital and health system pharmacies to continue to provide adequate care during the scenarios pointed out above via regulation change proposed below. References:  FDA Akorn recall.pdf 1. 2. Drug Shortages Statistics - ASHP

		Recommendation updated: We thank the board for making significant changes to 1736.1(e). These changes enhance the ability of pharmacists to better care for patients. We recommend that the Board harmonize this section with the proposed language in 1736.1(e) as it is currently written. **Recommended Language** (**BOLD**): 1735.1 Introduction and Scope. (e)(1) Is essentially a copy of one or more commercially available drug products, unless: (A) that 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 dispensing, **or in a health care facility licensed pursuant to Health and Safety Code Section 1250 where the drug product cannot be obtained from the manufacturer or wholesaler and documentation is maintained, or** (B) The pharmacist determines and documents that the **preparation** produces a clinically significant difference based on the medical need of an identified individual patient (C) Documentation describing the conditions in subsections (1)(A) & (1)(B) is maintained in a readily retrievable format.
CCR 1735.7 Master Formulation and Compounding Records. subsection (c)(2):	(c)(2) The manufacturer, lot number, and expiration date for each component for the CSP.	**Rationale:** This is duplicative of the USP 795 requirement which states: "Name, vendor or manufacturer, lot number, and expiration date of each component." **Recommendation(BOLD):** To strike this line from the regulation. ~~**(c)(2) The manufacturer, lot number, and expiration date for each component for the CSP**~~.
1735.12. Quality Assurance and Quality Control. Subsection (b)	(b) The Board shall be notified in writing within 96 hours of the facility's receipt of a complaint of a potential quality problem or the occurrence of an adverse drug	**Rationale:** We thank the board for acknowledging and addressing concerns regarding the timeline for reporting and the change to a much more reasonable time of 96 hours.

	experience as defined in 21 CFR 310.305(b) involving a CNSP.	However, the addition of language to report all adverse drug experiences, regardless of severity, will increase administrative and personnel costs that is not captured by the Board's evaluation. The board's response to the question of "Business Impact" in the Initial Statement Of Reasons (ISOR) states; "the board anticipates minimal ongoing costs ranging from approximately $5,700 to $15,000 per year related to administrative and maintenance workload." This statement applies to the multiple proposed regulations requiring the addition of new administrative procedures inclusive of reporting requirements. The amount stated is a gross underestimation of the true cost to health systems. Understandably the Board lacks the internal expertise to accurately reflect those anticipated costs associated with development of policies and procedures, monitoring implementation of those procedures, correctly reporting to the Board as proposed by this regulation and others, cost of monitoring visits by the Board, implementation of technology to support the deployment of the policies and procedures and hiring of additional staff to support compliance with the proposed regulation. The Board further states in the ISOR under the header of "Business Impact" as it relates to the issue of cost the following: "This initial determination is based on the absence of testimony to that effect during the public discussion and development of the proposed regulation." The public meetings mandate testimony be limited to a few minutes and attendees tend to focus their input on the specific wording of the proposed regulation and not the cost. It is incumbent on the Board to actively pursue input from those that can accurately project the cost to health systems from the proposed regulation(s). The Board should, during public meetings or by other means, actively seek input from experts who can inform the Board's ISOR development as it relates to both "Business Impact" and "Economic Impact Assessment" to ensure it accurately reflects the impact on health care access, and cost. As to the proposed requirement of reporting all adverse drug reactions to the Board, it is with limited value and the benefit of the regulation to the public is questionable. Additionally, the cited reference to the 21 CFR is to the "definitions" section and fails to recognize section (a) of 21 CRF 310.305 which addresses what type of adverse reactions are reportable: "all serious, unexpected adverse drug experiences." The FDA is charged with public safety of medication use and its expected manufacturers and drug companies would be required to report serious and unexpected adverse drug experiences so the FDA may act such as removing the medication from the market or requiring additional packaging information requirements. The Board doesn't have the

		same expectation and authority. As such, what would the Board be doing with information reported on all adverse experiences given they are not the FDA? We believe that the intent might be to identify adverse drug experiences related to potential quality problems with CNSP's. If this is the intent, it is recommended to change the regulation language to the recommendation below (bold and strikeouts). If not, we recommend that this proposed regulation be deleted. **Recommendation (BOLD):** (b) The Board shall be notified in writing within 96 hours of the facility's receipt of a complaint of a potential quality problem ~~or~~ **and** the occurrence of a **serious and unexpected** adverse drug experience as defined in 21 CFR 310.305(b) involving a CNSP.
Sterile Compounding		
CCR 1736.1 Introduction and Scope. Subsection (b):	(b) CSPs for direct and immediate administration as provided in the Chapter shall only be done in those limited situations where the failure to administer could result in loss of life or intense suffering. Any such compounding shall be only in such quantity as is necessary to meet the immediate need. Documentation for each such CSP shall include identification of the CSP, compounded date and time, number of units, the patient's name and patient's unique identifier and the circumstance causing the immediate need. Such documentation may be available in the patient's medical record and need not be redocumented by the compounding staff if already available. (2) If the sterile compounding equipment or environment fail(s) to meet any required specification, an immediate use CSP may be compounded without the	**Rationale:** The previous regulations have not served us well and we thank the board for making changes to this section that addresses longstanding concerns for patient safety during medical emergencies. We also thank the board for providing the ability to care for hospital patients with immediate use CSP's during times where engineering controls may have temporary malfunctions. However, the newly proposed requirement to report each instance of immediate use compounding associated with a temporary engineering control malfunction will place a burden on both pharmacy personnel and board staff. The benefit of reporting each minor malfunction to the board is questionable and it is difficult to see how reporting to the board a temporary operational decision to utilize immediate-use compounding to care for patients while an issue is addressed with engineering controls will add value and enhance the safety of the public. Reporting of issues to regulatory agencies are usually reserved for serious matters and only those issues that are within the regulatory agency's' jurisdiction to act. It must be pointed out that immediate use compounding is an allowable action under USP797 standards, it is utilized routinely, regularly and safely in healthcare practice settings worldwide. Performing a simple and safe immediate-use compound for a patient by a pharmacy licensee while an engineering control malfunction is being addressed is not serious enough to warrant a report to the board. There is a possible

	requirement for there to be loss of life or intense suffering of an identifiable patient. This provision may only be used for 24 hours after such failure(s). All such failures must be documented in accordance with facility's SOP and shall be reported to the BOP	unintended consequence of entities shifting this simple temporary task to disciplines functioning outside the scope of these regulations and the jurisdiction of the Board. Requiring reporting of each instance of compounding of an immediate-use CSP will lead to increased administrative requirements, increased personnel needs, and will have the unintended consequence of potentially diverting resources from patient care activities or worse patients will be unable to access compounded medications due to onerous requirements and fear of inability to comply. The Board failed to capture the economic impact to health systems in their ISOR. The board's response to the question of "Business Impact" in ISOR states; "the board anticipates minimal ongoing costs ranging from approximately $5,700 to $15,000 per year related to administrative and maintenance workload." This statement applies to the multiple proposed regulations requiring the addition of new administrative procedures, reporting requirements, and enhanced testing. The amount stated is a gross underestimation of the true cost to health systems. Understandably the Board lacks the internal expertise to accurately reflect those anticipated costs associated with development of policies and procedures, monitoring implementation of those procedures, correctly reporting to the Board as proposed by this regulation and others, cost of monitoring visits by the Board, elanced testing requirements, purchase of additional inventory for PPE, implementation of technology to support the deployment of the policies and procedures and hiring of additional staff to support compliance with the proposed regulation. The Board further states in the ISOR under the header of "Business Impact" as it relates to the issue of cost the following: "This initial determination is based on the absence of testimony to that effect during the public discussion and development of the proposed regulation." The public meetings mandate testimony be limited to a few minutes and attendees tend to focus their input on the specific wording of the proposed regulation and not the cost. It is incumbent on the Board to actively pursue input from those that can accurately project the cost to health system of the proposed regulation. The Board should, during public meetings, or by other means seek input from experts who can inform the Board's ISOR development as it relates to both "Business Impact" and Economic Impact Assessment" to ensure the ISOR is an accurate reflection of the impact to health systems on cost and health care access.

		USP 797 provides sufficient guidance in their improved and updated standards for immediate-use compounding, and we once more implore the board to require USP's standards and not engage in additional regulations that are not based on an articulated and proven evidence that such proposed regulations will enhance patient safety efforts beyond the national standards. **Recommendation:** Remove the requirement to report to the board, There is no public benefit in reporting each immediate use compounding when there is a temporary engineering control malfunction. In fact, an immediate-use compound made by pharmacy staff, is considered the best practice in this situation since it is done by staff who are trained and experienced in sterile compounding and is widely acknowledged as the best professionals to do compounding. The requirement to document the failure of an engineering control per facility SOP is already enough in that it may be reviewed by board staff during both unannounced and annual re-licensing inspections. This is a much more reasonable use of time and resources, and it provides a mechanism for review that is incorporated into a task already being performed while also fulfilling the board's mandated mission for public safety. **1736.1 Sterile Compounding Scope. Subsection (b) (BOLD)** (2) If the sterile compounding equipment or environment fail(s) to meet any required specification, an immediate use CSP may be compounded without the requirement for there to be loss of life or intense suffering of an identifiable patient. This provision may only be used for ~~**24 hours**~~ **7 business days** after such failure(s). All such failures must be documented in accordance with facility's SOP and shall be available for inspection. ~~**reported to the BOP within 72 hours.**~~
CCR 1736.1 Introduction and Scope. Subsection (h):	(h) CSPs with human whole blood or human whole blood derivatives shall be	**Rationale:** The current health and safety code section 1602.5 states the following:

	produced in compliance with Health and Safety Code section 1602.5.	(a) No person shall engage in the production of human whole blood or human whole blood derivatives unless the person is licensed under this chapter and the human whole blood or human whole blood derivative is collected, prepared, labeled, and stored in accordance with both of the following:" The proposed regulation in its current state would cause confusion as it would enforce a law that is not applicable to any human whole blood or human whole blood derivative that is already manufactured by a pharmaceutical company (e.g. Albumin, Factor products, IVIG etc.) **Recommendation (BOLD):** Would recommend the board to revise the proposed language to provide clarification to state that the regulation does not apply to CSPs made with human blood/derivative that is manufactured by pharmaceutical companies. (h) CSPs with **patient's own** whole blood or human whole blood derivatives **from the patient** shall be produced in compliance with Health and Safety Code section 1602.5.
CCR 1736.2 Personnel Training and Evaluation. Subsection (b)	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 Standard Operating Procedures (SOPs) required by section 1736.17 related to compounding are identical. (2) The Secondary Engineering Control	**Rationale:** The current USP 797 chapter does not require the PEC unique identifier to be documented for personnel training. Requiring a PEC unique identifier only adds to the additional documentation burden. **Recommendation:** Recommend the Board of Pharmacy to consider removing the requirement of "PEC unique identifier". We once more reiterate the comments by both us and others at various stages through this rulemaking process that USP have already very high standards and the state of California does not need to exceed these minimum standards. **Proposed Regulation Revision (BOLD:** 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.

	(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.	
CCR. 1736.4 Facilities and Engineering Controls Subsection (c)	(1) Designated compounding area(s) shall typically be maintained at a temperature of 20° Celsius or cooler.	**Rationale:** The USP chapter 797 recommends maintaining a temperature of 20° Celsius or cooler in that it states the following: "The cleanroom suite should be maintained at a temperature of 20° or cooler and a relative humidity of 60% or below to minimize the risk of microbial proliferation and to provide comfortable conditions for compounding personnel attired in the required garb." This requirement is in essence the same as this regulation and is duplicative. **Recommendation (BOLD):** We recommend this requirement be removed since pharmacies will follow USP 797 standards for temperature requirement. Recommend the Board of Pharmacy to consider removing the requirement of CCR. 1736.4 subsection (c). ~~**(1) Designated compounding area(s) shall typically be maintained at a temperature of 20° Celsius or cooler.**~~
CCR 1736.11 Master Formulation and Compounding Records. subsection (c)(2):	(c)(2) The manufacturer, lot number, and expiration date for each component for the CSP.	**Rationale:** Current language in CCR 1735.3 below has a provision for CSPs compounded in health facilities to prevent delays in care to acutely ill patient, i.e. infections, cancer, critical care, etc. The current language states: (F) The manufacturer, expiration date and lot number of each component. If the manufacturer name is demonstrably unavailable, the name of the supplier may be substituted. If the manufacturer does not supply an expiration date for any component, the records shall include the date of receipt of the component in the pharmacy, and the limitations of section 1735.2, subdivision (l) shall apply. (i) Exempt from the requirements in this paragraph (1735.3(a)(2)(F)) are sterile preparations compounded in a single lot for administration within seventy-two (72) hours to a patient in a health care facility licensed under section 1250 of the Health and

		Safety Code and stored in accordance with standards for "Redispensed CSPs" found in Chapter 797 of the United States Pharmacopeia – National Formulary (USP37-NF32) Through 2nd Supplement (37th Revision, Effective December 1, 2014), hereby incorporated by reference. **Recommendation (BOLD):** We once more reiterate the comments by both us and others at various stages through this rulemaking process that USP standards adequately provide for safe and quality compounding of medications. The addition of this regulation exceeds the national standards in a manner that fails to demonstrate the benefit to patients. Add back the language above: 1736.11 Master Formulation and Compounding Records, subsection (c)(2): (c)(2) The manufacturer, lot number, and expiration date shall be recorded for each component for CSPs. **(i) Exempt from the requirements in this paragraph are sterile preparations compounded in a single lot for administration within seventy-two (72) hours to a patient in a health care facility licensed under section 1250 of the Health and Safety Code.**
CCR. 1736.17 Standard Operating Procedures (SOPS) subsection (d)	(d) 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 contact time required, and how contact time will be monitored and documented.	**Rationale:** Regarding board staff's response to comments of CSHP and others related to this section stating the following: *"Board staff have reviewed the comments and do not recommend a change to the proposed text. Staff note that this is consistent with the board's current regulation requirements in the SOP, CCR 1751.3(a)(22). Further, staff note that not all technology solutions are the same. The Board understands automation typically require some sort of confirmation step before compounding begins. These methods could be documented in the SOPs."* **The current regulation referenced by board staff states the following:** 1751.3(a)(22) The determination and approval by a pharmacist of ingredients and the compounding process for each preparation before compounding begins. It appears that the board staff referenced current regulation and the response is not relevant to the topic of contact times of products being used on items introduced from

		the classified space into the compounding area(s). Please clarify and explain the response and how the two regulations relate. We reiterate and clarify our initial concerns: • In many health-system pharmacies there are many items entering the sterile compounding spaces including into the SEC and PEC. The proposed language as it is written, could be interpreted to suggest that the SOP must state that how each item introduced from the unclassified space be cleaned and the contact time be timed and then this time be documented. For example, when a pharmacy staff member brings in 20 bags of 1 liter normal saline into the cleanroom, this means that each bag must be wiped, the contact time must be timed with a stopwatch, the time documented on a log and then this process being followed for each subsequent bag of normal saline. This could take a staff member up to an hour to only bring in 20 bags of normal saline into the anteroom. • Requiring monitoring and documentation of the monitoring of the dwell time for each individual item adds a significant burden to the workload of sterile compounding staff. It will take them away from performing the work of compounding medications for acutely ill patients and will further contribute to the potential for increased compounding while providing no demonstratable benefits. In practice, this requirement could be interpreted that the wiping and dwell time of medication and related sterile compounding items such as syringes, needles etc. sterile isopropyl alcohol be individually timed and documented when introduced to the PEC for sterile compounding. We suspect that the intent of this regulation is for SOPs to sufficiently address documentation and following manufacturer recommended dwell times as part of sterile compounding practice and wish to point out the potential for misinterpretation during enforcement inspections. **Recommendation (BOLD):** (d) 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.**~~
CCR. 1736.18 Quality Assurance and Quality Control subsection (c)	(c) In addition to subsection (b), all complaints made to the facility related to a potential quality problem with a CSP and all adverse drug experiences events shall be reviewed by the pharmacist-in-charge within 72 hours of receipt of the complaint or occurrence of the adverse drug experience. Such review shall be documented and dated as defined in the SOPs.	**Rationale:** The way that the proposed regulation is written, seems to suggest that the review must be completed within 72 hours since it states that "such review shall be documented and dated as defined in the SOPs." The proposed language requirement for a documentation and dating of the review together with the preceding sentence's requirement for review within 72 hours from the receipt of the compliant could be seen as requiring the review to be completed within the 72 hours timeframe. A requirement of 72 hours may not provide sufficient time for pharmacies to thoroughly investigate and determine root causes. It is reasonable to expect that a review after a complaint be started within three business days. Investigation could take longer than this due to many factors involved in such an investigation that needs to be looked at. Many of these may not be available or apparent within this timeframe. **Recommendation (BOLD):** We recommend that the intent of this proposed regulation be clarified with the following proposed language: *(*c) In addition to subsection (b), all complaints made to the facility related to a potential quality problem with a CSP and all adverse drug experiences events shall be reviewed by the pharmacist-in-charge **and shall start within three (3) business days ~~within 72 hours~~ of** receipt of the complaint or occurrence of the adverse drug experience. Such review shall be documented and dated as defined in the SOPs.
CCR 1736.21 Compounding Allergenic Extracts subsection (c)	(c) Any compounded stock allergy solution shall comply with the requirements established in USP Chapter 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.	**Rationale:** USP 797 states "Because of certain characteristics of allergenic extracts and allergy practice, preparation of allergenic extract prescription sets is not subject to all of the requirements in this chapter that are applicable to other sterile CSPs." Additionally, USP 797 does not require allergenic extracts to conduct antimicrobial effectiveness testing or packaging integrity evaluation related to container closure. It is apparent that USP 797 make a clear distinction in standards related to allergenic compounds and regular compounding. The board's initial statement of reasons regarding this regulation states that "this would ensure that stock solutions comply with the compounding requirements of USP Chapters 51 and 1207 due to the risk of patient safety from contamination." This statement is contrary to what USP states above where they state that "allergenic extracts sets is not subject to all the requirements in this chapter".

		● Organizations such as the American Academy of Allergy, Asthma & Immunology (AAAAI) and the American College of Allergy, Asthma & Immunology (ACAAI) highlight that allergenic extract compounding practices, conducted under general aseptic conditions, have maintained a strong safety record without requiring ISO-classified environments or extensive sterility controls. This long history of safe use has supported continued in-office compounding of allergenic extracts under specific guidelines to ensure patient safety and access to care. ● If this proposed testing requirement would become regulation, it would create an immediate and permanent inability for pharmacies to be able to compound allergenic extracts for patients. What the proposed rule would require in practice, is that every stock solution for every patient be sent in to a laboratory for testing according to the requirements. It would create a waiting time for the results and add enormous cost to pharmacies, health plans and patients. It would further place enormous pressure on the supply chain of these products that would in effect stop the provision of these products to patients' access to these treatments. There is not enough staff and there are not enough laboratories or laboratory supplies in existence to perform these tests on the stock solutions for each and every patient being treated in the state of California. Since this regulation would only apply to pharmacies, they may very likely decide to stop providing this service. This severe economic impact was not stated in the initial statement of reasons. The subsequent lack of access was not mentioned in the initial statement of reasons. In fact, the ISOR under "Economic Impact" state: "(4) this proposal will not eliminate existing businesses within California." That is not the case given the situation described above as a consequence of this proposed regulation. ● As an alternative to this required testing, an alternate strategy could be followed by compounding stock solutions from scratch for each patient visit. This will have equally impactful consequences as explained in the next bullet point. ● Requiring compounded stock solution to be compounded at the time of the appointment, with unused doses discarded, will create the following issues: ○ Increased Waste: unused doses that are discarded after each visit will generate significant pharmaceutical waste, raising environmental and resource utilization concerns. ○ Higher Costs for Patients and pharmacies: The need to compound a new stock solution for every visit will increase operational costs, which will likely be passed on to patients, leading to financial burden.

		○ Additional Workload: Compounding single-use stock solutions for each patient will add to the workload of pharmacy staff, placing further strain on health-systems already facing staffing challenges and resource limitations. ▪ These challenges would disrupt workflows and amplify the financial and operational pressures on healthcare institutions and their patients. ● If this rule gets approved, it is highly likely that most pharmacies will decide that the pressure on staffing, wait times and associated costs would make this an unviable business decision. They will stop providing this service and the compounding of these products will be shifted solely to physician practices and compounding by non-pharmacy personnel where these regulations would not apply and would not be enforceable. ● Allergen extract shortages are common, with nearly all surveyed providers reporting experiences of disruption, mainly involving venom, pollen, and mold extracts. 95% of providers reported patient care was affected, with varying degrees of severity. Interruptions may lead to worsened asthma or allergic reactions in untreated patients.[1] Reference: 1. Ezhuthachan ID, Banks TA, Cerise JE, Wong SC, Ponda P. Allergen immunotherapy extract shortages and their effects on clinical care: A work group report of the AAAAI Immunotherapy, Allergen Standardization, and Allergy Diagnostics Committee. J Allergy Clin Immunol Pract. 2022;10(2):444-452. doi:10.1016/j.jaip.2021.10.057 **Recommendations:** We once more reiterate the comments by both us and others at various stages through this rulemaking process that USP has sufficient standards to promote and protect patients. Additionally, the Board has failed to accurately assess the “Economic Impact” and “Business Impact” as noted in the ISOR. This regulation will increase administrative, enhanced testing, and personnel costs that is not captured by the Board’s evaluation. The board’s response to the question of “Business Impact” in the ISOR states; “the board anticipates minimal ongoing costs ranging from approximately $5,700 to $15,000 per year related to administrative and maintenance workload.” This statement applies

		to the multiple proposed regulations requiring the addition of new administrative procedures inclusive of enhanced testing, and reporting. The amount stated is a gross underestimation of the true cost to health systems. Understandably the Board lacks the internal expertise to accurately reflect those anticipated costs associated with development of policies and procedures, monitoring implementation of those procedures, correctly reporting to the Board as proposed by this regulation and others, cost of monitoring visits by the Board, implementation of technology to support the deployment of the policies and procedures and hiring of additional staff to support compliance with the proposed regulation. The Board further states in the ISOR under the header of "Business Impact" as it relates to the issue of cost the following: "This initial determination is based on the absence of testimony to that effect during the public discussion and development of the proposed regulation." The public meetings mandate testimony be limited to a few minutes and attendees tend to focus their input on the specific wording of the proposed regulation and not the cost given the abbreviated time to comment. It is incumbent on the Board to actively pursue input from those that can accurately project the cost to health systems of the proposed regulation. The Board should, during public meetings and if necessary by other means, seek testimony from experts who can inform the Board's ISOR development as it relates to both "Business Impact" and "Economic Impact Assessment." **Proposed Regulation (BOLD)**: **(c) ~~Any compounded stock allergy solution shall comply with the requirements established in USP Chapter 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.
Hazardous drugs		
CCR 1737.2 List of Hazardous Drugs subsection (a) and (b) :	(a) 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 (PIC), professional director of a clinic, or designated representative-in-charge, as	**Rationale:** With regards to board staff's response to multiple commenters regarding this subsection. Board staff commented that the PIC is responsible for compliance with all provisions of Pharmacy Law. This is correct and is mandated by statute and therefore need not be duplicated in this section. It must be noted that the PIC is responsible for compliance but need not to be doing all the work associated with following these laws.

	applicable. The designated person must be 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. (b) 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.	We therefore ask the board to recognize the operational matters in pharmacies are impacted by governing body influence for which there should be corresponding responsibility to those individuals. PIC's must be able to delegate operational and administrative matters according to their professional discretion. Pharmacists are practicing professionals, and this is associated with making many important patient care and operational decisions. The board needs to recognize this and treat them as such and let them make decisions appropriate to their professional status. **Recommendation:** Recommend revising the language to state the expectation of review of the HD list and leave it to the PIC to decide how they would like to accomplish this based on their operations and staffing. **CCR 1737.2 List of Hazardous Drugs subsections (BOLD):** (a) 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 (PIC) or designee, professional director of a clinic, or designated representative-in-charge, as applicable. The designated person must be 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.**~~ **And this** approval shall be documented at least every 12 months. (b) 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 or designee, professional director of a clinic, or designated representative-in-*charge, as applicable***~~.
1737.5 Facilities and Engineering Controls. Subsection (c)	(c) Effective [OAL insert six months following the effective date] A a pass-through is not allowed between the hazardous drug buffer room C-SEC into an unclassified space.	**Rationale:** We once more reiterate the comments by both us and others at various stages through this rulemaking process that USP has sufficient standards to promote an protect patients and this regulation doesn't enhance patient safety expectations in a meaningful way. Additionally, USP 800 does not prohibit using a pass-through between a classified space and an unclassified space. **Recommendation (BOLD):** Delete this requirement.

		~~**Effective [OAL insert six months following the effective date] A a pass-through is not allowed between the hazardous drug buffer room C-SEC into an unclassified space.**~~
CCR 1737.7. Personal Protective Equipment (PPE), subsection (c).	(c) Outer gloves used for HD compounding shall be changed between each different HD preparation.	**Rationale:** Many health-systems use closed system transfer device (CSTD) when compounding antineoplastic HDs. The use of CSTD has shown to significantly reduce overall chemical contamination (12.24% vs. 26.39%).[1] Double-gloving is primarily designed to offer extra protection against hazardous drug compounds, with the outer glove serving as a first line of defense. If the outer glove is repeatedly removed or exposed to rough conditions, it may wear down, possibly increasing the risk of puncturing or compromising the inner glove. This could lead to reduced protection, especially when handling hazardous drug compound.[2,3] Frequent removal and disposal of outer glove changes creates significant waste.[2] Board staff's response that they performed an online search of the pricing and availability of appropriate gloves reflects a lack of understanding of the practice of pharmacy and the intricacies of purchasing contracts at large organizations. Pharmacies cannot simply go to an online vendor of these sterile gloves and buy it on a credit card. Purchasing is usually done on contracts with vetted suppliers to ensure supply chain integrity. Due to this, the pricing advertised online from unvetted suppliers, is generally unavailable to organizations. Furthermore, the cheapest online price may not reflect the product that is selected for use by the pharmacy since there are factors to be considered such as easy of use, quality of the product and in some cases, impact on staff that could experience allergic skin reactions to cheap products. As noted with other proposed regulations the "business impact" and "economic impact" of the ISOR fails to accurately reflect the cost and impact to businesses by this and other regulations. The board's response to the question of "Business Impact" in the Initial Statement Of Reasons (ISOR) states; "the board anticipates minimal ongoing costs ranging from approximately $5,700 to $15,000 per year related to administrative and maintenance workload." This statement applies to the multiple proposed regulations requiring the addition of new administrative procedures, increased purchase of PPE, increased testing

		and enhanced reporting requirements. The amount stated is a gross underestimation of the true cost to health systems. Understandably the Board lacks the internal expertise to accurately reflect those anticipated costs associated with development of policies and procedures, monitoring implementation of those procedures, correctly reporting to the Board as proposed by this regulation and others, cost of monitoring visits by the Board, implementation of technology to support the deployment of the policies and procedures and hiring of additional staff to support compliance with the proposed regulation. The Board further states in the ISOR under the header of "Business Impact" as it relates to the issue of cost the following: "This initial determination is based on the absence of testimony to that effect during the public discussion and development of the proposed regulation." The public meetings mandate testimony be limited to a few minutes and attendees tend to focus their input on the specific wording of the proposed regulation and not the cost. It is incumbent on the Board to actively pursue input from those that can accurately project the cost to health system of the proposed regulation. The Board should, during public meetings, or by other means seek input from experts who can inform the Board's ISOR development as it relates to both "Business Impact" and "Economic Impact Assessment." . **Reference** 1. Simon N, Vasseur M, Pinturaud M, et al. Effectiveness of a Closed-System Transfer Device in Reducing Surface Contamination in a New Antineoplastic Drug-Compounding Unit: A Prospective, Controlled, Parallel Study. Ahmad A, ed. PLoS One 2016;11:e0159052. Available at: https://dx.plos.org/10.1371/journal.pone.0159052. 2. Kirk H. Double gloving when handling cytotoxic drugs. *Hospital Pharmacy Europe*. Published March 2, 2009. Available from: https://hospitalpharmacyeurope.com/news/editors-pick/double-gloving-when-handling-cytotoxic-drugs/ 3. McNeilly L. Double gloving: Myth versus fact. *Infection Control Today*. Published May 5, 2011. Available from: https://www.infectioncontroltoday.com/view/double-gloving-myth-versus-fact **Recommendations**:

		We once more reiterate the comments by both us and others at various stages through this rulemaking process that USP has sufficient standards to promote and protect patients and this regulation fails to demonstrate its expected enhancement of patient safety efforts. Delete the proposed language: ~~**c) Outer gloves used for HD compounding shall be changed between each different HD preparation.**~~
CCR 1737.14. Administering subsection (a)	(a) When furnishing a compounded antineoplastic HD for administration, the facility shall: (1) Place the HD in a decontaminated plastic container with an HD label on the outside of the container; and (2) For an infused antineoplastic HD, attach and prime tubing and attach a CSTD when appropriate.	**Rationale:** The proposed language appears to presume that there is only one method for providing an HD's for administration. When compounding HD's, the finished product is placed in a plastic bag with Hazardous Drug print on it. This is then placed into another zip-lock bag that also has Hazardous Drug printing. This final package is then sent to the nursing unit/infusion center where it is placed in a plastic bin where the nurse will pick it up for administration to the patient. It is not clear if the interpretation of "plastic container" requires a rigid plastic container and/or if a zip-lock bag type is allowable. It is not clear if said single use zip-lock bag must be decontaminated, generally if it is a single use bag decontamination is not needed. Absent clarifying language, the proposed language could be misinterpreted and appears to require that all HD's be placed and furnished in a rigid plastic container when compounding is complete. **Recommendations (BOLD):** It is recommended that the proposed language be changed to the following: (a) When furnishing a compounded antineoplastic HD for administration, the facility shall: (1) **<u>Double bag or</u>** place the HD in a decontaminated plastic container with an HD label on the outside of the ***<u>bag or</u>*** container; and (2) For an infused antineoplastic HD, attach and prime tubing and attach a CSTD when appropriate.
Radiopharmaceutical- Preparation, Compounding, Dispensing, and Repackaging		
CCR 1738.4 Personnel Qualifications, Training, and Hygiene subsection (c)	(c) Aseptic manipulation competency initial training and competency and ongoing training and competency	**Rationale:**

	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.	The current USP 825 chapter does not require the PEC unique identifier to be documented for personnel training. Requiring a PEC unique identifier only adds to the additional documentation burden. **Recommendation:** We once more reiterate the comments by both us and others at various stages through this rulemaking process that USP has sufficient standards to promote and protect patients. Recommend the Board of Pharmacy remove the requirement of "PEC unique identifier". **Recommendation (BOLD):** (c) 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.
CCR 1738.10. Preparation subsection (c)	(c) 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.	**Rationale:** The proposed language is inconsistent with USP 825 recommendations, and will require health-systems to incorporate patient need which may not be pertinent information. **Recommendation (BOLD):** We once more reiterate the comments by both us and others at various stages through this rulemaking process that USP has sufficient standards to promote and protect patients. This proposed regulation fails to demonstrate the necessity for patient safety beyond that required by USPR. We recommend that this subsection be deleted. ~~(c) **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 radionuclides purity) as specified in individual monographs,~~**

		~~and other applicable parameters as clinically appropriate in the professional judgment of the pharmacist.~~
CCR 1738.14. Quality Assurance and Quality Control subsection (b)	(b) The board shall be notified in writing within 72 hours of a complaint involving a radiopharmaceutical. Recalls and adverse events must be reported to the Board and other agencies in compliance with relevant provisions of law.	**Rationale:** A requirement of 72 hours may not provide sufficient time for health-systems to investigate and notify the necessary regulatory bodies in cases where it occurs over an extended weekend. **Recommendation (BOLD):** (b) The board shall be notified in writing within **~~72 hours~~ three (3) business days** of a complaint involving a radiopharmaceutical. Recalls and adverse events must be reported to the Board and other agencies in compliance with relevant provisions of law.
CCR 1738.14. Quality Assurance and Quality Control subsection (c)	(c) In addition to subsection (b), all complaints related to a potential quality problem with a radiopharmaceutical and all reported 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.	**Rationale:** The way that the proposed regulation is written, seems to suggest that the review must be completed within 72 hours since it states that "such review shall be documented and dated as defined in the SOPs." The proposed language requirement for a documentation and dating of the review together with the preceding sentence's requirement for review within 72 hours from the receipt of the compliant could be seen as requiring the review to be completed within the 72 hours timeframe. A requirement of 72 hours may not provide sufficient time for pharmacies to thoroughly investigate and determine root causes. It is reasonable to expect that a review after a complaint be started within three business days. Investigation could take longer than this due to many factors involved in such an investigation that needs to be looked at. Many of these may not be available or apparent within this timeframe. **Recommendation (BOLD):** We recommend that the intent of this proposed regulation be clarified with the following proposed language: (c) In addition to subsection (b), all complaints made to the facility related to a potential quality problem with a CSP and all adverse drug experiences, as defined in 21 CFR 310.305(b) shall be reviewed by the pharmacist-in-charge **and shall start within three (3) business days ~~within 72 hours~~** of receipt of the complaint or occurrence of the adverse drug experience. Such review shall be documented and dated as defined in the SOPs.

Mark Johnston, R.Ph
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12/9/24

California Board of Pharmacy,

I am writing to you in my capacity as Executive Director of Pharmacy Regulatory Affairs for CVS Health and its family of pharmacies. CVS Health, the largest pharmacy health care provider in the United States, is uniquely positioned to provide diverse access points of care to patients in the state of California through our integrated offerings across the spectrum of pharmacy care that includes over 1,000 pharmacies located within California. We appreciate the opportunity to submit comments on the Board's proposed compounding regulations.

Article 4.5: Nonsterile Compounding:

As proposed 1735.10 clearly dictates that "(BUDs) assigned with only a date shall expire at 11:59pm on that date", the recording of the time of compounding is extraneous. To relieve unnecessary administrative burden, CVS suggests the following edits to proposed 1735.7.

1735.7 Master Formulation and Compounding Record

(c) A compounding record (CR) shall be maintained and, upon request, be produced as a single document developed in compliance with USP Chapter 795, and includes the following additional elements:

***(1)** The date ~~and time~~ of compounding, which is the time when compounding the CNSP started, and which determines when the assigned BUD starts*

1735.10 Establishing Beyond-Use Dates

***(a)** Beyond-use dates (BUDs) assigned with only a date shall expire at 11:59 pm on that date*

CVS Health is supportive of prescription flavoring within our pharmacies and supportive of the overwhelming majority of states who do not consider flavoring as compounding. We believe that the increased potential for adherence to medication regimens and thus increased public safety for California residents (particularly children) is evident and any perceived risk to public safety has not been substantiated with data or evidence. While we appreciate Enforcement and Compounding Committee Chair Serpa's comments at the 11/7/2024 full meeting of the Board that indicate her desire to exempt the requirement of a valid patient specific prescription for each flavoring, these modified regulations do not contain such an allowance, and the requirement of a valid patient specific prescription is not the only roadblock to flavoring in California. If the Board is to consider flavoring as compounding, CVS Health requests an exemption to labeling. We also believe that the compounding cleaning and record keeping requirements are excessive for flavoring. While we prefer that flavoring is exempted from compounding, we understand the Board to not be amenable. Thus, in order for CVS Health to

consider flavoring prescriptions in California, we request the following, which is mainly derived from the Missouri Board of Pharmacy's 2020 Pharmacy Practice Guide:

1735.1. Introduction and Scope.

(i) Using sound professional judgment, a pharmacist may authorize the flavoring of a prescription unless the prescriber expressly prohibits flavoring upon issuing the prescription.

1735.5. Cleaning and Sanitizing In addition to the standards set forth in USP Chapter 795, the following requirements apply to nonsterile compounding.

(c) When flavoring a prescription, this section is satisfied when cleaning and sanitizing measuring devices only.

1735.7. Master Formulation and Compounding Records.

(d) When flavoring a prescription, this section is satisfied by only notating the act of flavoring in the pharmacy's prescription record, including in a logbook or in the prescription record.

1735.9. Labeling. In addition to the standards set forth in USP Chapter 795, the following requirements apply to nonsterile compounding.

(d) When flavoring a prescription, this section is satisfied byindicating that the product was flavored on the patient's container.

Article 4.7 Hazardous Drugs

On 7/31/2024 during a full meeting of the Board, President Oh requested that Article 4.7 only pertain to compounding of hazardous drugs and not handling of hazardous drugs. This was memorialized in the minutes of said meeting on page 17-18, where a motion reads in part: "adding an introductory sentence to the article on hazardous drugs that the following requirements apply to the compounding of hazardous drugs". While the modified text published on 11/8/2024 does indeed strike the word "handling", without direction from the Board, modified Article 4.7 now pertains to "other manipulations included in Table 1 of the Chapter of antineoplastic HDs established by United States Pharmacopeia (USP) General Chapter 800".

While USP 800 does not require competency training for Table 1 manipulations, the Board's staff has determined that a portion of the Table 1 manipulations necessitate competency training, such as "withdrawing or diluting injectable HDs from parenteral containers", "expelling air or HDs from syringes", "weighing or mixing components", "constituting or reconstituting powdered or lyophilized HDs" and "crushing or splitting tablets or opening capsules". However, as written if a pharmacy partakes in any listing within Table 1, competency training must be performed. CVS Health believes that competency training for "pouring oral or topical liquids from one container to another", disposing of gloves and cleaning counting trays is overly burdensome and that safe procedures can easily be achieved via less rigorous requirements, such as through computer-based training and SOPs.

Additionally, requiring "ongoing evaluation and training" is an undefined mandate that CVS Health believes is satisfied when any listing within Table 1 is performed, as such "manipulations" in our retail pharmacies are performed under the direct supervision and control of a pharmacist, fostering a greater opportunity for a day-to-day safety competency assessment of colleague skills, negating the need for a periodic process.

Therefore, CVS Health requests that the training of both the person assigned to provide training and the personnel responsible for "other manipulations of antineoplastic HDs" be determined according to professional judgment and documented within required SOPs, as redlined below:

1737.9 Personnel Training

In *addition to the standards in USP Chapter 800, the following requirements apply to a facility where the compounding of HDs is performed or when a facility's SOPs require training to perform certain ~~one where~~ "other manipulations" included in Table 1 of the Chapter of antineoplastic HDs ~~is performed~~.*

(a) Any person assigned to provide training 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 facility's SOPs as referenced in section 1737.17. Documentation must be maintained demonstrating compliance with training requirements, and for compounding demonstrated~~ing~~ competency must be maintained.
(b) All personnel responsible for compounding HDs or "other manipulations of antineoplastic HDs" who fail any aspect of ongoing evaluation and training shall not compound HDs or perform other manipulations until after successfully passing reevaluations in the deficient area(s), as ~~As~~ detailed in the facility's SOPs. Any failure in competency shall comply with the provisions of 1735.2(c) or 1736.2(d), as applicable.

1737.17. Documentation and Standard Operating Procedures (SOPs).

In addition to the standards in USP Chapter 800, the following requirements apply to the compounding of HDs or performing "other manipulations" included in Table 1 of the Chapter of antineoplastics HDs.

(a) Any facility shall maintain and follow written SOPs for all situations in which HDs are compounded or

antineoplastic HDs are "otherwise manipulated".

(b) A facility where compounding HDs is performed or one where "other manipulations"

antineoplastic HDs is performed shall have SOPs that include at least the following:

(17) Training. including demonstrated competency if compounding.

Sincerely,

Mark Johnston, R.Ph

Executive Director

Pharmacy Advocacy and Regulatory Affairs

Public Comment Submission to CA BOP
By Donald Cottman, RPH
Individual, Licensed California Pharmacist
Stockton, CA

Title 16. Board of Pharmacy
"Modified Regulation Text"
Proposed changes to the current regulation. August 29, 2024.

Section, subdivision	Proposed language	Comments
1735.1. Introduction and Scope. (d)	~~(c)~~ (d) 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 no~~t~~ more than 7-day supply, or up to no more than 14 days for antibiotics, for an individual patient~~,~~ as fairly estimated by the prescriber, and documented on the purchase order or other documentation submitted to the pharmacy prior to furnishing for an individual patient.	As written has the effect of limiting what can be provided for office dispensing to a quantity for an individual patient that has to be known prior to furnishing it to the office. This defeats the purpose of providing office stock for the vet to be able to make an immediate dispense to a patient at the office.
1735.1. Introduction and Scope, (g)	~~(h)~~ (g) 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 "shall be provided" is not always within the pharmacy's control. Language should be included to accommodate if consultation is denied.
1735.3. Personnel Hygiene and Garbing. (a)	(a) Facilities shall require individuals entering the compounding area to report if the rashes, recent tattoos or oozing sores, conjunctivitis, active respiratory infection, or any other medical condition, to determine if such condition could contaminate a CNSP or the environment per the facility's SOPs. Prior to admitting any personnel into a compounding area, the supervising pharmacist shall evaluate whether ~~compounding~~ personnel is experiencing any of the above conditions ~~following: rashes, recent tattoos or oozing sores, conjunctivitis, active respiratory infection, or any 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.	There is no precise definition of "could contaminate" and has a requirement of "shall not allow". Without a definition, there is no way to objectively determine if compliance has been achieved.
1735.8. Release Inspections and Testing.	A pharmacist performing or supervising the nonsterile compounding and the dispensing pharmacist are ~~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~~ so long as label instructions for storage and handling are followed after the preparation is dispensed.	Inclusion of "and the dispensing pharmacist" creates an unreasonable liability for a pharmacist who was not involved in formulation or supervising of the compounding process. It forces employee RPHs to accept liability for the formulation and dating determinations made by management.
1735.10. Establishing Beyond-Use Dates. (b)	(b) 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.	There is no definition defining what "compatibility" nor "degradation" means in this context and has a "shall not" requirement. There is no clarity on when compliance has been achieved. Also, inclusion of "e.g. possible leaching, interaction, and storage conditions" implies

		an expectation of evaluating finished preparation for those kinds of parameters. This is completely impractical and not economically feasible for extemporaneously compounded formulations.
1735.12. Quality Assurance and Quality Control. (b) (c)	(b) The Board shall be notified in writing within ~~72~~ 96 hours of the facility's receipt of a complaint of a potential quality problem or the occurrence of an adverse drug experience as defined in 21 CFR 310.305(b) ~~drug event~~ involving a CNSP. (c) All complaints made to the facility related to a potential quality problem with a CNSP and all adverse drug experiences ~~events~~ shall be reviewed by the pharmacist-in-charge within 72 hours of receipt of the complaint or occurrence of the adverse drug experience ~~event~~. Such a review shall be documented and dated as defined in the SOPs.	There is no definition of what "a potential quality problem" is and there is no definition of what an "adverse drug experience" is. There is a "Board shall be notified" requirement, but without a definition of what defines the event, compliance with the notification cannot be determined.
1735.14. Documentation. (b)	In addition to the standards set forth in USP Chapter 795, the following requirements apply to nonsterile compounding. (a) Records shall be maintained as required by USP Chapter 795 and this article in a readily retrievable form, for at least three years from the date the record was created or relied upon to meet the requirements of this article. 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 (b) Records ~~created~~ 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, for at least three years from the date the record was created or relied upon, in a readily retrievable format and include the changes to the document, identification of the individual who made the change, and the date of each change.	The broad nature of this record keeping requirement requires that every record, which includes master formulations and SOPs, must have a complete audit trail of any revision with retention of prior versions of those documents. This creates an incredible burden on the pharmacy, requiring it to be able to produce not only the record of the formula, current formula and current P&P for operations, but also be able to produce that entire body of pharmacy operating documents that were in effect at the time any compound was made during the prior three years.
STERILE COMPOUNDING		
1736.1. Introduction and Scope. (d) (2)	(d) A reasonable quantity of a ~~compounded drug preparation~~CSP 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 a 120-hour supply for an individual patient, 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 ophthalmic where up to a 28-day supply may be furnished to veterinarian's office for an individual patient. Such topical ophthalmics shall be compliant with USP 797 section 14.5, Multiple-Dose CSPs.	Comment: As written, it limits the provision of compounds for a vet to furnish to "an individual patient… and documented…prior to furnishing." The furnishing to the office for an individual patient prevents the office from having products available for immediate furnishing, when needed. The "for an individual patient" requirement requires the

		office to provide a name, then the pharmacy can send it to the office, who could then furnish it to the patient. This is the same as the pharmacy dispensing it themselves to an individual patient. Pharmacy law already allows a pharmacy to send a patient's prescription to the office for the office to then furnish to the patient. This regulation, if that is the intent, would be redundant of existing regulation.
1736.1. Introduction and Scope. (e)(3)	(e) In addition to prohibitions and requirements for compounding established in federal law, no CSP may be compounded that: (3) Is made with a non-sterile component for which a conventionally manufactured sterile component is available and appropriate for the intended CSP, unless the CSP is compounded in full compliance with USP 797 Category 3 requirements, or the conventionally manufactured sterile component appears in an American Society of Health-System Pharmacists (ASHP) or FDA Drug Shortages Database.	The regulation would completely precludes the compounding of any non-sterile to sterile items except when performed under USP Category 3 requirements. This is in complete contradiction to the existence of USP Category 2 requirements that explicitly allow for non-sterile to sterile compounding under those conditions. This regulation will completely exclude licensed pharmacies, typically smaller ones, from the ability to provide compounding in an environment that have been accepted as a standard of practice, have been implemented in compliance with those standards, and have established patient populations dependent on access to their services. To suddenly have these pharmacies and their compounds be excluded from serving patients is a grave injustice to pharmacy owners, California prescribers, and California patients. Additionally, to state that a non-sterile to sterile preparation can be made as a category 2 if it is in shortage, but not at other times is illogical with respect to protecting the public. If it is not safe for a

		licensed pharmacy to prepare a particular non-sterile to sterile product in a Category 2 environment on a routine basis, why is it suddenly acceptable for the public to get it from them during a shortage? The Board should decide that it is either appropriate, or not appropriate, for non-sterile to sterile compounding to be performed under USP Category 2 conditions. If the intent of the CA BOP to limit non-sterile to sterile compounding to only licensed pharmacies operating under Category 3 conditions, then it should recognize this will reduce the accessibility of compounded preparations to the public and limit access from those unusual items that are typically made by smaller entities operating under Category 2 conditions. I cannot understate the extreme hardship this regulation would impose on licensed pharmacies to the detriment it represents to California patient access to medications.
1736.3. Personnel Hygiene and Garbing (a)	In addition to the requirements in USP Chapter 797, the following requirements apply to sterile compounding. (a) The pharmacist with supervision and control ~~overseeing~~ of compounding shall not allow personnel with potentially contaminating conditions to enter the designated compounding area.	Comment: There is no definition of "potentially contaminating condition" and there is a "shall not allow" requirement. Without a definition, it cannot be determined if compliance has been achieved.
1736.3. Personnel Hygiene and Garbing (d) (e)	(d) 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. (e) Except as provided in subsection (d), dynamic interactions between areas and rooms with classified air and unclassified air shall be controlled through a heating, ventilation, and air condition (HVAC) system.	What is being affected by this regulation is the prevention of passive-air movement, typically though low in doors, from an ante-room and uncontrolled room air. This requirement would require the ante-room be sealed off from the room air so only the HVAC system would push air into the room (through HEPA filters) and remove air from

		the room through return ducting. This is contrary to basic design principles of HVAC systems. HVAC systems REQUIRE the ability to have air flow out of the area to accommodate normal variations between the air flowing in from supply and the air leaving by returns. Due to the fluid-dynamics of air flow, these are NEVER in perfect balance and need passive points of overflow. In addition, the point of overpressuring a room's supply relative to its return is so that when the door is opened, the positive pressure pushes air out of the room. The industry standard design, and long standing history of success, and the basic physics of HVAC design REQUIRE passive airflow connections between the cleanroom and the surrounding room air.
1736.5 Certification and Recertification (b)	(b) 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.	The pharmacy cannot control the output of reports from vendors, so having a “shall be recorded on the report” is overly restrictive. It is reasonable to instruct that the PIC shall document what standard the vendor used in preparing the report.
	1736.8 Introducing Items into the SEC and PEC. In addition to the requirements in USP Chapter 797, the following requirement applies to sterile compounding. Introducing items into the SEC and PEC shall comply with the SOPs as required in section 1736.17. Note: Authority cited: Sections 4005, 4126.8, and 4127, Business and Professions Code. Reference: Sections 4005, and 4126.8, Business and Professions Code.	Having a regulation stating that you must comply with another regulation is redundant. Delete.

1736.9 Equipment, Supplies, and Components (d)	(d) All APIs ~~and excipient components~~ used to compound a CSP shall be manufactured by an FDA-registered facility, be accompanied by a Certificate of Analysis (COA), and be 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. An API ~~and excipient components~~ provided with a COA without this data shall not be used in a CSP.	FDA registered wholesalers consider source manufacturer information proprietary and will not provide it directly to pharmacies. Language that would allow a PIC to have an agreement with wholesalers that they are willing to provide, under NDA, this information directly to the BOP upon request, would accomplish the same effect and be agreeable to wholesalers.
1736.9 Equipment, Supplies, and Components (e)(1)	(e)(1)Except as provided in (2), ~~When~~ 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, or unless authorized by a public health official in an emergency use situation for a patient-specific compounded sterile preparation.	There is no definition of what a "public health official" nor "emergency use situation". This allows that person to approve for use in compounding a drug without a monograph, nor having been FDA approved drug, not on on the bulks list… which means this allows a public health official can approve the compounding of an unapproved drug, for a specific patient, upon their definition of an emergency use situation. This does not seem to be in the public's best interest.
1736.17 Standard Operating Procedures (SOPS) (a)(2)(E)	In addition to the requirements in USP Chapter 797, the following requirements apply to sterile compounding. (a) Standard operating procedures (SOPs) for sterile compounding shall be followed and shall: (2) Define the following: (E) The methods by which the pharmacist compounding or supervising the compounding pursuant to 1736.9(f) related to use of a bulk drug substance published in the 503A Category 1 bulk substances list, will ensure each lot of the bulk drug substance is representatively sampled per USP 1097 (bulk powder sampling procedures), tested, and found to be in compliance with at least: (i) USP Chapter 1, Injections and Implanted Drug Products (Parenterals) – Product Quality Tests (ii)USP Chapters 232 and 233 related to Elemental Impurities. (iii) USP Chapter 467 – Residual Solvents. (iv)USP Chapter 85 – *Bacterial Endotoxins* and (v) any other USP Chapters deemed appropriate based on the clinical judgment of the pharmacist developing the SOPs.	It is unclear if "..the pharmacist… will ensure each lot… is representative samples…tested and found to be in compliance" requires that the pharmacist obtain samples and perform the tests or if having documentation from the FDA licensed wholesaler that testing was performed.

1736.17 Standard Operating Procedures (SOPS) (a)(2)(f)	In addition to the requirements in USP Chapter 797, the following requirements apply to sterile compounding. (a) Standard operating procedures (SOPs) for sterile compounding shall be followed and shall: (2) Define the following: (f) The SOPs shall specify which pharmacist is responsible for the review of all complaints related to a potential quality problem with a CSP and all adverse drug experiences in the event that the PIC is not available within 72 hours of the receipt of the complaint or occurrence.	There is no definition of "potential quality problem" to determine if compliance has been achieved.
HAZARDOUS DRUGS		
1737.6. Environmental Quality and Control.	**1737.6. Environmental Quality and Control.** In addition to the standards in USP Chapter 800, the following requirements apply to a facility where compounding of HDs is performed. ~~Hazardous Drugs - Handling in Healthcare Setting shall meet the following requirements of this article.~~ The SOPs of a premises ~~where HDs are handled~~ shall address environmental wipe sampling for HD surface residue, its frequency, and areas of testing~~, levels of measurable contamination, and actions when these levels are exceeded~~. ~~(b) When any actionable level of contamination is found, at a 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).~~	Given the lack of industry standards or clarity on how surface testing can, could, or should be done and evaluated, and given the retraction of attempts to add such language into regulation as shown above, it is clear having regulations about this is premature. Rather than having a "shall" requirement for a completely vague policy for an undefined behavior that leaves great interpretation about how to achieve compliance or how it will be enforced, it should be deleted.
1737.7. Personal Protective Equipment (PPE). (c)	(c) Outer gloves used for HD compounding shall be changed between each different HD preparation.	Given the vast efforts made to prevent contaminating events, such as using closed-system-transfer-devices, the occurrence of any actual contamination is extremely low. Requiring a compounder to change gloves between different HD preparations defies logic. If a compounder is handling product A and there is a suspicion, or assumption, of exposure precluding them from handling product B, what is the logic that is ok to handle product A-2? Would not item A-2 be just as contaminated as product B? Should

		not avoiding contamination of product A-2 be of the same priority as preventing contamination of product B? If there is a contaminating event, regardless of what is being handled, then that contamination should be contained to prevent contaminating any other product. The purpose of contamination containment is to prevent exposure to the workers handling the product and the patients receiving them. If contamination of gloves is presumed, then the regulation should read "change gloves every HD preparation." However, if we acknowledge that such regulation would create an unreasonable consumption of sterile-gloves, since a single compounder could easily use 20 pairs of gloves in one compounding session, then we have to reject the presumption that gloves become contaminated simply from that act of engaging in compounding. If we reject the presumption that gloves are inherently contaminated by engaging in compounding, then having regulations that require them to be changed between HD drugs is arbitrary and nonsensical. This regulation should be deleted, or restated to say changing of gloves should be done when contamination is suspected.
1737.7. Personal Protective Equipment (PPE). (d)	(d) PPE removal process shall be done in a manner ~~shall be removed~~ to avoid transferring contamination to skin, the environment, and other surfaces. Outer 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.	Comment: The C-SEC if the physical space the PEC is located, also known as the buffer room. This is under positive pressure from the ante-room, which has HEPA filtered air feeding into it, so that only HEPA filtered air is pushed into the buffer room.

		As written, this requires PPE be removed inside the buffer room, leaving a person standing inside the buffer room, with exposed skin and clothing. This creates a profound risk of contamination of the C-SEC buffer room by having un-gowned personnel in that space. This defies all logic for clean-room particle reduction practices. The assumption being proposed is that the PPE worn by the staff is inherently contaminated by the simple act of compounding HD drugs, regardless of all containment efforts being employed, such as biologic safety cabinets and closed system transfer devices. In this assumption scenario, it is logical that garb should be removed in a negative pressure environment that is externally vented, which would require doffing PPE in the C-SEC buffer room. This is because the ante-room, by definition and design, is a positive pressure room with HEPA filtered air exiting into both uncontrolled space, as well as the C-SEC buffer room. Any contamination in the ante-room would be ejected into the uncontrolled space, so doffing in this space would create a risk to those outside of the ante room. However, if we make the assertion that the simple act of compounding does not contaminate a worker's PPE, given the precautions used during the process that include the PEC, CSTDs, regular cleaning of gloves, and attention to potential contamination events, then the risk of HD contaminated PPE is extremely low. In contrast, the risk of introducing microbial contamination to the C-SEC buffer room is

		plainly obvious if workers are removing their PPE inside the buffer room. This is a flaw in current USP <800> regulations regarding the removal of PPE in sterile HD compounding. Having an un-gowned person past the line of demarcation in the ante-room, standing un-gowned in the buffer room, is substandard practice for cleanroom protocols. This regulation should be rewritten to state PPE should not be removed in the C-SEC, but rather doffed in the ante-room.
1737.13. Compounding. (a)	(a) If a ~~A~~ disposable preparation mat is used for compounding a CSP it must be sterile and it must be changed immediately if a spill occurs, after each different HD preparation, and at the end of the daily compounding activity. ~~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.~~	The requirement that the mat be changed "after each different HD preparation" defies logic. If product A is prepared and regulation requires that the mat must be changed before making product B, then there is a presumption that there is contamination on the mat. But what is the logic that it is ok to prepare product A-2 on that contaminated mat? If there is contamination on the mat, then spreading contamination from A-1 to A-2 should not be allowed. To be consistent with logic, the regulation should be that the mat must be changed after every HD preparation. However, if it is recognized that changing a mat after every HD preparation would result in an unreasonable use of sterile mats, given that 20 mats could be used by one compounder in one compounding session, then one must reject the presumption that a mat is contaminated simply by the process of being used in HD compounding. If we reject the presumption of contamination

		simply by the act of compounding, then it should not matter if a mat is used for the same HD drug or a different HD drug, since there is no contamination present. This regulation should be limited to stating that the mat should be changed immediately if a spill occurs.
1737.13. Compounding. (b)	(b) Only one HD preparation may be handled in a C-PEC at one time.	This regulation suggests that having two HDs prepared in a C-PEC at the same time is due to the risk of cross contamination, and not microbial contamination, as there is no limitation to performing non-hazardous sterile compounding on more than one drug. If there is a presumption that the HD compounding space is contaminated by the presence of HD Drug 1 such that one cannot have HD Drug 2 in the same space, then regulations should require the complete cleaning and decontamination of the compounding space between each compound. This is not the case, so clearly the BOP and USP<800> do not assert that the simple act of compounding an HD drug contaminates the compounding space. If the compounding space is not contaminated by HD drug, and it is accepted practice that when using good aseptic techniques one may prepare multiple sterile compounds at the same time, in the same space, there is no logic to this restrictive regulation. This regulation should be deleted.

1737.15. Deactivation, Decontamination, Cleaning, and Disinfecting.	In addition to the standards in USP Chapter 800, the following requirements apply to a facility where compounding HDs is performed or one where "other manipulations" included in Table 1 of the Chapter of antineoplastic HDs is performed. ~~Hazardous Drugs – Handling in Healthcare Setting shall meet the following requirements of this article.~~ (a) Deactivating, decontaminating, cleaning, disinfecting, and sporicidal agents shall be used in accordance with manufacturers' specifications and shall be surface compatible. (b) Agents used for deactivation, decontamination, cleaning, and disinfecting all areas and equipment involved in the compounding of HDs ~~handling~~ or performing "other manipulations" of antineoplastics HDs shall be applied through the use of wipes wetted with the appropriate solution ~~and shall not be applied or delivered to the wipe by use of a spray bottle to avoid spreading HD residue~~. ~~(c) 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.~~	There is no definition of the word "deactivation" and the regulation includes a "shall" preventing clarity on when compliance has been achieved. In every publication, from the FDA, to the EPA, to USP, there is the use of the word "deactivation" with no clarity on what it means. Even the FDA says "use of a registered oxidizing agent" where the EPA has no list of products that are registered as deactivating agent. Also, the word has no scientific meaning. An antineoplastic agent that is "deactivated" means what? That doesn't treat cancer anymore? There is published literature showing that antineoplastic drugs, when subject to "deactivating" procedures, like heating in hydrogen peroxide solution for hours, will change their chemical structure so they are no longer the same chemical. But it turns out those new structures were more carcinogenic than the original compound. California should not participate in adding into its regulatory language the vague and undefined word "deactivate". It can still accomplish the intent of this section of the regulation section by removing the word.

End of document

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December 9, 2024

President Oh and Members of the California State Board of Pharmacy,

Thank you for seeking solutions to bring medication flavoring back to California's pharmacies and families. It is encouraging to see not only recognition from this Board that access to a valuable pharmacy service has been greatly diminished but also a willingness to fix the problem.

For your reference, below is a comprehensive listing of every mention of medication flavoring at the state level, either in statute, rule, or guidance. In each of these states, flavoring continues to be made available to pharmacy patients with little to no hesitation. I trust you will find somewhere in these 33 examples, language that works for you and your licensees. As you will see, much of this language has been adopted since USP first published revisions to Chapter 795 back in November of 2022. In that time, not a single pharmacy has run afoul of the FDA for the simple act of flavoring medicines.

More importantly, in the 25+ years pharmacies in California and all across the country have been flavoring children's medications, there have been no reported incidents of harm. We're talking hundreds of millions of use cases in that time. The flavorings pharmacists use are safe. So, while I understand the desire to place reasonable safety guardrails on your licensees when it comes to flavoring, common sense should tell you a light regulatory touch is appropriate.

Please do not hesitate to reach out to me if you have any questions.

Chad Baker
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STATE FLAVORING LANGUAGE CURRENT AS OF DECEMBER 2024

ARIZONA

(Updated 2024)

Link to Language Below

1. A pharmacist may add flavoring agents, up to a maximum of five (5) percent (%) of the total volume, to a prescription at the request of a patient, the patient's care-giver, or the prescriber. The pharmacist shall label the flavored prescription with a beyond-use-date that shall be no longer than fourteen days if stored in a refrigerator unless otherwise documented and maintain electronic or manual documentation of the flavoring agent and quantity added. Documentation of beyond-use-dates longer than fourteen days, including the flavoring agent and quantity added, shall be maintained by the pharmacy electronically or manually and made available to agents of the Board on request.

2. The addition of flavoring agents over five (5) percent (%) of the total volume to a prescription requires the permission of the prescriber and compliance with the requirements of the Current Good Compounding Practices rule (A.A.C. R4-23-410).

3. A pharmacist may not add flavoring to an over-the-counter product at the request of a patient or patient's care-giver unless the pharmacist first obtains a prescription for the over-the-counter product from the patient's

CALIFORNIA

(Updated 2017 – Pending Deletion)

Link to Language Below

(b) "Compounding" does not include reconstitution of a drug pursuant to a manufacturer's direction(s), nor does it include the sole act of tablet splitting or crushing, capsule opening, or the addition of flavoring agent(s) to enhance palatability.

COLORADO

(Updated 2024)

Link to Language Below

3.00.55 Prescription Flavoring. A flavor additive may be incorporated into a non-sterile prescription under the following conditions: a. The patient, patient's caregiver, or practitioner who authorized the original prescription shall authorize the flavoring of each new and, if applicable, refilled prescription; b. The flavor additive shall in no way compromise the stability, safety, or efficacy of the dispensed drug. c. No expired flavor additive shall be incorporated into a prescription. No flavor additive shall be incorporated which will expire prior to utilization by the patient, based on the practitioner's directions for use. d. For flavoring additives that do not have expiration dates assigned by the manufacturer or supplier, a pharmacist shall clearly and legibly label the container with the date of receipt and assign a conservative expiration date, not to exceed three years after receipt, to the flavoring additive. In no event shall the labeled date of receipt or assigned expiration date be later altered after originally labeling the container. e. The following information shall be recorded and maintained in a suitable hard-copy or electronic dispensing record for a period of two years from the date of flavoring the

corresponding new or refilled prescription. This record shall be made available, in printed form, for the Board or its representatives immediately upon the request of the Board or its representatives. 1) Additive's flavor; 2) Flavor additive's manufacturer 3) Flavor additive's lot number (if available); and 4) Flavor additive's expiration date. f. The pharmacist responsible for conducting the final evaluation of a new or refilled prescription shall also be responsible for the flavoring of the prescription as specified in subsections a., b., and c. of this Rule 3.00.55. g. The pharmacist manager shall be responsible for subsection d. of this Rule 3.00.55 and the maintenance of records as specified in subsection e. of this Rule 3.00.55.

CONNECTICUT

(Updated 2023)

Link to Language Below

Sec. 20-617a. Flavoring agent added to prescription product. (a) For purposes of this section, "flavoring agent" means an additive used in food or drugs when such additive: (1) Is used in accordance with good manufacturing practice principles and in the minimum quantity required to produce its intended effect, (2) consists of one or more ingredients generally recognized as safe in food and drugs, has been previously sanctioned for use in food and drugs by the state or the federal government, meets United States Pharmacopeia standards or is an additive permitted for direct addition to food for human consumption pursuant to 21 CFR 172, (3) is inert and produces no effect other than the instillation or modification of flavor, and (4) is not greater than five per cent of the total weight of the product.

(b) A flavoring agent may be added to a prescription product by: (1) A pharmacist upon the request of the prescribing practitioner, patient for whom the prescription is ordered or such patient's agent, or (2) a pharmacist acting on behalf of a hospital, as defined in section 19a-490.

(P.A. 12-12, S. 1.)

DELAWARE

(Discussed in 2024)

The following language is being considered for adoption by the Delaware Board of Pharmacy:

Pursuant to 24 **Del.C.** §2506(a)(1), the Delaware Board of Pharmacy ("Board") has proposed revisions to its Rules and Regulations. First, the Board proposes to amend subsection 5.1.6, pertaining to compounding, to state **that the definition of "compounding" does not include flavoring of conventionally manufactured medications provided that the flavors used are inert, tested, and do not alter a medication's concentration beyond USP's accepted level of variance.**

STATE FLAVORING LANGUAGE CURRENT AS OF DECEMBER 2024

IDAHO

(Updated 2023)

Link to Language Below

700. COMPOUNDING DRUG PREPARATIONS.

01. Application. This rule applies to any person, including any business entity, authorized to engage in the practice of non-sterile compounding, sterile compounding, and sterile prepackaging of drug products in or into Idaho, except these rules do not apply to: (3-28-23)

d. The addition of a flavoring agent to a drug product; and (3-28-23)

ILLINOIS

(Updated 2020)

Link to Language Below

(o) "Compounding" means the preparation and mixing of components, excluding flavorings, (1) as the result of a prescriber's prescription drug order or initiative based on the prescriber-patient-pharmacist relationship in the course of professional practice or (2) for the purpose of, or incident to, research, teaching, or chemical analysis and not for sale or dispensing.

IOWA

(Updated 2022)

Link to Language Below

“Compounding” means the combining, mixing, diluting, pooling, flavoring, or otherwise altering of a drug or bulk drug substance to create a drug. Compounding includes the preparation of drugs or devices in which all bulk drug substances and components are nonprescription products. Compounding does not include the use of a flavoring agent to flavor a drug pursuant to rule 657—20.13(124,126,155A), nor does it include mixing or reconstituting a drug according to the product’s manufacturer label. “Flavoring agent” means a therapeutically inert, nonallergenic substance consisting of inactive ingredients that is added to a drug to improve the drug’s taste and palatability.

657—20.13(124,126,155A) Use of flavoring agents. A flavoring agent may be added to a drug at the discretion of the pharmacist or upon the request of the prescriber, the patient, or the patient’s agent. The pharmacist may add flavoring agents not to exceed 5 percent of the total volume of the drug to which the flavoring agents are added. The pharmacist shall label the flavored drug with a beyond-use date no greater than 14 days past the date the flavoring agent is added if the drug is required to be stored in a refrigerator. A different beyond-use date or alternate storage conditions may be indicated if such variation is supported by peer-reviewed medical literature. The pharmacist shall electronically or manually document that a flavoring agent was added to a drug, and such documentation shall be made available for inspection and copying upon the request of the board or an agent of the board.

STATE FLAVORING LANGUAGE CURRENT AS OF DECEMBER 2024

KENTUCKY

(Updated 2023)

Link to Language Below

201 KAR 2:076. Compounding.

Section 2. (1) All non-sterile compounded preparations shall be compounded pursuant to United States Pharmacopeia (USP) 795, unless specified portions submitted by a pharmacist have been waived by the board. Notwithstanding any USP guidance to the contrary, the addition of flavoring to a drug shall not be considered non-sterile compounding, if the additive:

(a) Is inert, nonallergenic, and produces no effect other than the instillation or modification of flavor; and (b) Is not greater than five (5) percent of the drug product's total volume.

LOUISIANA

(Updated 2019)

Link to Language Below

Louisiana Board of Pharmacy Policies & Procedures

Title: Addition of Flavors to Medications- Policy No. I.A.31

Resolved, that the Board adopt an enforcement policy, such that the addition of nonallergenic and inert flavoring agents to commercially available liquid oral products resulting in a change in the final product volume of less than 5% shall not require a prescriber's order or a full compounding log.

MASSACHUSSETTS

(Updated 2023)

Link to Language Below

II. General

B. Patient-specific prescriptions are required to dispense any compounded preparation into, within, or from Massachusetts. Note: Flavoring may be added upon request of the patient or their agent for Schedule VI medications if it has not been requested by the prescriber. The prescription may be updated with this information in accordance with Policy 2018-01: Permitted Prescription Changes and Additions

III. Non-Sterile Compounding Process

C. Flavoring agent(s) added to conventionally manufactured non-sterile drug products is considered compounding. In addition to a policy and procedure, a pharmacy must ensure that the addition of the flavoring agent does not affect stability or alter the final concentration beyond the parameters outlined

in USP . Available scientific data or studies, whether published or unpublished, may be utilized for this purpose.

IV. Facility and Equipment

A. Pharmacies not engaged in complex non-sterile compounding must have a designated compounding area that should have at least 10 square feet of counter space that should not have carpeting. This area must be separated or otherwise protected from water sources (i.e., sink). Note: Flavoring agents may be added in a separate designated area (e.g., reconstitution area).

V. Labeling / BUDs

B. In addition to standard prescription labeling, a statement that the preparation is a non-sterile compounded drug preparation must also be included (MGL c. 94C § 21). If applicable, a statement that the product was flavored (e.g., auxiliary label, noted on label, etc.) must also be included on the patient's container.

VI. Documentation

C. In the case of pre-measured compounding kits and flavoring agents added to conventionally manufactured non-sterile drug products, the compounding record may also serve as the master formulation record and may be in the form of a log sheet. The following information must be documented and be readily retrievable: 1. date of preparation; 2. prescription number; 3. name, vendor / manufacturer / NDC, lot number, and expiration date of each component; 4. any relevant calculations and quantities/volumes of additives (e.g., water, flavoring agent(s), etc.); 5. BUD and any special storage requirements (e.g., refrigerate); and 6. identifier (e.g., name, initials, etc.) of individual who prepared the product (e.g., reconstitution, etc.).

MICHIGAN

(Updated 2022)

Link to Language Below

R 338.501 Definitions.

"Compounding" does not include any of the following:

> (iv) Flavoring agents added to conventionally manufactured and commercially available liquid medications. Flavoring agents must be nonallergenic and inert, not exceeding 5% of a drug product's total volume.

MINNESOTA

(Updated 2024)

Link to Language Below

Q: Is adding flavoring to a conventionally manufactured nonsterile product considered compounding?

A: Yes. United States Pharmacopeia ("USP") has determined adding a component such as flavoring not stipulated in the labeling to a conventionally manufactured nonsterile product is compounding and has been within the scope of USP <795> since 2004. USP has reemphasized this in its November 1, 2022 guidance document entitled "<795>: Adding Flavor to Conventionally Manufactured Nonsterile Products."

Additionally, Minnesota Rule 6800.3300, subpart 1 sets forth the standards for nonsterile compounding. The rule states that if pharmacies engage in nonsterile compounding, they must follow USP <795> standards.

The Minnesota Board of Pharmacy ("Board") recognizes the importance of this service, particularly in the pediatric population. Furthermore, the Board is aware the majority of states, including those states who border with Minnesota and whose resident pharmacies may directly serve Minnesota patients, have either enacted rules or statutes creating exceptions for flavoring, or have indicated they may use enforcement discretion when applying USP <795> standards to its licensees who add flavoring.

Accordingly, at this time, if a licensed Minnesota pharmacy elects to add flavoring to a conventionally manufactured product for the purpose of improving palatability, the Board may exercise its enforcement discretion regarding the applicable USP <795> requirements with the exception of the following USP <795> requirements:

- Flavoring agents must still consist of inactive ingredients and must not exceed 10% variance from the labeled strength.
- If a pharmacy adds flavoring to a manufactured product it must still take into account the manufacturer's Beyond Use Date ("BUD") and the effect on stability caused by adding flavoring.
- The addition of flavoring including the flavor manufacturer or product, lot number, and expiration date must still be documented in the patient record notes for the prescription. This includes any relevant calculations and quantities/volumes of additives (e.g., water, flavoring agent(s), etc.). Such documentation must still be made available for inspection and copying upon the request of the Board or an agent of the Board.

The Board also expects its licensees to follow and adhere to all other applicable state and federal rules and laws while conducting pharmacy operations.

STATE FLAVORING LANGUAGE CURRENT AS OF DECEMBER 2024

MISSISSIPPI

(Updated 2024)

Link to Language Below

ARTICLE XXXI COMPOUNDING GUIDELINES

1. GENERAL PROVISIONS

C. For the purpose of this Article, flavoring is not considered compounding

MISSOURI

(Updated 2023)

Link to Language Below

H.12 FLAVORING

Licensees may flavor a legend product unless the prescriber indicates otherwise. OTC products may only be flavored by prescription. Licensees should indicate that the product was flavored on the patient's container and the added flavoring must be documented in the pharmacy's prescription record (e.g., in a flavoring book or in the prescription record). As defined by the Board's rules, flavoring does not constitute compounding. Licensees may not flavor a prescription dispensed by another pharmacy.

The Board is aware that USP is reviewing whether flavoring constitutes compounding. The Board has not adopted USP's proposed revision at this time but may reconsider this approach in the future.

NEBRASKA

(Updated 2023)

Link to Language Below

(4) Any authorized person splitting a scored tablet along scored lines or adding flavoring to a commercially available drug product is not engaged in compounding.

STATE FLAVORING LANGUAGE CURRENT AS OF DECEMBER 2024

NEVADA

The following language was approved by the Nevada State Board of Pharmacy on July 18, 2024 and is now being promulgated.

Link to the Language Below

NAC Chapter 639 – Compounding and Dispensing Drug Products

Sec. 4.

1. A pharmacist, pharmaceutical technician or dispensing practitioner may add flavoring to an oral drug product at the request of a patient or a legal guardian of the patient, as applicable. A pharmacist, pharmaceutical technician or dispensing practitioner who adds flavoring to an oral drug product pursuant to this subsection shall: 2818 --4-- LCB Draft of Proposed Regulation R053-24

(a) Make a record contemporaneous with the completion of the mixture, including, without limitation, the ingredients of the oral drug product;

(b) Ensure that the flavor additive does not compromise the stability, safety or efficacy of the dispensed oral drug product; and

(c) Assign the applicable beyond-use date to the oral drug product pursuant to chapter 795 of the United States Pharmacopeia - National Formulary, as adopted by reference in paragraph (b) of subsection 1 of NAC 639.670.

NEW HAMPSHIRE

(Updated 2024)

Link to Language Below

"Compounding" shall not include the reconstitution of powdered formulations before dispensing or the addition of flavoring. "Compounding" shall not include the simple addition of flavoring, nor shall it include the preparation of a single dose of a nonhazardous commercially available drug or licensed biologic for administration within 2 hours of preparation to an individual patient when done in accordance with the manufacturer's approved labeling or instructions consistent with that labeling.

NEW JERSEY

(Updated 2024)

Link to Language Below

c) A compounding record shall not be required for:

2) Product flavoring.

STATE FLAVORING LANGUAGE CURRENT AS OF DECEMBER 2024

NEW MEXICO

(Updated 2024)

Link to Language Below

16.19.30.7 DEFINITIONS

D. "Compounding" the preparation, mixing, assembling, packaging, or labeling of a drug or device (reconstitution of commercial products is not considered compounding for purposes of this article).

(4) the addition of a flavoring agent to a conventionally manufactured product is not considered compounding as long as the following conditions are met:

(a) the flavoring agent is inert, nonallergenic, and produces no effect other than the instillation or modification of flavor;

(b) the flavoring agent does not alter a medication's concentration beyond USP's accepted level of variance;

(c) the addition of flavoring agent(s) is documented in the prescription record.

NORTH CAROLINA

(Updated 2023)

Link to Language Below

Adding flavoring to Conventionally Manufactured Products

Q. Is adding flavoring to a conventionally manufactured product considered compounding?

A. USP considers adding flavoring to a conventionally manufactured product to fall within the scope of compounding, because there are known instances when flavoring components have destabilized a product. If a pharmacy adds flavoring to a manufactured product it must take into account the manufacturer's Beyond Use Date (BUD) and the effect on stability caused by adding flavoring. If a flavoring component is added to a manufactured product that does not contain a preservative (e.g., reconstitution of amoxicillin oral suspension) the BUD is 14 days refrigerated or shorter if indicated in the manufacturer's labeling. If a flavoring component is added to a manufactured product that contains a preservative (e.g., pyridostigmine oral solution), then the BUD is 35 days in controlled room temperature or refrigerated or shorter if indicated in the manufacturer's labeling. When adding flavoring the compounding record must include the flavor manufacturer or product, lot number, and expiration date. All of this information about the flavoring must be documented in the patient record notes for the prescription

STATE FLAVORING LANGUAGE CURRENT AS OF DECEMBER 2024

OHIO

(Updated 2021)

Link to Language Below

A pharmacy engaged in the following shall not be required to comply with the provisions of this chapter:

(4) The addition of a flavoring agent to a conventionally manufactured drug product.

OREGON

(Updated 2024)

Link to Language Below

DRUGS

- SECTION 1. Section 2 of this 2024 Act is added to and made a part of ORS chapter 689.
- SECTION 2. The addition of flavoring to a drug intended for dispensation may not be considered compounding if the flavoring:
  - (1) Is inert, nonallergenic and has no effect other than imparting a flavor to the drug or modifying the flavor of the drug; and
  - (2) Does not constitute more than five percent of the total volume of the drug.

PENNSYLVANIA

(Updated 2019)

https://www.dos.pa.gov/ProfessionalLicensing/BoardsCommissions/Pharmacy/Pages/default.aspx

At the October 22, 2019 Pennsylvania State Board of Pharmacy (Board) Meeting, the Board discussed issues related to USP's decision to delay implementation of the revisions to chapters 795 and 797 pending resolution of appeals. The following decisions were approved by the Board and placed on record:

1. The Board is enforcing USP 795 and 797 as *currently* written. Board Regulation Section 27.601 was finalized on June 22, 2019 and requires compliance with section 503a of the federal Food, Drug and Cosmetic Act, federal regulations promulgated thereunder and the *current* version of the USP chapters governing compounding.

2. The Board is delaying the enforcement of USP 800 until the appeals of certain provisions of the revised USP 795 and 797 are resolved. While enforcement of USP 800 is being delayed, pharmacies should do their best to comply with the requirements of USP 800, including the sections related to the handling of hazardous medications, as these requirements will be enforced at some time in the future, dependent on resolution of the appeals of the revised USP 795 and 797.

3. The Board voted to adopt the following position and will be amending its regulations to reflect this information:

The definition of "compounding" does not include the unencumbered flavoring of conventionally manufactured medications provided that the flavors used are inert, tested and do not alter a medication's concentration beyond USP's accepted level of variance.

SOUTH CAROLINA

(Updated 2023)

Link to Language Below

Simple compounding that does not precipitate the application of this form include: 1) Reconstituting or manipulating commercial products that may require the addition of one or more ingredients as directed by the manufacturer; 2) Making twenty or less compounds of an oral liquid or topical dosage form utilizing five or less non-hazardous APIs over any 30 day period (not exempt from 40-43-86(CC)(6), "Formulas and Logs Maintained").

SOUTH DAKOTA

(Pending Rules Promulgation)

20:51:31:38. Non-hazardous, non-sterile drugs exclusions. The following of medication manipulations are excluded from USP requirements:

(2) The addition of a flavoring agent to a drug product

TENNESSEE

(Updated 2024)

Link to Language Below

1140-07-.09 NONSTERILE SIMPLE COMPOUNDING PREPARATIONS

(2) Solely adding flavoring to medications is not considered compounding.

TEXAS

(Updated 2024)

Link to Language Below

(H) A pharmacist may add flavoring to a prescription at the request of a patient, the patient's agent, or the prescriber. The pharmacist shall label the flavored prescription with a beyond-use-date that shall be no longer than fourteen days if stored in a refrigerator unless otherwise documented. Documentation of beyond-use-dates longer than fourteen days shall be maintained by the pharmacy electronically or manually and made available to agents of the board on request. A pharmacist may not add flavoring to an over-the-counter product at the request of a patient or patient's agent unless the pharmacist obtains a prescription for the over-the-counter product from the patient's practitioner.

STATE FLAVORING LANGUAGE CURRENT AS OF DECEMBER 2024

UTAH

(Updated 2023)

Link to Language Below

Flavoring Rule Utah Admin Code R156-17b-102

(13) "Compounding," as defined in Subsection 58-17b-102(18), in accordance with 21 U.S.C. 353a(e) Pharmacy Compounding, does not include:

(b) the addition of flavoring agents to conventionally manufactured and commercially prepared available liquid medications, if the flavoring agents:

(i) are therapeutically inert; and

(ii) do not exceed 5% of a preparation's total volume.

VERMONT

(Pending Rules Promulgation)

This language was approved by the Vermont Board of Pharmacy in 2023 and is entirely new.

Addition of flavoring agents to conventionally manufactured products is not considered compounding; provided that the flavoring agent is inert and does not alter the product's concentration beyond USP's accepted level of variance, and that the pharmacy labels the product with an expiration date and storage instructions consistent with any effect on stability caused by the addition of flavoring. The addition of flavoring must be documented as part of the prescription record, reconstitution log, or other similar documentation. The documentation shall include the agent's flavor, manufacturer, lot number, and expiration date.

VIRGINIA

(Updated 2024)

Link to Language Below

8. Does USP consider flavoring to be compounding? Yes, but the Board will exercise enforcement discretion of USP compounding standards for flavoring.

STATE FLAVORING LANGUAGE CURRENT AS OF DECEMBER 2024

WISCONSIN

(Language Currently in Rules Promulgation)

Phar 15.02 Incorporation of Standards. (1) PHARMACEUTICAL COMPOUNDING - NONSTERILE PREPARATIONS. USP-NF general chapter 795, official as of November 1, 2023, is incorporated by reference into this chapter, subject to the exception that nonsterile compounding does not include the addition of nonallergenic, therapeutically inert flavoring agents to a conventionally manufactured drug product. The pharmacist shall also comply with the following requirements when adding flavoring agents to a drug product: (a) The pharmacist shall ensure that the flavoring agent is not more than 5 percent of the product's total volume. (b) The pharmacist shall label the flavored prescription with a beyond-use-date that shall be no longer than fourteen days if stored in a refrigerator unless otherwise documented. (c) The pharmacist shall document the addition of flavoring as part of the prescription record. The documentation shall include the type of flavoring agent, manufacturer, lot number, and expiration date. (d) A prescription is required before a pharmacist may add flavoring to an over-thecounter product.

WEST VIRGINIA

(Updated 2024)

Link to Language Below

2.1.7.c. The following are not "compounding" and are exempt from USP 795 Compounding Standards:

2.1.7.c.3. upon the request of the prescribing practitioner and/or the patient for whom the prescription is ordered or such patient's agent, the addition of therapeutically inert, nonallergenic flavoring agents to a commercially manufactured product, not in excess of five percent (5%) of the preparation's total volume;

WYOMING

(Updated 2018)

Link to Language Below

Compounding does not include mixing, reconstituting, adding flavoring or other such acts that are performed in accordance with directions contained in approved labeling provided by the product's manufacturer and other manufacturer directions consistent with the labeling.

CALIFORNIA® VETERINARY MEDICAL ASSOCIATION

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November 8, 2024

Maria D. Serpa, PharmD
Chair, Enforcement and Compounding Committee
California Board of Pharmacy
2720 Gateway Oaks Drive, Suite 100
Sacramento, CA 95833

RE: 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.

Specifically: Amend 1735.1(e)(2) and 1736.1(e)(2) to include reference to the Federal Food and Drug Administration Guidance for Industry 256.

Specifically: Add a statement indicating that the regulations do not apply to veterinarians who compound medications for patients during the course of practice.

Dear Dr. Serpa:

The California Veterinary Medical Association (CVMA), representing approximately 7,000 veterinarians, registered veterinary technicians, and veterinary students, is requesting an amendment to the Board of Pharmacy's proposed California Code of Regulations, Title 16 (16 CCR), section 1735.1(e)(2) and 1736.1(e)(2) to include reference to the Federal Drug Administration's Guidance for Industry #256 (GFI 256), in addition to the current reference to the Animal Medicinal Drug Use Clarification Act (AMDUCA).

While AMDUCA is relevant to the provisions at issue, it alone does not provide the level of detail and specific guidance needed for licensees to understand what is allowable in compounding compounded nonsterile preparations and compounded sterile preparations. AMDUCA amended the Federal Food, Drug, and Cosmetic Act to legalize extralabel drug use (ELDU) under a valid veterinarian-client-patient relationship (VCPR), and to specify conditions and requirements for use, record keeping, and labeling according to FDA regulations.

In August of 2022, the FDA developed and published GFI 256, which serves as an inclusive list of active pharmaceutical ingredients permissible for use in compounding medications for animal patients. FDA has generally exercised enforcement discretion with regard to animal drug compounding from bulk drug substances under certain circumstances. Namely, the FDA recognizes that many vital animal drugs are unavailable in FDA-approved form and that veterinarians must be able to treat animals with needed medications, despite the pharmaceutical

industry's inability or unwillingness to bring them to market. GFI 256 is intended to provide clarity to veterinarians and pharmacists about the FDA's current thinking on compounding from APIs. The guidance identifies the FDA's enforcement priorities regarding animal drugs compounded from bulk drugs substances and describes the circumstances under which the FDA does not intend at this time to take enforcement action for violations of the Food, Drug and Cosmetic Act with respect to the compounding of animal drugs from bulk drug substances.

Should you agree with this request, the proposed 1735.1 (e)(2) and 1736.1(e)(2) could be changed as follows:

"Is made with any component not suitable for use in a CNSP for the intended ~~veterinary~~ animal population, unless allowable under the Animal Medicinal Drug Use Clarification Action of 1994 (AMDUCA) and, if applicable, the Federal Food and Drug Administration Guidance for Industry #256 (GFI 256)."

In addition, the CVMA requests that a specific statement be included in this proposed regulatory revision to affirmatively state that it does not apply to veterinarians who compound medications for patients in their practices. California Business and Professions Code section 4826.5 provides statutory authority for veterinarians to compound medications in practice pursuant to regulations promulgated by the Veterinary Medical Board. California Code of Regulations, Title 16, Article 11 in turn specifies requirements for veterinarians to perform compounding in practice. The CVMA has received multiple inquiries from confused veterinarians regarding which regulations apply to them. A clear statement from the Board of Pharmacy that its proposed regulations do not apply to veterinarians would alleviate that unnecessary confusion.

Thank you for your consideration.

Dan Baxter
Executive Director

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December 6, 2024

Lori Martinez
California State Board of Pharmacy
2720 Gateway Oaks Drive, Ste 100
Sacramento, CA 95834

Submitted via electronic mail to: Lori Martinez, California State Board of Pharmacy

RE: ***Compounded Drug Products Regulations***

Dear Ms. Martinez:

Kaiser Permanente appreciates the opportunity to respond to the California Board of Pharmacy's request for comments on the proposed regulations addressing nonsterile compounding, sterile compounding, and hazardous drugs. Kaiser Permanente comprises the non-profit Kaiser Foundation Health Plan, the non-profit Kaiser Foundation Hospitals; and the Permanente Medical Groups, self-governed physician group practices that exclusively contract with Kaiser Foundation Health Plan. These entities work together seamlessly to meet the health needs of Kaiser Permanente's nine million members in California. Kaiser Permanente's pharmacy enterprise in California is comprised of hundreds of licensed pharmacies that are staffed by thousands of individual pharmacy licentiates. The frontmatter of this letter comprises our general comments on the entirety of the proposed regulations; our comments on specific elements of the regulations are in the table that follows (in the table, the Board's proposed changes are denoted in purple font with a single strikethrough for deletions and Kaiser Permanente's proposed changes are denoted in red font with a double strikethrough for deletions).

In our view, the Board's continued efforts to advance these proposed compounding regulations demonstrate that the Board is either unwilling or unable to critically evaluate whether there is a bona fide need for regulations that exceed the compounding standards published in the United States Pharmacopeia (USP). First, throughout the proposed regulation, the Board suggests onerous requirements that are not supported by any empirical evidence; specifically, the Board does not reference any peer-reviewed studies, systematic reviews, or even any case reports to support the notion that additional regulations exceeding the USP standards are necessary to protect California patients. It seems that the Board's analysis hinges on the logical fallacy that more must be better. For example, the Board assumes that if requiring gloves used for Hazardous Drug (HD) compounding to be changed at least every 30 minutes, then requiring gloves to be changed after compounding each different HD preparation must be better. Second, time and again, the Board fails to consider the behaviors that its proposed regulations will incentivize and the second order effects that those practices will likely precipitate. For example, the proposed restrictions on immediate use compounding will incentivize organizations to shift immediate use compounding to non-pharmacy personnel, arguably increasing risks to the health and safety of Californians.

During its November 2024 discussion of the proposed compounding regulations, the Board received two presentations about federal and California requirements for compounding and the Board's approach to

the regulation of compounding.[1, 2] As part of the second presentation, entitled "Compounding," Board staff provided four "examples of items not covered in USP or where USP defers to the state," ostensibly to justify the need for the Board's proposed compounding regulations. The four items identified were: (1) recall provisions and notification to the Board, (2) adverse event reporting, (3) terms lacking definitions, and (4) pharmacist-in-charge responsibility. First, if these four areas are the only reasons that additional regulation beyond the USP standards are necessary, then we believe that these issues could be effectively addressed in one or two pages of regulations rather than the 50 pages of regulation put forward by the Board. Second, and more importantly, as we will show below, requirements in the Pharmacy Law already address most of these areas.

With respect to recalls of compounded products and notification to the Board, sections 4126.9, 4127.1(e)(3), and 4127.8 of the Business and Professions Code identify the conditions under which a pharmacy is required to issue a recall notice for non-sterile and sterile compounded drug products.[3, 4, 5] Section 4127.1(f) of the Business and Professions Code establishes a requirement for a pharmacy licensed to prepare sterile compounds to "report adverse effects that are reported or potentially attributable to a pharmacy's sterile drug products to the Board within 12 hours".[6] Second, section 4036.5 of the Business and Professions Code clearly indicates that the pharmacist-in-charge is "responsible for ensuring the pharmacy's compliance with all state and federal laws and regulations pertaining to the practice of pharmacy," and Business and Professions Code section 4126.8 requires "the compounding of drug preparations by a pharmacy… be consistent with standards established in the pharmacy compounding chapters of… USP." [7, 8] Taken together, these two sections of code clearly establish that the pharmacist-in-charge is responsible for a pharmacy's compliance with USP compounding standards. Finally, during its presentation, the Board did not provide any concrete examples of relevant terms that are not already defined either in the Pharmacy Law or in the USP chapters. Moreover, if the Board chooses to simply enforce the USP standards, as required under existing law, we expect that the definitions provided in the USP chapters would suffice.

Given the lack of evidence to support the need for these regulations and the negative second order effects that the regulations will almost certainly precipitate, Kaiser Permanente supports the following alternative approach:

1. The Board should accept the proposal to repeal sections 1708.3. 1708.4, and 1708.5 of Title 16, Division 17, Article 2 of the California Code of Regulations and to repeal 1735 et seq of Title 16, Division 17, Article 4.5 of the California Code of Regulations and to repeal 1751 et seq of Title 16, Division 17, Article 7 of the California Code of Regulations.
2. The Board should reject the proposal to add new sections 1735 et seq of Title 16, Division 17, Article 4.5 of the California Code of Regulations, and to add new sections/Article 1736 et seq of

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[1] California Board of Pharmacy, *Federal and California Requirements for Human Drug Compounding: An Overview,* https://www.pharmacy.ca.gov/meetings/agendas/2024/24_nov_bd_mat_presentation1.pdf (last visited Dec. 5, 2024).

[2] California Board of Pharmacy, *Compounding,* https://www.pharmacy.ca.gov/meetings/agendas/2024/24_nov_bd_mat_presentation2.pdf (last visited Dec. 5, 2024).

[3] Cal. Bus. & Prof. Code § 4126.9.

[4] Cal. Bus. & Prof. Code § 4127.1.

[5] Cal. Bus. & Prof. Code § 4127.8.

[6] Cal. Bus. & Prof. Code § 4127.1.

[7] Cal. Bus. & Prof. Code § 4036.5.

[8] Cal. Bus. & Prof. Code § 4126.8.

Title 16, Division 17, Article 4.6 of the California Code of Regulations, and to add new sections/Article 1737 et seq of Title 16, Division 17, Article 4.7 of the California Code of Regulations, and to add new sections/Article 1738 et seq of Title 16, Division 17, Article 4.8 of the California Code of Regulations.

3. The Board should enforce the provisions of the USP compounding chapters as required by Business and Professions Code section 4126.8.

During the November 2024 full Board meeting, the Board asked for stakeholders to include suggestions in their written comments for a "path forward" for the addition of flavoring agents to oral liquid medications. As the Board is aware, pharmacists have added flavoring to liquid medications for decades to make them less foul-tasting. Without citing any health or safety risk with these long-standing flavoring practices, the Board has decided that flavoring a medication is compounding and that pharmacists must meet burdensome compounding requirements if they add flavoring to a medication. Predictably, pharmacies have responded by declining to offer flavoring services to their patients. As a result, a safe and effective tool to help children take their medications is no longer available to California families. Regrettably, the Board has repeatedly demonstrated that they are not willing to consider commonsense solutions that would facilitate flavoring of prescription medications. Therefore, Kaiser Permanente has no additional suggestions to offer for a regulatory framework for the addition of flavoring agents to oral liquid medications. For two years in a row, the legislature has offered the Board a way out of this problem of the Board's own making in the form of Assembly Bills 782 (2023) and 3063 (2024), both of which the Board opposed—a position that likely contributed to the veto of both bills. The Board's dogmatic approach to regulating the flavoring of medications has removed an important tool that pharmacists have used for decades to make it easier for children to take their medications. Now the Board should take responsibility for solving this problem that it has created.

Finally, if the Board elects to finalize the proposed regulations, we continue to encourage the Board to establish a rational effective date for these regulations that will provide the regulated public with ample time to come into compliance with these new requirements. In its previous response to our request for a delayed effective date, the Board rejected our proposal because the USP compounding standards have been in effect since November 1, 2023, and because some of the provisions in the proposed regulations are in the Board's current compounding regulations. Both of those observations, which we do not dispute, are immaterial to the work that organizations will need to do to come into full compliance with the proposed regulations. We expect that, if this regulation is finalized as written, Kaiser Permanente will need to make extensive updates to our policies and standard operating procedures, update our pharmacy information systems, and remodel some of our compounding facilities. These tasks are time-consuming, costly, or both and, as such, the Board should establish a delayed effective date for organizations to do the work needed to meet these requirements. We suggest that at least one year from the date that the regulation is filed with the Secretary of State would be a reasonable effective date.

Kaiser Permanente appreciates the opportunity to provide feedback in response to the proposed regulations addressing nonsterile compounding, sterile compounding, and hazardous drugs. If you have questions, please contact John Gray (562.417.6417; john.p.gray@kp.org) or Rebecca Cupp (562.302.3217; rebecca.l.cupp@kp.org).

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Respectfully,

John P. Gray, PharmD, MSL
Director, National Pharmacy Legislative and Regulatory Affairs
Kaiser Permanente

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Section, Subdivision	Proposed Language	Recommendation/Comment
Article 4.5 Nonsterile Compounding		
1735.4(b)	~~Purified water, distilled water, or reverse osmosis water, or higher quality water shall be used for rinsing equipment and utensils.~~	The Board has still not provided any empirical evidence of untoward effects associated with the water used to rinse equipment and utensils used for non-sterile compounding. Instead of providing actual evidence to substantiate the purported risk, the Board has added additional unreferenced, unsubstantiated risks to its Modified Initial Statement of Reasons.[9] Because the Board has no concrete evidence to support the need for this regulation and because USP Chapter 795 adequately addresses the recommended use of purified, distilled, or reverse osmosis water for rinsing equipment and utensils, we continue to recommend that this requirement be deleted. If the Board chooses not to delete this requirement, then we encourage the Board to provide a definition of the term "higher quality water."
1735.7(c)(1)	The date ~~and time~~ of compounding, which is the time when compounding of the CNSP started, and which determines when the assigned BUD starts.	The Modified Initial Statement of Reason erroneously states that the requirement to document the date and time of compounding in the compounding record is "included within the USP Chapter."[10] In fact, the USP 795 chapter provides the flexibility to record either the date or the date and time. Since it appears that the Board's intent is to align with the USP chapter, we recommend deleting "and time" from the regulation.
1735.12(a)	(a) The facility's quality assurance program shall comply with section 1711 and the standards contained in USP Chapter 1163, ~~entitled~~ Quality Assurance in Pharmaceutical Compounding. In addition, the program shall include the following: (1) 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. ~~(2) A written procedure for responding to out-of-range temperature variations within the medication storage areas~~	The USP 795 chapter addresses temperature monitoring, documentation, and follow-up for areas where CNSPs are stored in sufficient detail that requiring a written standard operating procedure would be duplicative. In the Modified Initial Statement of Reasons, the Board claims that this regulation is necessary to "ensure appropriate action will be taken timely should it be needed to ensure patient safety."[11] The Board fails to recognize that existing regulations (e.g. 16 CCR 1714(b)) require all pharmacies to ensure that medications are "safely and properly maintained and secured" and that existing law (e.g. BPC 4084 and 4086) prohibits pharmacies from trading in adulterated drugs. Because the USP 795 Chapter and

[9] California Board of Pharmacy, *Modified Initial Statement of Reasons Compounded Drug Products*, https://www.pharmacy.ca.gov/laws_regs/1708_1735_1751_misr.pdf (last visited December 5, 2024).
[10] Modified Initial Statement of Reasons, *supra*.
[11] Modified Initial Statement of Reasons, *supra*.

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Section, Subdivision	Proposed Language	Recommendation/Comment
	~~where a furnished drug may be returned for furnishing to another patient.~~	existing law and regulation require pharmacies to store drugs at the appropriate temperature, the proposed regulation in 1735.12(a)(2) is unnecessary.
1735.12(b)	~~The Board shall be notified in writing within 72-96 hours of the facility's receipt of a complaint of a potential quality problem or the occurrence of an adverse drug experience as defined in 21 CFR 310.305(b) drug event involving a CNSP.~~	The modified regulation text references the definition of the term "adverse drug experience" provided in federal regulations pertaining to drug manufacturers and distributors.[12, 13] The referenced definition of the term adverse drug experience is too broad and would explicitly include untoward effects resulting from "intentional overdoses, drug abuse, and failures of expected pharmacological action." Business and Professions Code section 4126.9 already requires a pharmacy that issues a recall notice for a CNSP to notify the patient, prescriber, and Board within 12 hours of the recall notice if certain conditions are met. The requirement in existing law ensures that the Board is notified of serious quality and safety issues while reducing the administrative burden associated with reporting events that are in no way related to the quality of products compounded by the pharmacy (e.g., intentional overdose). One could argue that, as written, the proposed regulation would require a pharmacy to report cases in which it becomes aware that an individual died after ingesting an aid-in-dying drug under the California End of Life Option Act.[14] Given these factors, we recommend deleting this requirement from the proposed regulation. If the Board believes that this additional requirement to report adverse drug events to the Board be maintained in the regulation, then we encourage the Board to modify the regulation to align the requirement with Business and Professions Code section 4127.1(f).
Article 4.6 Sterile Compounding		
1736.1(b)	~~(b) (1) Except as allowed in paragraph (2), 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~~	While we acknowledge that this proposed regulation is similar to the existing requirements for immediate use compounding in 16 CCR 1751.8(e), we continue to assert that neither the current regulation nor the proposed regulation are necessary. First, the USP 797 Chapter provides sufficient guidance on the preparation of immediate use

[12] Modified Initial Statement of Reasons, *supra*.
[13] 21 C.F.R. § 310.305(b).
[14] Cal. Health & Safety Code §§ 443.

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Section, Subdivision	Proposed Language	Recommendation/Comment
	~~compounding shall be only in such quantity as is necessary to meet the immediate need of the patient. If not already documented in the patient's medical record, documentation for each such CSP shall also include identification of the CSP, the 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.~~ ~~(2) If the sterile compounding equipment or environment fail(s) to meet any required specification, an immediate use CSP may be compounded without the requirement for there to be loss of life or intense suffering of an identifiable patient. This provision may only be used for 24 hours after such failure(s). All such failures must be documented in accordance with facility's SOP and shall be reported to the BOP within 72 hours.~~	CSPs. More importantly, continuing to enforce these requirements will incentivize organizations to shift compounding to non-pharmacy personnel in situations in which immediate use compounding is necessary. If the Board's desired outcome is that non-pharmacy personnel are more frequently engaged in compounding sterile products for Californians, then we believe that the Board has written a regulation that will achieve that result. If, instead, it is the Board's intent to incentivize immediate use compounding by pharmacy personnel who complete extensive training and competency validation and are subject to the Board's oversight, then we strongly encourage the Board to delete this proposed regulation and enforce the USP standards for immediate use compounding.
1736.4(c)	~~(c)(1) Designated compounding area(s) shall typically be maintained at a temperature of 20° Celsius or cooler.~~	California law requires regulations to be "drafted using a coherent and easily readable style."[15] California regulations specify that a regulation does not comply with the clarity standard of the Administrative Procedures Act if "the regulation can… be reasonably and logically interpreted to have more than one meaning," or "the regulation uses terms which do not have meanings generally familiar to those 'directly affected' by the regulation."[16] The proposed regulation states "compounding areas ***shall typically*** be maintained at a temperature of 20° Celsius or cooler." The phrase "shall typically be maintained" could logically be interpreted by the regulated public in a myriad of ways. One stakeholder might argue that if 51% of all temperature readings taken in the compounding suite are at most 20° Celsius, then the standard has been met since more often than not, the temperature is less than 20° Celsius. Other stakeholders might contend that 90% of temperature readings must be less than 20°

[15] Cal. Gov't Code § 11346.2(a)(1).
[16] Cal. Code Regs. tit. 1 § 16.

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Section, Subdivision	Proposed Language	Recommendation/Comment
		Celsius to meet the requirement. Both interpretations are rational and logical based on the plain language of the proposed regulation. Because the proposed regulation is not clear, we suggest that this section of regulation be deleted and that the Board simply enforce the USP standard for the temperature of the compounding suite. If the Board believes that a regulation addressing the temperature of the compounding suite is necessary, then we suggest that the Board modify the regulation to read: Designated compounding area(s) should be maintained at a temperature of 20° or cooler.
1736.18(a)	(a) The quality assurance program shall comply with section 1711 and the standards contained in USP Chapter 1163, Quality Assurance in Pharmaceutical Compounding. In addition, the facility's quality assurance program shall include the following: (1) 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. (2) 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.	We anticipate that hospitals and other health care facilities are the most likely entities to be impacted by the requirement for a facility's quality assurance program to include a written procedure for responding to out-of-range temperature variations within medication storage areas when a furnished drug may be returned for furnishing to another patient. In some cases, the procedure for managing this kind of temperature excursion might be jointly managed by several departments within the facility. We suggest amending the proposed regulation to clarify that a facility-wide procedure would meet this requirement.
Article 4.7 Hazardous Drugs		
1737.5(c)	~~Where a pass-through is installed in a containment secondary engineering control (C-SEC), the doors must be gasketed and interlocking. Effective [OAL insert six months following the effective date] a pass-through is not allowed between the hazardous drug buffer room C-SEC into an unclassified space.~~	We appreciate the Board's reference to the restriction on pass-throughs from a hazardous buffer room to unclassified space in the California Building Code. Because existing state regulations already address this restriction, we encourage the Board to delete this provision from the proposed regulations. While we recognize that the Board cannot change the requirement in the Building Code, we continue to believe that a restriction on pass-throughs from a hazardous buffer room to unclassified space is misguided. Undoubtedly, increased human traffic in and out of the buffer room presents the greatest risk of microbial contamination and migration of Hazardous Drug (HD) residues. A properly configured

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Section, Subdivision	Proposed Language	Recommendation/Comment
		pass-through that is used appropriately is a commonsense tool to mitigate these risks.
1737.7(c)	~~Outer gloves used for HD compounding shall be changed between each different HD preparation.~~	In our written comments during the 45-day comment period, we provided the results of a literature review that we performed to assess whether there are data to support the practice of changing the outer glove between each different HD preparation. None of the studies that we found even addressed the question of changing gloves after each different HD preparation and they certainly did not provide any data to support that practice. It is disappointing that the Board only deigned to respond to our comprehensive comments on this proposed requirement with a vague reference to an uncited ASHP guidance document. We believe that the Board's reference to "ASHP guidance" might be to ASHP's Guidelines on Handling Hazardous Drugs.[17] If that is the case, that guideline recommends that the gloves be changed "every 30 minutes during compounding or immediately when damaged or contaminated."[18] The guideline makes no reference to changing gloves after each different HD preparation. As is emblematic of the Board's failure to provide evidence of the need for these regulations broadly—which has repeatedly been requested by the regulated public in hearings and written comments—the Board has utterly failed to meet the Administrative Procedure Act's substantial evidence standard for this proposed requirement. In the Modified Initial Statement of Reasons, the Board states, "an online search reveals that the cost of a pair of gloves is about $.14 [per] pair."[19] This cost estimate is a fantasy. A properly executed search will reveal that sterile, ASTM D6978 gloves cost between $1 and $4 per pair. We conservatively estimate that if this regulation is finalized as written, our annual supply cost would increase by between one and two million dollars. As such, the Board's estimated cost impact of "$150,000 over a ten-year period for administrative

[17] American Society of Health-System Pharmacists, *ASHP Guidelines on Handling Hazardous Drugs*, https://www.ashp.org/-/media/assets/policy-guidelines/docs/guidelines/handling-hazardous-drugs.ashx (last visited December 5, 2024).
[18] *Id*.
[19] Modified Initial Statement of Reasons, *supra*.

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Section, Subdivision	Proposed Language	Recommendation/Comment
		and maintenance workload and supplies," underestimates the financial impact of this proposed regulation by a factor of 100 for Kaiser Permanente alone. A recent study published in Health Affairs found that US health care greenhouse gas emissions accounted for approximately 8.5% of domestic US greenhouse gas emissions," and recommend that the health care sector "decrease unnecessary consumption of resources" to "reduce the sector's outsized environmental footprint."[20] Establishing a requirement to change gloves between each different HD preparation will increase the unnecessary consumption of resources and increase the environmental footprint of California pharmacies, which is at tension with Governor Newsom's bold climate goals articulated in his 2019 Executive Order on California's Climate Agenda.[21] Based on (1) the Board's failure to provide any evidence that this regulation is necessary, (2) the massive cost impact the proposed regulation would have on California businesses, and (3) the negative environmental impacts associated with the wasteful overuse of sterile chemotherapy gloves, we implore the Board to delete this requirement from the proposed regulation.
1737.15(a)	Deactivating, decontaminating, cleaning, disinfecting, and sporicidal agents shall be used in accordance with manufacturers' specifications or specifications established in published scientific studies and shall be surface compatible.	There are agents that have been shown to be effective in deactivating, decontaminating, cleaning, disinfecting, and/or killing bacterial and fungal spores but for which a manufacturer does not provide instructions for such a use. We encourage the Board to amend the regulation to provide organizations the flexibility to choose an agent that has been shown to be effective in published studies in accomplishing one or more of these required activities.

[20] Matthew J. Eckelman et al., *Health Care Pollution and Public Health Damage in the United States: an Update*, 39 HEALTH AFF. 2071 (2020).

[21] State of California Executive Department, *Executive Order N-19-19: Climate Agenda*, https://www.gov.ca.gov/wp-content/uploads/2019/09/9.20.19-Climate-EO-N-19-19.pdf (last visited December 5, 2024).

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December 9, 2024

Lori Martinez
Anne Sodergren, Executive Officer
California State Board of Pharmacy
2720 Gateway Oaks Drive, Suite 100
Sacramento, CA 95833

RE: Comment to the Proposed Regulatory Action Concerning Division 17 of Title 16 of the California Code of Regulations: Compounded Drug Products

Dear Ms. Martinez, Director Sodergren, and Members of the California State Board of Pharmacy:

Thank you for the opportunity to comment on the Notice of Proposed Regulatory Action Concerning: Compounded Drug Products issued by the California State Board of Pharmacy.

Medisca is a global company specializing in personalized pharmaceutical solutions, with over 2,000 product solutions to meet the unique needs of diverse healthcare sectors. Medisca supplies ingredients to 503A and 503B human drug compounders with the primary goal of facilitating and advancing patient access to safe and effective medications. Committed to bridging the gaps in healthcare, Medisca works to ensure the availability of individualized drug products tailored to the patients that need them.

This comment refers to the proposed amendments and repeals to Division 17 of Title 16 of the California Code of Regulations. Specifically, Medisca wishes to address the use of 503A Category 1 bulk drug substances (inclusive of dietary supplements) in compounded sterile preparations.

While the source of an ingredient and the available specifications and tests performed need to be considered as part of the overall qualification of the ingredient, Medisca would like to highlight that there exist in the marketplace today bulk drug substances listed under 503A Category 1 (inclusive of dietary supplements) that have been manufactured in compliance with Current Good Manufacturing Practice (cGMP) for Finished Pharmaceuticals (21 C.F.R. Part 210-211). Medisca respectfully requests that the Board consider the availability of these products and amend the regulations to allow pharmacies to compound sterile preparations using such bulk drug substances without the additional requirements listed in 1736.17(a)(2)(E) if the supplier and/or manufacturer can provide evidence of compliance with 1736.17(a)(2)(E) and cGMP.

When a 503A Category 1 bulk drug substance has been sourced, tested, and manufactured by a supplier and/or manufacturer in compliance with the cGMP standards for finished pharmaceuticals,

pharmacists should be able to consider use of such bulk drug substances when compounding sterile preparations. Further, pharmacies should not have to repeat testing at the ingredient level where a supplier and/or manufacturer has provided evidence of cGMP compliance along with available data demonstrating successful testing for the defined ingredient specifications, as listed in the ingredient-specific Certificate of Analysis. Requiring pharmacies to perform such testing, instead of the suppliers and manufacturers, dilutes wholesalers and places undue restrictions on pharmacies, inevitably decreasing access to patients.

In our view, California's pharmacy regulations should account for innovations and advancements in the industry, whether or not fully implemented. Medisca requests that the Board consider the products that both *are* and *can be* made available in the marketplace and amend the regulations to provide for that inevitability. If a supplier, like Medisca, can ensure the quality and safety of 503A Category 1 bulk drug substances with evidence of compliance with cGMPs for finished pharmaceuticals, the regulations should allow for their use in compounded sterile preparations. Doing so will promote patient access to high quality compounded drug products and ensure that the residents of California receive the same level of care as all other patients in the nation.

Thank you for your attention to our concerns. We look forward to a constructive dialogue and are happy to provide any additional information if needed. Please do not hesitate to reach out to me at mdestefano@medisca.com and (514) 333-7811, EXT. 1301 with any questions or to continue this important dialogue.

Institution/Contact Name	Medisca	Maurizio De Stefano, VP Compliance & Education
Section, Subdivision	**Proposed Language**	**Recommendation/Comment**
1736.17(a)(2)(E)	In addition to the requirements in USP Chapter 797, the following requirements apply to sterile compounding. (a) Standard operating procedures (SOPs) for sterile compounding shall be followed and shall: (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;	There exist in the marketplace today 503A Category 1 bulk drug substances (inclusive of dietary supplements) that have been manufactured in compliance with Current Good Manufacturing Practice (cGMP) for Finished Pharmaceuticals (21 C.F.R. Part 210-211). Medisca respectfully requests that the Board consider the availability of these products and amend the regulations to allow pharmacies to compound sterile preparations using such bulk drug substances without the additional requirements listed in 1736.17(a)(2)(E) if the

		(B) If applicable, 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. (E) The methods by which the pharmacist compounding or supervising the compounding pursuant to 1736.9(f) related to use of a bulk drug substance published in the 503A Category 1 bulk substances list, will ensure each lot of the bulk drug substance is representatively sampled per USP 1097 (bulk powder sampling procedures), tested, and found to be in compliance with at least: (i) USP Chapter 1, Injections and Implanted Drug Products (Parenterals) – Product Quality Tests	supplier and/or manufacturer can provide evidence of compliance with 1736.17(a)(2)(E) and cGMP. Pharmacies should not have to repeat testing at the ingredient level where a supplier and/or manufacturer has provided evidence of cGMP compliance along with available data demonstrating successful testing for the defined ingredient specifications, as listed in the ingredient-specific Certificate of Analysis. If a supplier, like Medisca, can ensure the quality and safety of 503A Category 1 bulk drug substances with evidence of compliance with cGMPs for finished pharmaceuticals, the regulations should allow for their use in compounded sterile preparations.

		(ii) USP Chapters 232 and 233 related to Elemental Impurities, (iii) USP Chapter 467 – Residual Solvents, (iv) USP Chapter 85 – Bacterial Endotoxins and (v) any other USP Chapters deemed appropriate based on the clinical judgment of the pharmacist developing the SOPs.	

Sincerely,

Maurizio De Stefano
VP, Compliance & Education
Medisca

Lorri Walmsley, RPh., FAzPA
Director, Pharmacy Affairs
Walgreen Co.
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lorri.walmsley@walgreens.com

December 6th, 2024

Dear Executive Director Sodergren and members of the California Board of Pharmacy,

On behalf of all pharmacies owned and operated by Walgreen Co. licensed in the State of California, we thank the Board for the opportunity to comment on the proposed rules. We ask the board to review our concerns and ensure that the compounding standards in California can be practically applied to ensure patient access to compounding services.

We feel that as suggested throughout the proposed language, the additional requirements go above and beyond the recommendations and guidance in the General Chapters of USP and intend to hold California pharmacies to a higher standard than currently established without the evidence of additional patient safety benefits. Walgreens thanks the board for reviewing our concerns and ensuring a balance is made for pharmacies in California and to reduce unnecessary regulatory burdens on the practice of pharmacy that may impact patient access to compounded products.

Sincerely,

Lorri Walmsley

Lorri Walmsley, RPh, FAzPA

Institution/Contact Name: Lorri Walmsley, RPh., FAzPA Director, Pharmacy Affairs Walgreen Co. 5330 E. Washington St, Ste. 105 Phoenix, AZ 85034 p: 602-214-6618 lorri.walmsley@walgreens.com		
Section, Subdivision	**Proposed Language**	**Recommendation / Comment**
1735.1. Introduction and Scope. (f)(1)(A)	(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 dispensing, or	It is understandable that the Board would like to impose strict and clear guardrails for compounding to inspect and enforce when commercially available products are on the market. However, the language as proposed will cause issues for patients and limit their ability to access compounded medications, especially in times of need. In many cases, there is urgency for a patient to receive their compounded medication and pharmacists should be able to utilize professional judgement to ensure that an urgent need is met for the patient. Product shortages can be short-term or long-term. It can take months for a product to "officially" appear on the FDA shortage list, as it is self-reported by the manufacturer. However, many times products remain on short-term shortages, backorders, or limited supply causing issues for patients as they struggle to find needed medication, these issues may often be regional and affect patients differently across the nation. It is not prudent to prohibit products, such as Tamiflu, from compounding until it is on the FDA Drug Shortages Database, as it may significantly impact patient health outcomes to wait for the product's availability. Additionally, there may be times that a product was compounded for a patient and appeared in an American Society of Health-System Pharmacists (ASHP) or FDA Drug Shortages Database that are in short supply at the time of

		compounding, but then at the time of dispensing that designation has changed. It would be incredibly wasteful of the products and create financial hardships for compounding pharmacies to discard that product solely because the product was no longer on a shortage list when the patient actually receives the medication. The board should continue to monitor for pharmacies that compound products excessively or in bulk without a patient specific order to capitalize or profit on shortages of products, however, the board should also ensure that delays in patient care do not occur due to the rigidity of the language as proposed. Of note, this language appears to come from an FDA guidance document; however, commercial products become unavailable for patients long before they appear on the referenced databases and the board should weigh the pros and cons of trusting manufacturers to appropriately report shortages of their medications. Walgreens suggests the board allow the compounding of a copy or essentially a copy of a commercial product so long as there is a clinically significant, therapeutic reason, such as a documented allergy or product shortage. The pharmacy must document the commercial product shortage on the prescription or the Compounding Formulation Record, if applicable. The board should require that pharmacy teams review the American Society of Health-System Pharmacists (ASHP) or Food and Drug Administration (FDA) list of drugs in short supply but not require that this product is listed. **Recommended Language:** (A) the drug product appears in an American Society of Health-System Pharmacists (ASHP) or FDA Drug Shortages Database ~~that~~ or are in short supply at the time of compounding ~~and at the time of dispensing,~~ or
1735.4. Building and Facilities.(b)	(b) Purified water, distilled water, reverse osmosis water or higher quality water shall be used for rinsing equipment and utensils.	The board is adopting language from various parts of the guidance in USP but expanding and applying it inappropriately to non-sterile compounded preparations. Purified water, distilled water, reverse osmosis water or higher quality water is utilized when preparing a non-sterile product and continues to be a standard of practice during the compounding process. However, during the cleaning process, when it comes to rinsing equipment and utensils, there is no evidence that this practice would reduce or prevent contamination of non-sterile products. The board is taking language from USP guidance

		and best practices and turning it into a mandate without evidence of improved patient safety. We request that this language be removed as this topic is already addressed in USP <795>. **Recommended language:** ~~(b) Purified water, distilled water, or reverse osmosis water shall be used for rinsing equipment and utensils.~~
1735.5. Cleaning and Sanitizing (a) and (b)	(a) The facility's documentation of each occurrence of the cleaning and sanitizing of the compounding area shall include the identity of the person completing the cleaning and sanitizing, as well as the product name(s) of the cleaning and sanitizing agent(s) used.	This is unnecessary and overly burdensome language that does not improve patient safety. Does the board have evidence that requiring the product names improves patient safety? This language could be interpreted to require pharmacies to list the specific brand or manufacturer of commonly used cleaning and sanitizing products. For example, does the board feel there is a significant difference between the various manufacturers or isopropyl alcohol and must know which one was used during the cleaning and sanitizing process? Requiring pharmacy teams to follow USP guidelines and instructions for cleaning is sufficient to ensure patient safety. **Recommended language:** (a) The facility's documentation of each occurrence of the cleaning and sanitizing of the compounding area shall include the identity of the person completing the cleaning and sanitizing, as well as ~~the product name(s) of~~ the cleaning and sanitizing agent(s) used.
1735.7. Master Formulation and Compounding Records. (a)(1)	(1) If a source is referenced to support the assigned beyond-use date (BUD), ~~each~~ the source referenced shall be readily retrievable at the time of compounding and shall be maintained for three years from the date each CNSP is dispensed.	We ask the board to clarify and specify the requirement for readily retrievable at the time of compounding. Does the board intend for this information to be immediately available to the compounding pharmacist or just available and retrievable if requested by the pharmacist or board. If the board's intent is for the pharmacist to have the source referenced for the master formulation record in hand at the time of compounding, this would further limit locations that could provide compounding services. USP monographs are widely referenced for beyond-use date assignments; however, access to these monographs is limited and cost prohibitive for many pharmacies. Often, if requested by the compounding pharmacist, a copy of the materials supporting the extended BUD will and can be provided but are not sent to the pharmacist for review, unless requested.

		Recommended language: (1) If a source is referenced to support the assigned beyond-use date (BUD), each source referenced shall be available upon request prior to compounding ~~readily retrievable at the time of compounding~~ and shall be retrievable ~~maintained~~ for three years from the date each CNSP is dispensed.
1737.5. Facilities and Engineering Controls. (e)	(e) 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.	As stated previously, the board is adopting language from various parts of the guidance in USP but expanding and applying it inappropriately to non-sterile compounded HD preparations. This proposed requirement exceeds the standards listed in USP <800> 5.3. Additionally, CAG-003 specifically only applies to the Certification of Sterile Compounding Facilities. Does the board have evidence that this requirement is necessary for non-sterile products? This reg applies it broadly to all healthcare settings compounding hazardous materials. We request this language is removed to prevent further confusion and ensure alignment with USP guidelines. **Recommended Language:** ~~(e) 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.~~
1737.7. Personal Protective Equipment (PPE)(b) and (c)	(b) The outer pair of gloves that meets the ASTM D-6978 standard chemotherapy gloves shall be changed ~~every 30 minutes during HD compounding unless otherwise~~ as recommended by the manufacturer's documentation. Documentation from the manufacturer shall be readily retrievable. For sterile HD compounding, both pairs of gloves labeled to meet the ASTM D-6978 standard shall be sterile. (c) Outer gloves used for HD compounding shall be changed between each different HD preparation.	Walgreens requests clarity on what defines "different". For example, if a pharmacist is compounding back-to-back progesterone creams, are those considered different and would require a change in gloves? If so, then c and b in combination will create confusion. We suggest that the board adds language to clarify that their intent is for gloves to be changed when active ingredients are different between compounds, but not necessarily between every compound made. Walgreens also is concerned that with this requirement if a change in gloves is required between every HD preparation, you are introducing touchpoint for contamination and exposure. We strongly feel that gloves should only be changed between each different HD API preparation and if there is a gap between the compounding of those products. We agree that gloves should be changed per manufacturer's recommendations or if switching to a different HD API preparation.

		Recommended language: (c) Outer gloves used for HD compounding shall be changed between each different HD API preparation.
1737.14. Administering.	(b) When furnishing dispensing a compounded antineoplastic HD to a patient or patient's agent a sufficient supply of ASTM D6978 gloves ~~that meet the ASTM D 6978 standard~~ shall be provided to allow for appropriate administration, handling, and disposal of HD ~~drugs by the patient or the patient's agent shall be provided.~~	Mandating the supply of gloves for antineoplastic HD compounded products is overreaching. However, we do feel that the dispensing pharmacy and the administering facility should ensure that the appropriate gloves are available for administration. Often the patient or patient's agent, such as a nurse, already has the appropriate supplies to administer the product and providing the gloves without the patient or patient's agent requesting them may be wasteful and contribute to excessive and unnecessary HD refuse and waste. **Proposed language:** (b) When ~~furnishing~~ dispensing a compounded antineoplastic HD to a patient or patient's agent the dispensing pharmacy must ensure a sufficient supply of ASTM D6978 gloves ~~that meet the ASTM D 6978 standard~~ is available and shall be provided upon request to allow for appropriate to allow for appropriate administration, handling, and disposal of HD ~~drugs by the patient or the patient's agent shall be provided.~~

UNIVERSITY OF CALIFORNIA HEALTH

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December 9, 2024

Maria Serpa, Chair
Enforcement and Compounding Committee
California State Board of Pharmacy
2720 Gateway Oaks Drive, Suite 100
Sacramento, California 95833

Re: Recommended Changes to Proposed Regulation: Compounded Drug Products

Dear Maria Serpa:

The University of California Health (UC Health) hospital pharmacy leaders appreciate the opportunity to provide comments on the Board of Pharmacy's proposed changes to 16 C.C.R. §§ 1735, 1736 and 1737, related to sterile compounding regulations.

Sterile and non-sterile compounding standards published by USP have allowed UC hospital pharmacies to find ways to enhance patient safety through facility updates, improved compounding practices, and updated purchasing methods. UC Health Pharmacy Departments have been actively planning for the updates to USP 797, 795, and 800 because these updates were provided as guidance for several years prior to their final implementation. UC Health Chief Pharmacy Officers are concerned that the Board's regulations propose additional, conflicting, or unduly burdensome changes to our UC Health hospital pharmacies. That, coupled with uncertainty of the 503b supply chain, has made the path forward on proposed regulations difficult to accommodate.

The UC Health Chief Pharmacy Officers agree with the Board's mission to protect the consumers of California and believe that addressing these hurdles will enable us to better provide for our patients' care and safety. However, we are also broadly concerned that the proposed regulations, while intended to improve patient safety, will have the undesirable effect of reducing the ability of all California hospitals to safely serve their patients.

We request that the Board revisit the proposed compounding regulations for acute care hospitals and consider USP 797, 795, and 800 standards as the target.

Our specific considerations are attached to this letter (Appendix 1).

Thank you again for the opportunity to provide input on the Board's proposed regulations. We welcome any future opportunities to collaborate with the Board on addressing these issues. If any further information is needed, please feel free to contact me.

Sincerely,

Cedric Terrell on behalf of
UCD, UCI, UCLA, UCSF, UCSD

Appendix 1

1. 1735.7 Master Formulation and Compounding Records. subsection (c)(2):
    a. **Proposed Regulation**: *(c)(2) The manufacturer, lot number, and expiration date for each component.*

    b. **Comments**: Current language in 16 CCR § 1735.3(a)(F)(i) (copied below) has a provision for CSPs compounded in licensed health facilities to prevent delays in care to acutely ill patient, i.e. infections, cancer, critical care, etc. The current language states:

    (F) The manufacturer, expiration date and lot number of each component. If the manufacturer name is demonstrably unavailable, the name of the supplier may be substituted. If the manufacturer does not supply an expiration date for any component, the records shall include the date of receipt of the component in the pharmacy, and the limitations of section 1735.2, subdivision (l) shall apply.

    (i) Exempt from the requirements in this paragraph (1735.3(a)(2)(F)) are sterile preparations compounded in a single lot for administration within seventy-two (72) hours to a patient in a health care facility licensed under section 1250 of the Health and Safety Code and stored in accordance with standards for "Redispensed CSPs" found in Chapter 797 of the United States Pharmacopeia – National Formulary (USP37-NF32) Through 2nd Supplement (37th Revision, Effective December 1, 2014), hereby incorporated by reference.

    c. **Recommendation**: To prevent delays in care to acutely ill patients, we recommend the Board consider including parallel exemption language found under current 16 C.C.R. § 1735.3(a)(F)(i) to the proposed § 1735.7(c)(2) to read as follows:

    (c)(2) The manufacturer, lot number, and expiration date for each component.

    (i) ***Exempt from the requirements in this paragraph are non-sterile preparations compounded in a single lot for administration within seventy-two (72) hours to a patient in a health care facility licensed under section 1250 of the Health and Safety Code.***

2. 1736.1 Sterile Compounding Scope. Subsection (b)(2):
    a. **Proposed Regulation**: *(b)(2) If the sterile compounding equipment or environment fail(s) to meet any required specification, an immediate use CSP may be compounded without the requirement for there to be loss of life or intense suffering of an identifiable patient. This provision may only be used for 24 hours after such failure(s). All such failures must be documented in accordance with facility's SOP and shall be reported to the BOP within 72 hours.*

    b. **Comments**: While we appreciate the Board's efforts to provide impacted facilities with flexibility in the event of an equipment or environment failure, a 24-hour timeframe is insufficient. Remedying equipment or environment failures within 24 hours may not be feasible due to a variety of reasons why there could have been such failures (including if such failures were due to a cause out of the control of the impacted facility). Often times, it may take more than 24 hours to remedy an equipment failure. To identify and use an outside facility or vendor to provide compounding preparations within such limited timeframe would pose a safety risk as the vendor/facility may not be following the health systems' processes and procedures. We urge the Board to embrace a 'Just Culture' framework, which emphasizes accountability and learning over punitive measures.

    c. **Recommendation**: To revise proposed § 1736.1(b)(2) to (i) apply the immediate use compounding requirements of USP 797, (ii) extend the period under which immediate use CSP may be compounded under the subsection, and (iii) amending the reporting requirement for documentation:

    (b)(2) If the sterile compounding equipment or environment fail(s) to meet any required specification, an immediate use CSP may be compounded ***under the immediate use compounding requirements of USP 797****. This provision may only be used for* ***7 business days*** *after such failure(s). All such failures must be documented in accordance with facility's SOP and shall be* ***available upon inspection****.*

3. 1736.1 Introduction and Scope. Subsection (h):
    a. **Proposed regulation**: *(h) CSPs with human whole blood or human whole blood derivatives shall be produced in compliance with Health and Safety Code section 1602.5.*

    b. **Comments:** The proposed subsection (h) would cause confusion as it would encompass any human whole blood or human whole blood derivative that is already manufactured by a pharmaceutical company (e.g. Albumin, Factor products, IVIG etc.).

    c. **Recommendation:** To revise proposed § 1736.1(h) to clarify that the regulation does not apply to CSPs made with human blood/derivative that is manufactured by pharmaceutical companies:

    (h) CSPs with ***patient's own*** *whole blood or human whole blood derivatives* ***from the patient*** *shall be produced in compliance with Health and Safety Code section 1602.5.*

4. 1736.2 Personnel Training and Evaluation. Subsection (d)
    a. **Proposed regulation**: *(d) Compounding personnel or persons with direct supervision and control of compounding personnel who fail any aspect of the aseptic manipulation ongoing training and competency evaluation shall not be involved in compounding 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 supervision and control of personnel who fails any aspect of the aseptic manipulation ongoing training and competency evaluation may continue to provide only direct supervision and control of personnel for no more than 30 days after a failure of any aspect while applicable aseptic manipulation ongoing training and competency evaluation results are pending.*

    b. **Comments:** Multiple factors can contribute to failure of staff in aseptic technique training and competency evaluation including environmental testing failure and engineering control failure. Prohibiting compounding personnel from compounding without an evaluation of contributing factors and timeframe would significantly disrupt patient treatment and jeopardize health systems' ability to operate.

    c. **Recommendation:** To revise § 1736.2(d) as follows:

        (d) Compounding personnel or persons with direct supervision and control of compounding personnel who fail any aspect of the aseptic manipulation ongoing training and competency evaluation shall not be involved in compounding 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 supervision and control of personnel who fails any aspect of the aseptic manipulation ongoing training and competency evaluation may continue to provide only direct supervision and control of personnel ***including performing in-process checks, final verification, and dispensing of CSPs*** *for no more than 30 days after a failure of any aspect while applicable aseptic manipulation ongoing training and competency evaluation results are pending.*

5. 1736.11 Master Formulation and Compounding Records. subsection (c)(2):
    a. **Proposed regulation**: *(c)(2) The manufacturer, lot number, and expiration date for each component for the CSP.*

    b. **Comments:** Similarly to our Comment #1 above, current language in 16 CCR § 1735.3(a)(F)(i) (copied below) has a provision for CSPs compounded in health facilities to prevent delays in care to acutely ill patient, i.e. infections, cancer, critical care, etc. The current language states:

        (F) The manufacturer, expiration date and lot number of each component. If the manufacturer name is demonstrably unavailable, the name of the supplier may be substituted. If the manufacturer does not supply an expiration date for any component, the records shall include the date of receipt of the component in the pharmacy, and the limitations of section 1735.2, subdivision (l) shall apply.

            (i) Exempt from the requirements in this paragraph (1735.3(a)(2)(F)) are sterile preparations compounded in a single lot for administration within seventy-two (72) hours to a patient in a health care facility licensed under section 1250 of the Health and Safety Code and stored in accordance with standards for "Redispensed CSPs" found in Chapter 797 of the United States Pharmacopeia – National Formulary (USP37-NF32) Through 2nd Supplement (37th Revision, Effective December 1, 2014), hereby incorporated by reference.

    c. **Recommendation:** To prevent delays in care to acutely ill patients, we recommend the Board consider including parallel exemption language found under current 16 C.C.R. § 1735.3(a)(F)(i) to the proposed § 1736.11(c)(2) to read as follows:

        (c)(2) The manufacturer, lot number, and expiration date for each component for the CSP.

            (i) Exempt from the requirements in this paragraph are sterile preparations compounded in a single lot for administration within seventy-two (72) hours to a patient in a health care facility licensed under section 1250 of the Health and Safety Code.

6. 1737.5 Facilities and Engineering Controls. Subsection (c)
    a. **Proposed Regulation***: (c) Effective [OAL insert six months following the effective date] a pass-through is not allowed between the hazardous drug buffer room into an unclassified space.*

    b. **Comments:**

        - USP 800 does not prohibit using a pass-through between a classified space and an unclassified space.. Complying with the proposed language would be a major operational challenge on existing facilities and may negatively impact patient care.

- In speaking with many experts who design and construct clean rooms there has never been an issue with a pass-through between classified to unclassified as long as the doors are interlocking. The FDA in their guidance for 503b compounding facilities states material flow directly between unclassified room and sterile compounding area is allowed as long as it is classified so a HEPA filtered pass-through would be permissible to use.

- If the intent is for the pass-through that is between a classified space and unclassified space to be HEPA purge type only, then we would recommend the below language. Alternatively, if the intent of the language is to be cautious of some presumed contamination requiring some sort of wipe sampling, we urge the Board to revise the language to accomplish such goal.

c. **Recommendation**: Revise language as follows:

(c) Effective [OAL insert six months following the effective date], ***a material flow directly between an unclassified area and a room in which sterile compounding is conducted (e.g., unclassified pass-through) is not allowed. Notwithstanding the foregoing, any secondary engineering control that has a pass-through between classified and unclassified space existing prior to such date may continue to be used if the facility's SOPs document that two doors are interlocking and the facility SOPs outline hazardous wipe sampling to monitor for contamination****.*

7. 1737.7 Personal Protective Equipment (PPE), subsection (c).
   a. **Proposed Regulation***: (c) Outer gloves used for HD compounding shall be changed between each different HD preparation.*

   b. **Comments:**

   - USP 800 says the following:
     - Chemotherapy gloves should be changed every 30 minutes unless otherwise recommended by the manufacturer's documentation and must be changed when torn, punctured, or contaminated.
   - Many health systems use closed system transfer device (CSTD) when compounding antineoplastic HDs. The use of CSTD has shown to significantly reduce overall chemical contamination (12.24% vs. 26.39%).[1]
   - Double gloving is primarily designed to offer extra protection against hazardous drug compounds, with the outer glove serving as a first line of defense. If the outer glove is repeatedly removed or exposed to rough conditions, it may wear down, possibly increasing the risk of puncturing or compromising the inner glove. This could lead to reduced protection, especially when handling hazardous drug compound.[2,3]
   - Frequent removal and disposal of outer glove changes creates significant waste.[2]

   Reference

   1. Simon N, Vasseur M, Pinturaud M, et al. Effectiveness of a Closed-System Transfer Device in Reducing Surface Contamination in a New Antineoplastic Drug-Compounding Unit: A Prospective, Controlled, Parallel Study. Ahmad A, ed. PLoS One 2016;11:e0159052. Available at:
      a. https://dx.plos.org/10.1371/journal.pone.0159052.

   2. Kirk H. Double gloving when handling cytotoxic drugs. Hospital Pharmacy Europe. Published March 2, 2009. Available from: https://hospitalpharmacyeurope.com/news/editors-pick/double-gloving-when-handling-cytotoxic-drugs/

   3. McNeilly L. Double gloving: Myth versus fact. Infection Control Today. Published May 5, 2011. Available from: https://www.infectioncontroltoday.com/view/double-gloving-myth-versus-fact

   c. **Recommendation**: Revise language to be consistent with USP 800 or as follows:
      - *(c) Outer gloves used for HD compounding shall be changed between each different HD preparation* ***if a closed system transfer device (CSTD) is not used****.*

8. 1737.14 Administering, subsection (b)
   a. **Proposed Regulation:** *(b) When dispensing a compounded antineoplastic HD to a patient or patient's agent, a sufficient supply of ASTM D-6978 standard gloves, shall be provided to the patient or the patient's agent, to allow for appropriate administration, handling, and disposal of the HD.*

b. **Comments:** In licensed health facilities where antineoplastic HD are dispensed and administered by licensed health care professionals who are trained to handle HDs, supplies such as ASTM D-6978 grade gloves and HD disposal bins are readily available.

Recommendation: Recommend adding the following exemption language to the current proposed language for facilities licensed under Health and Safety Code § 1250(a) as the administration of compounded medications to patients are done by health care personnel trained and authorized to administer HD medications and not dispensed for outpatient use:

Exempt from this requirement are health facilities, as defined in Section 1250 of the Health and Safety Code, if the prescriptions are administered by a licensed health care professional.

Alliance for Pharmacy Compounding

Compounding the Joy of Living®

December 9, 2024

Anne Sodegren, Executive Officer
Seung Oh, President
California State Board of Pharmacy
2720 Gateway Oaks Drive, Suite 100
Sacramento, CA 95833

Dear President Oh, Director Sodegren, and Members of the California State Board of Pharmacy:

Thank you for the opportunity to comment on **the Notice of Proposed Regulatory Action Concerning: Compounded Drug Products** issued by the California State Board of Pharmacy. Our comments and concerns here are backed up by the considerable patient-facing compounding experience of our members – experience that we believe can provide the board with a well-informed perspective that can improve its regulatory proposal.

The Alliance for Pharmacy Compounding is the industry trade association and the voice for pharmacy compounding, representing more than 600 compounding small businesses — including compounding pharmacists and technicians in both 503A and 503B settings, as well as prescribers, educators, researchers, and suppliers.

Our comments on specific provisions of the proposed regulations are attached here and refer to the amendments and repeals outlined in the proposal affecting Division 17 of Title 16 of the California Code of Regulations.

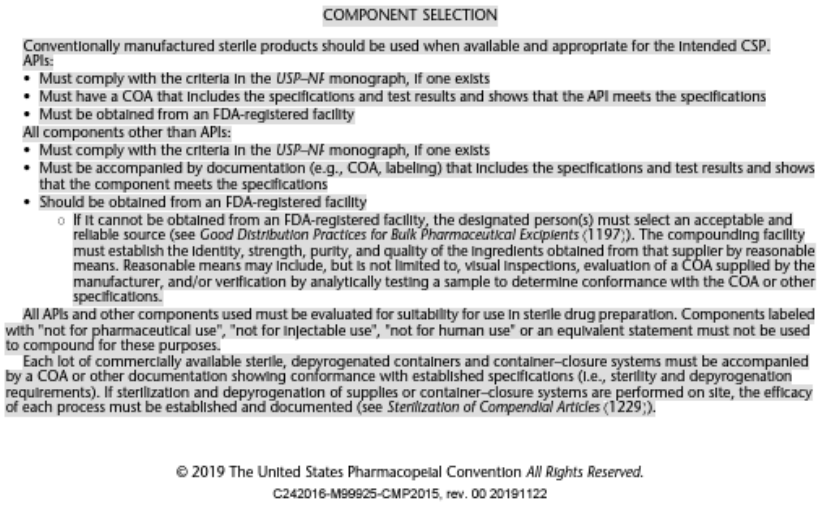
We are grateful that the board has heeded public comments and has made some adjustments to the initially proposed compounding regulations. However, we continue to have significant concern with proposed regulations that exceed USP guidelines, and we are frustrated that the Board seems to be unwilling to produce any evidence that the proposals that exceed the USP standards keep patients safer. For instance, requiring stability studies before compounding — irrespective of beyond-use date — and additional testing of the active pharmaceutical ingredients impose unnecessary barriers to patient access with no evidence that the additional studies and testing are needed, particularly for specialized preparations like inhaled glutathione.

We were particularly concerned to learn that if these proposed regulations are not adopted, the Board does not intend to allow future compounding of certain substances, implying that these preparations are non-compliant with FDA standards, which is demonstrably not the case.

We urge the Board to recognize that while these APIs are not on the FDA's final bulks list, they are on an interim list that the FDA currently permits for compounding as they undergo evaluation. Indeed, compounding with these APIs is allowed in all other 49 states.

No Other State Compounding Regulation (Proposed or Passed) Prohibits Compounding with Category 1 Bulk Drug Substances

During the November 7, 2024 Board meeting, a presentation was given by Director Anne Sodegren and Board Counsel Corinne Gartner. Several states were mentioned during the presentation with commentary about how those states are interpreting and applying federal and state law. Kansas was mentioned, and indeed the Kansas Board is proposing updating regulation K.A.R. 68-13-4. In the update, the “must” and “should” terminology becoming “shall” only applies to the USP chapter it is adopting, which in this case is USP 797. The Board also includes a similar provision in K.A.R. 68-13-3, which adopts USP 795. This is in alignment with language in the USP chapters on compounding. In USP 797, the section on component selection already includes USP’s requirements for API selection – including allowing for compounding with API in FDA’s interim Category 1.



COMPONENT SELECTION

Conventionally manufactured sterile products should be used when available and appropriate for the intended CSP.
APIs:

- Must comply with the criteria in the *USP–NF* monograph, if one exists
- Must have a COA that includes the specifications and test results and shows that the API meets the specifications
- Must be obtained from an FDA-registered facility

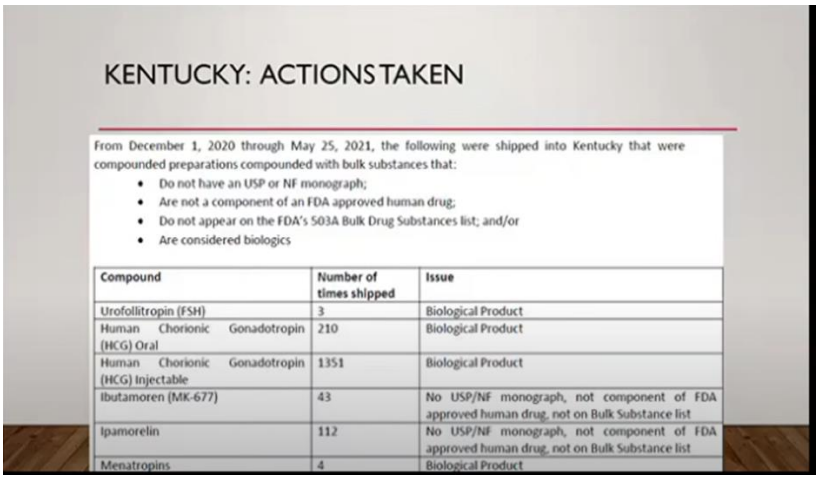
All components other than APIs:

- Must comply with the criteria in the *USP–NF* monograph, if one exists
- Must be accompanied by documentation (e.g., COA, labeling) that includes the specifications and test results and shows that the component meets the specifications
- Should be obtained from an FDA-registered facility
    - If it cannot be obtained from an FDA-registered facility, the designated person(s) must select an acceptable and reliable source (see *Good Distribution Practices for Bulk Pharmaceutical Excipients* ⟨1197⟩). The compounding facility must establish the identity, strength, purity, and quality of the ingredients obtained from that supplier by reasonable means. Reasonable means may include, but is not limited to, visual inspections, evaluation of a COA supplied by the manufacturer, and/or verification by analytically testing a sample to determine conformance with the COA or other specifications.

All APIs and other components used must be evaluated for suitability for use in sterile drug preparation. Components labeled with "not for pharmaceutical use", "not for injectable use", "not for human use" or an equivalent statement must not be used to compound for these purposes.

Each lot of commercially available sterile, depyrogenated containers and container–closure systems must be accompanied by a COA or other documentation showing conformance with established specifications (i.e., sterility and depyrogenation requirements). If sterilization and depyrogenation of supplies or container–closure systems are performed on site, the efficacy of each process must be established and documented (see *Sterilization of Compendial Articles* ⟨1229⟩).

That same presentation included a misleading slide that suggested other states are acting against compounders for using API in FDA’s interim Category 1. The information presented on the slide, from a case in Kentucky, showed that the pharmacy in question was compounding with a biologic agent, not a drug, and with API listed on FDA’s interim Category 2. APC agrees with the Kentucky Board’s assessment that these API were not appropriate for use in compounded drugs. Biologics are not eligible for use in compounding, and API in FDA’s interim Category 2 are expressly prohibited from being used in a compounded preparation.



Similarly, Kentucky's most recent compounding rules align with the FDA rules: Pharmacies may only use bulk drug substances that have a USP/NF monograph, are a component of an FDA approved medication, or appear on the 503A bulks list. While the interim bulks list isn't specifically called out in the Kentucky regs, the notice of proposed rulemaking included this question: "Will this administrative regulation impose stricter requirements, or additional or different responsibilities or requirements than those required by the federal mandate?" The Kentucky Board's response was: "No, this regulatory amendment only imposes the floor requirement of the federal rule." This shows that Kentucky was not and is not attempting to require stricter interpretation of the federal compounding law, guidance, and standards than the FDA does.

Massachusetts was also mentioned, again with misleading information. On that state's Board of Pharmacy website, this document outlines requirements for the API used in compounded products. It says that compounding of non-sterile preparations using bulk drug substances must comply with FDA's guidance "Bulk Drug Substances Used in Compounding Under Section 503A of the FD&C Act"; and bulk drug substances must be accompanied by a valid certificate of analysis. The linked FDA webpage highlights the final *and* interim policy for compounding with bulk drug substances under Section 503A. The proposed Massachusetts compounding rule changes presented by California Board staff showed that Massachusetts has indicated that all pharmacies performing sterile compounding shall be required to comply with ALL chapters of the current USP (emphasis added). Compliance with "all" USP chapters is defined by USP in USP's General Notices:

> *"Applicable general chapters" means general chapters numbered below 1000 or above 2000 that are made applicable to an article through reference in General Notices, a monograph, or another applicable general chapter numbered below 1000."*
>
> *"General chapters numbered 1000 to 1999 are for informational purposes only. They contain no mandatory tests, assays, or other requirements applicable to any official*

article, regardless of citation in a general chapter numbered below 1000, a monograph, or these General Notices."

USP clearly does not intend for chapters numbered between 1000 and 1999 to be used for compliance purposes. The Massachusetts BOP does not intend for literally all chapters within USP to be used for compliance, which is shown by the state's Board specifically calling out USP 1163. USP does not intend that chapter to be used for compliance purposes either, despite the valuable information it contains. There is no mention in the proposed Massachusetts compounding rule changes that would prohibit compounding with API in FDA's interim Category 1.

In fact, APC has found no evidence of enforcement action by any other state board of pharmacy against a pharmacy simply for compounding with API in FDA's interim Category 1. In California, however, the Board has disciplined six different sterile compounding pharmacies for using API in the interim Category 1 list. There is no current rule against using these API, but the Board has been using "underground" regulation and threats of/or actual license revocations to prohibit compounding with them, thus removing availability of these medications from patients in the state. Two of those six disciplined pharmacies requested administrative law hearings for their cases. The administrative law judges sided with the pharmacies in both cases, ruling that compounding with interim Category 1 substances was currently allowed under both federal and state law. However, the Board audaciously rejected both judges' rulings and disciplined the pharmacies with license revocation and/or probation, against the judges' recommendations. These actions by the Board have created a chilling effect, stopping pharmacies from making these medications – not because it is impermissible in law or unsafe, but rather from fear of reprisal by the Board.

During a recent presentation to the Board by Board Counsel Corinne Gartner, Ms. Gartner illustrated plainly what the FDA says about the topic of compounding with items in interim Category 1 – presenting a slide that details the FDA's interim enforcement policy. FDA allows the use of API in interim Category 1, provided that the bulk drug substance was manufactured by an entity registered with the FDA, is accompanied by a valid certificate of analysis, and that it is used in compliance with other sections of 503A.

The FDA does not require additional testing of the bulk drug substance API before use, as proposed by the California Board. This proposed additional testing of bulk drug substances increases costs to pharmacies and patients – which will create barriers to access – without demonstrating that doing so makes patients one iota safer. Despite some of these bulk drug substances having a dietary supplement USP monograph, there does exist in the marketplace API other than dietary supplement grade – for example, one wholesaler sells EP (European Pharmacopoeia) grade glutathione and methylcobalamin which are both labeled for use as an API.

The presentation delivered by Board staff highlighted instances where compounded preparations caused patient harm. It is, of course, important to investigate the root cause of any such instance and implement strategies for prevention. However, using isolated examples to create onerous and unnecessary regulations that apply to the entire industry and restrict patient access is simply not a rational approach to the Board's patient-safety focused mission. The example given about patient harm from a compounded product with excessive levels of endotoxins illustrates a case where a pharmacy did not follow existing guidelines by not performing currently required endotoxin testing. It is a circumstance covered by existing regulation. The Board seems to be arguing that violation of existing regulation by some demands not simply robust enforcement, but more stringent regulation of all compounding pharmacies – as if more regulation will lead to more compliance. It's simply not a rational approach to regulating an industry.

We also note that the most recent examples provided by the Board of patient harm were caused by non-sterile compounding errors and had nothing to do with compounding with the API in question or due to inappropriate component selection.

The board presentation also left the false impression that only compounded drugs result in adverse event reports or cause patient harm. The FDA Adverse Events Reporting database/website allows for reports of adverse events related to drugs, including both FDA-approved and compounded medications. The website cautions that existence of a report does not establish causation. In 2024 alone, there have been nearly 800,000 adverse events reported to FDA, and 100,000 have been associated with a patient death. Nearly all of these unfortunate events were attributed by the reporting individual to FDA-approved drug products. Moreover, the mere reporting of these adverse events does not mean the manufactured drug products are unsafe. It is a misuse of the FAERS data to claim that a reported adverse event is serious or that the product associated with the AE is unsafe. Again, the FDA's FAERS database states this very clearly: "Existence of a report does not establish causation."

That hour-long presentation by Board staff was not available prior to the meeting, and stakeholders had no opportunity to provide context. The Board claims to desire transparency in the rulemaking process and says it wants stakeholder input. But that one-sided and misleading presentation contained inaccuracies that appeared to be offered in an attempt to persuade Board members that compounding is inherently bad and should be curtailed. There was no time allowed for questions or clarifications from the public, and there was no chance for knowledgeable, experienced pharmacists and others who understand public policy associated with pharmacy compounding to respond to allegations made in the presentation before the Board was asked to vote on moving the proposed regulations forward. As a result, it was not informed policymaking by a regulatory agency. It was manipulation of supposed facts to achieve a pre-ordained end.

Again, with the Board's modest updates to the originally proposed rules, some progress has been made. However, these proposed regulations still need considerable revision. We strongly

recommend realigning with USP standards. It is indisputable that USP intends chapters numbered under 1000 to be used as enforceable standards, while chapters above 1000 are for informational purposes only – meaning they were not developed or intended for the purpose of being enshrined in legislation or regulation. USP clearly states in the General Notices that "Chapters above 1000 **contain no mandatory tests, assays, or other requirements applicable to any article, regardless of citation in a general chapter below 1000**, a monograph or these General Notices." That one reason the Board's assertion that it is just listing out all the tests required for bulk drug substances in interim Category 1 (and other requirements in Chapters above 1000) is misleading at best. Per USP, these tests are not required.

USP standards provide a scientifically sound and safety-focused approach to compounding and when aligned with the FDA's enforcement discretion, permits pharmacies to use APIs on the interim Category 1 bulks list. In areas where USP defers to the state, such as recall procedures, adverse event reporting, terms lacking definition, and PIC responsibilities, certainly California can provide clarity through reasonable regulations.

We would be happy to meet with the Board to foster collaboration in creating a set of regulations that protect patients without unduly hindering access.

We ask again that you conduct a serious and informed evaluation of our concerns.

Sincerely,

Scott Brunner, CAE
Chief Executive Officer
scott@a4pc.org

Comments of The Alliance for Pharmacy Compounding Regarding
The Notice of Proposed Regulatory Action Concerning: Compounded Drug Products

Notice of Proposed Action Concerning: Compounded Drug Products	Fiscal Impact and Related Estimates	The board indicates that the proposed changes will not have a significant adverse economic impact, including the inability of California businesses to compete with businesses in other states. The board makes these statements without

		conducting interviews gathering stakeholder feedback. The board also indicates that it does not have data to determine if its licensees are “small businesses,” which of course, many are. Holding pharmacies to a higher standard than is required by FDA and USP will cost these pharmacies, including those that are small businesses, more money to comply. The term “Small Business” is defined in California Code. The California Board of Pharmacy has over 40 inspectors who physically visit those establishments regulated by the Board. It can be assumed that Board Inspectors have the capability to determine which licensed entities they visit would qualify as a “Small Business.” We respectfully request that the Board of Pharmacy refrain from implementing these proposed regulations until an actual economic impact analysis can be performed, determining the adverse effect the proposed regulations will have on small businesses.

Discussion: As we discussed before, the proposed regulations will require small-business pharmacies to incur significant expense to come into compliance. In the initial statement of reasons, the Board said:

“While the board does not have, nor does it maintain, data to determine if any of its licensees (pharmacies and clinics) are a “small business,” as defined in Government Code section 11342.610, the board has made an initial determination that the proposed regulatory action will not affect small businesses as the proposal aligns 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.”

APC Recommendation. This determination was made without stakeholder input or feedback and is demonstrably false. APC recommends the board conduct stakeholder interviews to determine the true economic impact of the proposed compounding rules.

1735(a)	“Approved labeling” means the Food and Drug Administration’s (FDA’s) approved labeling in accordance with sections 201.56 and 201.57 of title 21, Code of Federal Regulations that include FDA approved information for the diluent, the resultant strength, the container closure system, and storage time.	As written, this definition assumes that all FDA-approved drugs have a diluent, resultant strength, and storage me. This will not always be the case.

Discussion: Proposed modified text moved “as applicable” to after “FDA approved information.” Comment accepted.

APC recommendation: Accept change.

1735(c)	“Diluent” means a liquid with no pharmacological activity used in reconstitution, such as purified water or sterile water.	If this is specifically related to manufactured products, it will work. If this is used when speaking to compounded preparations, it must specify that it is referring to USP grade purified water or USP grade sterile water. USP grade water is required as a component of nonsterile compounds.

Discussion: Comment not accepted. Staff note that section 1735.4(b) further identify the types of water.

APC recommendation: Accept section 1735.4(b) identification of water types.

1735(d)	"Essentially a copy" of a commercially available drug product means a preparation that includes the same active pharmaceutical ingredient(s) (APIs) as the commercially available drug product, except that It does not include any preparation in which there has been a change made for an identified individual patient that produces for that patient a clinically significant difference, as determined by the prescribing practitioner, between that compounded preparation and the commercially available drug product.	The FDA defines an "essential copy" as the same API; same route of administration; same, similar, or easily substitutable strength; and same characteristics as the combination of two or more commercially available drug products in the 503A copies guidance. The proposed definition makes many compounded medications copies of manufactured drugs for simply sharing the same API. Recommend aligning with the FDA approach.

Discussion: Comment not accepted. Staff note that the language provides flexibility for the clinician to use their clinical judgement when determining if a compound is essentially a copy.

APC recommendation: We continue to recommend that California aligns its definition of "essentially a copy" with the FDA's for clarity and ease of compliance.

Was 1735.1(b)	Repackaging of a conventionally manufactured drug product is not considered compounding if compliant with USP Chapter 1178, *Good Repackaging Practices*.	USP chapters over 1000 are not written for compliance purposes. See this quote from the USP General Notices: "General chapters numbered 1000 to 1999 are for informational purposes only. They contain no mandatory tests, assays, or other requirements applicable to any official article, regardless of citation in a general chapter numbered below 1000, a monograph, or these General

		Notices." Generally pharmacists can dispense an oral capsule or tablet and the patient can store it in a prescription bottle for up to one year provided that the expiration date of the product is at least that long. Following the guidance in USP 1178, the same drug could only be given no more than 6 months of dating and many times this could be shorter. This is not logical. Recommend to move away from this guidance and to not use chapters over 1000 as regulation.

Discussion: Updated modified text removes this. Comment accepted.

APC recommendation: Accept change.

Was 1735.1 (e)(2) Now 1735.1(d)(2)	For furnishing of not more than a 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.	Finishing a course of medica on, like antibiotics, is important, and many pet owners will not fill the remainder of the prescription if a full course is not provided. Veterinarians should be able to provide a full course of antibiotic agents to the owners of the animals for which they are prescribed. APC is requesting a carve-out (similar to that for ophthalmic agents) for antibiotic medications.

Discussion: Updated modified text allows for 14 day supply to be provided for antibiotics. Comment accepted.

APC recommendation: Accept change.

Was 1735.1 (f) Now 1735.1(e)	In addition to the prohibitions and requirements for compounding established in federal law, no CNSP shall be prepared that:	Prior version cited 21CFR353a. Replacing the citation with “federal law” is vague and could apply to any federal law.

Discussion: Comment not accepted.

APC recommendation: We still assert that referencing specific regulations instead of the general “federal law” provides clarity and specificity to which laws this applies.

Was 1735.1(f)(1)(A,B,C) Now 1735.1(e)(1)(A,B,C)	Is essentially a copy of one or more commercially available drug products, unless:	There is no accommodation for veterinary compounds, which are regulated under different provisions of federal law. A reference should be made to the appropriate guidance, and a section should be added to allow for compounded preparations being sold for veterinary office use where the API appears on the lists of approved or under consideration APIs for veterinary use. Subpoint A indicates that the drug must be on shortage ‘at the time of compounding and at the time of dispensing’. There should be a transition period from the time of the end of shortage. We recommend a 30-day transition period.

Discussion: Comment not accepted. Staff note that pharmacists must remain knowledgeable of current practice standards and legal requirements of the industry while exercising their professional judgement including any guidance for industry, including those issued by the FDA for veterinary patients.

APC recommendation: The final compounding regulations should reference GFI #256 where it applies to animal drug compounders.

Was 1735.1(f)(1)(B) Now 1735.1(e)(B)	Considers a compounded preparation "essentially a copy" unless the compounding produces a clinically significant different for the medical need of an identified patient, as determined by: the prescriber, the compounding pharmacist and the dispensing pharmacist.	Is it necessary to have two pharmacists involved? What if the compounding pharmacist is also the dispensing pharmacist? This is not a pharmacist's job. Furthermore, it puts the pharmacist in an adversarial position to the prescriber, questioning the prescriber's judgement. How would the pharmacy document pharmacist(s) assessment of the reason for compounding?

Discussion: Updated modified text has been changed to require only one pharmacist document the medical need for "essentially a copy" of an FDA-approved medication. This is in the supplemental responses, not the original one. Comment partially accepted.

APC recommendation: APC recommends aligning with what is required in the FDA's Essential Copy Guidance document, which does require documentation when a pharmacist dispenses a medication for which a change is made so it is not a copy of an FDA-approved product. The *prescriber* makes the determination that the compound is required, and the Board should not intend to question the prescriber's judgement. We also recommend that California provide examples of appropriate documentation to allow for all inspectors to apply the rule consistently. The Board's own definition of "essentially a copy" is as determined by the prescribing practitioner, not the pharmacist. Likewise, the pharmacist is not the one that makes the determination that the medication is required, but does document the determination on the prescription.

Was 1735.1(f)(2) Now 1735.1(e)(2)	Is made with any component not suitable for use in a CNSP for the intended patient population, unless allowable under the Animal Medicinal Drug Use Clarification Action of 1994 (AMDUCA).	As written, this eliminates the compounding of drugs for animals from API because AMDUCA does not address this. The statement says that it has to be specifically allowed under AMDUCA, and AMDUCA does not address this topic. California should align with FDA GFI 256 in

		their approach to animal compounding to maintain patient access.

Discussion: Proposed modified text changes “intended patient population” to “intended veterinary population.” Staff notes that pharmacists must remain knowledgeable of current practice standards and legal requirements while exercising their professional judgement.

APC recommendation: Sections 1735.1(e)(2) of the proposed regulations state: “No CNSP shall be prepared that is made with any component not suitable for use in a CNSP for the intended veterinary population, unless allowable under the Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA).” However, the phrase “not suitable for use in the intended veterinary population” is ambiguous and unnecessary. If a drug or excipient is toxic to a specific animal population, professional judgment and existing pharmacy practice standards already preclude its use. For decades, veterinarians have safely prescribed, and pharmacists have compounded, medications using bulk drug substances without incident. The lack of clarity in this regulation raises concerns about how the Board intends to determine “suitability.”

The reference to AMDUCA in this context is also problematic. AMDUCA permits the off-label use of FDA-approved human and animal drugs in veterinary patients but does not address compounding or bulk drug substances. The law neither explicitly allows nor prohibits compounding from bulk drug substances, and its inclusion in the regulation creates unnecessary confusion. FDA’s Guidance for Industry 256 allows for the use of bulk drug substances in compounded animal medications when there is a clinical rationale, but this guidance is not a law or regulation restricting such practices.

We are concerned that referencing AMDUCA could be misinterpreted to restrict the compounding of animal medications from bulk drug substances, a practice permitted by FDA. To avoid confusion and ensure veterinarians and pharmacists can continue providing essential compounded medications, we strongly recommend removing the reference to AMDUCA or revising the regulation to explicitly protect the ability to compound using bulk drug substances.

1735.2(a)	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…	There are many people that may handle the CNSP (lab assistants, dispensary technicians, shipping associates) who do not need to be trained on topics such as container closure, equipment selection, and component selection and handling.

Discussion: Proposed modified text removes the words “verifying, handling.” Comment accepted.

APC recommendation: Accept change.

Was 1735.2(c) Now 1735.2(b)	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.	Having people that fail any aspect of training be removed from compounding is too broad. A more nuanced approach needs to be taken based on what training was failed. If the person fails washing their hands properly, they should be excluded from compounding entirely. If they fail compounding of capsules, it does not generally mean they could not continue to compound suspensions provided that they had passed the training for that dosage form. Wording should be amended to allow the supervising pharmacist to determine the appropriate course of action based on the training needed and the training that was not passed.

Discussion: Updated modified text was changed to “shall not be involved in compounding of a CNSP until after successfully passing training and competency in the deficient…” In other words, they are still allowed to oversee compounding. Staff are offering recommended changes to the section to focus on core competencies established in the USP Chapter. Comment partially accepted.

APC recommendation: Accept change.

1735.3(a)	Prior to admitting any personnel into a compounding area, the supervising pharmacist shall evaluate them.	Is it reasonable for every employee to check in with a pharmacist at the beginning of the day to check them for rashes, oozing sores, conjunctivitis, etc.? It is typical in GMP facilities that

		it is a requirement of each person to report these symptoms to management as opposed to the pharmacist responsible to inspect each person and admit them to compounding. Requiring the pharmacist to inspect their team prior to compounding for all the listed items will create HR-related challenges and is not realistic.

Discussion: Modified proposed text was changed to "facilities shall require individuals entering the compounding area to report if the rashes, recent tattoos or oozing sores, conjunctivitis, active respiratory infection, or any other medical conditions, to determine if such condition could contaminate a CNSP or equipment." But the staff notes do not recommend a change to the language. Comment partially accepted.

APC recommendation: Accept change.

1735.3(c)	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.	As written, this would allow for the reuse of any and all disposable garb during a shift. Of the disposable garb items, only the disposable gown should be reused.

Discussion: Modified proposed text was changed to replace "all garb removed during a shift" with "gowns intended for reuse during the shift." Comment accepted.

APC recommendation: Accept change.

1735.3(e)	Non-disposable garb should be cleaned with a germicidal cleaning agent and sanitized with 70% isopropyl alcohol before re-use.	It is possible that the proposed language was intended for items such as goggles. However, it is possible that some pharmacies may have non-disposable garb, including gowns, which are laundered either by the pharmacy or by third party services. These

		gowns would be typically cleaned with the combination of agents specified in the proposed language. Clarity should be created in the wording of this language as to what non-disposable garb this is expected to be used with.

Discussion: Proposed modified text changed to “Reusable garb and equipment” and added “any reusable gowns must be laundered, per the facility’s SOPs before use.” Comment accepted.

APC recommendation: Accept change.

1735.4(b)	Purified water, distilled water, or reverse osmosis water shall be used for rinsing equipment and utensils.	USP 795 offers this as a should statement and is not required. Should this be required as written it should also allow for other waters of equal or better quality such as sterile water for irrigation or sterile water for injection.

Discussion: Modified proposed text was edited to “or higher quality water.” Comment accepted.

APC recommendation: Accept change.

1735.4(c)	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.	Recommend specifying the following as: • Vermin (e.g., insects, rodents) or other animals (e.g., dogs) or evidence of their presence (e.g., urine, feces) in the production area or adjacent areas • Visible microbial contamination (e.g., bacteria, mold) in the production area or adjacent areas. Foreign ma er in the production area (e.g., rust, glass shavings, hairs, paint chips)

		• Producing drugs while construction is underway in a nearby area without adequate controls to prevent contamination of the production area and product • Standing water or evidence of water leakage in the production area or adjacent areas • Handling bulk drug substances or drug products that are hazardous, sensi zing, or highly potent (e.g., hormones) with inadequate controls to prevent cross-contamination. • Using active ingredients, inactive ingredients, or processing aides, that have or may have higher levels of impurities compared to compendial or pharmaceutical grade equivalents (e.g., ingredients with potentially harmful impurities, ingredients labeled with “not for pharmaceutical use” or an equivalent statement)

Discussion: Comment not accepted. Staff note that pharmacists should use professional judgement and that it is not possible to develop a list that encompasses every potential scenario.

APC Recommendation: California regulations could reference FDA’s Insanitary Conditions guidance for clarity.

1735.7(c)(1)	The date and me of compounding, which is the me when compounding of the CNSP started, and which	Time becomes relevant when BUDs are relatively short (<72 hours). This would be highly uncommon for CNSPs. Recommend that the

	determines when the assigned BUD starts	language be updated to only include the day that the CNSP was compounded.

Discussion: Comment not accepted. Staff acknowledge that date OR date and time are required in USP 795 but that date AND time are required in USP 797, and their proposed regulation text ensures consistency.

APC recommendation: Reject staff reasoning, APC still encourages CABOP to align with USP.

1735.7(c)(2)	The manufacturer, lot number, and expiration date for each component.	The manufacturer of each component is a trade secret that is not required to be disclosed by federal law or federal regulation. Suggest changing the word manufacturer to supplier.

Discussion: Comment not accepted. Staff note that in USP, it requires the recording of the manufacturer or vendor, but FDA guidance indicates that the facility needs to have transparency into the supply chain and awareness of the manufacturer. They also argue that identifying the manufacturer does not appear to be requiring the disclosure of a trade secret under Civil Code 3426.1(d).

APC recommendation: Per the Civil Code, “Trade secret” means information, including a formula, pattern, compilation, program, device, method, technique or process that (1) derives independent economic value, actual or potential, from being generally known to the public or to other persons who can obtain economic value from its disclosure or use, and (2) is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.

Some pharmacy vendors maintain that the manufacturers they source API from is a trade secret and disclosure would cause economic injury.

1735.7(c)(4)	The total quantity compounded, which shall include the number of units made and the volume or weight of each unit.	Compounding software programs typically require the metric quantity of a batch prepared, but do not document the quantity of each individual unit.

Discussion: Proposed modified text was edited to “the total quantity, or amount compounded, which shall include the number of units made and the volume or weight of each unit, where applicable.” Comment partially accepted (when is it applicable?)

APC recommendation: Recommend aligning with USP Chapter <905>, *Uniformity of Dosage Units*, for ease of compliance.

1735.10(b)(1)	The chemical and physical stability data of the active pharmaceutical ingredient (API) and any added component in the preparation.	Components such as pH adjusters should be excluded from impacting the BUD of the formula on. These are typically made fresh, used, and disposed of. If the pharmacy were to document a 1-day BUD for the pH adjuster, then this language as written would cause the final preparation to have a 1-day BUD. Recommend aligning with USP's approach to exclude pH adjusters from the determination of the BUD.

Discussion: Per the staff comments "Board staff have reviewed the comment and recommend a change to the proposed regulation text to address the comment."

APC recommendation: We do not see a change in the proposed rules. Language still exists as:

1735.10. Establishing Beyond-Use Dates.

In addition to the standards set forth in USP Chapter 795, the following requirements apply to nonsterile compounding.

(a) Beyond-use dates (BUDs) assigned with only a date shall expire at 11:59 p.m. on that date.

(b) 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.

1735.10(b)(2)	(e.g. possible leachables, interactions, and storage conditions.)	Leachables per USP are extensive studies that cost several hundred thousand dollars for each drug product. It is not reasonable for compounding pharmacy to study leachables.

Discussion: Comment not accepted. Board staff argues that this is required in USP 795 Section 10.2.

APC recommendation: There are several USP chapters that apply to leachables and extractables. They apply to manufacturers making packaging materials and do not apply to pharmacies. USP 795 10.2 does indicate that a pharmacy should consider leachables, but does not indicate that the pharmacy itself must conduct leachable studies.

1735.11(a)(1)	Comply with USP Chapter 1163, Quality Assurance in Pharmaceutical Compounding	USP chapters over 1000 are not written for compliance purposes. See this quote from the USP General Notices: "General chapters numbered 1000 to 1999 are for informational purposes only. They contain no mandatory tests, assays, or other requirements applicable to any official article, regardless of citation in a general chapter numbered below 1000, a monograph, or these General Notices."

Discussion: Comment not accepted. Board staff say that the initial statement of reasons documents the basis for inclusion of USP Chapters above 1000 and that Business and Professions Code section 4126.8 establishes compliance with pharmacy compounding chapters.

APC recommendation: USP Chapters above 1000 are for informational purposes only. They **contain no mandatory tests, assays, or other requirements applicable to any article, regardless of citation in a general chapter below 1000**, a monograph or these General Notices. The Board's assertion that it is just listing out all the tests required on API (and other requirements in Chapters above 1000) is untrue. Per USP, these tests are not required, even if they are cited in chapters below 1000. We recommend removing all requirements for pharmacies outlined in the proposed regulations that reference USP chapters above 1000.

1735.11(a)(2)(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 statement "validated processes" is unclear and undefined.

Discussion: Proposed modified text added “as applicable” after shipping containers and temperature sensitive CSPs. The board staff disagrees that “validated processes” is unclear but will change to “process validation” (as defined by FDA) if needed.

APC recommendation: APC recommends changing the wording to “process validation” as it has a specified definition and is not up for interpretation.

1735.12(a)	The facility’s quality assurance program shall comply with section 1711 and the standards contained in USP Chapter 1163, entitled Quality Assurance in Pharmaceutical Compounding. In addition, the program shall include the following:	USP chapters over 1000 are not written for compliance purposes. See this quote from the USP General Notices: "General chapters numbered 1000 to 1999 are for informational purposes only. They contain no mandatory tests, assays, or other requirements applicable to any official article, regardless of citation in a general chapter numbered below 1000, a monograph, or these General Notices."

Discussion: Comment not accepted. See above.

APC recommendation: USP Chapters above 1000 are for informational purposes only. They **contain no mandatory tests, assays, or other requirements applicable to any article, regardless of citation in a general chapter below 1000**, a monograph or these General Notices. The Board’s assertion that it is just listing out all the tests required on API (and other requirements in Chapters above 1000) is untrue. Per USP, these tests are not required, even if they are cited in chapters below 1000. We recommend removing all requirements for pharmacies outlined in the proposed regulations that reference USP chapters above 1000.

1735.12(b)	The Board shall be notified in writing within 72 hours of the facility’s receipt of a complaint or a potential quality problem or the occurrence of an adverse drug event involving a CNSP.	Adverse events are expected as a potential occurrence with the use of a drug and may not represent a quality-related problem with the compounded medication. As written, the board will have to hear about every adverse effect related to a CNSP whether it is related to the

		quality of the CNSP or not. This type of reporting may drown out the reports the board needs to be aware of for a CNSP that has a quality problem. Suggest that this be changed to have the reporting occur when the adverse drug event is related to a quality problem and is not an adverse event that is generally expected to occur with the use of the drug. Pharmacies should investigate potential quality problems. It will take longer than 72 hours to conduct those investigations, as well. The board will be notified of occurrences prior to them being able to be fully investigated.

Discussion: The proposed modified text was change to 96 hours and "drug event" was changed to "adverse drug experience as defined in 21 CFR 310.305(b)." Comment partially accepted.

APC recommendation: Expanding the timeline to 96 hours is an improvement, however, we still assert that pharmacies should fully investigate an adverse drug experience before notifying the Board.

1735.13	In addition to the standards set forth in USP 795, the facility shall ensure appropriate processes for storage, shipping containers and temperature sensitive CNSPs as provided for in the facility's SOPs.	The statement "validated processes" is unclear and undefined.

Discussion: Comment not accepted. See above.

APC recommendation: APC recommends changing the wording to "process validation" as it has a specified definition and is not up for interpretation.

1736.1(e)	"Essentially a copy" of a commercially available drug product means a preparation that includes the same active pharmaceutical ingredient(s) (APIs) as the commercially available drug product, except that It does not include any preparation in which there has been a change made for an identified individual patient that produces for that patient a clinically significant difference, as determined by the prescribing practitioner, between that compounded preparation and the commercially available drug product.	The FDA defines an "essential copy" as the same API; same route of administration; same, similar, or easily substitutable strength; and same characteristics as the combination of two or more commercially available drug products. Recommend that California align with FDA's description used in the 503A copies guidance.

Discussion: Comment not accepted.

APC recommendation: APC recommends aligning with what is required in the FDA's Essential Copy Guidance document, which does require documentation when a pharmacist dispenses a medication for which a change is made so it is not a copy of an FDA approved product. The *prescriber* makes the determination that the compound is required, and the Board should not intend to question the prescriber's judgement. We also recommend that California provides examples of appropriate documentation to allow for all inspectors to apply the rule consistently. The Board's own definition of "essentially a copy" is as determined by the prescribing practitioner, not the pharmacist. Likewise, the pharmacist is not the one that makes the determination that the medication is required, but does document the determination on the prescription.

1736.1(b)	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 CSPs could result in loss of life or intense suffering of an identifiable patient…	There are many other times that CSPs should be compounded for direct and immediate administration other than loss of life or intense suffering. USP removed the emergency situation requirement for immediate-use CSPs. An

		example of when this might be required is during the shortage of lidocaine with epinephrine. Clinics could use available ingredients (lidocaine vials, epinephrine vials) to compound multiple syringes for use in multiple patients over a 4- hour period. This medication is often needed for infiltration and nerve block.

Discussion: Proposed modified text adds a section allowing this compounding for immediate use if the compounding equipment or environment fails to meet any required specifications without the "loss of life" provision, but only for 24 hours after the failure and the failure must be reported to the BOP within 72 hours. Subdivision (c) allows for a limited quantity of CSPs to be prepared and stored in advance of receipt of a patient specified prescription document where, and solely in such quantity, as is necessary to ensure continuity of care for identified patients based on a documented history of prescriptions for that patient population.

APC recommendation: APC recommends that 24 hours is not enough time after an equipment or environmental failure to always be corrected, and reporting to the Board of each equipment or environmental failure within 72 hours is excessive.

1736.1(e)(1)(A,B,C)	Is essentially a copy of one or more commercially available drug products, unless:	There is no accommodation for veterinary compounds, which are regulated under different provisions of federal law. A reference should be made to the appropriate guidance, and a section should be added to allow for compounded preparations being sold for veterinary office use where the API appears on the lists of approved or under consideration APIs for veterinary use.

Discussion: Comment not accepted.

APC recommendation: The final compounding regulations should reference GFI #256 where it applies to animal drug compounders.

1736.1(e)(2)	Is made with any component not suitable for use in a CSP for the intended patient population, unless allowable under the Animal Medicinal Drug Use Clarification Action of 1994 (AMDUCA).	As written, this eliminates the compounding of drugs for animals from API because AMDUCA does not address this. The statement says that it must be specifically allowed under AMDUCA, and AMDUCA does not address this topic. California should align with FDA GFI 256 in their approach to animal compounding to maintain patient access.

Discussion: Proposed modified text changes “intended patient population” to “intended veterinary population.” Comment not accepted.

APC recommendation: Sections 1736.1(e)(2) of the proposed regulations state: “No CSP shall be prepared that is made with any component not suitable for use in a CSP for the intended veterinary population, unless allowable under the Animal Medicinal Drug Use Clarification Act of 1994 (AMDUCA).” However, the phrase “not suitable for use in the intended veterinary population” is ambiguous and unnecessary. If a drug or excipient is toxic to a specific animal population, professional judgment and existing pharmacy practice standards already preclude its use. For decades, veterinarians have safely prescribed, and pharmacists have compounded, medications using bulk drug substances without incident. The lack of clarity in this regulation raises concerns about how the Board intends to determine “suitability.”

The reference to AMDUCA in this context is also problematic. AMDUCA permits the off-label use of FDA-approved human and animal drugs in veterinary patients but does not address compounding or bulk drug substances. The law neither explicitly allows nor prohibits compounding from bulk drug substances, and its inclusion in the regulation creates unnecessary confusion. FDA’s Guidance for Industry 256 allows for the use of bulk drug substances in compounded animal medications when there is a clinical rationale, but this guidance is not a law or regulation restricting such practices.

We are concerned that referencing AMDUCA could be misinterpreted to restrict the compounding of animal medications from bulk drug substances, a practice permitted by FDA. To avoid confusion and ensure veterinarians and pharmacists can continue providing essential compounded medications, we strongly recommend removing the reference to AMDUCA or revising the regulation to explicitly protect the ability to compound using bulk drug substances.

1736.1(e)(3)	Is made with a non-sterile component for which conventionally manufactured sterile component is available and appropriate for the intended CSP.	In some cases, starting with the non-sterile component would be more appropriate (excipients in the conventionally manufactured product, tonicity, concentration). Depending on batch size and compounding set-up, using a conventionally manufactured sterile product as opposed to bulk ingredients could cause more sterility issues and potency variability among units prepared (e.g., exponentially increased manual manipulations by repetitively entering vials or bags to transfer a portion of liquid to the finished preparation increases the potential for contamination and variability as these processes are primarily manual.) Additionally, starting with nonsterile ingredients already shortens the BUD of the final product. Does “conventionally manufactured” mean commercially available?

Discussion: Proposed modified text was edited to “is made with a non-sterile component for which a conventionally manufactured sterile component is available and appropriate for the intended CSP, unless the CSP is compounded in full compliance with USP 797 Category 3 requirements, or the conventionally manufactured sterile component appears on the ASHP or FDA shortage list.” Comment partially accepted.

APC recommendation: APC recommends allowing for compounding with non-sterile starting ingredients outside of full Category 3 requirements or shortages when it makes more sense for the product to be compounded with API rather than finished form injectable products.

1736.1(e)(4)	Requires end-product sterilization unless sterilization occurs within the same licensed compounding location.	This would prevent the use of e-beam or gamma-irradiation sterilization methods, which are performed off-site at validated facilities. Can the board demonstrate the harm caused to patient care by offsite sterilization?

Discussion: Comment not accepted. Staff notes that in September 2019, counsel advised members that sterile compounding has to occur in a single pharmacy.

APC recommendation: E-beam sterilization is an FDA approved process. It is recognized and accepted by international standards organizations, and should be allowed.

1736.2(d)	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 a er a failure of any aspect while applicable aseptic manipulation ongoing training and competency evaluation results are pending.	The person with direct oversight who fails will need more than 14 days after the failure if this involves a media-fill failure. The incubation of a media-fill takes 14 days at a minimum per 797. Unless the person can do a media-fill on the same day that their media-fill failure is known, they will not be able to continue to provide that direct oversight for some number of days. Recommend that this me be extended to 21 days. Similar to the comment in nonsterile compounding, removing people from performing all compounding due to a failure in any training area is not appropriate. A more nuanced approach should be used. If a person fails in their use of an autoclave, they could still compound solutions that are prepared aseptically or by

		filtration, assuming that they passed all training and competency for those processes. The supervising pharmacist needs to be able to determine areas of training and competency that would cause the compounder to be completely removed from all compounding of CSPs.

Discussion: Proposed modified text removes the section that does not allow oversight of the preparation of a CSP until after passing training and competency in a deficient area, and changes the timeframe to 30 days. Comment partially accepted.

APC recommendation: Accept change.

Was 1736.6(a) Now 1736.6	At a minimum of every six months, air and surface sampling results should be identified to at least the genus level. Investigation must be consistent with the deviation and must include evaluation of trends.	The second sentence is not clear. What deviation is this referring to? Is there an assumption that the sampling will result in a deviation or there will be results exceeding the action limits?

Discussion: This was removed. Comment accepted.

APC recommendation: Accept change.

1736.9(d)	All API and excipient components used to compound a CSP shall be manufactured by an FDA-registered facility, be 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	Most excipient components are sold by FDA-registered wholesalers but are not manufactured by FDA-registered facilities. FDA registration is required of manufacturers of food, beverages, dietary supplements, cosmetics, animal and veterinary products, medical devices, drug products, tobacco

	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 with a COA without this data shall not be used in a CSP.	products, radiation-emiting devices, and biologics. What is meant by "suitable for use in sterile pharmaceuticals?" Additionally, not all wholesalers or repackagers include the original manufacturer name or address on the COA, as they assert that is a trade secret. Trade secrets should be protected under California law.

Discussion: Proposed modified text was changed to remove components/excipients. Comment partially accepted, but industry still does not put the original manufacturer's name and address on the COA. They do not agree that requiring this would be requiring a disclosure of a trade secret under Civil Code 3426.1(d).

APC recommendation: Per the Civil Code, "Trade secret" means information, including a formula, pattern, compilation, program, device, method, technique or process that (1) derives independent economic value, actual or potential, from being generally known to the public or to other persons who can obtain economic value from its disclosure or use, and (2) is the subject of efforts that are reasonable under the circumstances to maintain its secrecy.

Some pharmacy vendors maintain that the manufacturers they source API from is a trade secret and disclosure would cause economic injury.

1736.9(e)	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 21 CFR 216, unless authorized by a public health official in an emergency use situation for a patient-specific compounded sterile preparation.	21 CFR 216 only includes items on the Final FDA bulks list, and not anything on the interim bulks list (category 1 items). Removal of the ability to use these agents in a CSP will harm California patients who require these medications, and who cannot get them otherwise.

Discussion: Proposed modified text was edited to “except as provided in 2…” which allows for compounding with bulk drug substances which FDA has determined that a nomination included adequate information for the FDA to evaluate the substance, it does not present safety risks, and is included on 503A category 1 interim list BUT must be compounded only after completion of a full stability study, and then dispensed after receipt of a prescription that documents the clinical need of a BDS from interim bulks list 1. The stability study is required no matter the category of USP compounding being performed. This will limit compounding with specialized dosage forms and strengths/combinations as pharmacies will likely only perform stability studies on one dosage form/strength. Additionally, in 1736.17(e), the proposed text requires testing of these BDS in category 1 above and beyond what is required by USP or FDA – testing per USP 1097. USP Chapters about 1000 are for informational purposes only. They contain no mandatory tests, assays, or other requirements applicable to any official article, regardless of citation in a general chapter numbers below 1000. Comment partially accepted.

APC recommendation: Items in FDA’s Interim Bulks List 1 are allowed to be used in compounded drug products by the FDA and every other state. They should not have requirements that are different than any other API. Pharmacies must use a grade of API that is appropriate for sterile compounding. Stability studies are not required for other API compounded under Category 1 or 2, and will limit patient access to specialized therapies like inhaled glutathione. There is no point in endotoxin testing API and then also requiring endotoxin testing of the CSP.

1736.10	The entire section references various USP chapters numbered over 1000.	From USP's General Notices: "General chapters numbered 1000 to 1999 are for informational purposes only. They contain no mandatory tests, assays, or other requirements applicable to any official article, regardless of citation in a general chapter numbered below 1000, a monograph, or these *General Notices*."

Discussion: Comment not accepted. See above.

APC recommendation: USP Chapters above 1000 are for informational purposes only. They **contain no mandatory tests, assays, or other requirements applicable to any article, regardless of citation in a general chapter below 1000**, a monograph or these General Notices. The Board’s assertion that it is just listing out all the tests required on API (and other requirements in Chapters above 1000) is untrue. Per USP, these tests are not required, even if

they are cited in chapters below 1000. We recommend removing all requirements for pharmacies outlined in the proposed regulations that reference USP chapters above 1000.

1736.10(e)	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.	This would prevent the use of e-beam or gamma-irradiation sterilization methods, which are performed off-site at validated facilities

Discussion: Comment not accepted. See above.

APC recommendation: E-beam sterilization is an FDA approved process. It is recognized and accepted by international standards organizations, and should be allowed.

1736.12(b)	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 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.	This places the burden of ensuring validation of an alternative method for sterility testing is done in compliance with USP Chapter 1223 on the pharmacist. Valida on should be provided by the Analytical Laboratory performing the alternative method and maintained by the pharmacy as part of the compounding record.

Discussion: Proposed modified text includes mild wording edits that did not change meaning. Comment not accepted.

APC recommendation: USP Chapters above 1000 are for informational purposes only. They **contain no mandatory tests, assays, or other requirements applicable to any article, regardless of citation in a general chapter below 1000**, a monograph or these General Notices. The Board's assertion that it is just listing out all the tests required on API (and other requirements in Chapters above 1000) is untrue. Per USP, these tests are not required, even if they are cited in chapters below 1000. We recommend removing all requirements for pharmacies outlined in the proposed regulations that reference USP chapters above 1000.

1736.12(c)	A pharmacist performing or supervising sterile compounding is responsible for ensuring injectable CSPs made from nonsterile components, regardless of Category, are tested to ensure they do not contain excessive bacterial endotoxins, as established in USP Chapter 85, Bacterial Endotoxins. Results must be reviewed and documented in the compounding records prior to furnishing.	For Category 2 CSPs that are not sterility tested, it is impractical and would hinder patient care to wait for endotoxin testing to release the CSP. In addition, CSPs that use nonsterile starting components and are not sterility tested only have a 4-day BUD. Typical endotoxin testing would not be available before the end of the BUD.

Discussion: Proposed modified text includes wording edits that did not change the endotoxin testing requirements. Board staff note that endotoxin testing can be performed in-house and that it is limited to injectable CSPs. Comment not accepted.

APC recommendation: Recommend aligning with USP standards for endotoxin testing.

1736.13(a)(2)	The solution utilized, if applicable.	Clarify what this means.

Discussion: Proposed modified text changed to “for CSPs administered by infusion, the solution utilized.” Comment accepted.

APC recommendation: Accept change.

1736.14(a)(1)	The chemical and physical stability data of the active pharmaceutical ingredients(s) and any added substances in the preparation.	Components such as pH adjusters should be excluded from impacting the BUD of the formulation. These are typically made fresh, used, and disposed of. If the pharmacy were to document a 1-day BUD for the pH adjuster, then this language as written would cause the final preparation to have a 1-day BUD. Recommend aligning with USP’s approach to exclude pH adjusters from

		the determination of the BUD.

Discussion: Per notes, Board staff considered the comment and recommended a change in the proposed language as it is consistent with appropriate compounding practices.

APC recommendation: We do not see the change referenced by the Board. Still reads:

(a) 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;

1736.14(c)	Prior to furnishing a CSP, the pharmacist performing or supervising sterile compounding is responsible for ensuring that sterility and endotoxin testing for the BUD determination is performed and has received and reviewed the results. Results must be within acceptable USP limits. Test results must be retained as part of the compounding record.	Sterility testing can take more than 2 weeks for results to be reported, and patients may need access to the compounded preparations before testing results are available. Restricting formulations to release after testing creates a situation where patients could be denied a medication if testing cannot be performed fast enough to prevent suffering or patient harm.

Discussion: Proposed modified text includes some wording changes but still includes testing requirements and review prior to release. Comment not accepted.

APC recommendation: Recommend aligning with USP, allowing release before receipt of sterility and endotoxin results as long as the pharmacy has a program in place in the event they need to perform a recall.

1736.17(g)	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.	The statement "validated processes" is unclear and undefined. What does the Board consider to be a validated process? Temperature mapping, thermal mapping, or must standardized tests be used (International Safe Transit Association standards 3A, 20,

		7D and 7E or the ASTM International Standard D3103)?

Discussion: Comment not accepted.

APC recommendation: No change.

1736.18(c)	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 shal be documented and dated as defined in the SOPs.	Adverse events are expected as a potential occurrence with the use of a drug and may not represent a quality related problem with the compounded medica on. As written, the board will have to hear about every adverse effect related to a CSP, whether or not it is related to the quality of the CSP. This type of reporting may drown out the reports that the board needs to be aware of for a CSP that has a quality problem. Suggest that this be changed to have the reporting occur when the adverse drug event is related to a quality problem and is not an adverse event that is generally expected to occur with the use of the drug. Pharmacies should investigate potential quality problems. It will take longer than 72 hours conduct those investigations, as well. The board will be notified of occurrences prior to them being fully investigated.

Discussion: Proposed modified text changes language from “adverse event” to “adverse drug experience” which does not change the meaning or 72 hour requirement. Changed language to

allow for reporting of the event by someone other than the PIC when they are not available. Comment partially accepted.

APC recommendation: A requirement of 72 hours may not provide sufficient time for pharmacies to investigate and notify the necessary regulatory bodies in cases where it occurs over the holiday weekend. Additionally, the Board may be notified of adverse events before they have been investigated.

1736.21(a)	Any allergenic extract compounding shall take place in a dedicated PEC. No other CSP made be made in this PEC.	Compounding of allergenic extracts per USP may be done in a PEC or a dedicated Allergenic Extracts Compounding Area. The PEC is not required to be used only for allergenic extracts. This requirement is onerous and will restrict access of this vital medication therapy.

Discussion: Proposed modified text was changed to allow for compounding of other CSPs in the PEC after cleaning. Comment accepted.

APC recommendation: Accept change.

1736.21(b)	Compounding of allergenic extracts are limited to patient-specific prescriptions and conditions limited to Category 1 and Category 2 CSPs as specified in USP Chapter 797.	Allergenic extracts are in a category of their own, and USP allows up to a one-year BUD a er preparation without sterility testing. If pharmacies have to treat them as a category 1 or 2 CSP, the short BUDs will prevent patient access. Additionally, this is more onerous than FDA's approach to compounding these preparations, as discussed in their Biologics guidance document.

Discussion: Proposed modified text removes this section. Comments accepted.

APC recommendation: Accept change.

Was 1737.6(a)(b) Now 1737.6	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.	There are no standards for contamination action levels for HD drugs. Wipe sampling is recommended in USP 800 but not required, as there is no consensus on what to do with the results.

Discussion: Proposed modified text was changed remove “levels of measurable contamination, and actions when those levels are exceeded.” Comment partially accepted.

APC recommendation: Why perform wipe sampling when there are no limits and there is no action required based on results. Recommend wipe sampling not be a requirement, as in USP 800.

1737.7(d)	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	As written, this assumes that there is only a positive pressure anteroom which would require the PPE to be removed in the CSEC. Some facilities have a negative pressure anteroom where the PPE could be removed so that it does not have to be removed in the negative pressure buffer room. These facilities with a negative pressure anteroom also have a positive pressure gowning room.

Discussion: Proposed modified text changes to “PPE removal process shall be done in a manner to avoid transferring contamination to the skin…” and Added “Outer” to the PPE definition. Comment partially accepted.

APC recommendation: Accept change.

1737.9(b)	Personnel responsible for handling HDs who fail any aspect of training in handling HDs shall not handle HDs	As noted in other areas of compounding, failing one area of training may not mean that a person should

	until after successfully passing reevaluations in the deficient area(s), as detailed in the facility's SOPs.	be removed from handling of HDs entirely. The supervising pharmacist needs discretion to determine if the area failed should cause complete removal of the individual.

Discussion: Proposed modified text has changes in wording that allow for a 14-day period for the supervising pharmacist to continue while undergoing new assessment.

APC recommendation: Accept change.

1737.13(a)	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 the daily compounding activity.	Change "the mat must be sterile" to "the mat must be cleaned with germicidal cleaner and then sanitized with sterile 70% IPA prior to use."

Discussion: Proposed modified text changed to "if a disposable preparation mat is used…" Comment accepted.

APC recommendation: Accept change.

1737.14(b)	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.	Who bears liability if the patient refuses to pay for the gloves? Who bears liability if the patient does not use the gloves that shall be made available for purchase?

Discussion: Proposed modified text wording changed that did not change the requirement. Comment not accepted.

APC recommendation: 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 should be made available, when needed.

UC San Diego Health

December 1st, 2024

California Board of Pharmacy
2720 Gateway Oaks Drive, Suite 100
Sacramento, CA 95833

Dear Anne Sodergren,

This letter is to provide comments on the proposed California Code of Regulations 1735-1738.14

1. 1735.7 Master Formulation and Compounding Records. subsection (c)(2):
    a. Proposed Regulation: (c)(3) The manufacturer, lot number, and expiration date for each component for the CSP.

    b. Comments: Current language in CCR 1735.3 below has a provision for CSPs compounded in health facilities to prevent delays in care to acutely ill patient, i.e. infections, cancer, critical care, etc. The current language states:
        - (F) The manufacturer, expiration date and lot number of each component. If the manufacturer name is demonstrably unavailable, the name of the supplier may be substituted. If the manufacturer does not supply an expiration date for any component, the records shall include the date of receipt of the component in the pharmacy, and the limitations of section 1735.2, subdivision (l) shall apply. Exempt from the requirements in this paragraph (1735.3(a)(2)(F)) are sterile preparations compounded in a single lot for administration within seventy-two (72) hours to a patient in a health care facility licensed under section 1250 of the Health and Safety Code and stored in accordance with standards for “Redispensed CSPs” found in Chapter 797 of the United States Pharmacopeia – National Formulary (USP37-NF32) Through 2nd Supplement (37th Revision, Effective December 1, 2014), hereby incorporated by reference.

    c. **Recommendation**: To prevent delays in care to acutely ill patients, recommend the board consider including the same exemption language to the 1735.7 Master Formulation and Compounding Records, subsection (c)(2):

        The manufacturer, lot number, and expiration date for each component.
        (i) **Exempt from the requirements in this paragraph are non-sterile preparations compounded in a single lot for administration within seventy-two (72) hours to a patient in a health care facility licensed under section 1250 of the Health and Safety Code.**

2. 1736.1 Sterile Compounding Scope. Subsection (b)(2):
    a. **Proposed Regulation**: *2) If the sterile compounding equipment or environment fail(s) to meet any required specification, an immediate use CSP may be compounded without the requirement for there to be loss of life or intense suffering of an identifiable patient. This provision may only be used for 24 hours after such failure(s). All such failures must be documented in accordance with facility’s SOP and shall be reported to the BOP within 72 hours.*

    b. **Comments**: Requiring health-system pharmacies to remedy equipment failures within 24 hours may not be feasible due to a variety of reasons why there could have been equipment failures. Often times, it may take more than 24 hours to remedy. To use outside facility or vendor to provide compounding preparations would still pose a safety risk as they may not be following the health-systems processes and procedures. Given the concerns about potential audits, institutions may hesitate to report issues to the Board of Pharmacy. We urge the Board to embrace a 'Just Culture' framework, which emphasizes accountability and learning over punitive measures.

    c. **Recommendation**: To remove the requirement for immediate use compounding under this provision to be used for 24 hours after such failure(s), and requiring such failures must be documented in accordance with facility’s SOP and shall be reported to the BOP within 72 hours.

    CCR 1736.1 Introduction and Scope. Subsection (b) (2):
    (2) *If the sterile compounding equipment or environment fail(s) to meet any required specification, an immediate use CSP may be compounded under the immediate use compounding requirements of USP 797. This provision may only be used for 7 business days after such failure(s). All such failures must be documented in accordance with facility’s SOP and shall be available upon inspection.*

3. 1736.1 Introduction and Scope. Subsection (h):
    a. **Proposed regulation**: *h) CSPs with human whole blood or human whole blood derivatives shall be produced in compliance with Health and Safety Code section 1602.5.*

    b. **Comments:** The current health and safety code section 1602.5 states the following:
    (a) No person shall engage in the production of human whole blood or human whole blood derivatives unless the person is licensed under this chapter and the human whole blood or human whole blood derivative is collected, prepared, labeled, and stored in accordance with both of the following:"

    The proposed regulation in its current state would cause confusion as it would enforce a law that is not applicable to any human whole blood or human whole blood derivative that is already manufactured by a pharmaceutical company (e.g. Albumin, Factor products, IVIG etc.)

    c. **Recommendation:** Would recommend the board to revise the proposed language to provide clarification to state that the regulation does not apply to CSPs made with human blood/derivative that is manufactured by pharmaceutical companies.

    (h) CSPs with patient's own whole blood or human whole blood derivatives from the patient shall be produced in compliance with Health and Safety Code section 1602.5.

4. 1736.2 Personnel Training and Evaluation. Subsection (d)
    a. **Proposed regulation**: *(d) Compounding personnel or persons with direct supervision and control of compounding personnel who fail any aspect of the aseptic manipulation ongoing training and competency evaluation shall not be involved in compounding 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 supervision and control of 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 30 days after a failure of any aspect while applicable aseptic manipulation ongoing training and competency evaluation results are pending*

    b. **Comments:** Multiple factors can contribute to failure of staff in aseptic technique training and competency evaluation including environmental testing failure, and engineering control failure. Prohibiting compounding personnel from compounding without an evaluation of contributing factors and timeframe would significantly disrupt patient treatment and for jeopardize health-systems ability to operate.

    c. **Recommendation:** (d) 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 including performing in-process checks, final verification, and dispensing of CSPs for no more than 30 days after a failure of any aspect while applicable aseptic manipulation ongoing training and competency evaluation results are pending.**

5. 1736.11 Master Formulation and Compounding Records. subsection (c)(2):
    a. **Proposed regulation**: (c)(2) The manufacturer, lot number, and expiration date for each component for the CSP.
    b. **Comments:** Current language in CCR 1735.3 below has a provision for CSPs compounded in health facilities to prevent delays in care to acutely ill patient, i.e. infections, cancer, critical care, etc. The current language states: (F) The manufacturer, expiration date and lot number of each component. If the manufacturer name is demonstrably unavailable, the name of the supplier may be substituted. If the manufacturer does not supply an expiration date for any component, the records shall include the date of receipt of the component in the pharmacy, and the limitations of section 1735.2, subdivision (l) shall apply.
    (i) *Exempt from the requirements in this paragraph (1735.3(a)(2)(F)) are sterile preparations compounded in a single lot for administration within seventy-two (72) hours to a patient in a health care facility licensed under section 1250 of the Health and Safety Code and stored in accordance with standards for "Redispensed CSPs" found in Chapter 797 of the United States Pharmacopeia – National Formulary (USP37-NF32) Through 2nd Supplement (37th Revision, Effective December 1, 2014), hereby incorporated by reference.*

    c. **Recommendation:**
    Add back the language above: 1736.11 Master Formulation and Compounding Records, subsection (c)(3) The manufacturer, lot number, and expiration date shall be recorded for each component for CSPs.

(i) Exempt from the requirements in this paragraph are sterile preparations compounded in a single lot for administration within seventy-two (72) hours to a patient in a health care facility licensed under section 1250 of the Health and Safety Code.

6. 1737.5 Facilities and Engineering Controls. Subsection (c)
    a. **Proposed Regulation***: (c)Effective [OAL insert six months following the effective date] A a pass-through is not allowed between the hazardous drug buffer room C-SEC into an unclassified space*

    b. **Comments:**

        - USP 800 does not prohibit using a pass-through between a classified space and an unclassified space. The way this is currently worded it would make it so having a pass-through would be very difficult and to be in compliance. This would be a major operational challenge and may impact patient care.

        - In speaking with many experts who design and construct clean rooms there has never been an issue with a pass-through between classified to unclassified as long as the doors are interlocking. Even the FDA in their guidance for 503b compounding facilities states material flow directly between unclassified room and sterile compounding area is allowed as long as it is classified so a HEPA filtered pass through would be ok to use. Of note the FDA does not call out hazardous compounding only so not sure why hazardous is being singled out with this requirement.

        - If the intent is for the pass-through that is between a classified space and unclassified space to be HEPA purge type only then I would recommend the below language. Alternatively, if the intent is to be cautious of some presumed contamination requiring some sort of wipe sampling would more appropriate to accomplish this goal.

    c. **Recommendation**: Revise language to be consistent with USP 800 or FDA language.

        1737.5 Facilities and Engineering Controls:
        (c) Effective [OAL insert six months following the effective date] a material flow directly between an unclassified area and a room in which sterile compounding is conducted (e.g., unclassified pass-through) is not allowed.
            - An existing secondary engineering control that has a pass-through between classified and unclassified may continue to be used if the SOP's document that two doors are interlocking and the facilities SOP's outline hazardous wipe sampling to monitor for contamination.

7. 1737.7 Personal Protective Equipment (PPE), subsection (c).
    a. **Proposed Regulation***: (c) Outer gloves used for HD compounding shall be changed between each different HD preparation.*

    b. **Comments:**

        - USP 800 says the following:
            - Chemotherapy gloves should be changed every 30 minutes unless otherwise recommended by the manufacturer's documentation and must be changed when torn, punctured, or contaminated.

        - Many health-systems use closed system transfer device (CSTD) when compounding antineoplastic HDs. The use of CSTD has shown to significantly reduce overall chemical contamination (12.24% vs. 26.39%).1
        - Double-gloving is primarily designed to offer extra protection against hazardous drug compounds, with the outer glove serving as a first line of defense. If the outer glove is repeatedly removed or exposed to rough conditions, it may wear down, possibly increasing the risk of puncturing or compromising the inner glove. This could lead to reduced protection, especially when handling hazardous drug compound.2,3
        - Frequent removal and disposal of outer glove changes creates significant waste.2

        Reference

            - Simon N, Vasseur M, Pinturaud M, et al. Effectiveness of a Closed-System Transfer Device in Reducing Surface Contamination in a New Antineoplastic Drug-Compounding Unit: A Prospective, Controlled, Parallel Study. Ahmad A, ed. PLoS One 2016;11:e0159052. Available at: https://dx.plos.org/10.1371/journal.pone.0159052.

            - Kirk H. Double gloving when handling cytotoxic drugs. Hospital Pharmacy Europe.

Published March 2, 2009. Available from: https://hospitalpharmacyeurope.com/news/editors-pick/double-gloving-when-handling-cytotoxic-drugs/

- McNeilly L. Double gloving: Myth versus fact. Infection Control Today. Published May 5, 2011. Available from: https://www.infectioncontroltoday.com/view/double-gloving-myth-versus-fact

c. **Recommendation**: Revise language to be consistent with USP 800 or as follows:
   - *(c) Outer gloves used for HD compounding shall be changed between each different HD preparation if a closed system transfer device (CSTD) is not used*

8. 1737.14 Administering subsection (b)

a. **Proposed Regulation:** *(b) When dispensing a compounded antineoplastic HD to a patient or patient's agent, a sufficient supply of ASTM D-6978 standard gloves, shall be provided to the patient or the patient's agent, to allow for appropriate administration, handling, and disposal of the HD.*

Comments: In health facilities where antineoplastic HD are dispensed and administered by licensed health care professionals who are trained to handle HDs. Supplies such as ASTM D-6978 grade gloves, and HD disposal bins are readily available.

Recommendation: Recommend adding exemption language to the current proposed language for HSC 1250 (a) licensed facilities as the administration of compounded medications to patients are done by health care personnel trained and authorized to administer HD medications and not dispensed for outpatient use. Exempt from this requirement are health facilities, as defined in Section 1250 of the Health and Safety Code, if the prescriptions are administered by a licensed health care professional.

Sincerely,

Sam Martinez

Sam Martinez, PharmD, BCOP
Outpatient Infusion Pharmacy Manager
UC San Diego Health

Stanford MEDICINE | Health Care

December 6th, 2024

Lori Martinez
California State Board of Pharmacy
2720 Gateway Oaks Dr., Ste. 100
Sacramento, CA 95833

Re: Title 16. Board of Pharmacy Proposed Regulation

Dear Ms. Martinez,

Stanford Health Care Pharmacy leadership would like to thank the California State Board of Pharmacy (Board) for the opportunity to provide public comment on the proposed rulemaking for compounded drug products and the handling of hazardous drugs. We share the Board's values and unwavering commitment to enhancing the practice of pharmacy while promoting the health and safety of Californians.

While we appreciate the Board's rationale outlined in the Initial Statement of Reasons document for the proposed changes, we do not share the sentiment that additional requirements are necessary to "strengthen" United States Pharmacopeia (USP) chapters <795>, <797>, or <800> standards. **We strongly urge the Board to adopt USP chapters <795>, <797>, and <800> as currently written**.

We acknowledge that in the past, additional requirements for compounded drug products from the Board were necessary due to outdated USP standards; however, this is no longer a concern. The published revisions of USP <795>, <797>, and <800> have undergone extensive review and careful decision-making by an expert committee. Revised chapters are now both current and comprehensive. Furthermore, creating new requirements that do not align with other regulatory and accreditation bodies (e.g., California Department of Public Health, The Joint Commission) can lead to confusion and unnecessary challenges in maintaining compliance.

Should the Board decide to proceed with further clarification and strengthening of USP standards, we have provided our public comments on the original and modified proposed amendments to Article 4.5, and the additions of Articles 4.6 and 4.7 attached to this message.

On behalf of the pharmacists-in-charge (PICs) and the pharmacy leadership at Stanford Health Care, we would like to thank the Board for its consideration. Should you have any questions, please do not hesitate to contact us.

Sincerely,

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Stanford MEDICINE | Health Care

Comments on the Board of Pharmacy's Proposed Regulation

Section, Subdivision	Proposed Language	Recommendation/Comment
Articles 4.5, 4.6, 4.7		
1735(b)	*"Designated person(s)" means 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 CNSPs for the purposes of this article.*	**Comment:** Can the pharmacist-in-charge assign themselves to be the designated person? For smaller pharmacies with a limited number of employees, it may be difficult to identify someone interested and willing to take on the responsibilities of the designated person. **Recommendation:** Revise language to allow the pharmacist-in-charge the option to assign themselves to be the designated person.
1736(c)	*"Designated person(s)" means 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 CNSPs/compounded sterile preparations.*	
1737.2(a)	*The designated person must be 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.*	
Article 4.5 Nonsterile Compounding		
1735.3(a)	*Prior to admitting any personnel into a compounding area, the supervising pharmacist shall evaluate whether personnel is experiencing any of the above conditions could contaminate a CNSP or the environment. After such evaluation and determination, the supervising pharmacist shall not allow personnel with potentially contaminating conditions to enter the compounding area.*	**Comment:** This language does not align with the BOP's requirement for sterile compounding. The BOP's proposed section 1736.3 does not require a supervising pharmacist to evaluate all sterile compounding personnel for specific contaminating conditions before entering the compounding area. This requirement may not be feasible for a high-volume pharmacy (e.g., a large hospital pharmacy) with numerous employees who may be asked to compound at any given time. Additionally, supervisors have raised concerns that this may require them to ask staff personal questions about their health conditions, which may be seen as inappropriate.

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		Recommendation: Remove language to be consistent with USP 795, where it is the responsibility of the compounding person to report contaminating conditions to the designated person(s); or Revise the language to read: "If the supervising pharmacist observes personnel experiencing any of the conditions mentioned above and determines that such personnel pose a risk to CNSPs or the environment, the supervising pharmacist shall prohibit the individual from entering the compounding area."
1735.6(a)	*Any equipment used to compound a CNSP shall be used in accordance with the manufacturer's specifications.*	**Comment:** Manufacturer specifications are not always available for all compounding equipment (e.g., mortar and pestle). **Recommendation:** Revise language to read: *"Any equipment used to compound a CNSP shall be used in accordance with the manufacturer's specification or, in the absence of such specifications, in accordance with professional standards of use."*
1735.7(c)(1)	*(c) A compounding record (CR) shall be maintained and, upon request, be produced as a single document developed in compliance with USP Chapter 795, and includes the following additional elements:* *(1) The date and time of compounding, which is the time when compounding the CNSP started, and which determines when the assigned BUD starts.*	**Comment:** Clarify statement. **Recommendation:** Revise language to read: *"(1) The date and time of compounding, which is the time when compounding the CNSP began, and is the time from which the assigned BUD is determined."*
1735.7(c)(5)	*(c) A compounding record (CR) shall be maintained and, upon request, be produced as a single document developed in compliance with USP Chapter 795, and includes the following additional elements:* *(5) The identity of personnel performing the compounding, pharmacist who has direct supervision and control of compounding, and the pharmacist verifying the final drug preparation.*	**Comment:** The pharmacist who has direct supervision and control of compounding is often the pharmacist verifying the final drug preparation. **Recommendation:** Revise language to read: *"(5) The identity of personnel performing the compounding, the pharmacist verifying the final drug preparation, as well as the pharmacist who has direct supervision and control of*

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		compounding if different from the pharmacist verifying the final drug preparation."
1735.10(a)	*Beyond-use dates (BUDs) assigned with only a date shall expire at 11:59 p.m. on that date*	**Comment:** Electronic health record (EHR) systems use the 24-hour format for time entries. **Recommendation:** Revise language to include 24-hour time format (e.g., 23:59).
Article 4.6 Sterile Compounding		
1736.2(b)	*Aseptic qualifications from one premises may be used for another premises if all of the following conditions are met…*	**Comment**: It is unclear whether "aseptic qualifications" include hand hygiene and garbing competencies (observational competency and gloved fingertip and thumb sampling) or if it pertains to aseptic technique competencies only. **Recommendation:** To avoid confusion, be more specific with what sterile compounding competencies are transferrable between pharmacy locations or define "aseptic qualifications."
1736.4(c)(1)	*Designated compounding area(s) shall typically be maintained at a temperature of 20° Celsius or cooler.*	**Comment:** This requirement will significantly affect all Stanford Health Care pharmacy locations that support investigational drug studies and store investigational medications in the cleanroom (e.g., hazardous drugs in the negative pressure buffer room). Sponsor protocols have strict drug storage temperature requirements which cannot be deviated. USP defines room temperature storage as a temperature range of 20° C to 25°C. **Recommendation:** Remove language to align with USP 797 where a temperature less than 20° or cooler is a recommendation and not a requirement.
1736.11(c)(4)	*(c) A compounding record (CR) shall be maintained and, upon request be produced as a single document. The document shall satisfy the requirements of USP Chapter 797, and also contain the following:* *(4) The identity of personnel performing the compounding, pharmacist who has direct supervision and*	**Comment:** The pharmacist who has direct supervision and control of compounding is often the pharmacist verifying the final drug preparation. **Recommendation:** Revise language to read:

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	control of compounding, and pharmacist verifying the final drug preparation.	*"(4) The identity of personnel performing the compounding, the pharmacist verifying the final drug preparation, as well as the pharmacist who has direct supervision and control of compounding, if different from the pharmacist verifying the final drug preparation."*
1736.14(b)	*A CSP labeled with a BUD with only a date shall expire at 11:59 p.m. on that date.*	**Comment:** Electronic health record (EHR) systems use the 24-hour format for time entries. **Recommendation:** Revise language to include 24-hour time format (e.g., 23:59).
Article 4.7 Hazardous Drugs		
1737.2 (a)	*… The designated person must be 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…*	**Comment:** For a large health system pharmacy department, it is common for multiple people to assume the responsibilities of the designated person. Additionally, proposed sections 1735 and 1736 define the designated person(s) as "one or more individuals." The USP <800> FAQ further supports this by clarifying that the designated person may be more than one person. **Recommendation:** Revise language to allow the designated person for hazardous drug handling to be "one or more individuals."
1737.7(c)	*Outer gloves used for HD compounding shall be changed between each different HD preparation.*	**Comment:** The requirement for compounding personnel to change outer HD gloves between each different HD preparation will result in significant increases in costs and generation of HD waste. Additionally, there is likely minimal benefit if a pharmacy is using CSTDs for HD compounding. **Recommendation:** Remove language to be consistent with USP 800 or revise language to require changing outer HD gloves, between each different HD preparation, if compounding is performed without a CSTD.

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1737.13 (b)	*Only one HD preparation may be handled in a C-PEC at a time.*	**Comment:** There are other effective strategies to prevent drug mix-up and cross-contamination besides limiting one HD preparation in a C-PEC at a time. These include clearly defined segregation between different HD preparations (e.g., dividers, bins, barriers), compounding multiple HD preparations of the same drug, and compounding different HD preparations for the same patient. Front-line staff have commented that there are HD drugs that take a long time to dissolve and not being able to continue compounding other medications would negatively affect patient care. This is especially true for our locations with only one or a limited number of hoods. **Recommendation:** Revise language to allow exceptions for more than one HD preparation in a C-PEC at a time under the following circumstances 1. Implemented methods that create clearly defined segregation between different HD preparations. 2. Multiple HD preparations of the same drug are being compounded. 3. Multiple HD preparations for the same patient are being compounded.

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Section, Subdivision	Proposed Language	Recommendation / Comment
Non-Sterile Compounding		
CCR 1735 Compounding Definitions. Subsection (e)	(e) "Essentially a copy" of a commercially available drug product means a preparation that includes the same active pharmaceutical ingredient(s) (API(s)) as the commercially available drug product, except that it does not include any preparation in which there has been a change made for an identified individual patient that produces for that patient a clinically significant difference, as determined by the prescribing practitioner, between that compounded preparation and the comparable commercially available drug product	**Rationale:** • The proposed language does not distinguish commercially available drug products with the same active pharmaceutical ingredient(s) (API(s)) with drug dosage form(s). • To make it clear that drug dosage forms not available commercially can be compounded for patient specific clinical needs. **Recommendation:** Recommend the board to add language to the definition of "essentially a copy" to include "the same dosage form" in addition to the same active ingredient(s) (API(s)).
CCR 1735.1 Introduction and Scope. Subsection (e) (1) (A):	(e) In addition to prohibitions and requirements for compounding established in federal law, 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 dispensing, or	**Rationale:** • The ASHP and FDA drug shortage lists do not always reflect real-time real time drug shortages. As an example, the 2023 Akorn recall was posted after the State Board notification of the company shut down which resulted in multiple drug shortages. (see attached) [1] Health systems have monitoring strategies in place to track these drug shortages real-time from drug manufacturers or wholesalers before these shortage drugs get added to the ASHP and FDA drug shortage lists. • Additionally, wholesalers themselves often run out of supply of critical medications (pre-shortage situations). Inability to procure medications or restrictions to compound in these events would have contribute to heightened risk and safety concerns for patients. With the growing number of medications going on shortage[2] and recent manufacturer bankruptcies (i.e. Akorn, Apotex) it is becoming more challenging for Health-Systems to obtain commercially available products. References:  FDA Akorn recall.pdf 1. 2. Drug Shortages Statistics - ASHP

		Recommendation: Recommend the board to revise language to be consistent with language changes in section 1736.1 subsection (e) (1) (A). ***1735.1 Introduction and Scope. Subsection (f) (1) (A):*** *(e) In addition to prohibitions and requirements for compounding established in federal law, no CNSP shall be prepared that:* *(1) Is essentially a copy of one or more commercially available drug products, unless:* *(A) that 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 dispensing, or in a health care facility licensed pursuant to Health and Safety Code Section 1250 where the drug product cannot be obtained from the manufacturer or wholesaler and documentation is maintained, or*
CCR 1735.7 Master Formulation and Compounding Records. subsection (c)(2):	(c)(3) The manufacturer, lot number, and expiration date for each component for the CSP.	**Rationale:** Current language in CCR 1735.3 below has a provision for CSPs compounded in health facilities to prevent delays in care to acutely ill patient, i.e. infections, cancer, critical care, etc. The current language states: (F) The manufacturer, expiration date and lot number of each component. If the manufacturer name is demonstrably unavailable, the name of the supplier may be substituted. If the manufacturer does not supply an expiration date for any component, the records shall include the date of receipt of the component in the pharmacy, and the limitations of section 1735.2, subdivision (l) shall apply. (*i) Exempt from the requirements in this paragraph (1735.3(a)(2)(F)) are sterile preparations compounded in a single lot for administration within seventy-two (72) hours to a patient in a health care facility licensed under section 1250 of the Health and Safety Code and stored in accordance with standards for "Redispensed CSPs" found in Chapter 797 of the United States Pharmacopeia – National Formulary (USP37-NF32) Through 2nd Supplement (37th Revision, Effective December 1, 2014), hereby incorporated by reference.* **Recommendation:** To prevent delays in care to acutely ill patients, recommend the board consider including the same exemption language to the 1735.7 Master Formulation and Compounding Records, subsection (c)(2):

		The manufacturer, lot number, and expiration date for each component. *(i) Exempt from the requirements in this paragraph are non-sterile preparations compounded in a single lot for administration within seventy-two (72) hours to a patient in a health care facility licensed under section 1250 of the Health and Safety Code.*
1735.12. Quality Assurance and Quality Control. Subsection (c)	(c) All complaints made to the facility related to a potential quality problem with a CNSP and all adverse drug experiences events shall be reviewed by the pharmacist-in charge within 72 hours of receipt of the complaint or occurrence of the adverse drug experience event. Such a review shall be documented and dated as defined in the SOPs.	**Rationale:** • A 72-hour requirement might not offer adequate time for health systems to investigate and notify the requisite regulatory bodies, particularly if the incident occurs over a holiday weekend. ~~A requirement of 72 hours may not provide sufficient time for health-systems to investigate and notify the necessary regulatory bodies in cases where it occurs over the holiday weekend.~~ **Recommendation** *(c)All complaints related to a potential quality problem with a CNSP and all adverse events shall be reviewed by the pharmacist-in-charge within 3 business days ~~72 hours~~ of receipt of the complaint or occurrence of the adverse event. Such review shall be documented and dated as defined in the SOPs.*
Sterile Compounding		
CCR 1736.1 Introduction and Scope. Subsection (b) (2):	(2) If the sterile compounding equipment or environment fail(s) to meet any required specification, an immediate use CSP may be compounded without the requirement for there to be loss of life or intense suffering of an identifiable patient. This provision may only be used for 24 hours after such failure(s). All such failures must be documented in accordance with facility's SOP and shall be reported to the BOP within 72 hours.	**Rationale:** • Requiring health-system pharmacies to remedy equipment failures within 24 hours may not be feasible due to a variety of reasons why there could have been equipment failures. Often, it may take more than 24 hours to remedy. • To use outside facility or vendor to provide compounding preparations would still pose a safety risk as they may not be following the health-systems processes and procedures. • Given the concerns about potential audits, institutions may hesitate to report issues to the Board of Pharmacy. We urge the Board to embrace a 'Just Culture' framework, which emphasizes accountability and learning over punitive measures. • **Recommendation:** • To remove the requirement for immediate use compounding under this provision to be used for 24 hours after such failure(s) and requiring such failures must be documented in accordance with facility's SOP and shall be reported to the BOP within 72 hours.

		CCR 1736.1 Introduction and Scope. Subsection (b) (2): *(2) If the sterile compounding equipment or environment fail(s) to meet any required specification, an immediate use CSP may be compounded without the requirement for there to be loss of life or intense suffering of an identifiable patient. This provision may only be used for 7 business days after such failure(s). All such failures must be documented in accordance with facility's SOP and shall be available upon inspection. ~~and shall be reported to the BOP within 72 hours.~~*
CCR 1736.2 Personnel Training and Evaluation. Subsection (d)	(d) Compounding personnel or persons with direct supervision and control of compounding personnel who fail any aspect of the aseptic manipulation ongoing training and competency evaluation shall not be involved in compounding 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 supervision and control of 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 30 days after a failure of any aspect while applicable aseptic manipulation ongoing training and competency evaluation results are pending	**Rationale:** Multiple factors can contribute to failure of staff in aseptic technique training and competency evaluation including environmental testing failure, and engineering control failure. Prohibiting compounding personnel from compounding without an evaluation of contributing factors and timeframe would significantly disrupt patient treatment and for jeopardize health-systems ability to operate. **Recommendation:** Recommend to the following revisions to section 1736.2 subsection (d) to allow personnel who fail any aspect of aseptic manipulation training to continue to perform in-process checks, final verification and dispensing of CSPs for no more than 30 days. **Proposed Regulation Revision:** *(d) 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 including performing in-process checks, final verification, and dispensing of CSPs for no more than 30 days after a failure of any aspect while applicable aseptic manipulation ongoing training and competency evaluation results are pending*

CCR. 1736.4 Facilities and Engineering Controls Subsection (c)	(1) Designated compounding area(s) shall typically be maintained at a temperature of 20° Celsius or cooler.	**Rationale:** • The USP chapter 797 recommends maintaining a temperature of 20° Celsius or cooler for staff comfort within the classified compounding areas where multiple layers of PPE are worn. • The term "designed compounding area" is defined by CCR. 1736 as a restricted location within a facility that limits access, where only activities and items related to compounding are present. This definition would include both classified compounding areas and segregated compounding areas. • If the language remains as is, 'shall typically' this can lead to severe consequences for many health systems, as many would have to make significant changes to their Heating, Ventilation, and Air Conditioning (HVAC) systems to be compliant with this requirement. Additionally, many of these classified compounding rooms and segregated compounding areas maintain room temperature medication which must be stored in temperatures defined in USP Chapter 659 as 20°–25° (68°–77° F). • The manufacturer storage label for medications include a range 20°–25° (68°–77° F). If the temperatures in the compounding areas must be below 20° Celsius, the medications would be exposed to temperature excursion and would not be considered safe to use. • If the requirement remains as written, many institutions will need to build new storage rooms for all medications, including HD medications, and upgrade HVAC systems. This would involve large construction projects, adding significant strain to already overburdened healthcare facilities. **Recommendation:** (1) Designated compounding area(s) ~~shall~~ *should* typically be maintained at a temperature of 20° Celsius or cooler.
CCR. 1736.4 Facilities and Engineering Controls Subsection (f)	(f) No CSP shall be compounded if the compounding environment fails to meet criteria specified in law or the facility's SOPs.	**Rationale:** In smaller rural hospitals, this proposed law in combination with CCR 1736.1 Introduction and Scope. Subsection (b) would lead to severe consequences for patients. For example, if a designated compounding area fails to meet the criteria specified in the law, and hospitals are unable to compound for immediate use, they would have to cease operations as they would not be able to provide appropriate patient care. **Recommendation:**

		Recommend the Board of Pharmacy to consider removing the requirement of CCR. 1736.4 subsection (f) and defer to USP 797.
CCR 1736.11 Master Formulation and Compounding Records. subsection (c)(2):	(c)(2) The manufacturer, lot number, and expiration date for each component for the CSP.	**Rationale:** Current language in CCR 1735.3 below has a provision for CSPs compounded in health facilities to prevent delays in care to acutely ill patient, i.e. infections, cancer, critical care, etc. The current language states: (F) The manufacturer, expiration date and lot number of each component. If the manufacturer name is demonstrably unavailable, the name of the supplier may be substituted. If the manufacturer does not supply an expiration date for any component, the records shall include the date of receipt of the component in the pharmacy, and the limitations of section 1735.2, subdivision (l) shall apply. *(i) Exempt from the requirements in this paragraph (1735.3(a)(2)(F)) are sterile preparations compounded in a single lot for administration within seventy-two (72) hours to a patient in a health care facility licensed under section 1250 of the Health and Safety Code and stored in accordance with standards for "Redispensed CSPs" found in Chapter 797 of the United States Pharmacopeia – National Formulary (USP37-NF32) Through 2nd Supplement (37th Revision, Effective December 1, 2014), hereby incorporated by reference.* **Recommendation:** Add back the language above: 1736.11 Master Formulation and Compounding Records, subsection (c)(3): *(c)(3) The manufacturer, lot number, and expiration date shall be recorded for each component for CSPs.* *(i) Exempt from the requirements in this paragraph are sterile preparations compounded in a single lot for administration within seventy-two (72) hours to a patient in a health care facility licensed under section 1250 of the Health and Safety Code.*
CCR 1736.13 Labeling subsection (a):	(a) A CSP label shall include all of the following: (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	**Rationale:** Most health-systems utilize electronic health record (EHR) system that can provide the required label components in readily retrievable format. **Recommendations:** Recommend updating the regulation to: *(a) A CSP label shall include all of the following and these can also be readily retrievable from the EHR:*

	as prescribed, or the duration for the entire CSP to be administered.	*(1) Route of intended administration;* *(2) The solution utilized, if applicable;* *(3) Instructions for administration;* *(A) For an admixed CSP that are to be infused, the rate of infusion, or range of rates of infusion as prescribed, or the duration for the entire CSP to be administered.*
CCR. 1736.17 Standard Operating Procedures (SOPS) subsection (a)(2)(c)	(a)(2)(c) The methods a pharmacist will use to determine and approve the ingredients and the compounding process for each preparation before compounding begins;	**Rationale:** Many health-systems currently utilize IV room workflow system that utilizes barcode scanning to check for correct components before allowing technicians to proceed with compounding. Moreover, with pharmacy recruitment issues, it would become challenging for health-systems to provide manual individual checks for a large number of CSPs. **Recommendations:** The methods a pharmacist will use to determine and approve the ingredients and the compounding process for each preparation before compounding begins; *(i) A sterile compounding workflow system may be utilized for verification of correct components used for preparing a CSP.*
CCR. 1736.17 Standard Operating Procedures (SOPS) subsection (d)	(d) 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.	**Rationale:** In many health-systems there are many items entering the sterile compounding spaces including into the PEC. Requiring documentation of monitoring dwell time adds a significant burden to the workload of sterile compounding staff which could increase the risk of causing an error in compounding. Additionally, USP 797 does not require monitoring or documentation. **Recommendation:** *d) 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.~~*
CCR. 1736.18 Quality Assurance and Quality Control subsection (c)	(c) 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	**Rationale:** A requirement of 72 hours may not provide sufficient time for health-systems to investigate and notify the necessary regulatory bodies in cases where it occurs over the holiday weekend. **Recommendation:**

	review shall be documented and dated as defined in the SOPs.	*(c) 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 3 business days ~~72 hours~~ of receipt of the complaint or occurrence. Such review shall be documented and dated as defined in the SOPs.*
Hazardous drugs		
CCR 1737.2 List of Hazardous Drugs subsection (a) and (b) :	(a) 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 (PIC), professional director of a clinic, or designated representative-in-charge, as applicable. The designated person must be 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. (b) 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.	**Rationale:** Often times, the designated person may be the pharmacist-in-charge **Recommendation:** Recommend revising the language to allow the Pharmacist-in-charge or designated person to review and approve the facility's list of HDs annually. ***CCR 1737.2 List of Hazardous Drugs subsections:*** *(a) The facility's list of HDs as required by USP Chapter 800 must be reviewed and approved by the designated person ~~and~~ or the pharmacist-in-charge (PIC), or professional director of a clinic, or designated representative-in-charge, as applicable. The designated person must be 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.* *(b) If an assessment of risk approach is taken as authorized in USP Chapter 800, it shall be approved by the designated person ~~and~~ or the pharmacist-in-charge, or professional director of a clinic, or designated representative-in-charge, as applicable.*
1737.5 Facilities and Engineering Controls. Subsection (c)	(c)Effective [OAL insert six months following the effective date] A a pass-through is not allowed between the hazardous drug buffer room C-SEC into an unclassified space	**Rationale:** USP 800 does not prohibit using a pass-through between a classified space and an unclassified space. In addition, this requirement without an exemption for previously built classified areas will put a significant burden financially and operationally on institutions that utilize a passthrough to be compliant with the new regulations. **Recommendation:** Revise language to remove the requirement and to align with USP 800 to read as follows:

		CCR 1737.5 Facilities and Engineering Controls: *(c) Effective [OAL insert six months following the effective date] a pass-through is not allowed between the hazardous drug buffer room C-SEC into an unclassified space* • *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.*
CCR 1737.6 Environmental Quality and Control. Subsection (a)	(a) 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.	**Rationale:** • USP 800 only recommends performing environmental wipe sampling for HD surface residue routinely. • Currently, there is currently no standard for acceptable limits for HD surface contamination.[1] • Additionally, requiring additional sampling will add an undue burden to test without any concrete actionable limits. **Reference** 1. Connor et al. Surface wipe sampling for antineoplastic (chemotherapy) and other hazardous drug residue in healthcare settings: Methodology and recommendations. Journal of Occupational and Environmental Hygiene. **Recommendations**: Request the board to consider removing the section or revise language to "should" to be consistent with USP 800 Chapter and to provide guidance on the specific requirement such as action level, frequency what to do when actionable levels have been reached as there is no standards provided. ***CCR 1737.6 Environmental Quality and Control*** *a) The SOPs of a premises where HDs are handled ~~shall~~ should address environmental wipe sampling for HD surface residue, its frequency, areas of testing, levels of measurable contamination, and actions when those levels are exceeded.*
CCR 1737.7. Personal Protective Equipment (PPE), subsection (c).	(c) Outer gloves used for HD compounding shall be changed between each different HD preparation.	**Rationale:** • Many health-systems use closed system transfer device (CSTD) when compounding antineoplastic HDs. The use of CSTD has shown to significantly reduce overall chemical contamination (12.24% vs. 26.39%).[1] • Double-gloving is primarily designed to offer extra protection against hazardous drug compounds, with the outer glove serving as a first line of defense. If the outer glove is repeatedly removed or exposed to rough

		conditions, it may wear down, possibly increasing the risk of puncturing or compromising the inner glove. This could lead to reduced protection, especially when handling hazardous drug compound.[2,3] • Frequent removal and disposal of outer glove changes creates significant waste.[2] **Reference** 1. Simon N, Vasseur M, Pinturaud M, et al. Effectiveness of a Closed-System Transfer Device in Reducing Surface Contamination in a New Antineoplastic Drug-Compounding Unit: A Prospective, Controlled, Parallel Study. Ahmad A, ed. PLoS One 2016;11:e0159052. Available at: https://dx.plos.org/10.1371/journal.pone.0159052. 2. Kirk H. Double gloving when handling cytotoxic drugs. *Hospital Pharmacy Europe*. Published March 2, 2009. Available from: https://hospitalpharmacyeurope.com/news/editors-pick/double-gloving-when-handling-cytotoxic-drugs/ 3. McNeilly L. Double gloving: Myth versus fact. *Infection Control Today*. Published May 5, 2011. Available from: https://www.infectioncontroltoday.com/view/double-gloving-myth-versus-fact **Recommendations**: Revise the proposed language to: *(c) Outer gloves used for HD compounding shall be changed between each different HD preparation if a closed system transfer device (CSTD) is not used.*
CCR 1737.14. Administering subsection (b)	(b) When dispensing a compounded antineoplastic HD to a patient or patient's agent, a sufficient supply of ASTM D-6978 standard gloves, shall be provided to the patient or the patient's agent, to allow for appropriate administration, handling, and disposal of the HD.	**Rationale:** In health facilities where antineoplastic HD are dispensed and administered by licensed health care professionals who are trained to handle HDs. Supplies such as ASTM D-6978 grade gloves, and HD disposal bins are readily available. **Recommendations:** Recommend adding exemption language to the current proposed language for HSC 1250 (a) licensed facilities as the administration of compounded medications to patients are done by health care personnel trained and authorized to administer HD medications and not dispensed for outpatient use.

		(i) Exempt from this requirement are health facilities, as defined in Section 1250 of the Health and Safety Code, if the prescriptions are administered by a licensed health care professional.

Public Comment to proposed text in Title 16, California Code of Regulations

Add new sections 1735 et seq of Title 16, Division 17, Article 4.5 of the California Code of Regulations
Add new sections/Article 1736 et seq of Title 16, Division 17, Article 4.6 of the California Code of Regulations
Add new sections/Article 1737 et seq of Title 16, Division 17, Article 4.7 of the California Code of Regulations

Institution: Contact:	Kaweah Health Medical Center Rheta Silvas, Pharm.D., Inpatient Assistant Director of Pharmacy	
Section	Proposed Language	Recommendation/Comments
1735.1 e(1)(A)	(A) the drug product appears in an American Society of Health-System Pharmacist (ASHP) or FDA Drug Shortages Database that are in short supply at the time of compounding at the time of dispensing, or	Recommend: Add language consistent with the staff recommended modified changes to 17**36**.1(e)(1)(B) "or in a health care facility licensed pursuant to Health and Safety Code Section 1250 where the drug product cannot be obtained from the manufacturer or wholesaler and documentation is maintained". Rationale: to provide provisions for drug shortages. There were a number of concerns communicated during the 45-day comment period April 19th, 2024 to June 3, 2024 related to the ASHP and FDA Drug shortage databases not consistently reflecting shortages in a timely manner. It appears that these concerns were acknowledged and addressed with the staff recommended modified changes to 1736.1(e)(1)(B) but perhaps an oversight to not acknowledge similarly in 1735.1 f(1)(A)? While the proposed text is consistent with current regulations (CCR Section 1735.2(d)(3)), when that language was proposed in 2014, similar concerns were shared via public comment. The state of drug shortages experienced in the hospital setting in particular is vastly different than it was a decade ago and according to the U.S. Senate Committee on Homeland Security & Governmental Affairs' report "Short Supply The Health and National Security Risks of Drug Shortages" shortages of critical medications continues to rise. While the FDA drug shortage website updates daily, the info is limited to data provided from drug manufacturers with a focus only on shortages that have the greatest impact on public health. The FDA list may not include shortages with an anticipated short resolution or those that involve select product presentations. Verification that a shortage exists does not take into account what the pharmacy is experiencing in the buying process. Instead, information from manufacturers, distributors and market share data is used by the FDA to determine if a shortage exists. ASHP's site lists reported shortages after investigation and confirmation, usually within 24 – 72 hours. https://www.govinfo.gov/content/pkg/GOVPUB-Y4_G74_9-PURL-gpo194920/pdf/GOVPUB-Y4_G74_9-PURL-gpo194920.pdf

1735.1 e(1)(B)	(B) The pharmacist determines and documents that the compounding produces a clinically significant difference for the medical need of an identified individual patient~~,~~ ~~as determined by~~: ~~(i) the prescribing practitioner,~~ ~~(ii) the compounding pharmacist~~ (iii) the dispensing pharmacist(s), if not the same as the compounding pharmacist.	Recommend: strike (B)(iii) to be consistent with proposed language in 17**36**.1(e)(1)(B) unless there is a compelling reason the language for CNSPs in this section needs to vary. If staff do not agree with the above recommendation, the staff recommended modified changes should be clarified to improve readability and at minimum a renumbering is required. There is a B(iii) without a B(i) or B(ii). If the staff recommended modified changes are approved as proposed, the section would read: B) The pharmacist determines and documents that the compounding produces a clinically significant difference for the medical need of an identified individual patient**:** **(iii)** the dispensing pharmacist(s), if not the same as the compounding pharmacist.
1736.1 (b)(2)	(2) if the sterile compounding equipment or environment fail(s) to meet any required specification, an immediate use CSP may be	Appreciate the staffs' efforts with the modified text to introduce flexibility not currently provided in current CCR 1751.8(e). Recommendation #1: strike the language "this provision may only be used for 24 hours after such failure(s). **Preferred.** Recommendation #2: Alternatively, modify the language so it provides impacted facilities even greater flexibility. Consider modifying the language to read "this provision may only be used for the shortest timeframe necessary to evidence full remediation of the failure". **Less Preferred.**

	compounded without the requirement there to be loss of life or intense suffering of an identifiable patient. This provision may only be used for 24 hours after such failure(s). All such failures must be documented in accordance with the facility's SOP and shall be reported to the BOP within 72 hours.	Concerns: The 24-hour timeframe for the immediate use "criticality" provision specified in 1736.1 (b)(2) is not long enough to allow for certain failures to be remedied and then evidenced as fully remediated. Without question, to the extent that is possible, contingencies should be in place that support service continuity. With that said, a few scenarios are offered to illustrate the concern and provide some practice perspective. Scenario 1 - In the case of a PEC failure, compounding can immediately cease in the effected PEC and compounding can be shifted to an alternate PEC that meets the required specifications. No concern with the 24-hour limit to using the immediate-use provision. Scenario 2 - In the case of an environmental failure (e.g. surface sample in an ISO 7 ante-room) where the CFU count exceeds the threshold, corrective action can be taken and the area re-sampled. It would take at minimum 14 days to obtain sampling results to evidence that the environment meets the required specification. Scenario 3 In the case of a ceiling HEPA filter failure in an ISO 7 Ante-room, pharmacies could reasonably install a new filter from replacement filters kept on hand within 24 hours but it is not always possible to have the filter re-certified within 24 hours depending on the schedule of the certifier. In the gap between environmental failure and evidence of full remediation, compounding can proceed without quality compromise by reducing the longest permitted BUD for Category 2 to the longest permitted BUD for Category 1. As proposed, 1736.1 (b)(2) would permit compounding in a Cleanroom suite with a 4-hour maximum BUD for only a 24- hour period of time in the absence of patient "criticality" in this this scenario while pharmacies licensed as segregated compounding areas are permitted a BUD to be < 12 hours at room temperature, < 24 hours refrigerated without requiring a ceiling HEPA filter at all. Concerned that pharmacies unable to evidence full remediation of a compounding equipment or environment failure within 24 hours as would be the case in scenario 2 and 3 above would be unable to compound preparations for acute care needs as the condition for which the CSP is needed may not meet the criteria "loss of life or intense suffering" (unless CCR 1736.1(b)(2) is violated).
1736.3 (c)	1736.3 – Personnel Hygiene and Garbing - In addition to the standards set forth	Recommend: Revise language to read "*With the exception of sterile gloves*, garb shall be donned in an anteroom or immediately outside the segregated compounding area (SCA). *Sterile gloves must be donned in a classified room or 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.

	in USP Chapter 797, the following requirements apply to sterile compounding. (c) 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.	Recommended revisions are underlined in italics for emphasis. While there is no modified text to provide public comment on in this section, public comment was submitted for the proposed changes to the current language with acknowledgment of review by staff but no recommended changes to the proposed text, noting that the current proposed text provides for flexibility in where gloving can occur by stating that the facilities SOPs may define specific processes. Respectfully disagree with staff response, the proposed text as it reads provides flexibility specific to <u>simultaneous donning and doffing</u> in the anteroom. Please reconsider. <u>Rationale:</u> Current language as proposed is in conflict with USP 797 in regards to donning of sterile gloves. See section 3.2 Hand Hygiene (last sentence above Box 4). Allow compounding pharmacies to determine the best location for donning of gloves based on their facility design as long as they are donned in a classified space (and not in a C-PEC/PEC) or in the SCA. Note: USP Chapter <797> requires that gloves be donned in a classified room or SCA. The proposed language specifies "immediately outside the SCA". **Box 3. Hand Washing Procedures** • Clean underneath fingernails under warm running water using a disposable nail cleaner. • Wash hands and forearms up to the elbows with soap and water for at least 30 s. • Dry hands and forearms up to the elbows completely with low-lint disposable towels or wipers. The order of hand washing and garbing depends on the placement of the sink (see *4.4 Water Sources*). The order of garbing must be determined by the facility and documented in the facility's SOPs. Hands must be sanitized with alcohol-based hand rub before donning sterile gloves (see *Box 4*). Sterile gloves must be donned in a classified room or SCA.
1736.6 (a)	1736.6 – Microbial Air and Surface Monitoring - In addition to the standards set forth in USP Chapter 797, the following	<u>Recommend</u>: modify the language to include the current versioning and application guide title. Allow the public an opportunity to comment after having had an opportunity to review the specific version of the application guide the regulated public will be expected to comply with. <u>Rationale:</u> Proposed language presented for public comment during the 45-day comment period April 19th, 2024 to June 3, 2024 and the modified changes to the proposed language presented for public comment during the 30-day comment period November 8, 2024 to December 9, 2024 did not include

	requirements apply to sterile compounding. (a) Environmental sampling shall be done in compliance with Controlled Environment Testing Association's Certification Application Guide USP <797> Viable Environmental Sampling & Gowning Evaluation (CAG-009, Revised October ~~2022~~ 2020), which is hereby incorporated by reference.	the correct versioning or title of CAG-009. CAG-009 version 2020 document is not available for the regulated public to review to determine if compliance can be achieved. The most current version is 2023, the title of the current application guide is Viable Environmental Monitoring for Sterile Compounding Facilities. The current law (CCR section 1751.4(f) was specific to *certification completed by a qualified technician (i.e. third party certifier)*. The proposed language is not consistent with exiting law, CCR section 1751.4(f) as staff indicated in their response to public comment. The below public comment was provided for proposed changes to current regulation 1736.6(b) during the 45-day comment period April 19th, 2024 to June 3, 2024 but was not included in the staff prepared public comment summary and response. The comment was "recommend clarity if the intent is to require the qualified technician (i.e. third party certifier) to comply with CAG-009 or anyone performing environmental sampling. If the former, recommend modifying the language accordingly".
1737.5(c)	~~Where a pass-through is installed in a containment secondary engineering control (C-SEC),~~	Recommendation #1: strike the language in this section altogether (Preferred). Rationale: In addition to the rationale detailed below, there is an OSHPD Initial Express Terms and Initial Statement of Reasons indicating proposed changes to Title 24 1224.19.3.3.2.8 to align with USP 800; striking the specific language that is of concern. In looking at the Building Standards Commission, the proposed changes have not yet made it to the state where it hits the CA regulatory Notice Register. Providing helpful information regarding the proposal to amend the 2025 edition of the

	~~the doors must be gasketed and interlocking~~. Effective [OAL insert six months following the effective date] ~~A~~ a pass-through is not allowed between the C-SEC into an unclassified space.	California Building Code, Part 2, Volume 1, Title 24: ***1224.19.3.3.2.8 Pass-throughs.*** HCAI proposes an amendment to remove the prohibition of a pass-through between the hazardous drug buffer room and any unclassified area and to add a restriction for refrigerator pass-through. The proposed amendment is to align with United States Pharmacopeia General Chapter, USP-GC <800> Hazardous Drugs-Handling in Healthcare Settings (USP-GC <800>). The USP-GC <800> standards allow a passthrough from the buffer room to unclassified areas but not the refrigerator. This revision will align with USP-GC <800>. It will not cause financial burden to the facilities. Recommendation #2: if staff do not support recommendation #1, please allow facilities with clean room construction projects permitted under the 2016 California Building Code to be exempt from this requirement. Rationale: Title 24 1224.19.3.3.2.8, regulations that disallow a pass-through between the C-SEC into an unclassified space, is applicable to buildings permitted under **2019** building code which went into effect January 1, 2020. There are newly constructed or existing clean room suites at considerable costs in the state of California, permitted under the **2016** building code that incorporate this design feature as it is not prohibited by USP Chapter <800> and is was not prohibited under the OSHPD Advisory Guide for Sterile Compounding Pharmacies for hospital facilities (OSHPD 1 Buildings) or building codes in effect at the time of permitting. In a clean room suite with an ISO-7 Anteroom shared between an ISO 7 Positive Pressure Buffer Room and ISO 7 Negative Pressure Buffer Room, optimal placement of a pass-through is between the Negative Pressure Buffer room and adjacent unclassified space and/or placement between the Negative Pressure Buffer room and adjacent unclassified negative pressure hazardous drug storage room. There are contamination control benefits afforded from this design in that the design limits entry in/out of the anteroom thereby limiting the introduction of microbial contamination into the anteroom which is then introduced into the negative pressure buffer room as a result of the pressure relationship between the 2 rooms. The benefit of a pass-through between the negative pressure buffer room and adjacent unclassified negative pressure room storage room is it avoids the storage of bulk HD refrigerated and non-refrigerated inventory in the negative pressure buffer room optimizing microbial contamination control while minimizing the risk of HD exposure by better controlling

		material transfer. With respect to worker protections, material transfer between an unclassified negative pressure storage room into an IS0 7 Negative Pressure Buffer Room via a pass through is safer in the event a vial is accidently dropped in the process of wiping the component with disinfectant or sterile isopropyl alcohol before it is introduced to the clean side of the ante-room (a spill would occur in a negative pressure environment versus positive pressure environment).

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OFA

OUTSOURCING FACILITIES ASSOCIATION

December 9, 2024

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Re: Notice of Proposed Action: Compounded Drug Products

The Outsourcing Facilities Association ("OFA") is the trade association representing FDA-registered outsourcing facilities operating pursuant to Section 503B of the Federal Food, Drug, and Cosmetic Act ("FDCA"). OFA's members provide compounding and repackaging services to patients, healthcare providers, and healthcare facilities, and strive to ensure the specific needs of both providers and patients are met with safe and effective compounded and/or repackaged medications under the current Good Manufacturing Practices standards and guidance of the Food and Drug Administration and in compliance with all applicable laws and regulations.

OFA submits this comment concerning certain proposed amendments to Title 16 of the California Code of Regulations, as follows:

Outsourcing Facilities Association; c/o: Victoria Weatherford		
Section, Subdivision	Proposed Language	Recommendation / Comment
Proposed § 1735(d)	"Essentially a copy" of a commercially available drug product means a preparation that includes the same active pharmaceutical ingredient(s) (API(s)) as	This definition creates incoherence and confusion in conjunction with proposed § 1735.1(f), as explained in § A, *infra*.

	the commercially available drug product, except that it does not include any preparation in which there has been a change made for an identified individual patient that produces for that patient a clinically significant difference, as determined by the prescribing practitioner, between that compounded preparation and the comparable commercially available drug product.	
Proposed § 1735.1(f) and (f)(1)	(f) In addition to prohibitions and requirements for compounding established in federal law, 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 dispensing, or (B) the compounding produces a clinically	The proposed amendment should not be adopted, for the reasons stated in §§ A–D, *infra*.

	significant difference for the medical need of an identified individual patient, as determined by: (i) the prescribing practitioner, (ii) the compounding pharmacist, and (iii) the dispensing pharmacist(s).	

The Board should not adopt its proposed § 1735.1. When taken in conjunction with proposed § 1735(d), the proposed regulation is poorly drafted, to the point that it does not appear to achieve the Board's stated objective of requiring that a compounded drug "must produce a clinically significant difference for the patient as determined by the prescriber, compounding pharmacist, and dispensing pharmacist." Amended Initial Statement of Reasons at 12. Worse, that objective, if it were achieved by the proposed regulation (or in some other fashion), is misconceived, contrary to law, and arbitrary. The Board lacks authority to condition federally authorized compounding on findings of clinically significant difference by pharmacists, as Section 503A of the federal Food, Drug, and Cosmetic Act (FDCA) would preempt such a requirement. That requirement would also conflict with state law by requiring pharmacists to practice medicine without medical licenses. We explain these comments, and others, in more depth below.

A. The Proposed Regulation Is Incoherent

Contrary to the Board's stated objective of requiring that a compounded drug "must produce a clinically significant difference for the patient as determined by the prescriber, compounding pharmacist, and dispensing pharmacist," the proposed text of § 1735.1(f)(1) does not require a finding of clinically significant difference by a prescriber, compounding pharmacist, and dispensing pharmacist. Read with the definition of "essentially a copy," the draft creates a confusing and indeterminate system that may lack any practical effect.

Section 1735.1(f)(1) establishes a blanket ban on compounding if it results in a drug that "[i]s essentially a copy of one or more commercially available drug products." The subsection requiring prescriber and pharmacist findings of "a clinically significant difference" is phrased as an exception from this blanket ban (beginning "unless"). But the proposed definition in § 1735 of the term "[e]ssentially a copy" already contains an exception where:

> there has been a change made for an identified individual patient that produces for that patient a clinically

> significant difference, **as determined by the prescribing practitioner**, between that compounded preparation and the comparable commercially available drug product (emphasis added)

By consequence, where a practitioner makes a finding of clinically significant difference, the blanket ban on essentially-a-copy compounding is not implicated. No pharmacist's finding of clinically significant difference is necessary for this definitional exception to apply; a practitioner's determination is sufficient.

As a result, the scenario addressed by the proposed blanket ban of § 1735.1(f) will not arise. In relevant part, it provides:

> no CNSP shall be prepared that … (1) Is **essentially a copy** of one or more commercially available drug products, unless … (B) the compounding produces a clinically significant difference for the medical need of an identified individual patient, as determined by: (i) **the prescribing practitioner**, (ii) the compounding pharmacist, and (iii) the dispensing pharmacist(s). (emphasis added).

Because the definition of the first boldface term ("essentially a copy") already excludes compounding where the second boldface term is satisfied (prescriber finds "clinically significant difference"), there will apparently never be a need for a compounding or dispensing pharmacist to make the same finding. The Board's proposed text does not appear to accomplish its intended purpose. At a minimum, it will create confusion in application and potential litigation.

B. The Board's Objective of Requiring Pharmacist Determinations of Clinically Significant Difference Is Preempted by Federal Law

Assuming § 1735.1(f)(1)(B) accomplishes the Board's stated purpose, or were revised to do so, it would (if adopted) conflict with federal law and be preempted. The U.S. Constitution's Supremacy Clause renders federal law "supreme … any Thing in the Constitution or Laws of any State to the Contrary notwithstanding." U.S. Const. art. VI, cl. 2. The provision gives Congress "power to preempt state law." *Crosby v. Nat'l Foreign Trade Council*, 530 U.S. 363, 372 (2000). Preemption occurs, *inter alia*, where "Congress enacts a law that imposes restrictions or confers rights on private actors; a state law confers rights or imposes restrictions that conflict with the federal law; and therefore the federal law takes precedence and the state law is preempted." *New Jersey Thoroughbred Horsemen's Ass'n v. NCAA*, 584 U.S. 453, 477 (2018).

Federal law would preempt any requirement by the Board that compounding be permitted (in the absence of a drug shortage) only if both the compounding and dispensing pharmacists make determinations of clinically significant difference. Section 503A establishes a reticulated regime in which pharmacy compounding is conducted. It exempts a compounded drug product from the new-drug-approval process and various other FDCA prohibitions that would otherwise bar the sale of compounded drugs if a long list of factors are satisfied. *See* 21 U.S.C. § 353a(a)–(e). The implication is that a pharmacy that runs the gauntlet under federal law is entitled to engage in compounding. *See, e.g.*, *Barnett Bank of Marion Cnty., N.A. v. Nelson*, 517 U.S. 25, 31 (1996); *Maine Forest Prod. Council v. Cormier*, 51 F.4th 1, 9 (1st Cir. 2022).

Specifically, Section 503A generally prohibits pharmacy compounding "regularly or in inordinate amounts (as defined by the Secretary [of Health and Human Services] any drug products that are essentially copies of a commercially available drug product." 21 U.S.C. § 353a(b)(1)(B). Section 503A, however, expressly exempts from the term "essentially a copy of a commercially available drug product" the following:

> [Any] drug product in which there is a change, made for an identified individual patient, which produces for that patient a significant difference, **as determined by the prescribing practitioner**, between the compounded drug and the comparable commercially available drug product.

Id. § 353a(b)(2) (emphasis added). This text establishes that, where a practitioner makes a finding of clinically significant difference, compounding cannot be deemed within the general prohibition on compounding of drugs that are essentially copies of commercially available drug products. It reflects Congress's judgment that the determination of whether a clinically significant difference exists is to be made by prescribing practitioners. While Congress could have assigned that decision to compounding or dispensing pharmacists, it did not.

Requiring clinically-significant-difference findings by the compounding and dispensing pharmacists, in addition to the prescribing practitioner, clashes with Congress's carefully calibrated scheme. Adding that requirement would at a minimum create "an obstacle to the regulatory system Congress chose," *Arizona v. United States*, 567 U.S. 387, 406 (2012), by directing pharmacists to make the judgment call Congress delegated to practitioners alone, and it is, for that reason, preempted. In addition, any attempt by the Board to enforce the proposed regulation's requirement of a prescribing practitioner finding would be expressly preempted. *See* 21 U.S.C. § 337(a); *Nexus Pharms., Inc. v. Cent. Admixture Pharmacy Servs., Inc.*, 48 F.4th 1040, 1048 (9th Cir. 2022).

To the extent that the draft regulation would impair the dispensing of compounded drugs compounded by federally regulated outsourcing facilities, it would also be preempted. FDCA Section 503B authorizes compounding at outsourcing facilities and establishes 11 independent requirements comprehensively regulating them and the drugs they compound, beginning with active ingredients and embracing labelling and quality and safety standards. *See* 21 U.S.C. § 353b(a)–(c). Like Section 503A, this provision establishes a federally recognized prerogative to engage in compounding once all requirements are met that states may not frustrate with requirements that destroy that prerogative. Proposed § 1735.1(f) may have that effect by requiring both the "compounding" and "dispensing" pharmacist to make findings of clinically significant difference. If applied to outsourcing facilities, this would be unworkable because Section 503B provides that outsourcing facilities need "not obtain prescriptions for identified individual patients" and need not even be licensed pharmacies. 21 U.S.C. § 353b(4)(B) and (C). As permitted by Section 503B, outsourcing facilities produce large quantities of compounded drugs with no individualized patient assessment. It is therefore not possible for outsourcing facilities to make individualized findings of clinically significant difference when operating under the model Congress expressly permits. Such a requirement would conflict with Section 503B and be preempted.

C. Requiring Pharmacist Findings of Clinically Significant Difference Would Unlawfully Require Pharmacists to Engage in the Unlicensed Practice of Medicine

Assuming § 1735.1(f)(1)(B) accomplishes the stated purpose, or were revised to do so, it would (if adopted) contravene state law, which prohibits the practice of medicine by anyone lacking a medical license. *See* Cal. Bus. & Prof. Code § 2052(a). Because the practice of medicine is defined by statute, a regulation that commands the unlawful (indeed, criminal) practice of medicine is unlawful. *See, e.g.*, *Ass'n of California Ins. Cos. v. Poizner*, 180 Cal. App. 4th 1029, 1044 (2009).

Under California law, one engages in the practice of medicine if she "diagnoses, treats, operates for, or prescribes for any ailment, blemish, deformity, disease, disfigurement, disorder, injury, or other physical or mental condition of any person." *Id.* "This section proscribes not only the practice of a mode of treating the sick, but also prohibits unlicensed persons from diagnosing, treating or prescribing for any ailment, disease or other mental or physical condition." 62 Cal. Op. Att'y Gen. 792, at *2 (1979) (quotation marks omitted).

In directing pharmacists to ascertain whether "the compounding produces a clinically significant difference for the medical need of an identified individual patient," the proposed regulation directs the practice of medicine by pharmacists who are not so licensed. The draft regulation refers to a type of diagnosis, which "is the recognition

of a disease from its symptoms." *People v. Cantor*, 198 Cal. App. 2d Supp. 843, 847 (1961); 62 Cal. Op. Att'y Gen. 792, at *2 (1979). To make the requisite determination, a pharmacist would need to understand "the medical need of an individual identified patient" and determine whether a compounded drug produces a "clinically significant difference" as compared to a commercially available drug. As the text indicates, this is an individualized assessment of patient medical need that must entail a diagnosis. Indeed, the draft regulation seems to recognize (along with the FDCA) that this determination involves the practice of medicine because it also requires that a "prescribing practitioner" make the same determination.

The draft regulation proposes an expansion of the practice of pharmacy beyond recognition. "The pharmacist is in the business of selling prescription drugs, and his role begins and ends with the sale." *Murphy v. E. R. Squibb & Sons, Inc.*, 40 Cal. 3d 672, 679 (1985). While pharmacists do provide services, their role is "to assure that the drug prescribed is properly selected, measured and labelled." *Id.* at 678. To be sure, pharmacists, in addition, "must be alert to errors in prescriptions written by doctors," but their role is not to override the doctor but to "contact the doctor in case of doubts or questions regarding the drug prescribed." *Id.* "A key factor is that the pharmacist who fills a prescription … cannot offer a prescription for sale except by order of the doctor" and thus "is providing a service to the doctor and acting as an extension of the doctor in the same sense as a technician who takes an X-ray or analyzes a blood sample on a doctor's order." *Id.* at 679.

In requiring pharmacists to make medical decisions assigned to medical practitioners (by federal and state law) in filling each prescription for a compounding drug, the proposed regulation takes the startling step of authorizing pharmacists to override the judgment of prescribing practitioners. Given the requirements of federal law, *see* § B, *supra*, the draft regulation's only practical application is to instances where a doctor finds clinically significant impact and the compounding or dispensing pharmacist *disagrees* with the practitioner's medical judgment. This conclusively confirms that the draft regulation requires pharmacists to engage in the practice of medicine, in plain violation of California law.

D. Requiring Pharmacists To Make Findings of Clinically Significant Difference Would Be Arbitrary, Capricious, and Bad Policy

Assuming § 1735.1(f)(1)(B) accomplishes the stated purpose, or were revised to do so, it would (if adopted) establish an arbitrary and unjustified system that, in addition, makes for bad policy.

The Board proposes that prescribers and pharmacists "all are responsible for using their professional judgment with respect to patient safety" and that pharmacists'

"professional obligation to patient care" includes "the selection of the drug therapy being provided to their patient." Amended Initial Statement of Reasons at 12. But a determination of clinically significant difference is not a safety-related determination. A compounded drug may be safe even if a pharmacist finds it not to achieve a clinically significant difference, and a non-compounded drug may be unsafe in a given case. Moreover, as explained, the respective professional roles of pharmacists and doctors are not traditionally (or legally) the same, so it would be arbitrary for the Board to require these different professionals to make the exact same determination successively. That system would endanger mistrust and strife among professionals by requiring pharmacists to second-guess and overrule doctors and create regulatory confusion, as pharmacists and doctors—tasked with making the *same* determination—are governed by different licensing and disciplinary bodies and regimes.

This is an irrational choice inexplicable as anything other than an attempt to discourage compounding under federal law. The proposed series of vetoes on access to practitioner-prescribed compounded drugs would create a one-way ratchet that only reduces patient access to compounded drugs deemed proper by doctors. But Congress permits compounding because (subject to proper regulation) it is safe, effective, and beneficial for patients. If implemented, the proposed regulation will deny Californians access to medicines that their practitioners have determined are necessary for their treatment, raise costs, and ultimately raise the price of drugs in California.

Finally, it would be irrational in the extreme to apply the proposed pharmacist-determination requirement to compounded drugs manufactured by outsourcing facilities. As explained, outsourcing facilities compound drugs in bulk without prescriptions, as Congress expressly permitted. From the standpoint of pharmacies that purchase their products, outsourcing facilities are the functional equivalent of manufacturers. Accordingly, outsourcing facilities have no competency or practical ability to determine whether a given batch of compounded drugs would produce a clinically significant difference for any individual patient. To require that type of assessment of an outsourcing facility—and privilege it above a doctor's assessment—would be completely absurd, just as any individualized assessment of consumer need from a manufacturer would be absurd.

The Board should not adopt proposed § 1735.1.

Respectfully submitted, December 9, 2024

/s/ Victoria Weatherford

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Re: Notice of Proposed Action: Compounded Drug Products

Dear President Oh and Board Members,

Thank you for the opportunity to provide further comment on the proposed compounding regulations. We appreciate the effort that has gone into developing the draft regulations and are happy to provide feedback to help make certain that California patients are protected and provided access to this important class of medication. We respect the Board's responsibility to the consumers of California and hope the recommendations that we and others submit are taken seriously and considered when finalizing the draft. While many aspects of the initial draft have been updated in a manner that we appreciate, we continue to strongly advocate that the compounding standards in these draft regulations default to the standards set in United States Pharmacopeia Chapters 795, 797, and 800. Much work was done by industry experts in developing the new chapters and the Board yet to convince the regulated public that these proposals will provide added protections to the consumers of California. We have submitted all of our comments in the format requested as you will see below, but there is one aspect of these draft regulations that we still find deeply troubling and we will address in more detail here.

Wedgewood Pharmacy is the largest animal compounding pharmacy in the United States. We have been in business compounding for animal patients for almost 40 years and in that time, we have helped to treat millions of pets, horses, zoo animals, pocket pets, and many other animals. Our mission is to improve the lives of animals and those that love and care for them. In the last year our compounds have helped improve compliance for approximately 65,000 California based customers and many more nationally. We have a formulary of roughly 45,000 unique compounds in a variety of dosage forms, flavors, and concentrations specifically designed to improve compliance for our animal patients.

Our concern lies primarily with sections 1735.1(e)(2) and 1736 (e)(2) of the proposed regulations that provide in part that "No CNSP [compounded non-sterile preparation] is permitted … that is made with any component not suitable for use in a CNSP for the intended patient population, unless allowable under the Animal Medicinal Drug Use Clarification Action of 1994 (AMDUCA)."

The phrase "not suitable for use in the intended patient population" in the proposed regulations is ambiguous and confusing. Hundreds of different Bulk Drug Substances have been used in compounded medications

treating animals for decades and are regularly prescribed and ordered for office administration by veterinarians treating their patients. We would strongly argue that because substantially all of the drugs we make are made from bulk drug substances and veterinarians order these drugs for administration and dispensing to their patients, the components "are suitable for use …[in] the intended patient population". The veterinarian who monitors and is responsible for the treatment and health of the patient is in the best position to determine what is suitable for their patient. Because of the ambiguity of this clause, however, we are concerned that the Board will apply some undefined standard in determining suitability for use. More clarity needs to be provided as to what this statement means so that pharmacies can understand what compliance will mean and the public can understand how this will impact their ability to access compounded medications.

In addition, the reference to AMDUCA in the regulations is both ambiguous and inappropriate.

AMDUCA , as passed by Congress, allows for off-label use of animal and human FDA-approved medications in animal patients (plain text of AMDUCA is attached in Appendix 1). As you can see in the attached text, compounding is neither referenced nor mentioned at all in the text. Prior to the passage of AMDUCA, prescription medication could only be used exactly as labeled, i.e., no off-label prescribing. The direction Congress gave the FDA in AMDUCA was to draft regulations expanding a veterinarian's ability to prescribe medications off-label. Nothing more.

One often cited and more often misinterpreted section of the regulations the FDA promulgated is 21 CFR Part 530.13 of the Code of Federal Regulations (attached in Appendix 2) that provides that "Nothing in this part shall be construed as permitting compounding from bulk drug". Notably and relevant for this discussion in no way does this prohibit compounding for animal patients from bulk drug substances. Additionally, nowhere in this regulation is "suitability of ingredients for a CNSP in specific patient populations" discussed. For these reasons, we do not understand the intent of the inclusion of the reference to AMDUCA nor do we understand how compliance with the regulation would be achieved.

Because AMDUCA does not address suitability for use in a CNSP, it's reference in Sections 1735.1 and 1736.1 is confusing. We would like to better understand the reasoning of the Board as to why this provision is included and what are the practical implications of this provision.

We are concerned that in the context of the Board's proposed regulations, because AMDUCA does not specifically allow for compounding from bulk, the proposed regulation could be applied to mean that the only components suitable for use in a compounded preparation are those specifically addressed in 21 CFR Part 530.13 and thus this reference could be used by the Board to prohibit the compounding of animal preparations from bulk drug substances (or Active Pharmaceutical ingredients (API)), a practice that is specifically acknowledged and allowed by FDA.

As the Board is likely aware, the FDA has promulgated Guidance for Industry 256, which is non-binding guidance, not a law or regulation. The guidance in no way prohibits the production of drugs from Bulk Drug Substances. In fact, GFI#256 specifically allows for the compounding of animal medications from Bulk Drug Substances for both veterinarian office use and for patient specific application and dispensing.

For these reasons we strongly believe that Sections 1735.1(e)(2) and 1736 (e)(2) of the proposed regulations should be removed or revised in a way that provide clear guidance to pharmacies. If our concerns are valid, this would have devastating consequences for the animal patients and veterinarians of California. As mentioned above, we have almost 45,000 unique compounds in our catalog, the vast majority of which are made using bulk drug substance. We estimate that 60% of our dosage forms would be negatively impacted and no longer available to California patients if bulk drug substances were deemed unsuitable by this Board. The impact of this on California animal patients would be devastating. Dr. Grant Miller has already spoken before this Board on the difficulty his practice has experienced sourcing needed compounds that used to be readily available to him. This problem would be significantly amplified if compounders are unable to utilize bulk drug substance. Many of the bulk drug substance ingredients commonly used in animal medication are also utilized in human medicine, for which there would be no such restriction. How would the Board justify to animal owners that a substance that can be an ingredient in a compound for use by them (a human) is not "suitable" for use in their pets or animals?

We would very much like to work with the Board to determine a path forward that both protects the animals and animal owners of California and still allows them access to life saving compounded medications. We hope you will consider and take seriously our concerns.

Comments Regarding The Notice of Proposed Regulatory Action Concerning: Compounded Drug Products		
Section, Subdivision	Proposed Language	Recommendation/Comment
1735 (d)	"Essentially a copy" of a commercially available drug product means a preparation that includes the same active pharmaceutical ingredient(s) (API(s)) as the commercially available drug product, except that it does not include any preparation in which there has been	While similar to the current definition in CA regs, we feel this is a good opportunity to align with Federal definitions. This very broad definition makes drugs that are in different dosage forms and contain substantially different ingredients copies of each other for purposes of the statute (see example below). This broad definition

	a change made for an identified individual patient that produces for that patient a clinically significant difference, as determined by the prescribing practitioner, between that compounded preparation and the comparable commercially available drug product.	leads to delays in patient care, causes an undue administrative burden on both pharmacists and prescribers, and provides no patient benefit. If the Board intends to move forward with this definition, it should provide justification as to how this protects the patient population as compared to the FDA definition. Otherwise, the Board should align with the definition of a copy used by the FDA which includes the route of administration. Additionally, limiting the exception in this provision to patient specific prescriptions effectively prohibits pharmacies from compounding anticipatory stock (which will in turn make it extraordinarily difficult to produce adequate quantities of sterile preps). This provision could also be used by the Board to prohibit production of drugs for office stock if there is any commercial product that includes the same API because for these orders there is no identified individual patient. Thus, an unintended consequence of this change would be that veterinarians could no longer stock in their offices the

		drugs they need to begin immediate care of their patients. Example of undue burden: Tacrolimus as an eye drop. There is no commercial equivalent dosage form and this is widely prescribed for dry eye conditions in dogs. Considering this a copy of the commercial tablet or injection is non-sensical as it is utilized in a completely different manner. Requiring the pharmacist and prescriber to document justification for a novel route of administration leads to delays in care while each side ensures the other is maintaining proper documentation.
1735.1 (e)(1)(B), 1736.1 (e)(1)(B)	1735.1 (e)(1)(B) The pharmacist determines and documents that the compounding produces a clinically significant difference for the medical need of an identified individual patient~~, as determined by: (i) the prescribing practitioner, (ii) the compounding pharmacist, and~~ (iii) the dispensing pharmacist(s), if not the same as the compounding pharmacist.	Recommendation: Edit 1735.1 (e) to align with the language that is more appropriate in 1736.1 (e)

	1736.1 (e)(1)(B) The pharmacist determines and documents that the preparation produces a clinically significant difference based on the medical need of an identified individual patient, ~~as determined by: (i) the prescribing practitioner, (ii) the compounding pharmacist, and (iii) the dispensing pharmacist(s).~~	
1735.1 (d) & 1736.1 (d)	(d) 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 7-day supply, or up to no more than 14 days for antibiotics, for an individual patient, as fairly estimated by the prescriber, and documented on the purchase order or other documentation submitted to the pharmacy prior to furnishing for an individual patient.	"Reasonable quantity" needs to be defined clearly to avoid ambiguity, provide clear compliance standards, and make clear what enforcement will entail. It is unfair to place the burden of determining a "reasonable quantity" on the pharmacist when it is a) an unclear standard and b) the pharmacist doesn't know the prescriber's patient base nor their needs. Recommendations: Change terminology "veterinary office" to "veterinary practice". Mobile veterinarians practice in the field, not an office. Eliminate the words "Reasonable quantity". Clauses 1 and 2 of this

		provision and the phrase "estimated by the prescriber" establish clear criteria for the amount of office stock drugs that can be ordered and sold. The prescriber is in the best position to determine based on their practice the amount of drugs that are appropriate. A pharmacy has no reasonable basis to determine what a particular practice may need particularly when the practice is permitted to both administer drugs in office and dispense. Align sterile and non-sterile to the 7-day supply standard. Current language in 1736.1 (d)(2) lists 120 hours.
135.1 (e)(1) & 1736.1 (e)(1)	(e) In addition to prohibitions and requirements for compounding established in federal law, no CSP may be compounded that: (1) Is essentially a copy of one or more commercially available drug products, unless: (A) that 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 dispensing, or in a health care facility licensed pursuant	Prescribers and pharmacies often become aware that a drug is likely to be in short supply or out of stock in the near future. Without the changes below, pharmacies will not be able to compound a drug until is actually in short supply rather than in anticipation of short supply. Thus, there may be a significant interruption in supply. The critical factor is dispensing and selling only copies that are in short supply not the actual compounding of these drugs.

	to Health and Safety Code Section 1250 where the drug product cannot be obtained from the manufacturer or wholesaler and documentation is maintained, or (B) The pharmacist determines and documents that the preparation produces a clinically significant difference based on the medical need of an identified individual patient	"e) In addition to prohibitions and requirements for compounding established in federal law, no CSP may be ~~compounded~~ <u>dispensed or sold</u> that:…." ".....that are in short supply at the time of ~~compounding and at the time of~~ dispensing,…." "(B) The pharmacist ~~determines and~~ documents that the preparation produces a clinically significant difference…." **The pharmacist is not in a position to determine if a preparation will produce a clinical difference, that is the purview of the prescriber. The pharmacist should only be required to document the need.** ".....based on the medical need of an identified individual patient <u>or patient population</u>" **Updating this language will allow for office use in veterinary practice as well as population-based prescriptions.**

1735.1 (e)(2) & 1736.1 (e)(2)	Is made with any component not suitable for use in a CNSP for the intended veterinary population, unless allowable under the Animal Medicinal Drug Use Clarification Action of 1994 (AMDUCA).	AMDUCA is a statute that does not address compounding (text of the statute is in the attachments). While the intent of this inclusion is unclear, referencing AMDUCA in this manner has the effect of eliminating animal compounding in the state of CA as there is no substance "allowable under AMDUCA" that can be utilized in compounding. We believe the Board's actual intent is to reference CFR 21 Part 530.13 (which is also included in the attachments). This is also problematic as the only ingredients mentioned under this section of regulation are FDA approved commercially available products. This has the effect of essentially eliminating the use of bulk drug (API) in animal compounding. It would significantly reduce the number of compounded dosage forms available to CA patients. Please see our introductory statements for more detail. Recommendation: Remove ambiguous and irrelevant reference to AMDUCA and

		provide a clear pathway for compounding veterinary preparations from bulk drug API in compliance with USP. Under USP, compounders already must use the highest quality APIs available from FDA-registered manufacturers. If the Board intends to add "suitability" requirements, please clearly explain to CA pet owners how substances that are suitable for use in compounding for human patients are not suitable for use in their pet's medication.
1735.11 (a)(1) & 1736.17 (a)(1)	Comply with USP Chapter 1163, Quality Assurance in Pharmaceutical Compounding.	This has been mentioned in previous comment sections, USP Chapters above 1000 are for reference only and not intended to be a regulatory requirement.
1736.1 (e)(1)(A)	(A) that 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 dispensing, or in a health care facility licensed pursuant to Health and Safety Code Section 1250 where the drug product cannot be obtained from the manufacturer or wholesaler and documentation is maintained,	Retail compounders will face the same struggles in obtaining out of stock ingredients as health systems and should be able to utilize the same exemption with proper documentation of inaccessibility of product. Recommendation: Expand this language to include retail compounders and veterinary practices.

1736.1 (e)(4)	Requires end product sterilization unless sterilization occurs within the same licensed compounding location.	Requiring end product sterilization to occur onsite removes viable sterilization methods such as gamma irradiation and ethylene oxide that provide terminal sterilization but are typically outsourced. Removing these options will have unintended consequences that may lead to improperly sterilized products or insufficient sterilization procedures that could lead to patient harm. Recommendation: Remove this language entirely or add the possibility of validating an outsourced sterilization method.
1737.6	The SOPs of a premises where HDs are handled shall address environmental wipe sampling for HD surface residue, its frequency, and areas of testing	This language should be removed and deferred to the language in USP 800 which has this as a "should" and not a "shall". The industry is simply not ready for this and while theoretically it can provide a pharmacy with data on its cleaning practices, making this a requirement provides no patient protection or benefit. It will only add costs to the pharmacy with limited to no benefit until the testing industry can provide good data for trending purposes.
1737.14 (b)	(b) When ~~furnishing~~ dispensing ~~an~~ a compounded	Recommendation: Change "shall be provided" to "shall

	antineoplastic HD to a patient or patient's agent, a sufficient supply of ASTM D-6978 standard gloves, ~~that meet the ASTM D-6978 standard~~, shall be provided to the patient or the patient's agent, to allow for appropriate administration, handling, and disposal of the HD	be made available for purchase".
1737.17 (a) and 1737.17 (b)	(a) Any ~~premises entity~~ facility ~~engaged in the compounding or handling of HDs~~ shall maintain and follow written SOPs for all situations in which HDs are compounded or antineoplastics are otherwise manipulated antineoplastic ~~HDs are handled throughout the facility~~. (b) A facility where the compounding of HDs is performed or otherwise manipulates antineoplastic HDs shall have ~~The~~ SOPs ~~for compounding or handling HDs shall~~ that include at least the following	Subpoint (a) is confusingly worded as written and should be further cleaned up to clarify the intent of the subpoint. Subpoint (b) seems to be saying almost the same thing as subpoint (a), but without clarifying (a) it is hard to tell. Recommendation: Either clarify language in subpoint (a) or consider consolidating subpoints (a) and (b) if intent is the same.

Thank you for your consideration.

Erik Clausen, PharmD/MBA
Vice President Pharmacy Compliance
Wedgewood Pharmacy LLC

APPENDIX 1: AMDUCA

Public Law 103-396
103d Congress

An Act

To amend the Federal Food, Drug, and Cosmetic Act to clarify the application of the Act with respect to alternate uses of new animal drugs and new drugs intended for human use, and for other purposes.

Oct. 22, 1994
[S. 340]

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

Animal Medicinal Drug Use Clarification Act of 1994.
21 USC 301 note.

SECTION 1. SHORT TITLE.

This Act may be cited as the "Animal Medicinal Drug Use Clarification Act of 1994".

SEC. 2. UNAPPROVED USES.

(a) GENERAL RULE.—Section 512(a) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360b(a)) is amended by adding the following new paragraphs at the end:

"(4)(A) Except as provided in subparagraph (B), if an approval of an application filed under subsection (b) is in effect with respect to a particular use or intended use of a new animal drug, the drug shall not be deemed unsafe for the purposes of paragraph (1) and shall be exempt from the requirements of section 502(f) with respect to a different use or intended use of the drug, other than a use in or on animal feed, if such use or intended use—

"(i) is by or on the lawful written or oral order of a licensed veterinarian within the context of a veterinarian-client-patient relationship, as defined by the Secretary; and

"(ii) is in compliance with regulations promulgated by the Secretary that establish the conditions for such different use or intended use.

The regulations promulgated by the Secretary under clause (ii) may prohibit particular uses of an animal drug and shall not permit such different use of an animal drug if the labeling of another animal drug that contains the same active ingredient and which is in the same dosage form and concentration provides for such different use.

"(B) If the Secretary finds that there is a reasonable probability that a use of an animal drug authorized under subparagraph (A) may present a risk to the public health, the Secretary may—

"(i) establish a safe level for a residue of an animal drug when it is used for such different use authorized by subparagraph (A); and

"(ii) require the development of a practical, analytical method for the detection of residues of such drug above the safe level established under clause (i).

The use of an animal drug that results in residues exceeding a safe level established under clause (i) shall be considered an unsafe use of such drug under paragraph (1). Safe levels may be established under clause (i) either by regulation or order.

"(C) The Secretary may by general regulation provide access to the records of veterinarians to ascertain any use or intended use authorized under subparagraph (A) that the Secretary has determined may present a risk to the public health.

"(D) If the Secretary finds, after affording an opportunity for public comment, that a use of an animal drug authorized under subparagraph (A) presents a risk to the public health or that an analytical method required under subparagraph (B) has not been developed and submitted to the Secretary, the Secretary may, by order, prohibit any such use.

"(5) If the approval of an application filed under section 505 is in effect, the drug under such application shall not be deemed unsafe for purposes of paragraph (1) and shall be exempt from the requirements of section 502(f) with respect to a use or intended use of the drug in animals if such use or intended use—

"(A) is by or on the lawful written or oral order of a licensed veterinarian within the context of a veterinarian-client-patient relationship, as defined by the Secretary; and

"(B) is in compliance with regulations promulgated by the Secretary that establish the conditions for the use or intended use of the drug in animals.".

(b) OTHER AMENDMENTS.—

(1) SECTION 301.—Section 301 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 331) is amended—

(A) in paragraph (e), by striking "507(d) or (g)," and inserting "507(d) or (g), 512(a)(4)(C),"; and

(B) by adding at the end the following:

"(u) The failure to comply with any requirements of the provisions of, or any regulations or orders of the Secretary, under section 512(a)(4)(A), 512(a)(4)(D), or 512(a)(5).".

(2) SECTION 512(e).—Section 512(e)(1)(A) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 360b(e)(1)(A)) is amended by inserting before the semicolon the following: "or the condition of use authorized under subsection (a)(4)(A)".

(3) SECTION 512(l).—Section 512(l)(1) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 360b(l)(1)) is amended by striking "relating to experience" and inserting "relating to experience, including experience with uses authorized under subsection (a)(4)(A),".

21 USC 360b note.

(c) REGULATIONS.—Not later than 2 years after the date of the enactment of this Act, the Secretary of Health and Human Services shall promulgate regulations to implement paragraphs (4)(A) and (5) of section 512(a) of the Federal Food, Drug, and Cosmetic Act (as amended by subsection (a)).

21 USC 360b note.

(d) EFFECTIVE DATE.—The amendments made by this section shall take effect upon the adoption of the final regulations under subsection (c).

SEC. 3. MAPLE SYRUP.

(a) PREEMPTION.—Section 403A(a) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 343–1(a)) is amended—

(1) in paragraph (1), by inserting at the end the following: "except that this paragraph does not apply to a standard of

identity of a State or political subdivision of a State for maple syrup that is of the type required by sections 401 and 403(g),";

(2) in paragraph (2), by inserting at the end the following: "except that this paragraph does not apply to a requirement of a State or political subdivision of a State that is of the type required by section 403(c) and that is applicable to maple syrup,"; and

(3) in paragraph (3) by inserting at the end the following: "except that this paragraph does not apply to a requirement of a State or political subdivision of a State that is of the type required by section 403(h)(1) and that is applicable to maple syrup,".

(b) PROCEDURE.—Section 701(e)(1) (21 U.S.C. 371(e)(1)) is amended by striking "or maple syrup (regulated under section 168.140 of title 21, Code of Federal Regulations).".

Approved October 22, 1994.

LEGISLATIVE HISTORY—S. 340:

CONGRESSIONAL RECORD, Vol. 140 (1994):
Oct. 4, considered and passed Senate.
Oct. 6, considered and passed House.

Appendix 2: 21 CFR Part 530

Title 21—Food and Drugs
Chapter I—Food and Drug Administration, Department of Health and Human Services
Subchapter E—Animal Drugs, Feeds, and Related Products

Part 530 Extralabel Drug Use in Animals
Subpart A General Provisions
§ 530.1 Scope.
§ 530.2 Purpose.
§ 530.3 Definitions.
§ 530.4 Advertising and promotion.
§ 530.5 Veterinary records.
Subpart B Rules and Provisions for Extralabel Uses of Drugs in Animals
§ 530.10 Provision permitting extralabel use of animal drugs.
§ 530.11 Limitations.
§ 530.12 Labeling.
§ 530.13 Extralabel use from compounding of approved new animal and approved human drugs.
Subpart C Specific Provisions Relating to Extralabel Use of Animal and Human Drugs in Food-Producing Animals
§ 530.20 Conditions for permitted extralabel animal and human drug use in food-producing animals.
§ 530.21 Prohibitions for food-producing animals.
§ 530.22 Safe levels and analytical methods for food-producing animals.
§ 530.23 Procedure for setting and announcing safe levels.
§ 530.24 Procedure for announcing analytical methods for drug residue quantification.
§ 530.25 Orders prohibiting extralabel uses for drugs in food-producing animals.
Subpart D Extralabel Use of Human and Animal Drugs in Animals Not Intended for Human Consumption
§ 530.30 Extralabel drug use in nonfood animals.
Subpart E Safe Levels for Extralabel Use of Drugs in Animals and Drugs Prohibited From Extralabel Use in Animals
§ 530.40 Safe levels and availability of analytical methods.
§ 530.41 Drugs prohibited for extralabel use in animals.

PART 530—EXTRALABEL DRUG USE IN ANIMALS

Authority: 15 U.S.C. 1453, 1454, 1455; 21 U.S.C. 321, 331, 351, 352, 353, 355, 357, 360b, 371, 379e.

Source: 61 FR 57743, Nov. 7, 1996, unless otherwise noted.

Subpart A—General Provisions

§ 530.1 Scope.

This part applies to the extralabel use in an animal of any approved new animal drug or approved new human drug by or on the lawful order of a licensed veterinarian within the context of a valid veterinary-client-patient relationship.

§ 530.2 Purpose.

The purpose of this part is to establish conditions for extralabel use or intended extralabel use in animals by or on the lawful order of licensed veterinarians of Food and Drug Administration approved new animal drugs and approved new human drugs. Such use is limited to treatment modalities when the health of an animal is threatened or suffering or death may result from failure to treat. This section implements the Animal Medicinal Drug Use Clarification Act of 1994 (the AMDUCA) (Pub. L. 103-396).

§ 530.3 Definitions.

(a) ***Extralabel use*** means actual use or intended use of a drug in an animal in a manner that is not in accordance with the approved labeling. This includes, but is not limited to, use in species not listed in the labeling, use for indications (disease or other conditions) not listed in the labeling, use at dosage levels, frequencies, or routes of administration other than those stated in the labeling, and deviation from the labeled withdrawal time based on these different uses.

(b) ***FDA*** means the U.S. Food and Drug Administration.

(c) The phrase *a reasonable probability that a drug's use may present a risk to the public health* means that FDA has reason to believe that use of a drug may be likely to cause a potential adverse event.

(d) The phrase *use of a drug may present a risk to the public health* means that FDA has information that indicates that use of a drug may cause an adverse event.

(e) The phrase *use of a drug presents a risk to the public health* means that FDA has evidence that demonstrates that the use of a drug has caused or likely will cause an adverse event.

(f) A *residue* means any compound present in edible tissues that results from the use of a drug, and includes the drug, its metabolites, and any other substance formed in or on food because of the drug's use.

(g) A *safe level* is a conservative estimate of a drug residue level in edible animal tissue derived from food safety data or other scientific information. Concentrations of residues in tissue below the safe level will not raise human food safety concerns. A safe level is not a safe concentration or a tolerance and does not indicate that an approval exists for the drug in that species or category of animal from which the food is derived.

(h) ***Veterinarian*** means a person licensed by a State or Territory to practice veterinary medicine.

(i) A *valid veterinarian-client-patient relationship* is one in which:

(1) A veterinarian has assumed the responsibility for making medical judgments regarding the health of (an) animal(s) and the need for medical treatment, and the client (the owner of the animal or animals or other caretaker) has agreed to follow the instructions of the veterinarian;

(2) There is sufficient knowledge of the animal(s) by the veterinarian to initiate at least a general or preliminary diagnosis of the medical condition of the animal(s); and

(3) The practicing veterinarian is readily available for followup in case of adverse reactions or failure of the regimen of therapy. Such a relationship can exist only when the veterinarian has recently seen and is personally acquainted with the keeping and care of the animal(s) by virtue of examination of the animal(s), and/or by medically appropriate and timely visits to the premises where the animal(s) are kept.

§ 530.4 Advertising and promotion.

Nothing in this part shall be construed as permitting the advertising or promotion of extralabel uses in animals of approved new animal drugs or approved human drugs.

§ 530.5 Veterinary records.

(a) As a condition of extralabel use permitted under this part, to permit FDA to ascertain any extralabel use or intended extralabel use of drugs that the agency has determined may present a risk to the public health, veterinarians shall maintain the following records of extralabel uses. Such records shall be legible, documented in an accurate and timely manner, and be readily accessible to permit prompt retrieval of information. Such records shall be adequate to substantiate the identification of the animals and shall be maintained either as individual records or, in food animal practices, on a group, herd, flock, or per-client basis. Records shall be adequate to provide the following information:

(1) The established name of the drug and its active ingredient, or if formulated from more than one ingredient, the established name of each ingredient;

(2) The condition treated;

(3) The species of the treated animal(s);

(4) The dosage administered;

(5) The duration of treatment;

(6) The numbers of animals treated; and

(7) The specified withdrawal, withholding, or discard time(s), if applicable, for meat, milk, eggs, or any food which might be derived from any food animals treated.

(b) A veterinarian shall keep all required records for 2 years or as otherwise required by Federal or State law, whichever is greater.

(c) Any person who is in charge, control, or custody of such records shall, upon request of a person designated by FDA, permit such person designated by FDA to, at all reasonable times, have access to, permit copying, and verify such records.

Subpart B—Rules and Provisions for Extralabel Uses of Drugs in Animals

§ 530.10 Provision permitting extralabel use of animal drugs.

An approved new animal drug or human drug intended to be used for an extralabel purpose in an animal is not unsafe under section 512 of the act and is exempt from the labeling requirements of section 502(f) of the act if such use is:

(a) By or on the lawful written or oral order of a licensed veterinarian within the context of a valid veterinarian-client-patient relationship; and

(b) In compliance with this part.

§ 530.11 Limitations.

In addition to uses which do not comply with the provision set forth in § 530.10, the following specific extralabel uses are not permitted and result in the drug being deemed unsafe within the meaning of section 512 of the act:

(a) Extralabel use in an animal of an approved new animal drug or human drug by a lay person (except when under the supervision of a licensed veterinarian);

(b) Extralabel use of an approved new animal drug or human drug in or on an animal feed;

(c) Extralabel use resulting in any residue which may present a risk to the public health; and

(d) Extralabel use resulting in any residue above an established safe level, safe concentration or tolerance.

§ 530.12 Labeling.

Any human or animal drug prescribed and dispensed for extralabel use by a veterinarian or dispensed by a pharmacist on the order of a veterinarian shall bear or be accompanied by labeling information adequate to assure the safe and proper use of the product. Such information shall include the following:

(a) The name and address of the prescribing veterinarian. If the drug is dispensed by a pharmacy on the order of a veterinarian, the labeling shall include the name of the prescribing veterinarian and the name and address of the dispensing pharmacy, and may include the address of the prescribing veterinarian;

(b) The established name of the drug or, if formulated from more than one active ingredient, the established name of each ingredient;

(c) Any directions for use specified by the veterinarian, including the class/species or identification of the animal or herd, flock, pen, lot, or other group of animals being treated, in which the drug is intended to be used; the dosage, frequency, and route of administration; and the duration of therapy;

(d) Any cautionary statements; and

(e) The veterinarian's specified withdrawal, withholding, or discard time for meat, milk, eggs, or any other food which might be derived from the treated animal or animals.

§ 530.13 Extralabel use from compounding of approved new animal and approved human drugs.

(a) This part applies to compounding of a product from approved animal or human drugs by a veterinarian or a pharmacist on the order of a veterinarian within the practice of veterinary medicine. Nothing in this part shall be construed as permitting compounding from bulk drugs.

(b) Extralabel use from compounding of approved new animal or human drugs is permitted if:

(1) All relevant portions of this part have been complied with;

(2) There is no approved new animal or approved new human drug that, when used as labeled or in conformity with criteria established in this part, will, in the available dosage form and concentration, appropriately treat the condition diagnosed. Compounding from a human drug for use in food-producing animals will not be permitted if an approved animal drug can be used for the compounding;

(3) The compounding is performed by a licensed pharmacist or veterinarian within the scope of a professional practice;

(4) Adequate procedures and processes are followed that ensure the safety and effectiveness of the compounded product;

(5) The scale of the compounding operation is commensurate with the established need for compounded products (e.g., similar to that of comparable practices); and

(6) All relevant State laws relating to the compounding of drugs for use in animals are followed.

(c) Guidance on the subject of compounding may be found in guidance documents issued by FDA.

Subpart C—Specific Provisions Relating to Extralabel Use of Animal and Human Drugs in Food-Producing Animals

§ 530.20 Conditions for permitted extralabel animal and human drug use in food-producing animals.

(a) The following conditions must be met for a permitted extralabel use in food-producing animals of approved new animal and human drugs:

(1) There is no approved new animal drug that is labeled for such use and that contains the same active ingredient which is in the required dosage form and concentration, except where a veterinarian finds, within the context of a valid veterinarian-client-patient relationship, that the approved new animal drug is clinically ineffective for its intended use.

(2) Prior to prescribing or dispensing an approved new animal or human drug for an extralabel use in food animals, the veterinarian must:

(i) Make a careful diagnosis and evaluation of the conditions for which the drug is to be used;

(ii) Establish a substantially extended withdrawal period prior to marketing of milk, meat, eggs, or other edible products supported by appropriate scientific information, if applicable;

(iii) Institute procedures to assure that the identity of the treated animal or animals is carefully maintained; and

(iv) Take appropriate measures to assure that assigned timeframes for withdrawal are met and no illegal drug residues occur in any food-producing animal subjected to extralabel treatment.

(b) The following additional conditions must be met for a permitted extralabel use of in food-producing animals an approved human drug, or of an animal drug approved only for use in animals not intended for human consumption:

(1) Such use must be accomplished in accordance with an appropriate medical rationale; and

(2) If scientific information on the human food safety aspect of the use of the drug in food-producing animals is not available, the veterinarian must take appropriate measures to assure that the animal and its food products will not enter the human food supply.

(c) Extralabel use of an approved human drug in a food-producing animal is not permitted under this part if an animal drug approved for use in food-producing animals can be used in an extralabel manner for the particular use.

§ 530.21 Prohibitions for food-producing animals.

(a) FDA may prohibit the extralabel use of an approved new animal or human drug or class of drugs in food-producing animals if FDA determines that:

(1) An acceptable analytical method needs to be established and such method has not been established or cannot be established; or

(2) The extralabel use of the drug or class of drugs presents a risk to the public health.

(b) A prohibition may be a general ban on the extralabel use of the drug or class of drugs or may be limited to a specific species, indication, dosage form, route of administration, or combination of factors.

§ 530.22 Safe levels and analytical methods for food-producing animals.

(a) FDA may establish a safe level for extralabel use of an approved human drug or an approved new animal drug when the agency finds that there is a reasonable probability that an extralabel use may present a risk to the public health. FDA may:

(1) Establish a finite safe level based on residue and metabolism information from available sources;

(2) Establish a safe level based on the lowest level that can be measured by a practical analytical method; or

(3) Establish a safe level based on other appropriate scientific, technical, or regulatory criteria.

(b) FDA may require the development of an acceptable analytical method for the quantification of residues above any safe level established under this part. If FDA requires the development of such an acceptable analytical method, the agency will publish notice of that requirement in the FEDERAL REGISTER.

(c) The extralabel use of an animal drug or human drug that results in residues exceeding a safe level established under this part is an unsafe use of such drug.

(d) If the agency establishes a safe level for a particular species or category of animals and a tolerance or safe concentration is later established through an approval for that particular species or category of animals, for that species or category of animals, the safe level is superseded by the tolerance or safe concentration for that species or category of animals.

§ 530.23 Procedure for setting and announcing safe levels.

(a) FDA may issue an order establishing a safe level for a residue of an extralabel use of an approved human drug or an approved animal drug. The agency will publish in the FEDERAL REGISTER a notice of the order. The notice will include:

(1) A statement setting forth the agency's finding that there is a reasonable probability that extralabel use in animals of the human drug or animal drug may present a risk to the public health;

(2) A statement of the basis for that finding; and

(3) A request for public comments.

(b) A current listing of those drugs for which a safe level for extralabel drug use in food-producing animals has been established, the specific safe levels, and the availability, if any, of a specific analytical method or methods for drug residue detection will be codified in § 530.40.

§ 530.24 Procedure for announcing analytical methods for drug residue quantification.

(a) FDA may issue an order announcing a specific analytical method or methods for the quantification of extralabel use drug residues above the safe levels established under § 530.22 for extralabel use of an approved human drug or an approved animal drug. The agency will publish in the FEDERAL REGISTER a notice of the order, including the name of the specific analytical method or methods and the drug or drugs for which the method is applicable.

(b) Copies of analytical methods for the quantification of extralabel use drug residues above the safe levels established under § 530.22 will be available upon request from the Communications and Education Branch (HFV-12), Division of Program Communication and Administrative Management, Center for Veterinary Medicine, 7500 Standish Pl., Rockville, MD 20855. When an analytical method for the detection of extralabel use drug residues above the safe levels established under § 530.22 is developed, and that method is acceptable to the agency, FDA will incorporate that method by reference.

§ 530.25 Orders prohibiting extralabel uses for drugs in food-producing animals.

(a) FDA may issue an order prohibiting extralabel use of an approved new animal or human drug in food-producing animals if the agency finds, after providing an opportunity for public comment, that:

(1) An acceptable analytical method required under § 530.22 has not been developed, submitted, and found to be acceptable by FDA or that such method cannot be established; or

(2) The extralabel use in animals presents a risk to the public health.

(b) After making a determination that the analytical method required under § 530.22 has not been developed and submitted, or that such method cannot be established, or that an extralabel use in animals of a particular human drug or animal drug presents a risk to the public health, FDA will publish in the FEDERAL REGISTER, with a 90-day delayed effective date, an order of prohibition for an extralabel use of a drug in food-producing animals. Such order shall state that an acceptable analytical method required under § 530.22 has not been developed, submitted, and found to be acceptable by FDA; that such method cannot be established; or that the extralabel use in animals presents a risk to the public health; and shall:

(1) Specify the nature and extent of the order of prohibition and the reasons for the prohibition;

(2) Request public comments; and

(3) Provide a period of not less than 60 days for comments.

(c) The order of prohibition will become effective 90 days after date of publication of the order unless FDA publishes a notice in the FEDERAL REGISTER prior to that date, that revokes the order of prohibition, modifies it, or extends the period of public comment.

(d) The agency may publish an order of prohibition with a shorter comment period and/or delayed effective date than specified in paragraph (b) of this section in exceptional circumstances (e.g., where there is immediate risk to the public health), provided that the order of prohibition states that the comment period and/or effective date have been abbreviated because there are exceptional circumstances, and the order of prohibition sets forth the agency's rationale for taking such action.

(e) If FDA publishes a notice in the FEDERAL REGISTER modifying an order of prohibition, the agency will specify in the modified order of prohibition the nature and extent of the modified prohibition, the reasons for it, and the agency's response to any comments on the original order of prohibition.

(f) A current listing of drugs prohibited for extralabel use in animals will be codified in § 530.41.

(g) After the submission of appropriate information (i.e., adequate data, an acceptable method, approval of a new animal drug application for the prohibited extralabel use, or information demonstrating that the prohibition was based on incorrect data), FDA may, by publication of an appropriate notice in the FEDERAL REGISTER, remove a drug from the list of human and animal drugs prohibited for extralabel use in animals, or may modify a prohibition.

(h) FDA may prohibit extralabel use of a drug in food-producing animals without establishing a safe level.

Subpart D—Extralabel Use of Human and Animal Drugs in Animals Not Intended for Human Consumption

§ 530.30 Extralabel drug use in nonfood animals.

(a) Because extralabel use of animal and human drugs in nonfood-producing animals does not ordinarily pose a threat to the public health, extralabel use of animal and human drugs is permitted in nonfood-producing animal practice except when the public health is threatened. In addition, the provisions of § 530.20(a)(1) will apply to the use of an approved animal drug.

(b) If FDA determines that an extralabel drug use in animals not intended for human consumption presents a risk to the public health, the agency may publish in the FEDERAL REGISTER a notice prohibiting such use following the procedures in § 530.25. The prohibited extralabel drug use will be codified in § 530.41.

Subpart E—Safe Levels for Extralabel Use of Drugs in Animals and Drugs Prohibited From Extralabel Use in Animals

§ 530.40 Safe levels and availability of analytical methods.

(a) In accordance with § 530.22, the following safe levels for extralabel use of an approved animal drug or human drug have been established: [Reserved]

(b) In accordance with § 530.22, the following analytical methods have been accepted by FDA: [Reserved]

§ 530.41 Drugs prohibited for extralabel use in animals.

(a) The following drugs, families of drugs, and substances are prohibited for extralabel animal and human drug uses in food-producing animals.

(1) Chloramphenicol;

(2) Clenbuterol;

(3) Diethylstilbestrol (DES);

(4) Dimetridazole;

(5) Ipronidazole;

(6) Other nitroimidazoles;

(7) Furazolidone.

(8) Nitrofurazone.

(9) Sulfonamide drugs in lactating dairy cattle (except approved use of sulfadimethoxine, sulfabromomethazine, and sulfaethoxypyridazine);

(10) Fluoroquinolones; and

(11) Glycopeptides.

(12) Phenylbutazone in female dairy cattle 20 months of age or older.

(13) Cephalosporins (not including cephapirin) in cattle, swine, chickens, or turkeys:

(i) For disease prevention purposes;

(ii) At unapproved doses, frequencies, durations, or routes of administration; or

(iii) If the drug is not approved for that species and production class.

(b) The following drugs, families of drugs, and substances are prohibited for extralabel animal and human drug uses in nonfood-producing animals: [Reserved]

(c) [Reserved]

(d) The following drugs, or classes of drugs, that are approved for treating or preventing influenza A, are prohibited from extralabel use in chickens, turkeys, and ducks:

(1) Adamantanes.

(2) Neuraminidase inhibitors.

[62 FR 27947, May 22, 1997, as amended at 67 FR 5471, Feb. 6, 2002; 68 FR 9530, Feb. 28, 2003; 68 FR 14134, Mar. 24, 2003; 71 FR 14377, Mar. 22, 2006; 77 FR 745, Jan. 6, 2012]

Keck Medicine of USC

December 5, 2024

SENT VIA ELECTRONIC MAIL TO CALIFORNIA BOARD OF PHARMACY (BOP) CONTACT PERSON: LORI MARTINEZ (PharmacyRulemaking@dca.ca.gov)

Re: Compounded Drug Preparations, Notice of Proposed Action, Proposed New Sections 1735-1738 of Title 16, Division 17, Articles 4.5-4.8 of the California Code of Regulations

Dear Ms. Martinez,

On behalf of the Keck Medicine of USC Department of Pharmacy and its seven licensed pharmacies, the following comments on the proposed regulations for compounded drug preparations are respectfully submitted.

Institution/ Contact Name	Keck Medicine of USC Pharmacies	Contact Name: Daniel I. Kudryashov
Section, Subdivision	**Proposed Language**	**Recommendation / Comment**
1735.1(f)	In addition to prohibitions and requirements for compounding established in federal law, **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 (C) Documentation describing the conditions in (1)(A) & (1)(B) is maintained in a readily retrievable format"	**Comment**: This requirement exceeds current FDA guidance for the industry and will impose an unjustified burden on health-system pharmacies, creating gaps in patient care and negatively affecting clinical outcomes. The FDA guidance uses the term "should" when discussing compounding in 503A facilities. By prohibiting this practice, the BOP would impose a burden on inpatient hospital pharmacy licensees and negatively impact patient outcomes when a drug is unavailable within the institution, yet there is an urgent clinical need. Additionally, determining that the compounded product produces a clinically significant difference for the medical need of a patient will be challenging and subjective. Maintaining retrievable justification documentation each time a medication is compounded will burden operations and may impact timely patient care. Furthermore, USP 795 allows for any CNSP compounding when the master formulation record (MFR) is available.

		Recommendation: To allow for continuity of care, change the language to "In addition to prohibitions and requirements for compounding established in federal law, **no CNSP should** be prepared that".
1736.1(b)	1736.1(b) 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.	**Comment:** The 24-hour limitation on immediate-use compounding in cases of inadvertent failure of standard engineering controls may adversely impact hospital pharmacies' ability to meet patient care needs adequately. Compounding with an immediate-use BUD could be a short-term plan while addressing the failure and determining a long-term plan. In the event of compounding equipment failure, ISO classified area(s) recertification may be needed and not feasible within a 24-hour period. Furthermore, it may take several weeks for a facility to develop alterative pathways for compounding in ISO classified areas or segregated compounding areas (SCA) to meet patient care needs (e.g. developing a memorandum of understanding with a neighboring facility, establishing a new SCA, or deploying a mobile compounding unit). A grace period of 24 hours is woefully inadequate. For patient safety, immediate-use compounding should be allowed if all USP 797 requirements are followed. **Recommendation:** Due to significant safety concerns and barriers for access to care in unexpected downtime situations, the Board is asked to remove this section completely and follow USP 797 recommendations with regards to immediate use compounding.
1736.13(a)(3)(A)	(a) A CSP label shall include all of the following: (3) Instructions for administration. (A) For CSPs, the rate of infusion, or range of rates of infusion as prescribed, or the	**Comment**: Displaying "rate of infusion, or range of rates of infusion" is not feasible to accomplish in many contemporary electronic medical record (EMR) systems. Most of labels for titratable medications display the rate as "As Directed", and the order details are specified in the EMR. This practice meets patient safety recommendations outlined in

	duration for the entire CSP to be administered.	The Joint Commission elements of performance (MM.04.01.02). It is a safer practice to maintain those elements in the EMR to make the most up-to-date information available to the administering nurse in real time. In acute care settings where provider orders frequently change, the source of truth regarding medication rates must remain the EMR . Furthermore, the size of labels will make it impossible to write all required labeling requirements, directions, barcode without covering the compound. It will be impacting the nursing bedside scanning process upon administration and increase the risk of medication errors. **Recommendation**: This new proposal is not aligned with CMS-approved accreditation agency standards for patient care and not feasible to achieve with some, of not all of the current EMR systems. It will likely result in higher risk of medication errors and adversely impact patient care. Recommend revising as follows: "A) For an admixed CSP, the <u>rate of infusion, or range of rates of infusion as directed (unless the infusion rate is specified in a shared electronic medical record system)</u>, or the duration for the entire CSP to be administered."
1737.5(c)	A pass-through is not allowed between the C-SEC into an unclassified space. (c.) Effective (OAL insert six months following the effective date) , a pass-through is **not allowed** between the hazardous buffer room into an unclassified space.	**Comment**: The prohibition on the presence of a pass-through between a C-SEC and unclassified space has not been a requirement in USP 797 nor USP 800 and would be a new mandatory requirement for pharmacies, if passed. The approval of this requirement will place extreme hardship on existing facilities that were compliant with applicable codes <u>at the time of construction</u>. Cleanroom designs were approved, and compounding pharmacies were licensed by the CA board and CDPH. Given extremely high cost of cleanroom re-design, construction and modifications, this requirement may lead to pharmacy closures, negatively affecting patient access to care.

		Additionally, C-SEC are ISO 7 classified areas with a mandatory air exchange of 30-60 per hour, allowing for purging of the limited air released from the pass-through. Furthermore, HEPA filtered pass-through are limiting airborne particle contamination and reducing the contamination of the air introduced in the C-SEC. **Per USP 800**, " Although not a recommended facility design, if the negative-pressure HD buffer room is entered though the positive-pressure non-HD buffer room, the following is also **required: …** A method to transport HDs, HD CSPs, and HD waste into and out of the negative pressure buffer room to minimize the spread of HD contamination. **This may be accomplished by use of a pass-through chamber between the negative-pressure buffer area and adjacent space.** The pass-through chamber must be included in the facility's certification to ensure that particles are not compromising the air quality of the negative-pressure buffer room." **Recommendation**: The BOP is asked to reconsider requiring this standard not specified in USP 800, or otherwise providing for a process to allow the presence in existing construction (e.g., grandfathering). For example: "(c) A pass-through is not allowed between the C-SEC into an unclassified space in cleanrooms if constructed after [insert date]." "Where an existing pass-through is already installed between the C-SEC into an unclassified space, the doors must be gasketed and interlocking and the pass-through must be included in the facility's certification"
1737.6 Subsection (a) and (b)	(a) 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.	**Comment**: Environmental quality and control utilizing wipe sampling for hazardous drug surface residue is not a mandatory requirement in USP 800. While this is a worthwhile effort that pharmacies compounding hazardous drugs *should* follow, there are several significant barriers that arise when this requirement is made mandatory.

		Per USP 800, "t*here are currently no certifying agencies for vendors of wipe sample kits.*" Existing common marker HDs that can be assayed include Cyclophosphamide, ifosfamide, methotrexate, fluorouracil, and platinum-containing drugs. However, pharmacies may not be compounding these NIOSH Group 1 antineoplastic drugs but other medications from Group 2 or 3. As previously stated, there is currently no kit available to test non -anti-neoplastic drugs. Therefore, a pharmacy attempting to comply with the new requirement and the apparent intent of the environment quality and control program, will not be successful in doing so at present. **Recommendation**: The Board's proposed requirement to establish an environmental wipe sampling cannot be justified given several significant concerns and barriers listed above. <u>We recommend the Board considers removing the proposed additional requirements and follow the standards outlined in USP 800 as it related to this section.</u>

Respectfully,

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