California State Board of Pharmacy
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Business, Consumer Services and Housing Agency
Department of Consumer Affairs
Gavin Newsom, Governor

COMPOUNDING COMMITTEE
MEETING MINUTES

DATE: March 13, 2019

LOCATION: Department of Consumer Affairs
First Floor Hearing Room
1625 N. Market Blvd.
Sacramento, CA 95834

COMMITTEE MEMBERS PRESENT: Maria Serpa, Licensee Member, Chairperson
Stan Weisser, Licensee Member, Vice Chairperson
Victor Law, Licensee Member
Allen Schaad, Licensee Member

COMMITTEE MEMBERS NOT PRESENT: Shirley Kim, Public Member

STAFF MEMBERS PRESENT: Anne Sodergren, Interim Executive Officer
Julia Ansel, Chief of Enforcement
Anna Kalantar, Supervising Inspector
MaryJo Tobola, Senior Enforcement Manager
Laura Freedman, DCA Staff Counsel
Kelsey Pruden, DCA Staff Counsel

1. **Call to Order and Establishment of Quorum and General Announcements**

   Chairperson Serpa called the meeting to order at 10:02 am. Board members present: Allen Schaad, Maria Serpa, Stan Weisser and Victor Law. A quorum was established.

2. **Public Comment on Items not on the Agenda/Agenda Items for Future Meetings**
   Board President Victor Law suggested current issues affecting practitioners as a future agenda item. Board counsel Laura Freedman recommended that specific issues could be presented to the board during Public Comment and placed on future agenda.

3. **Presentation on the Current Proposed Revisions to USP General Chapter 797, Regarding Pharmaceutical Compounding – Sterile Preparations**

The committee heard a presentation on the current proposed revisions to USP General Chapter <797> regarding pharmaceutical compounding for sterile preparations by Supervising Inspector Anna Kalantar.

Supervising Inspector Kalantar provided an overview of the United States Pharmacopeia (USP) 2015-2020 Council of Experts including Healthcare Quality Standards Collaborative Group which includes compounding. USP maintains resolutions to work with stakeholders in the development and maintenance of practice and quality standards in sterile and nonsterile compounding. USP includes General Chapters: <795> – Pharmaceutical Compounding – Nonsterile Products; <797> – Pharmaceutical Compounding – Sterile Preparations; <800> – Hazardous Drugs – Handling in Healthcare Settings; and <825> – Radiopharmaceutical Preparation, Compounding, Dispensing, and Repackaging. Dr. Kalantar updated the committee on the status of USP revising Chapter <797> and subsequent revisions. The committee was provided with a summary of the changes made in draft Chapter <797> based on the 18 sections.

Dr. Kalantar noted that the draft section "Introduction and Scope," describe the minimum standards to be followed when preparing compounded sterile human and animal drugs based on current scientific information and best practices for sterile compounding. The section defines sterile compounding as the process of combining, admixing, diluting, pooling, reconstituting, repackaging, or otherwise altering a drug or bulk drug substance to create a sterile medication. The section also defines common terms including preparing, administration, reconstitution and repackaging. The draft section clarifies docking and activation of proprietary bag and vial systems in accordance with the manufacturer's instructions for immediate administration to an individual patient is not considered compounding; however, the draft section specifies docking for future activation and administration is considered compounding.

Dr. Kalantar noted risk categories were eliminated as the risk categories (e.g., low, medium, or high) provided false security on sterility assurance as all sterile compounding has risk. Dr. Kalantar further explained the new model uses Category 1 and Category 2 based on conditions under which the compounded sterile preparations (CSP) are made including the probability for microbial growth and the time period for which they must be used.

Dr. Kalantar reviewed the draft section "Personnel Qualifications: Training, Evaluation and Requalification," noting delineated personnel qualifications and core competencies based on Categories 1-2 rather than risk categories. Personnel qualifications for visual observation of hand hygiene and garbing, gloved fingertip and thumb sampling and media fill testing must be completed every six months regardless of the category. If any of these are failed, they must be passed before allowed to compound. Core competencies must be completed every 12 months and include written and hands-on proficiency. Core competencies are now extended to non-compounding staff such as cleaning crews to establish competencies to maintain the proper environment.

Dr. Kalantar reviewed the draft section "Personal Hygiene and Garbing," which specify the minimum requirements that must be completed prior to entering a compounding area. The draft section notes acceptable hand hygiene methods and required hand hygiene procedures.

Dr. Kalanatar indicated that the order of garbing is to be determined by the facility and included in standard operating procedures (SOPS). Minimum garbing requirements to enter a buffer room or SCA are outlined. The draft chapter specifies if using RABS [compounding aseptic containment isolator (CACI) and compounding aseptic isolator (CAI)] disposable gloves either nonsterile or sterile are required inside of the gauntlet gloves and sterile gloves are required over the gauntlet gloves. Dr. Kalantar noted gowns may no longer be reused once removed from the sterile compounding area.

Dr. Kalantar reviewed the draft section "Facilities and Engineering Controls," which defines a cleanroom suite as an ante-room and buffer room and provided requirements for each room. Dr. Kalantar noted the HEPA filters are now required to be part of the ceiling and cannot be part of the HVAC systems. The draft section defined the Segregated Compounding Area (SCA) and provided the requirements. Dr. Kalantar noted all surfaces should be smooth, non-shedding and resistant to damage. The draft chapter defined Primary Engineering Controls (PEC) and provides requirements for the PECs. Dr. Kalantar noted smoke pattern tests must be performed initially and every 6 months. The draft chapter notes the minimum air exchange requirements based on the compounding area type. Dr. Kalantar added the new requirement for ISO Class 8 rooms.

Dr. Kalantar noted the certifications must be completed under dynamic conditions every six months in accordance with CETA guidelines or an equivalent guideline. Certifications required include airflow testing, HEPA filter integrity testing, total particle count testing and smoke visualization studies. The draft chapter notes when recertification is required.

Dr. Kalantar reviewed the draft section "Microbiological Air and Surface Monitoring," that requires the monitoring to be done under dynamic operating conditions. Further, the draft chapter specifies viable air sampling must be conducted initially and every 6 months and surface sampling must be completed initially and every monthly. Surface sampling will be increased to monthly as surface contamination poses the greatest risk. Monitoring functions must be completed again with new facility and equipment certification, after servicing of facilities/equipment and when problems are identified. Action levels are identified and if levels are exceeded, there must be an investigation and corrective action plan. The chapter no longer references highly pathogenic organisms and there is no need to identify every colony forming unit (CFU). If action levels are exceeded, the organism must be identified with the assistance of a microbiologist.

Dr. Kalantar reviewed the draft section "Cleaning and Disinfecting Compounding Areas," which defines cleaning, disinfecting and one-step disinfectant. Surfaces must be cleaned prior to disinfecting unless using EPA one-step disinfectant cleaner. Minimum requirements and frequencies for cleaning and disinfecting requirements are delineated as well as minimum requirements for cleaning supplies. If there is no daily compounding, these need to be initiated prior to compounding. Cleaning tools are only removed when disposed.

Dr. Kalantar reviewed the draft section "Equipment, Supplies and Components," defines the restricted-access barrier system (RABS); CACI; and CAI but specifies CAI and CACI are not isolators. Component and Active Pharmaceutical Ingredient (API) are defined. APIs must be

obtained from an FDA-registered facility; must comply with *USP-NF* monograph, if one exists; and must be accompanied by a certificate of analysis (COA). COA must demonstrate the specifications, test results and demonstrate the API meets the specifications of the *USP-NF*, if one exists.

Dr. Kalantar reviewed the draft section "Sterilization and Depyrogenation," which delineates the sterilization methods. Dr. Kalantar clarified that sterilized products may be compounded from sterile or nonsterile ingredients. When compounding from sterile ingredients, the sterility of the ingredients must be maintained. When compounding from nonsterile ingredients, the sterility must be achieved. The two methods for achieving sterilization are defined as aseptic preparation and terminal sterilization. Terminal sterility is preferred because it can achieve sterility assurance level of 10^{-6}.

Dr. Kalantar reviewed the draft section "Standard Operating Procedures, Master Formulation and Compounding Records," which establish the requirement for SOPs, master formulation records and compounding records. Dr. Kalantar clarified that a master formulation records is required if the CSP is prepared for a batch greater than one patient and the CSP is prepared from nonsterile ingredients. She noted that the chapter defines batch as more than one unit of CSP prepared in a single process. Dr. Kalantar stated compounding records are required for all CSPs. The compounding record form is not specified as long as the requirements are met. The record may be stored electronically but must be retrievable.

Dr. Kalantar reviewed the draft section "Release Testing," which requires visual inspection prior to release of any Category 1 and 2 CSPs. Sterility testing is required for Category 2 to extend the BUD. Sterility testing must be completed according to USP <71>. Bacterial endotoxin testing is excluded for inhalations and topical ophthalmics but is required for Category 2 CSPs if made from one or more nonsterile ingredients/components and if assigned Beyond Use Date (BUD) requires sterility testing.

Dr. Kalantar reviewed the draft sections "Labeling," "Establishing Beyond Use Dates (BUD)," Use of Conventionally Manufactured Products," and "Use of CSPs as Components" which detail the requirements for labeling, provide that compounders must consider stability factors and sterility factors when establishing BUDs. Dr. Kalantar noted that BUDs for Category 1 and 2 are included in the proposed chapter and that multi-dose containers are defined and must be prepared as a Category 2 CSP. Further Dr. Kalantar noted that the proposed chapter details the time within which a product must be used based on the type of container and the appropriate storage requirements related to BUDs.

Dr. Kalantar highlighted the draft section "Quality Assurance (QA) and Quality Control (QC)," including the required elements: recall SOP procedures; complaint handling; and adverse event reporting.

Dr. Kalantar discussed the draft "CSP Storage, Handling, Packaging, Shipping and Transporting," which outline requirements for packaging materials, storage and shipping/transporting of CSP as well as the draft section "Documentation," establishing the minimum requirements for when CSPs are prepared.

Board President Law inquired how inspectors verify documentation of all requirements. Dr. Kalantar advised that inspectors request documentation from the licensee at the time of inspection that is reviewed by board inspectors. Dr. Kalantar noted that typically, licensees have information ready for board inspectors. If additional information is required, the licensee retrieves it for the inspector.

Chairperson Serpa inquired about docking for future activation and administration being considered compounding. Dr. Serpa indicated this is a change in practice and asked Dr. Kalantar for additional comment. Dr. Kalantar responded it may be performed outside of ISO 5 but aseptic technique must be followed. If it is docked for future activation, under the proposed chapter, would be compounding, and this chapter will apply. Dr. Serpa indicated this will be a large area for education as it occurs in multiple environments and implications in some acute care settings like nursing homes.

Chairperson Serpa commented that another issue will be the temperature ranges and will be discussed in the future. Dr. Kalantar provided the chapter states what the temperatures should be rather than must be required.

Chairperson Serpa inquired about the components mentioned in the presentation and if that included supplies such as syringes, bags, shields, devices etc.. Dr. Kalantar indicated that was how she interpreted it as well. Dr. Kalantar indicated it was not discussed during the open mic but may be included in the future by the providers.

The committee took a break and returned at 11:47 am.

BJ Bartleson of the California Hospital Association referred to an educational tool put together by some of the associations. Dr. Serpa commented that the tool would have to be re-written to incorporate the changes to the USP compounding chapters. Discussion noted that updating the educational tool would be most beneficial after the proposed changes to the various chapters are finalized. Ms. Bartleson indicated the concern for the 430+ hospitals undergoing major construction based on what they think will happen and to stay on track with deadlines. Ms. Bartleson indicated she would appreciate continued collaboration. Ms. Bartleson commented with AB 973 would change regulations and USP standards and the hospitals will be looking forward to that change.

Paul Mahan of PETNET Solutions advised the committee he participated as a panel member on writing USP <825> and nondisclosure agreements are required for participants, so the participants are unable to comment.

Pharmacist Holly Strom commented and inquired how the presentation was compiled. Dr. Kalantar said it was based on the USP September 5th open mic and added to the information provided. Ms. Strom inquired about the definition for components and the comment “must be evaluated when received and before use.” Ms. Strom asked what the inspectors would be looking for during inspections for proof this was completed. Dr. Kalantar responded all components must be evaluated when received and before use. Interim Executive Officer Anne Sodergren added that these items would be clarified at the time the board pursues regulations and referred Ms. Strom to the documentation section of the draft USP <797>. DCA Counsel added comments can be added to USP as well.

Ms. Strom also inquired about packaging of materials and reference to shaking of the materials. Dr. Kalantar responded the draft chapter states the pharmacy will need to consider the shaking. Ms. Strom mentioned use of 3PLs should be considered with the development of the board's regulations.

Christine Versichele of Dynalabs provided an overview of what is provided to a customer who requests a stability study for an extended BUD.

A sterile compounding pharmacist inquired about the intention of the education for the board. Dr. Serpa commented there is a series of educational meetings regarding the future of USP and to determine what regulatory changes may be needed for our state. The pharmacist inquired about the fingertip testing. Dr. Kalantar provided the intent of the process is for the person to demonstrate they can go through the process without adding contamination to their hand. DCA Counsel referred the pharmacist to the USP for commenting on draft USP <797>.

4. Future Committee Meeting Dates

Chairperson Serpa announced the committee's next educational meeting is scheduled for April 16, 2019, in Sacramento.

5. Adjournment

Chairperson Serpa adjourned the meeting at 12:17 pm.