Alliance for Pharmacy Compounding

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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.

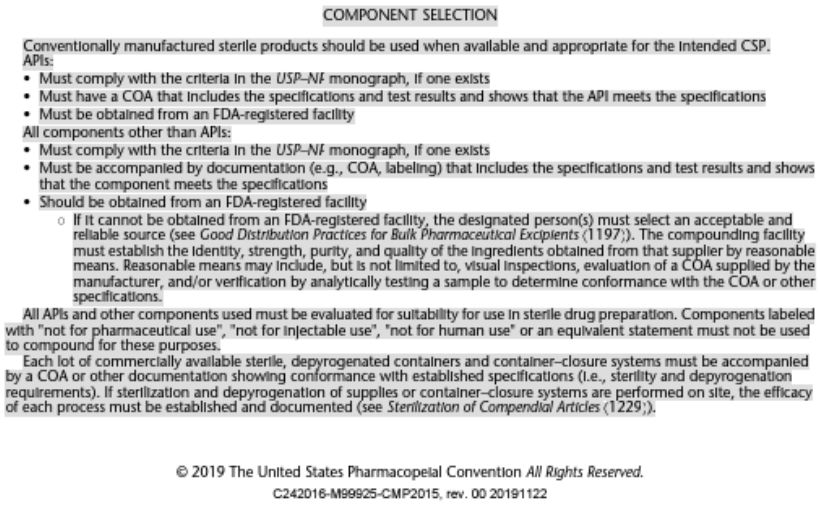
We are grateful that the board has heeded public comments and has made some adjustments to the initially proposed compounding regulations. However, we continue to have significant concern with proposed regulations that exceed USP guidelines, and we are frustrated that the Board seems to be unwilling 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⟩).

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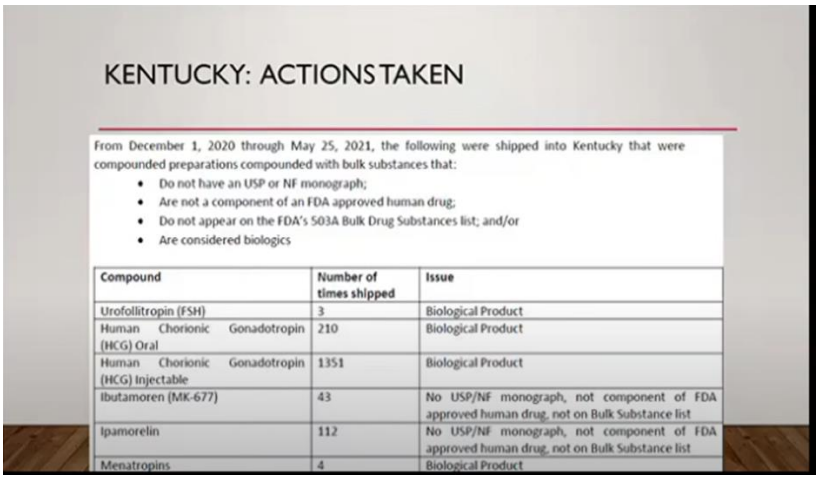
That same presentation included a misleading slide that suggested other states are acting against compounders for using API in FDA’s interim Category 1. The information presented on the slide, from a case in Kentucky, showed that the pharmacy in question was compounding with a biologic agent, not a drug, 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.