Comments on Proposed CA Sterile Compounding Regs

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1736 Sterile Compounding Definitions

"Certificate of Analysis" (COA) means a document produced by the manufacturer or supplier that certifies the quality of the component and demonstrates that the component conforms to the defined specifications, and, if applicable, meets the requirements in USP.

> **Reason:** The content in this definition is important for pharmacists to analyze, however, it may go beyond what a COA typically offers. Therefore, most COAs would likely be deficient. The supplier usually does not give the original COA from the manufacturer, instead it transcribes the data supplied by the manufacturer into a new COA. Also, I rarely see COAs that include the manufacturing conditions (ie. cGMP) and the suitability of use in pharmaceuticals. This could be accomplished by ensuring the manufacturer is registered with FDA and analyzing the grade of the material. There are other minor changes that I think would be more appropriate for compounders.
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> The following is the definition in USP <797>:
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> ***Certificate of analysis (COA):*** *A report from the supplier of a component, container, or closure that accompanies the supplier's material and contains the specifications and results of all analyses and a description of the material.*

(d) "Essentially a copy" of a commercially available drug product means all preparations that are comparable in active ingredients, strength, and dosage form to commercially available drug products, except that it does not include any preparations in which there has been a change, made for an identified individual patient, which produces for that patient a clinically significant difference, as determined by a prescribing practitioner, between that compounded preparation and the comparable commercially available drug product.

> **Reason:** The current definition may be interpreted quite broadly so that any compounded preparation with similar ingredients, but a different strength or route of administration might be considered an essential copy.

(j) "Quality" means the degree to which the components and preparation meets the intended characteristics , complies with relevant law and regulation, and means the

absence of harmful levels of contaminants, including but not limited to filth, putrid, or decomposed substances, the absence of active ingredients other than those listed on the label, or the absence of inactive ingredients other than those listed on the master formula record as specified in USP 797.

> **Reason:** The current definition may be confused with the effectiveness of the preparation (eg. the ability to cure an infection) instead of meeting the intended characteristics of the medication prescribed.

1736.1 Sterile Compounding Scope.

(d) In addition to prohibitions established in federal law, no licensed pharmacy personnel shall compound a CSP that:
(1) Is essentially a copy of one or more commercially available drug products, unless:
(A) that drug product appears on an ASHP (American Society of Health- System Pharmacists) or FDA list of drugs that are in short supply at the time of compounding and at the time of dispense, or
(B) the compounding of that CSP is justified by a specific, documented medical need made known to the pharmacist prior to compounding. Documentation of the shortage or the specific medical need shall be maintained in a readily retrievable format.
(2) Is made with any component not suitable for use in a CSP for the intended patient population.

(4) Cannot be sterilized within the licensed location.

> **Reason:** For subsection 2, I believe “suitable” may be better verbiage because it is difficult to know if the manufacturer intended the component for compounding. For subsection 3, it is unclear what this is referring to. Conventionally manufactured products are often used as components of CSPs.

(f) In addition to the provisions provided in Section 1707.2, consultation shall be provided orally or in writing to the patient and/or patient’s agent concerning proper use, storage, handling and disposal of the CSP and related supplies furnished.

> **Reason:** Many compounded medications are shipped to the patient with written instructions and an offer for a verbal consultation. The current language may be interpreted that oral consultations are always required for shipped prescriptions.

1736.2 PERSONNEL TRAINING AND EVALUATION

(b) Aseptic manipulation competency initial training and competency and ongoing training and competency documentation shall include the Primary Engineering Control (PEC's) type and 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 SOPs are identical
2. The facility designs are identical
3. The PECs are of the same type and sufficiently similar to accommodate the use of the same SOPs describing use and cleaning.

Reason: The current language may be interpreted to require the presterilization equipment and materials (eg. beakers, graduated cylinders, spin plates, etc) to be exactly the same during the media fill. These are irrelevant to the aseptic manipulation competency.

(c) Aseptic manipulation ongoing training and competency shall occur each time and for each staff member involved in an event where the quality assurance program yields an unacceptable result as defined in the SOPs referenced in section 1736.17 that may indicate microbial contamination of CSPs due to poor practices. Aseptic manipulation ongoing training and competency procedures shall be defined in the facilities SOPs

> **Reason:** It is not clear how to implement this requirement. For example, if a new staff member has poor aseptic technique, would all sterile compounders and supervising pharmacists need to redo training? Also, would this apply to environmental monitoring issues or component selection issues? I think it would be helpful to narrow this to the staff members involved in poor practices.

(d) Compounding personnel or persons with direct oversight over personnel performing compounding, verifying and/or handling CSPs who fail any aspect of aseptic manipulation 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, except that this does not apply to:

(1) Persons performing direct oversight, verifying and/or handling CSPs who retake and successfully pass the competency within 30 days of the original failed attempt.

> **Reason:** If a pharmacist overseeing compounding fails any aspect of the aseptic competency, the earliest they would be able to successfully complete a new competency is 2 weeks. This could be very problematic for pharmacies with fewer pharmacists. It is reasonable to require pharmacists to pass this competency for educational purposes, but I think giving more leeway would be helpful for compliance and would not adversely affect quality.

1736.6 MICROBIOLOGICAL AIR AND SURFACE MONITORING

(b) At a minimum, to trend for growth of microorganisms, viable air sampling must occur every 6 months, and any microorganism recovered (growth) shall be identified at least to the genus species, regardless of the CFU count. Professional judgement shall be used to determine the appropriate action necessary to remedy identified trends regardless on the action level. Investigation must be consistent with the deviation and must include evaluation of trends.

> **Reason:** I agree with this requirement, however it should be separated from certifications because viable air sampling is not required to be in conjunction to re-certification.

1736.9 EQUIPMENT, SUPPLIES, AND COMPONENTS

(d) All active pharmaceutical ingredients used to compound a CSP shall be manufactured by an FDA registered facility and suitable for use in sterile pharmaceuticals. A Certificate of Analysis (COA) which 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 manufactured drug products.

Reason: Some components such as container closures or sterile tubing are not manufactured in FDA registered facilities, however the details of the sterilization methods are on the COA.

1736.10 STERILIZATION AND DEPYROGENATION

(f) Sterilization of supplies and/or container–closure systems shall be done in compliance with USP Chapter 1229, Sterilization of Compendial Articles.

> **Reason:** This may be a typo, but USP <1229> doesn't address depyrogenation.

1736.11 MASTER FORMULATION AND COMPOUNDING RECORDS

(1) The source referenced to support the assigned beyond-use date (BUD), if it exists; each source referenced shall be readily retrievable at the time of compounding and shall be maintained for three years from the date each CSP is dispensed.

> **Reason:** Compounders are required to consider stability data for all BUDs assigned and it is appropriate to cite this data to support the BUD. However, some preparations don't have any stability data. If so, a conservative BUD must be assigned within the limits in USP <797>. The current language may be interpreted to mean that compounders must have stability studies for all preparations (instead of just for the Category 3 CSPs).

(1) The date, or date and time of preparation, if the BUD is listed in hours. The time of preparation is the time when compounding the CSP started, which also determines when the assigned BUD starts, if the BUD is listed in hours.

> **Reason:** This language is helpful to clarify that the date and/or time of compounding refers to when the compounding process started. However, this language may be confused to mean that the BUD must specify a day and time (eg. Discard after 06/15/2023 at 1PM). However, most BUDs are assigned in days only, which would make the time started irrelevant. The time compounded would only be applicable when the BUD is listed in hours.

1736.16. USE OF CSPS AS COMPONENTS

A compounded stock solution intended for use in a CSP must comply with all provisions of this article including Category 1, Category 2, or Category 3.

Reason: The language may be interpreted that CSPs as components must comply with all CSP categories, instead of only the one that is applicable.