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Blueprint for Inspection of Pharmacies

Module III – Compounding Sterile Preparations

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Introduction

United States Pharmacopeia (USP)

Chapter <797> Pharmaceutical Compounding - Sterile

The objective of USP Chapter <797> is to describe conditions and practices to prevent harm, including death, to patients that could result from:

- Microbial contamination (nonsterility);
- Excessive bacterial endotoxins;
- Variability in the intended strength of correct ingredients that exceeds either monograph limits for official articles or 10% for nonofficial articles;
- Unintended chemical and physical contaminants; and
- Ingredients of inappropriate quality in compounded sterile preparations (CSPs).

Despite the extensive attention in the chapter to the provision, maintenance, and evaluation of air quality, the avoidance of direct or physical contact contamination is paramount. It is generally acknowledged that direct or physical contact of critical sites of CSPs with contaminants, especially microbial sources, poses the greatest probability of risk to patients. Therefore, compounding personnel must be meticulously conscientious in precluding contact contamination of CSPs both within and outside ISO Class 5 areas.

To achieve the above five conditions and practices, the chapter provides minimum practice and quality standards for CSPs of drugs and nutrients based on current scientific information and best sterile compounding practices. The use of technologies, techniques, materials, and procedures other than those described in the chapter is not prohibited so long as they have been proven to be equivalent or superior with statistical significance to those described therein. The standards in the chapter do not pertain to the clinical administration of CSPs in patients via application, implantation, infusion, inhalation, injection, insertion, instillation, and irrigation, which are the routes of administration. Four specific categories of CSPs are described in the chapter: low-risk level, medium-risk level, high-risk level, and immediate use.

The standards in the chapter are intended to apply to all persons who prepare CSPs and all places where CSPs are prepared (e.g., hospitals and other healthcare institutions, patient treatment clinics, pharmacies, physician practice facilities, and other locations and facilities in which CSPs are prepared, stored, and transported). Persons who perform sterile compounding include pharmacists, nurses, pharmacy technicians, and physicians. These terms recognize that most sterile compounding is performed by or under the supervision of pharmacists in pharmacies and also that the chapter applies to all healthcare personnel who prepare, store, and transport CSPs. For the purposes of the chapter, CSPs include any of the following:

1. Compounded biologics, diagnostics, drugs, nutrients, and radiopharmaceuticals, including but not limited to the following dosage forms that must be sterile when they are administered to patients: aqueous, bronchial and nasal inhalations, baths and soaks for live organs and tissues, injections (e.g., colloidal dispersions, emulsions, solutions, suspensions), irrigations for wounds and body cavities, ophthalmic drops and ointments, and tissue implants.

2. Manufactured sterile products that are either prepared strictly according to the instructions appearing in manufacturers' approved labeling (product package inserts) or prepared differently than published in such labeling. [Note: The FDA states that "Compounding does not include mixing, reconstituting, or similar acts that are performed in accordance with the directions contained in approved labeling provided by the product's manufacturer and other manufacturer directions consistent with that labeling." However, the FDA-approved labeling (product package insert) rarely describes environmental quality (e.g., ISO Class air designation, exposure durations to non_ISO classified air, personnel garbing and gloving, and other aseptic precautions by which sterile products are to be prepared for administration). Beyond-use exposure and storage dates or times for sterile products that have been either opened or prepared for administration are not specified in all package inserts for all sterile products. Furthermore, when such durations are specified, they may refer to chemical stability and not necessarily to microbiological purity or safety.]

ISO Classification of Particulate Matter in Room Air

(limits are in particles of 0.5 microns and larger per cubic meter [ISO] and cubic feet [FS 209E]*)

ISO Class	Class Name		Particle Count	
	U.S. FS 209E	ISO, m ³	FS 209E, ft ³	
3	Class 1	35.2	1	
4	Class 10	352	10	
5	Class 100	3,520	100	
6	Class 1,000	35,200	1,000	
7	Class 10,000	352,000	10,000	
8	Class 100,000	3,520,000	100,000	

**Adapted from former Federal Standard No. 209E, General Services Administration, Washington, DC 20407 (September 11, 1992) and International Standards Organization (ISO) 14644-1:1999, Cleanrooms and associated controlled environments – Part 1: Classification of air cleanliness.*

Microbial Contamination Risk Levels of Compounded Sterile Preparations

Low Risk Level

Preparations compounded under all of the following conditions are at a low risk of contamination:

1. The compounded sterile preparations (CSPs) are compounded with aseptic manipulations entirely within ISO Class 5 or better air quality using only sterile ingredients, products, components, and devices.
2. The compounding involves only transfer, measuring, and mixing manipulations using not more than three commercially manufactured packages of sterile products and not more than two entries into any one sterile container or package (e.g., bag, vial) of sterile product or administration container/device to prepare the CSP.
3. Manipulations are limited to aseptically opening ampuls, penetrating disinfected stoppers on vials with sterile needles and syringes, and transferring sterile liquids in sterile syringes to sterile administration devices, package containers of other

sterile products, and containers for storage and dispensing.

4. For a low risk level preparation, in the absence of passing a sterility test, the storage periods cannot exceed the following time periods: before administration, the CSPs are properly stored and are exposed for not more than 48 hours at controlled room temperature, for not more than 14 days at a cold temperature, and for 45 days in solid frozen state.

Examples of Low Risk Compounding

1. Single-volume transfers of sterile dosage forms from ampuls, bottles, bags, and vials using sterile syringes with sterile needles, other administration devices, and other sterile containers. The solution content of ampuls should be passed through a sterile filter to remove any particles.
2. Simple aseptic measuring and transferring with not more than three packages of manufactured sterile products, including infusion or diluents solution to compound admixtures and nutritional solutions.

Medium Risk Level

When CSPs are compounded aseptically under Low Risk conditions and one or more of the following conditions exist, such CSPs are at a medium risk of contamination:

1. Multiple individual or small doses of sterile products are combined or pooled to prepare a CSP that will be administered either to multiple patients or to one patient on multiple occasions.
2. The compounding process includes complex aseptic manipulations other than the single-volume transfer.
3. The compounding process requires unusually long duration, such as that required to complete dissolution or homogenous mixing.
4. For a medium risk preparation, in the absence of passing a sterility test, the storage periods cannot exceed the following time periods: before administration, the CSPs are properly stored and are exposed for not more than 30 hours at controlled room temperature, for not more than 9 days at a cold temperature, and for 45 days in solid frozen state.

Examples of Medium Risk Compounding

1. Compounding of total parenteral nutrition fluids using manual or automated devices during which there are multiple injection, detachments, and attachments of nutrient source products to the device or machine to deliver all nutritional components to the final sterile container.
2. Filling of reservoirs of injection and infusion devices with more than three sterile drug products and evacuation of air from those reservoirs before the filled device is dispensed.
3. Transfer of volumes from multiple ampuls or vials into one or more final sterile containers.

High Risk Level

CSPs compounded under any of the following conditions are either contaminated or at a high risk to become contaminated:

1. Nonsterile ingredients, including manufactured products not intended for sterile

routes of administration (e.g., oral), are incorporated or a nonsterile device is employed before sterilization.

2. Any of the following are exposed to air quality worse than ISO Class 5 for more than 1 hour:
 - Sterile contents of commercially manufactured products;
 - CSPs that lack effective antimicrobial preservatives; and
 - Sterile surfaces of devices and containers for the preparation, transfer, sterilization, and packaging of CSPs.
3. Compounding personnel are improperly garbed and gloved.
4. Nonsterile water-containing preparations are stored for more than 6 hours before being sterilized.
5. It is assumed, and not verified by examination of labeling and documentation from suppliers or by direct determination, that the chemical purity and content strength of ingredients meet their original or compendial specifications in unopened or in opened packages of bulk ingredients.

Examples of High Risk Compounding

1. Dissolving nonsterile bulk drug and nutrient powders to make solutions that will be terminally sterilized.
2. Exposing the sterile ingredients and components used to prepare and package CSPs to room air quality worse than ISO Class 5 for more than 1 hour.
3. Measuring and mixing sterile ingredients in nonsterile devices before sterilization is performed.
4. Assuming, without appropriate evidence or direct determination, that packages of bulk ingredients contain at least 95% by weight of their active chemical moiety and have not been contaminated or adulterated between uses.

Immediate Use

The immediate use provision is intended only for those situations where there is a need for emergency or immediate patient administration of a CSP. Such situations may include cardiopulmonary resuscitation, emergency room treatment, preparation of diagnostic agents, or critical therapy where the preparation of the CSP under conditions described for *Low Risk Level* subjects the patient to additional risk due to delays in therapy. Immediate use CSPs are not intended for storage for anticipated needs or batch compounding. Preparations that are medium risk level and high risk level CSPs shall not be prepared as immediate use CSPs.

Immediate use CSPs are exempt from the requirements described for Low Risk Level only when all of the following criteria are met:

1. The compounding process involves simple transfer of not more than three commercially manufactured packages of sterile nonhazardous products or diagnostic radiopharmaceutical products from the manufacturers' original containers and not more than two entries into any one container or package (e.g., bag, vial) of sterile infusion solution or administration container/device. For example, antineoplastic agents shall not be prepared as immediate use CSPs because they are hazardous drugs.
2. Unless required for the preparation, the compounding procedure is a continuous process not to exceed 1 hour.

3. During preparation, aseptic technique is followed and, if not immediately administered, the CSP is under continuous supervision to minimize the potential for contact with nonsterile surfaces, introduction of particulate matter or biological fluids, mix-ups with other CSPs, and direct contact of outside surfaces.
4. Administration begins not later than 1 hour following the start of the preparation of the CSP.
5. Unless immediately and completely administered by the person who prepared it or immediate and complete administration is witnessed by the preparer, the CSP shall bear a label listing patient identification information, the names and amounts of all ingredients, the name or initials of the person who prepared the CSP, and the exact 1-hour BUD and time.
6. If administration has not begun within 1 hour following the start of preparing the CSP, the CSP shall be promptly, properly, and safely discarded.

Compounding in worse than ISO Class 5 conditions increases the likelihood of microbial contamination, and administration durations of microbially contaminated CSPs exceeding a few hours increase the potential for clinically significant microbial colonization and thus for patient harm, especially in critically ill or immunocompromised patients.

[Abstracted from 2016 USP Compounding Compendium, current with USP-39/NF-34 through First Supplement]

General Operations Information

001.00 Does the pharmacy dispense sterile compounded preparations pursuant to a prescription?

001.01 Are patient profiles complete and DUR performed for each prescription?

001.02 Are sterile compounded prescriptions picked up at the pharmacy?

001.03 Are sterile compounded prescriptions delivered/mailed to patients in their homes or residential facilities?

001.04 Are sterile compounded prescriptions delivered/mailed to the practitioner for administration to the patient in the office, clinic, or facility?

002.00 Does the pharmacy distribute sterile compounded preparations?

002.01 Does the pharmacy distribute sterile compounded preparations to practitioners for office use?

002.02 Does the pharmacy distribute sterile compounded preparation to hospitals, clinics, or surgery centers?

002.03 Is the pharmacy registered with the FDA as an Outsourcing Facility?

002.04 Does the pharmacy have a sales force that distributes samples containing active ingredients?

003.00 Does the pharmacy provide sterile compounded preparations to other pharmacies for dispensing?

003.01 If so, does the pharmacy have central fill contracts or agreements with these pharmacies for patient-specific preparations?

004.00 Which of the following sterile compounds are prepared?

004.01 Allergen extracts

004.02 Parenteral solutions

004.03 Parenteral suspensions

004.04 Preservative-free parenterals

004.05 Ophthalmic preparations

- 004.06 Oral or nasal inhalation preparations (not topical sprays)
- 004.07 Baths and soaks for live organs and tissues
- 004.08 Irrigations for wounds and body cavities
- 004.09 Any other sterile preparations (implants, pellets, etc.)
- 005.00 Does the pharmacy compound investigational drugs?
- 006.00 Does the pharmacy only make essential copies of a commercially available drug product on the Drug Shortage List or for a clinically justified reason for individual patients?
 - 006.01 Products are verified as appearing on the Drug Shortage List in effect under 506(E) of the Federal Act at the time of compounding, distribution, and dispensing.
 - 006.02 The Drug Shortage List is monitored and when a drug product is no longer on the list, any remaining stock is quarantined and not available for distribution or dispensing.
- 007.00 Does the pharmacy perform low-risk compounding?
 - 007.01 Are all low-risk compounds assigned BUDs within USP guidelines (48 hours at controlled room temperature, 14 days refrigerated, 45 days frozen)?
 - 007.02 If extended BUDs are used, list products with extended BUDs and maximum BUD in notes.
 - 007.03 If extended BUDs are used, is further testing being performed to justify the use of extended BUDs?
- 008.00 Does the pharmacy perform medium-risk compounding?
 - 008.01 Are all medium-risk compounds assigned BUDs within USP guidelines (30 hours at controlled room temperature, 9 days refrigerated, 45 days frozen)?
 - 008.02 If extended BUDs are used, list products with extended BUDs and maximum BUD in notes.
 - 008.03 If extended BUDs are used, is further testing being performed to justify the use of extended BUDs?
- 009.00 Does the pharmacy perform high-risk compounding?

- 009.01 Are all high-risk compounds assigned BUDs within USP guidelines (24 hours at controlled room temperature, 3 days refrigerated, 45 days frozen)?
- 009.02 If extended BUDs are used, list products with extended BUDs and maximum BUD in notes.
- 009.03 If extended BUDs are used, is further testing being performed to justify the use of extended BUDs?
- 010.00 Does the pharmacy provide sterile compounded preparations to be administered via an implantable infusion pump?
- 011.00 Does the pharmacy perform compounding for *immediate use*?
- 012.00 Does the pharmacy perform compounding with *hazardous drugs*?
- 012.01 Is the pharmacy aware of the more stringent requirements of the proposed USP Chapter <800>?
- 012.02 Are hazardous drugs segregated and stored in a room that is negative pressure (at least 0.01" water column) to adjacent areas and with at least 12 ACPH?
- 012.03 Is hazardous drug waste quarantined in a designated area and disposed of in compliance with local, state, and federal regulations?
- 013.00 Are Safety Data Sheets (SDS) [formerly known as Material Safety Data Sheets (MSDS)] available to personnel for drugs and chemicals used in the pharmacy (including those for compounding, if applicable)?
- 014.00 Does the pharmacy perform compounding using *blood products* (or other biological materials), such as wound care, autologous eye drops, etc?
- 015.00 Does the pharmacy compound using any *federally controlled substances I-V*?
- 016.00 Does the pharmacy make any sterile compounded preparations using bulk powder Active Pharmaceutical Ingredients (APIs)?
- 016.01 Does the pharmacy purchase APIs directly from the manufacturer?
- 016.02 Does the pharmacy verify that the source of the API is an FDA-registered facility?
- 016.03 Does the pharmacy use active ingredients that are not from an FDA-registered facility?

- 017.00** Does the pharmacy use scales/balances for sterile compounding?
- 017.01 If so, what type of scale/balance is used?
- 017.02 If the scale/balance is electronic, does the pharmacy use the automatic calibration?
- 018.00** Does the pharmacy have a lyophilizer?
- 018.01 Where is the lyophilizer located?
- 018.02 Note the products lyophilized and the volume or percent of products per week produced using the lyophilizer.
- 018.03 Is the lyophilizer part of the viable air and surface sampling, media fill testing procedures, and cleaning schedules and procedures?
- 019.00** Does the pharmacy perform any testing in-house (not sent to an outside lab)?
- 020.00** Does the pharmacy send samples to an outside lab to perform testing?
- 021.00** Quality Assurance/Quality Improvement. Does the pharmacy's continuous quality improvement program include sterile compounding measures? If so, review 021.01 – 021.12 below.
- 021.01 Does the CQI program include QREs related to the preparation of compounded products?
- 021.02 Does the CQI program include nonviable environmental monitoring and testing?
- 021.03 Does the CQI program include viable environmental testing?
- 021.04 Does the CQI program include personnel testing and validation?
- 021.05 Does the CQI program include equipment calibration, testing, and validation?
- 021.06 Does the CQI program include sterilization method testing and validation.
- 021.07 Does the CQI program include end product testing (such as: potency, particulates, sterility, endotoxins, etc.)?
- 021.08 Does the CQI program include patient or prescriber reports or complaints regarding CSPs?

- 021.09 Does the facility QA program identify action limits or thresholds and the appropriate follow-up mechanisms when action limits or thresholds are exceeded, including a recall system?
- 021.10 Does the recall system include communication with both the patient and prescriber regarding the potentially contaminated CSP administered and the potential risks?
- 021.11 Are QREs involving CSPs that may have been contaminated or are recalled reported to the appropriate agency such as the Board of Pharmacy and/or FDA?
- 021.12 Are all incidents (Colony-forming units [CFUs] detected by any personnel, environmental, or product testing, or any other checks or tests including endotoxin, purity, potency, etc.) remediated, appropriately investigated, cause determined, and processes implemented to prevent in the future?

Component Selection and Use

- 022.00** All bulk drug substances (APIs) used are:
- (1) Compliant with the standards of an applicable USP or NF monograph, if one exists; or
 - (2) A component of an FDA-approved human drug product; or
 - (3) On the list of bulk drug substances for use in compounding developed by the FDA and issued through regulation. [*Note: must comply with (1) or (2) above until the FDA list is issued*]
- 022.01 Certificates of Analysis (COAs) obtained for all bulk APIs used for compounding.
- 022.02 USP- or NF-grade substances used, if available.
- 022.03 If compendia quality components are not available, chemically pure, analytical reagent grade or ACS [American Chemical Society]-certified components are used and are determined to be free from impurities.
- 022.04 APIs or other components have labeling indicating use for pharmaceutical compounding or manufacturing. Labels do not indicate “for research purposes only”, “not for drug use”, or are handwritten labels from other pharmacies.
- 022.05 If compounding for humans and animals, APIs or other components that are labeled for veterinary use only are segregated or marked in such a way to prevent them from being used for human compounding.

- 022.06** All substances and components have a complete label including a batch control or lot number, and an expiration date.
- 022.07** For APIs without an expiration date assigned by the manufacturer or supplier, the pharmacy assigns a conservative expiration date. The expiration date assigned is not greater than one year, and is supported with data and/or testing.
- 022.08** All APIs are labeled with the date they were received.
- 022.09** If the pharmacy repackages the APIs into smaller containers for ease of use, the expiration date assigned is conservative (typically the lesser of one year or the actual expiration date from the original container). Product may be tested to extend the expiration date, but may not exceed the original package expiration.
- 022.10** Bulk component containers are labeled with appropriate OSHA hazard communication labels and hazardous substances are segregated.
- 022.11** Components from foreign sources that are derived from ruminant animals (cow, sheep, goat) have documentation that the component is in compliance with federal laws governing processing, use, and importation – that the animals were free from disease, and that they were born, raised, and slaughtered in locations where spongiform encephalopathy and scrapie are not known to exist.
- 023.00** No preparations for human use are made or ingredients used that appear on the FDA's list of drug products withdrawn or removed from the market for safety reasons. The facility should have a copy of the list or other way to determine.
- 024.00** No preparations are compounded that present demonstrable difficulties for compounding as identified by the FDA.
- 025.00** When manufactured products are used for compounding, all the other excipients (in addition to the active ingredient) in the manufactured product are considered relative to the use, effectiveness, and stability of the compounded preparation to be made.
- 026.00** For animal compounding, does the compounding meet the same standards as compounding for human patients?
- 026.01** The pharmacist is knowledgeable or has references regarding the individual species' limitations in physiology and metabolic capacity that can result in toxicity when certain drugs or excipients are used.

- 026.02** It is determined and documented if the animal is used for food (meat, milk, eggs, etc.) or that the animal is a pet.
- 026.03** The pharmacist is familiar with or has a reference regarding drug residues in the food chain and withdrawal times if compounding for food-producing animals.
- 026.04** The facility has a list of drugs and components not allowed when compounding for food-producing animals.
- 026.05** The pharmacist is familiar with or has a reference regarding regulations for drug use in performance animals (e.g., race or show horses, racing dogs).
- 027.00** If the pharmacy compounds stock solutions or components (that are then used to compound a finished product) using APIs, these stock solutions are categorized as high-risk compounding.
- 027.01** The stock solutions are assigned a BUD based on the USP <797> high-risk compound BUD, or there is documentation of stability or testing to support an extended BUD.
- 027.02** Compounded preparations using the stock solution are classified as high-risk compounds with appropriate handling with regard to BUD and testing requirements.

Environment

- 028.00** If the facility performs both sterile and nonsterile compounding, the areas are separate and distinct.
- 029.00** If the facility performs compounding using blood products (or other biological material), this compounding area is separate and distinct from the general compounding areas.
- 029.01** Are components used in compounding with blood products restricted to the blood compounding area (not used in other compounding areas)?
- 030.00** Entry into the sterile compounding area is limited to task-critical employees [limited to only the pharmacist(s) and other trained and authorized pharmacy personnel].
- 031.00** The anteroom has a line of demarcation or other separation of the dirty to clean side.
- 031.01** Carts used to bring supplies from the storeroom are kept on the outside of the line of demarcation.

- 031.02** Carts used in the clean/buffer room are kept on the clean side of the line of demarcation.
- 032.00** All surfaces of the sterile compounding area carts, shelves, stools, chairs and other items resistant to disinfectants, non-permeable, non-carpeted or upholstered, and low-particulate generating.
- 033.00** Walls are painted with epoxy-based paint or other impermeable surface, and are seamless or have sealed seams where panels meet and corners with no cracks.
- 034.00** The ceiling tiles are composed of a vinyl surface, with the tiles caulked and sealed, and the seams where the walls meet the ceiling are caulked and sealed.
- 035.00** The floor is overlaid with wide sheet flooring and seamless or with heat-welded seams, with coving to the sidewall, and a sealed seam where the coving meets the wall.
- 036.00** The clean/buffer room or anteroom does not have dust-collecting overhangs, such as ceiling utility pipes, ledges, pneumatic tube stations, sprinkler heads, emergency exit signs, etc.
- 037.00** The exposed surfaces of the light fixtures are smooth, mounted flush, and sealed.
- 038.00** A working sink, located on the clean side of the line of demarcation, is available that enables pharmacy personnel to wash hands and enter the sterile compounding area without contaminating his/her hands and is away from/not adjacent to any PECs.
- 039.00** There is no sink or drain in the clean/buffer room.
- 040.00** Hand drying is with non-linting paper towels or an electronic or HEPA-filtered hand dryer.
- 040.01** If using a hand dryer, particle count and smoke testing is performed when the dryer is in use (while someone is actively using the dryer to dry their hands) at certification, and the immediate area around the dryer is part of the viable air and surface testing program performed [not applicable if only using towels].
- 041.00** All air ducts controlling air flow into the sterile compounding clean/buffer room and anteroom are equipped with HEPA filters that maintains the clean/buffer room in an ISO Class 7 environment.
- 042.00** Incoming air ducts through HEPA filters are on or near the ceiling and air return ducts are low on the walls in the anteroom and clean/buffer room.

- 043.00** If there are particle generating equipment/appliances in the clean/buffer room or anteroom (e.g., computers, printers, refrigerators, dishwashers, etc.), they are located by an air return so air flows over and out of the room taking particles with it, and this air flow has been confirmed by smoke testing while the equipment was in use.
- 044.00** Beverages including drinking water, chewing gum, candy or food items are prohibited from the clean/buffer room or the anteroom.
- 045.00** If compounding occurs using nonsterile ingredients, products, components, or devices (e.g., compounding with nonsterile APIs or using nonsterile vials and closures), the pharmacy has appropriate equipment to sterilize the finished product.
- 045.01** Pre-sterilization procedures for high-risk CSPs (such as weighing and mixing) are performed in no worse than ISO Class 8 environment.
- 046.00** Completely enclosed anteroom and clean/buffer room (with a door) are equipped with monitors or gauges to measure differential pressure.
- 046.01** Anteroom is at least 0.02" water column positive pressure to general pharmacy areas.
- 046.02** Clean/buffer room is at least 0.02" water column positive pressure to the anteroom.
- 046.03** Hazardous compounding room and storage area is at least 0.01" water column negative pressure to ISO Class 7 anteroom.
- 046.04** Pressures are read and recorded each shift, or a minimum of once daily, or in the alternative, are continuously recorded.
- 046.05** There is a plan in place to detect and react to pressure differentials outside limits.
- 047.00** If the clean/buffer room and anteroom are not fully enclosed (open or with plastic strips – no door that closes), the air flow is measured across the openings.
- 047.01** The air flow is at least 40 feet per minute across the entire opening.
- 047.02** Airflow is read and recorded each shift (minimum of once daily) or continuously.
- 047.03** Plan in place to detect and react to airflow measurements outside of limits

- 047.04** This area is used only for low- and medium-risk compounding. (High-risk not allowed.)
- 048.00** The temperature of the compounding area is controlled by a thermostat and an air conditioning system is in place.
- 048.01** Temperature in the *compounding area* is maintained to provide controlled room temperature of 20°C or cooler (68°F or cooler), or more restrictive if warranted by specific drug product storage requirements. Recommended temperature range for performing sterile compounding while garbed is between 64-72°F (18-22°C).
- 048.02** Temperature monitoring in place to detect any excursions (24/7) by continuous monitoring or retroactive detection using min/max. Temperature records are maintained.
- 048.03** Temperature monitoring is also performed in *drug storage area* (if separate from the compounding area). Temperature is maintained at controlled room temperature of 20° to 25° C (68° to 77° F) or as specified by FDA approved labeling for drug product storage.
- 048.04** Temperature in the *refrigerator or cooler* is maintained to provide controlled cold temperature of 2° to 8°C (36° to 46°F) or as specified by FDA approved labeling for drug product storage.
- 048.05** Temperature monitoring in place to detect any excursions (24/7) by continuous monitoring or retroactive detection using min/max. Temperature records are maintained.
- 048.06** Temperature in the *freezer* is maintained to provide controlled frozen temperature of -10° to 25°C (-13° to 14°F), or as specified by FDA approved labeling for drug product storage.
- 048.07** Temperature monitoring in place to detect any excursions (24/7) by continuous monitoring or retroactive detection using min/ax. Temperature records are maintained.
- 048.08** Action plan in place for temperature excursions including evaluating excursion effects on drug product integrity.
- 049.00** Humidity: If warranted by specific drug products, humidity in the compounding area is maintained to provide humidity within the specified ranges. If drug products require storage in a “dry place”, humidity is not to exceed 40%. Generally recommended range is 35-60% for performing sterile compounding.
- 049.01** If applicable, humidity monitoring in place to detect any excursions (24/7) by continuous monitoring or retroactive detection using min/max. Humidity records are maintained.

- 049.02** If applicable, excursion action plan in place including evaluating excursion effects on drug product integrity.
- 049.03** If applicable, humidity monitoring is also performed in drug storage areas (if separate from the compounding areas).
- 050.00** Blowers on ISO-5 primary engineering controls are operated continuously during compounding activity, including during interruptions of less than eight hours.
- 051.00** When the ISO-5 laminar air LAFW blower is turned off, and before other personnel enter to perform compounding activities, only one garbed person is allowed to enter the buffer area for the purpose of turning on the blower (for at least 30 minutes) and of sanitizing the work surfaces.
- 052.00** The doors into the anteroom from the general pharmacy area and from the anteroom into the clean/buffer room are prevented from both being open at the same time (by interlocking, training of personnel, or signage).
- 053.00** The inside and outside doors of a pass-through are prevented from both being open at the same time (by interlocking, training of personnel, or signage).
- 053.01** Pass-throughs are located between outside areas and the anteroom, or between the anteroom and the buffer room (and NOT between the outside areas directly into the buffer room)
{Recommended}
- 054.00** The immediate area around the doorway or pass-through into the anteroom from the general area is free of particle-generating materials (such as corrugated cardboard, etc.) and is located in an area that limits particles (not next to an outside door or window, etc.) to limit potential contamination from being brought in through the entry. *{Recommended}*
- 055.00** For BSC or LAFW that is NOT located in an ISO-7 clean/buffer room, the BSC or LAFW has been certified to maintain ISO-5 during compounding activities.
- 055.01** Used only for low-risk compounded preparations with a 12-hour or less BUD assigned.
- 055.02** All garbing requirements adhered to.
- 055.03** Located in an area that is maintained under sanitary conditions and only traveled by persons engaging in the compounding of sterile preparations.

- 055.04** Location does not contain any unsealed windows or doors that connect to the outdoors or areas of high traffic flow, and is not adjacent to construction sites, warehouses, or food preparation areas.
- 055.05** The sink is separated from the immediate area of the ISO-5 workbench (not adjacent) and an eyewash station.
- 056.00** For CAI/CACI that is NOT located in an ISO-7 clean/buffer room, the CAI/CACI has been certified to maintain ISO-5 under dynamic conditions including transferring of ingredients, components, and devices, and during preparation of compounded sterile preparations.
- 056.01** The pharmacy has documentation from the manufacturer that the CAI or CACI will meet this standard when located in worse than ISO-7 environments.
- 056.02** The CAI or CACI is located in an area that is maintained under sanitary conditions and only traveled by persons engaging in the compounding of sterile preparations.
- 056.03** There is a sink in the compounding area, not directly adjacent to the CAI or CACI, that enables pharmacy personnel to wash hands and an eyewash station.
- 056.04** For NIOSH hazardous compounding in a CACI that is NOT located in a clean/buffer room, the CACI is located in a physically separated area that maintains a negative pressure of 0.01" water column pressure to adjacent areas and a minimum of 12 air changes per hour (ACPH).

Cleaning and Disinfection

- 057.00** Are all personnel performing cleaning appropriately garbed?
- 058.00** Is the sterile compounding area equipped with appropriate non-shedding cleaning equipment and supplies?
- 059.00** If cleaning tools are reused, is there a procedure to rinse and sanitize the tools and an appropriate clean storage area and are buckets inverted to prevent moisture accumulation?
- 060.00** Are reusable tools appropriately labeled to prevent them from being used inappropriately, e.g., a mop used for the floors cannot also be used for the ceilings and walls?
- 061.00** Are there formulas and instructions for mixing or diluting the cleaning and sanitizing agents prior to use and is the preparation of cleaning supplies

documented?

- 062.00** Are cleaning and sanitizing agents appropriately labeled including expiration dates?
- 063.00** Are appropriate cleaning agents used that are effective for bacteria, viruses, fungi, and spores?
- 064.00** Is the ISO-5 primary engineering control cleaned at the beginning of each shift, between compounding activities, at least every 30 minutes while compounding and after spills or suspected surface contamination?
- 064.01** If heavily soiled, cleaning includes the appropriate agent.
- 065.00** Does sanitizing of the ISO-5 primary engineering control include sanitizing with sterile 70% isopropyl alcohol using a nonlinting wipe?
- 066.00** Does daily cleaning and sanitizing include counters and easily cleanable work surfaces?
- 067.00** Does daily cleaning include the floors starting from the clean/buffer room and working outwards? Floor cleaning does not occur during compounding.
- 068.00** If fatigue mats are used, are they cleaned daily and let dry on both sides?
- 069.00** Is a tacky mat used and if so, is there a procedure in place regarding replacement?
- 070.00** Are the ceilings, walls, all shelving, bins, carts, chairs, and the tops and sides of the primary engineering controls thoroughly cleaned monthly? This includes removing everything from shelves and bins before cleaning, cleaning the undersides of cart surfaces and stools, wheels, etc.
- 071.00** Is enough time allocated for cleaning activities, including contact/dwell times for the cleaning/disinfection agents?

Training

- 072.00** There is documentation that compounding personnel are appropriately trained including policies and procedures, documentation, hazardous drug handling, and aseptic technique. Compounding personnel includes persons performing, supervising, and verifying compounding activities.
- 072.01** All personnel performing compounding are not allowed to compound until training and initial testing is successfully completed.

- 072.02** All personnel that supervise compounding and/or perform verifications of other's compounding are not allowed to supervise or verify compounding until training and initial testing is successfully completed.
- 073.00** All personnel of reproductive capacity who handle or compound hazardous drugs or chemicals have confirmed in writing that they understand the risks of handling hazardous drugs.
- 074.00** There is documentation that all personnel (including housekeeping or other outside personnel) that perform cleaning activities in the compounding areas including hazardous compounding areas are appropriately trained in garbing, cleaning, and disinfection.
- 075.00** There is documentation of training on the operation of any equipment that may be used when preparing compounded sterile preparations.
- 076.00** If the pharmacy uses relief personnel from outside agencies to perform sterile compounding, training and certifications are verified.
- 077.00** There is documentation that all compounding personnel (including those supervising or performing verifications) have passed an initial written exam, and subsequent annual written exams for the appropriate compounding risk levels and NIOSH hazardous drugs.
- 078.00** There is documentation that all compounding personnel have passed an initial and subsequent annual competency assessments of aseptic compounding skills using observational audit tools including handling NIOSH hazardous drugs.
- 079.00** There is documentation that new compounding personnel have passed an initial observed gowning procedure and three gloved fingertip sampling tests.
- 080.00** There is documentation that compounding personnel preparing low or medium risk-level products have passed an annual observed gowning procedures and gloved fingertip sampling test.
- 081.00** There is documentation that a media fill test procedure is performed for each compounding employee at least annually for individuals that prepare low or medium risk-level products.
- 082.00** The media fill testing procedures include:
- 082.01** Media selection (including obtaining COAs or growth promotion certificates from suppliers);
 - 082.02** Fill volume;

- 082.03 Incubation time and temperature (30-35°C for a minimum of 7 days then 20-25°C for 7 days);
- 082.04 Inspection of filled units;
- 082.05 Documentation;
- 082.06 Interpretation of results; and
- 082.07 Action levels set with the corrective actions required.

- 083.00 *High-Risk Sterile Compounding:* There is documentation that compounding personnel have passed an observed gowning procedure and gloved fingertip sampling test every six months.

- 084.00 *High-Risk Sterile Compounding:* There is documentation that a media fill test procedure is performed for each compounding employee at least every six months for individuals that prepare high-risk level products.

- 085.00 Employees who have failed any testing are prohibited from compounding until training is performed/reviewed and subsequent testing is performed successfully.
 - 085.01 Gloved fingertip tests that failed have the organisms identified down to the genus to determine the most likely source of the contamination. This data is used to develop plans to prevent contamination.
 - 085.02 There is a plan to evaluate the sterile compounds prepared by an employee with failed gloved fingertip tests or media fills to detect potential contamination of the sterile preparations compounded.

Garbing

- 086.00 Personnel are prohibited from compounding, or entering the clean/buffer room or anteroom if they have a rash, sunburn, weeping sores, conjunctivitis, or an active respiratory infection.

- 087.00 Personnel are required to remove all personal outer garments such as hats, scarves, sweaters, vests, coats, or jackets and any makeup or cosmetics before entering compounding areas.

- 088.00 Personnel are required to remove all hand and wrist jewelry, and all visible jewelry or piercings, such as earrings, lip or eyebrow piercings, etc. before entering clean/buffer room.

- 089.00** Personnel are prohibited from wearing artificial nails or extenders, and required to keep natural nails neat and trimmed.
- 090.00** Garbing with dedicated shoes or shoe covers that are donned as the line of demarcation is crossed (with the dedicated or covered shoe never touching the same side of the line of demarcation as the dirty shoe).
- 091.00** Garbing includes head and facial hair covers and masks. There is a mirror available to check that all hair is covered.
- 092.00** Hand cleaning is performed in the anteroom and includes removing debris from under the nails with a nail cleaner followed by a vigorous washing of the hands and forearms with soap for at least 30 seconds with hands and arms then dried with a non-linting disposable towel or a hand dryer.
- 093.00** The gown is non-shedding with sleeves that fit snugly around the wrists and enclosed at the neck.
- 094.00** All bare skin is covered on the arms and legs (no bare ankles, wrists, etc.).
- 095.00** Prior to donning sterile gloves, a waterless alcohol based surgical hand scrub with persistent activity is used and hands are allowed to dry.
- 096.00** Upon leaving the sterile preparation compounding area, gowns are taken off and disposed of, or if used for non-hazardous compounding they are left in the anteroom and not reused for longer than one shift.
- 097.00** Pharmacists or other personnel do NOT enter the anteroom and cross the line of demarcation without donning shoe covers or dedicated shoes.
- 098.00** Pharmacists or other personnel do NOT enter the clean/buffer room without fully washing and garbing (e.g., not wearing just a mask to check a technician's work).

Environmental Monitoring

- 099.00** The most recent primary engineering control and room certification report is available.
 - 099.01** All ISO Class 7 and 8 SECs (clean/buffer rooms and anterooms) have been certified within the last six months.
 - 099.02** All ISO Class 5 PECs (laminar airflow workbenches or areas, BSCs, CAIs, CACIs, and barrier isolators) have been certified within the last six months.

- 099.03 Certification procedures shall be performed by a qualified individual at least every 6 months and whenever the device or room is moved or major work is done to the space.
- 099.04 Certification procedures such as those outlined in the Controlled Environmental Testing Association (CETA)'s *"Certification Guide for Sterile Compounding Facilities"* (CAG-003-2006) shall be noted on the report.
- 099.05 If the certification procedures used are not those outlined in *"Certification Guide for Sterile Compounding Facilities"* (CAG-003-2006), the facility has performed a comparison and determined the procedures used are equivalent or better than the procedures outlined in *"Certification Guide for Sterile Compounding Facilities"* (CAG-003-2006).
- 099.06 The PIC or compounding supervisor is familiar with what testing is required and interpretation of results, ensures all testing is performed appropriately (under dynamic conditions where appropriate), has action levels identified, evaluates results to detect issues or trends, and action levels are further customized based on trended data of performance.
- 100.00 The certification report includes information about the equipment used for performing calibration test including: identification of the equipment used by model, serial number, last calibration date (or when next calibration is due).
- 100.01 The equipment used had not exceeded its calibration date at the time of certification.
- 101.00 The HEPA filtered air changes per hour (ACPH) were measured for the compounding rooms.
- 101.01 ISO Class 7 sterile compounding room is certified as having a minimum of 30 ACPE with at least 15 ACPH from outside air sources.
- 101.02 ISO Class 7 anteroom (required if connected to a NIOSH hazardous compounding clean/buffer room) is certified as having a minimum of 30 ACPH.
- 101.03 ISO Class 8 anteroom is certified as having the recommended minimum of 20 ACPH. {*Recommended*}
- 101.04 ISO Class 7 hazardous sterile compounding room is certified as having a minimum of 30 ACPH.

- 101.05** If a CACI is used in a non-HEPA filtered room, the room is certified to maintain a minimum of 12 ACPH.
- 102.00** Air pattern analysis using smoke testing was performed under dynamic conditions (people working in the hoods and rooms). The smoke flow is described in the report for the various tests as turbulent, sluggish, smooth, etc.
- 102.01** Air pattern analysis was conducted at the critical area (direct compounding area inside the ISO Class 5 PEC) to demonstrate unidirectional airflow and sweeping action over and away from the product under dynamic conditions (personnel compounding or simulating compounding in PEC).
- 102.02** Air pattern analysis was conducted to confirm positive pressure (and negative pressure into hazardous compounding rooms) at all points around all openings, doorways, and pass-throughs.
- 102.03** Air pattern analysis was conducted around particle generating equipment while the equipment was in operation to confirm airflow.
- 103.00** Differential air pressure between rooms was measured.
- 103.01** The differential pressure measured was at least 0.02" water column positive from the clean/buffer room to the anteroom and between the anteroom and all adjacent spaces with the doors closed.
- 103.02** The differential pressure measured was at least 0.01" water column negative from the hazardous clean/buffer room to the anteroom with the doors closed.
- 104.00** Displacement airflow between rooms or areas were measured; required for a clean/buffer room without a door that closes to the anteroom – may be an open space or may have plastic strips in doorways.
- 104.01** Displacement airflow (for low and medium-risk non-hazardous rooms only) was measured at a minimum differential velocity of 40 feet per minute from the clean/buffer room to the anteroom.
- 105.00** Particle counts of particles 0.5 um and larger were measured under dynamic conditions.
- 105.01** ISO Class 5 areas and hoods are certified as having less than 3,520 particles per cubic meter of air (100 particles per cubic foot).
- 105.02** ISO Class 7 areas are certified as having less than 352,000 particles per cubic meter of air (10,000 particles per cubic foot).

- 105.03 ISO Class 8 areas are certified as having less than 3,520,000 particles per cubic meter of air (100,000 particles per cubic foot).
- 106.00 HEPA filter tests were performed.
- 106.01 All room HEPA filters were leak tested and if leaks found, they were fixed.
- 106.02 All PEC HEPA filters were leak tested and if leaks found, they were fixed.
- 107.00 PECs with failed tests are not used for compounding until the conditions are corrected and verified by subsequent testing.
- 108.00 Viable air (every six months) and surface sampling (periodically) tests have been conducted.
- 108.01 Appropriate growth media used (containing tryptic soy agar medium with polysorbate and lecithin (TSApl) added to neutralize cleaning agents for surface sampling) with appropriate corresponding incubation time and temperature used.
- 108.02 Viable air sampling by active impaction using a volumetric air sampling device.
- 108.03 Air samples were taken in each ISO Class 5 PEC, and in each sterile compounding room and anteroom, and the samples are at least 400 liters in volume. *{Recommendation for ISO Class 5 PEC is 1,000 liters.}*
- 108.04 Surface samples performed on all direct compounding areas inside of each ISO Class 5 PEC, in each room, inside any pass-throughs, and on surfaces likely to be contaminated due to position relative to doorways, etc.
- 108.05 Viable air and surface samples did not exceed USP action levels (or internal action levels if more restrictive):
- | <i>Classification</i> | <i>Air Sample</i> | <i>Surface Sample</i> |
|-----------------------|--------------------------|-----------------------|
| ISO Class 5 | > 1 CFU/m ³ | > 3 CFU/plate |
| ISO Class 7 | > 10 CFU/m ³ | > 5 CFU/plate |
| ISO Class 8 | > 100 CFU/m ³ | > 100 CFU/plate |
- 108.06 CFUs detected by any means (viable air or surface sampling, gloved fingertip testing, failed sterility tests, etc.) are analyzed to determine the organism down to the genus.

- 108.07 If the number of CFUs detected in the rooms exceeds action levels, compounding ceases, immediate remediation and investigation into the cause conducted, and compounding not resumed until subsequent tests are performed successfully .
- 108.08 If the number of CFUs detected in the PECs exceeds action levels, begin immediate remediation, including recleaning, retraining and retesting, and conduct investigation into the causes.
- 108.09 If any highly pathogenic (i.e., mold, yeast, coagulase positive staphylococcus, or gram negative rods) were detected in the PECs (whether or not the number of CFUs exceeds action levels), begin immediate remediation including recleaning, retraining and retesting, and conduct investigation into the causes.
- 108.10 The testing report indicates growth promotion testing or documentation and sterility quality control testing of the media plates was performed. *{Recommendation}*
- 108.11 The testing results report includes media lot numbers and expiration dates and a signature of the laboratory analyst and/or reviewer. *{Recommendation}*
- 109.00 Facilities performing routine air or surface sampling with internal qualified personnel routinely verify sampling procedures.

Compounding Equipment

- 110.00 Appropriate equipment and utensils are available, clean, and in good working order. Automated, mechanical, or electronic equipment (autoclaves, ovens, etc.) are periodically inspected, and calibrated yearly or in accordance with the equipment manufacturer guidelines.
- 111.00 All environmental monitoring equipment and gauges (differential pressure gauges or probes, air flow and velocity measuring equipment for rooms not fully enclosed, etc.) are periodically inspected, and calibrated yearly or in accordance with the equipment manufacturer guidelines. Calibration is documented.
- 112.00 All temperature and humidity (where applicable) monitoring devices (thermometers, hygrometers, probes, etc.) are periodically inspected, and calibrated yearly or in accordance with equipment manufacturer guidelines. Calibration is documented.
- 113.00 PEC (hood) prefilters are checked and replaced regularly. *{Recommended}*

- 114.00** Where Automated Compounding Devices (ACDs) are used for sterile compounding (such as repeater pumps), there is a policy and procedure for their use and calibration.
- 114.01** There is documentation of the ACD tubing being changed or discarded every 24 hours.
- 114.02** The ACD is used when performing media fill testing.

Compounding Procedures

- 115.00** Gloves and critical sites are sanitized with adequate frequency and with an approved disinfectant, such as sterile 70% isopropyl alcohol (IPA) spray and a non-linting wipe.
- 116.00** Objects that shed particles are prohibited in the clean/buffer room area, including pencils, cardboard cartons, paper towels, reading material, and cotton items, e.g., gauze pads.
- 117.00** Essential paper related products (syringe overwraps, work records contained in a protective plastic sleeve) are wiped down with sterile 70% IPA before being brought into the clean/buffer room area.
- 118.00** Supplies required for the scheduled operations of the shift are prepared and decontaminated by wiping or spraying the outer surface with sterile 70% IPA (or removing the outer wrap as the item is introduced into the aseptic work area) and brought into the clean/buffer room in a bin or on a movable cart.
- 119.00** Compounding employees are using appropriate aseptic technique.
- 120.00** Compounding personnel ascertain that ingredients for compounded sterile preparations are of the correct identity and appropriate quality by reading vendors' labels, and a unit-by-unit physical inspection of the product before use.
- 121.00** All rubber stoppers of vials and bottles and the neck of ampoules are sanitized every time with sterile 70% IPA (and a wait of at least ten seconds to dry) prior to the introduction of a needle or spike for the removal of the product.
- 122.00** Single-dose vials exposed to ISO Class 5 or cleaner air are used within six hours of the initial puncture and any remaining contents discarded; if used in less than ISO Class 5 air, they are used within one hour of the initial puncture and any remaining contents discarded.
- 123.00** The remaining contents of opened single-dose ampoules (or vials where container closure system has been removed) are discarded immediately.

- 124.00** Multiple-dose vials formulated for removal of portions on multiple occasions are used within 28 days (or the manufacturer's specific BUD if less) after the initial entry or puncture and any remaining contents discarded.
- 125.00** The Compounding Record is complete with the following minimum data elements:
- 125.01 Official or assigned name, strength, and dosage of the preparation;
 - 125.02 Names, lot numbers, and expiration dates of all components;
 - 125.03 Total quantity or number of units compounded;
 - 125.04 Person compounding the preparation;
 - 125.05 Person performing the quality control procedures;
 - 125.06 Person who approved the preparation;
 - 125.07 Date of compounding;
 - 125.08 Assigned internal identification number or prescription number;
 - 125.09 Assigned BUD and reference if extended beyond USP guidelines;
 - 125.10 Duplicate label;
 - 125.11 Sterilization method (if applicable); and
 - 125.12 Indication of the quality control procedures to perform (testing, filter integrity, etc.) and results of the testing, quality control issues, and investigation and recall, if applicable.
- 126.00** Procedure for in-process checks is followed. These checks indicate that appropriate procedures and packaging are followed for each step, including addressing pharmacist verification of steps performed by non-pharmacists and visual inspection of product. Documentation of the compounding accuracy is *recommended* to be performed by someone other than the compounder to ensure proper measurement, reconstitution, and component usage.
- 127.00** Labels on batch preparations include the name and quantity of all contents, date, and time of preparation (or internal code indicating this information), preparer and verification pharmacist identifiers, stability (BUD), and any auxiliary labels indicated including appropriate packaging and labeling of hazardous materials.

- 127.01 Labels on batch single-use containers are clearly marked as “Single Use Only.” *{Recommended}*
- 128.00 Labels on patient-specific containers, in addition to standard label requirements, also include names and quantity or concentration of active ingredients, BUD, total volume, route of administration, storage conditions and other information for safe use.
- 128.01 Labels on patient-specific single-use containers are clearly marked as “Single Use Only.” *{Recommended}*
- 129.00 Inspect several different finished products and look for any particulates. Do any of the finished products inspected show any evidence of particulates? If so, list the products including lot and expiration date and obtain photos if possible. Request the product be quarantined and notify Board office immediately.
- 130.00 Preparations without additional stability testing or supported by data are assigned BUDs within USP <797> guidelines:
- *Low Risk*: 48 hrs room – 14 days refrigerated – 45 days frozen;
 - *Medium Risk*: 30 hrs room – 9 days refrigerated – 45 days frozen;
 - *High Risk*: 24 hrs room – 3 days refrigerated – 45 days frozen.
- 131.00 If extended BUDs are assigned, they are supported with stability documentation – preparation must exactly match the preparation tested by the facility including concentration of all active ingredients, excipients, etc.
- 132.00 If extended BUDs are assigned, has the facility has performed its own stability testing.
- 133.00 Compounded multiple-dose vials with extended BUDs assigned have additional instruction provided that indicates remainder must be discarded 28 days after first puncture or use.
- 134.00 Filter Sterilization in an ISO Class 5 environment and documentation includes:
- 134.01 If the compounded preparation contains large particles, a prefilter is placed upstream from the sterilizing filter.
- 134.02 The 0.2 micron sterile microporous membrane filter used to sterilize compounded sterile preparations is chemically and physically compatible with the compounded sterile preparation; and the filter is intended for human-use applications for sterilizing compounded sterile preparations (labeling does not indicate ‘research only’ or ‘laboratory use’ only);

- 134.03 Is the appropriate capacity filter being used for the volume being filtered?
- 134.04 Filtering is completed rapidly without filter replacement; and
- 134.05 Confirmation of filter integrity (bubble testing) is performed and value documented for each filter used with each batch sterilized by filtration.

135.00 Steam Sterilization documentation includes:

- 135.01 The autoclave has been validated for the exposure time and mass of the items to be sterilized;
- 135.02 Ensures live steam contacts all ingredients and surfaces to be sterilized, effectiveness verified with biological indicators and temperature sensing devices;
- 135.03 Solutions are passed through a 1.2 micron or small filter into the final containers to remove particulates before sterilization;
- 135.04 Heated filtered air is evenly distributed throughout the chamber with a blower;
- 135.05 That the compounded sterile preparation will not be adversely affected by the steam and heat; and
- 135.06 The description of steam sterilization includes conditions and duration for specific compounded sterile preparations.

136.00 Dry Heat Sterilization documentation includes:

- 136.01 Dry heat is only used for those items that cannot be sterilized by steam or would be damaged by moisture;
- 136.02 Sufficient space is left between materials to allow for air circulation;
- 136.03 The description of dry heat sterilization includes conditions and duration for specific compounded sterile preparations;
- 136.04 That the effectiveness of dry heat sterilization is verified each time using appropriate biological indicators; and
- 136.05 The oven is equipped with a system for controlling and recording temperature and exposure period.

137.00 Depyrogenation by Dry Heat documentation includes:

- 137.01 Dry heat depyrogenation is used to render glassware and containers (such as vials) free from pyrogens as well as viable microbes;
 - 137.02 The description of the cycle and duration for specific load items;
 - 137.03 The effectiveness of the cycle is verified using endotoxin challenge vials (EVCs); and
 - 137.04 Bacterial endotoxin testing is performed on the ECVs to verify the cycle is capable of achieving a three log reduction in endotoxins.
- 138.00 Other methods of sterilization are used with documented procedures and validation performed.

Finished Preparation Release Checks and Tests

- 139.00 Are products visually checked for particulates or other foreign matter against both a light and a dark colored background as a condition of release?
- 140.00 Are there checks for container, closure integrity, and any other apparent visual defects?
- 141.00 Is compounding accuracy documented by verification of steps?
- 142.00 Is verification of ingredient identity and quantity verified? Is there a reconciliation of components?
- 143.00 Are labels verified as being correct and is a copy of the label included in the record?
- 144.00 Sterility Testing complies with USP <71>. If testing is performed to a more stringent standard, describe in inspection notes.
 - 144.01 Sterility testing includes both bacterial and fungal testing.
 - 144.02 Sterility testing is performed on all compounded sterile preparations that have extended BUDs.
 - 144.03 Sterility testing is performed for high-risk compounded sterile preparations prepared in batches of more than 25 identical containers.
 - 144.04 Sterility testing is performed for compounded sterile preparations exposed longer than 12 hours at 2°C to 8°C or longer than 6 hours at warmer than 8°C before being sterilized.

- 144.05 The appropriate quantities of units are sterility tested:
- *For parenterals:*
 - For less than 100 units, test 10% or 4 units, whichever is greater;
 - For 100 to 500 units, test 10 units; and
 - For more than 500 units, test 2% or 20 units, whichever is less.
 - *For large-volume parenterals:*
 - 2% of the units or 10 containers, whichever is less.
 - *For non-parenterals (eye drops, inhalation, etc.):*
 - For less than 200 units, test 5% or 2 containers, whichever is greater;
 - For 200 or more units, test 10 containers; or
 - If the product is packaged in unit doses, use the parenteral testing parameters above.
- 144.06 For products failing testing, product is quarantined, and an investigation is performed including microbial identification and action taken.
- 144.07 If items are dispensed or distributed prior to sterility testing completion, there is a written procedure requiring daily observation of the incubated media. If there is any evidence of microbial growth, there is an immediate recall and both the patient and the physician/prescriber for the patient to whom a potentially contaminated compounded sterile preparation was administered are notified of the potential risk.
- 145.00 Endotoxin Testing complies with USP <85>. If testing is performed to a more stringent standard, describe in inspection notes.
- 145.01 Is endotoxin testing performed for all high-risk level compounded sterile preparations for administration by injection prepared in groups of more than 25 single-dose packages, such as ampoules, bags, syringes, vials, etc.?
- 145.02 High-risk compounded sterile preparations prepared in multiple dose vials for administration to multiple patients.
- 145.03 High-risk compounded sterile preparations exposed longer than 12 hours at 2°C to 8°C (25°F to 46°F) or longer than 6 hours at warmer than 8°C (46°F) before they are sterilized.
- 145.04 For products failing testing, product is quarantined, and an investigation is performed and action taken.
- 146.00 Potency Testing is performed. {Recommended}

Patient Counseling and Communication

- 147.00** Do patient/caregiver training programs or materials contain information and precautions regarding the handling and disposal of hazardous products such as chemotherapy medications?
- 148.00** Are required printed drug information materials (drug information, PPI, MedGuides, etc.) provided for the compounded products?
- 149.00** Are patients instructed on the signs of product instability or contamination (as appropriate) and to report any changes in the physical characteristics of the product to the pharmacy?
- 150.00** Product recalls include documentation that both the patient AND the physician/prescriber of the potentially contaminated compounded sterile preparation was administered are notified of the potential risk.

Revision History

08-30-2017	Version 1.1	006.00	Changed question relative preparation of copies of commercially approved products to limit it to certain circumstances.
		006.03	Deleted item due to specific data requested in 006.00.
		007.02	New question requests additional information relative to BUD in low-risk compounding.
		007.03	New question requests additional information about testing for BUD in low-risk compounding.
		008.02	New question requests additional information relative to BUD in medium-risk compounding.
		008.03	New question requests additional information about testing for BUD in medium-risk compounding.
		009.02	New question requests additional information relative to BUD in high-risk compounding.
		009.03	New question requests additional information about testing for BUD in high-risk compounding.
		010.01	Deleted item due to absence of parameter in USP chapter.
		012.02	Observation: when USP chapter is final, will need to change pressure parameter from "0.01" to "0.03".
		016.00	Deleted reference to nonsterile preparations.
		017.00	New question asking about use of scales or balances in compounding of sterile preparations.
		017.01	New question asking details about scales used.
		017.02	New question asking about electronic scales.
		021.00	Question about pharmacy's continuous quality improvement (CQI) program relative to

compounding of sterile preparations.

- 021.01 thru 021.12 Additional questions about different aspects of the pharmacy's CQI program.
- 023.00 Added clarification "for human use".
- 027.02 Deleted item; not covered in USP chapter.
- 027.03 Deleted item; not covered in USP chapter.
- 027.04 Deleted item; not covered in USP chapter.
- 038.01 Deleted recommendation re hand-free sink.
- 040.00 Observation: Future revision of USP 797 will removed heated hand dryer.
- 045.01 Clarification; requirement, not recommendation.
- 048.01 Clarification re temperature standards.
- 048.03 Clarification re temperature standards.
- 048.04 Clarification re temperature standards.
- 048.06 Clarification re temperature standards.
- 064.01 New item seeking additional detail.
- 065.00 Clarification – sanitizing vs cleaning.
- 067.00 Clarification re timing of floor cleaning.
- 071.00 Clarification re time for cleaning activities.
- 085.01 Clarification – deleted media fill tests.
- 099.04 Clarification; changed "standards" to "procedures."
- 099.05 Clarification allows for alternative procedures equivalent or superior to listed reference.
- 099.06 Adds additional person beyond PIC.
- 101.03 Clarification – recommendation, not requirement.

- 108.00 Clarification of timing of samples.
- 108.06 Clarification – deleted media fills.
- 108.07 Clarification re CFUs on clean rooms.
- 108.08 New question relative to CFUs in PECs; distinct from 108.07.
- 108.09 Clarification re action plans on CFUs.
- 108.10 Clarification; recommendation, not requirement.
- 108.11 Clarification; recommendation, not requirement.
- 109.00 Clarification re sampling procedures.
- 112.00 Clarification re monitoring devices.
- 113.00 Deleted this item due to its relocation.
- 123.00 Clarification on single-dose containers.
- 128.00 Clarification on labeling of patient-specific containers.
- 134.02 Added example of inappropriate use of filters.
- 134.03 New item for additional data point re filters.
- 139.00 Clarification of visual checks prior to release.
- 140.00 Additional detail re visual checks prior to release.
- 144.00 Allows for alternative but superior standard for sterility testing.
- 144.03 Clarification of standard for sterility testing in high-risk compounding.
- 145.00 Allows for alternative but superior standard for endotoxin testing.
- 147.00 Item deleted; standards incorporated elsewhere in blueprint.