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PHARMACY RULES COMMITTEE
of the
PHARMACY EXAMINING BOARD

Room 121C, 1400 East Washington Avenue, Madison, WI 53703
Contact: Dan Williams (608) 266-2112
November 18, 2015

Notice: The following agenda describes the issues that the Committee plans to consider at the meeting. At the time of the meeting, items may be removed from the agenda. ***A quorum of the Board may be present during any committee meetings.***

AGENDA

8:30 A.M.

OPEN SESSION – CALL TO ORDER

A. Approval of Agenda (1)

B. Legislation and Rule Matters – Discussion and Consideration (2-55)

1) Phar 2, 4 Relating to Application and Examination **(3-4)**
2) Phar 6 Relating to Temperature and Humidity Controls **(5)**
3) Phar 15 Relating to Compounding **(6-55)**
4) Update on Legislation and Pending or Possible Rulemaking Projects

C. Public Comments

ADJOURNMENT

State of Wisconsin
Department of Safety & Professional Services

AGENDA REQUEST FORM

1) Name and Title of Person Submitting the Request:	2) Date When Request Submitted:
Sharon Henes **Administrative Rules Coordinator**	**9 November 2015** Items will be considered late if submitted after 12:00 p.m. on the deadline date: ▪ 8 business days before the meeting

3) Name of Board, Committee, Council, Sections:

Pharmacy Rules Committee

4) Meeting Date:	5) Attachments:	6) How should the item be titled on the agenda page?
18 November 2015	☐ Yes ☐ No	**A. Approval of agenda** **B. Legislation and Rule Matters – Discussion and Consideration** **1) Phar 2, 4 Relating to Application and Examination** **2) Phar 6 Relating to Temperature and Humidity Controls** **3) Phar 15 Relating to Compounding** **4) Update on Pending Legislation and Pending or Possible Rulemaking** **C. Public Comments** **Adjournment**

7) Place Item in:	8) Is an appearance before the Board being scheduled?	9) Name of Case Advisor(s), if required:
☒ Open Session ☐ Closed Session ☐ Both	☐ Yes (Fill out Board Appearance Request) ☐ No	

10) Describe the issue and action that should be addressed:

11) Authorization

Sharon Henes — *9 November 2015*

Signature of person making this request — Date

Supervisor (if required) — Date

Executive Director signature (indicates approval to add post agenda deadline item to agenda) — Date

Directions for including supporting documents:
1. This form should be attached to any documents submitted to the agenda.
2. Post Agenda Deadline items must be authorized by a Supervisor and the Policy Development Executive Director.
3. If necessary, Provide original documents needing Board Chairperson signature to the Bureau Assistant prior to the start of a meeting.

Revised 8/13

TEXT OF RULE

SECTION 1. Phar 1.02(6m) is created to read:

Phar 1.02(6m) "NABP" means the National Association of Boards of Pharmacy.

SECTION 2. Phar 2.01 is repealed.

SECTION 3. Phar 2.02 (1) (intro) and (a) are amended to read:

Phar 2.02 Application procedure for original licensure. (1) Each applicant for original licensure as a pharmacist shall submit ~~a completed notarized application prior to the examination date on forms provided by the board. The application shall include~~ all of the following:

(a) ~~The~~ Completed application form with the signature of the applicant.

SECTION 4. Phar 2.02 (1) (f) and (g) are created to read:

Phar 2.02 (1) (f) Evidence of having passed the NAPLEX.

(g) Evidence of having passed the multi-state pharmacy jurisprudence examination with Wisconsin as primary state.

SECTION 5. Phar 2.03 and 2.04 is repealed.

SECTION 6. Phar 2.05 repealed and recreated:

Phar 2.05 Application procedure for persons licensed in another state. Each applicant licensed as a pharmacist in another state shall submit all of the following:
(1) Completed application and fee as determined by the department under s. 440.05, Stats.
(2) NABP Clearinghouse license transfer application.
(3) Evidence of having passed the multi-state pharmacy jurisprudence examination with Wisconsin as primary state.

SECTION 7. Phar 2.06 is repealed.

SECTION 8. Phar 4.01 is repealed.

SECTION 9. Phar 4.03 is amended to read:

Phar 4.03 Passing scores. (1) The passing scores set by the board represent the minimum competency required to protect public health and safety. The board may adopt the recommended passing score of the examination provider.

SECTION 10. Phar 4.03(3) is repealed.

SECTION 11. Phar 4.04, 4.045, 4.046 and 4.05 are repealed.

SECTION 12. EFFECTIVE DATE. The rules adopted in this order shall take effect on the first day of the month following publication in the Wisconsin administrative register, pursuant to s. 227.22 (2) (intro.), Stats.

(END OF TEXT OF RULE)

TEXT OF RULE

SECTION 1. Phar 6.075 is created to read:

Phar 6.075 Temperature. (1) DEFINITIONS. In this section:
(a) Dry place means a place that does not exceed 40% average relative humidity at 68 degree Fahrenheit or the equivalent water vapor pressure at other temperatures.
(a) Freezer means a place in which the temperature is maintained between -13 and 14 degrees Fahrenheit.
(c) Mean kinetic temperature means the calculated temperature at which the total amount of degradation over a particular period is equal to the sum of the individual degradations that would occur at various temperatures.
(b) Refrigerator means a place in which the temperature is maintained between 36 and 46 degrees Fahrenheit.
(2)

SECTION ?. EFFECTIVE DATE. The rules adopted in this order shall take effect on the first day of the month following publication in the Wisconsin administrative register, pursuant to s. 227.22 (2) (intro.), Stats.

(END OF TEXT OF RULE)

Dated _____ Agency _____
(Member of the Board or Secretary)
(board or department name)

DRAFT TEXT of Chapter Phar 15

[*NOTE: There are some areas which may not be contained in this draft due to my needing more input in order to address in the rule.*]

15.01 Definitions. In this chapter:
(1) Active pharmaceutical ingredient (API) means any substance or mixture of substances intended to be used in the compounding of a drug preparation and that, when used in the compounding of a drug preparation, becomes an active ingredient in the preparation intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment or prevention of disease in humans and animals or affecting the structure and function of the body.
(2) Added substances means ingredients that are necessary to compound a drug preparation that are not intended or expected to cause a pharmacologic response if administered alone in the amount or concentration contained in a single dose of the compounded preparation.
(3) Beyond Use Date (BUD) means the date after which a non-sterile compounded preparation shall not be used, or the date after which a sterile compounded preparation shall not be stored or transported.
(4) Component means any, active pharmaceutical ingredient, or added substances used in the compounding of a drug preparation.
(5) Compounding means the preparation, mixing, assembling, altering, packaging, and labeling of a drug, drug delivery device, or a device in accordance with a prescription, medication order or initiative. Compounding includes any of the following:

(a) Preparation of drug dosage forms for both human and animal patients.

(b) Preparation of drugs or devices in anticipation of prescription drug orders based on routine, regularly observed prescribing patterns.

(c) Reconstitution or manipulation of commercial products that may require the addition of one or more ingredients. Notwithstanding this paragraph, the reconstitution or mixing that is performed pursuant to the directions contained in approved labeling provided by the manufacturer of a commercially available product is not compounding.

(d) Preparation of drugs or devices for the purposes of, or as an incident to, research, teaching or chemical analysis.

(6) Controlled room temperature means a temperature maintained thermostatically that encompasses the usual and customary working environment of 68 degrees to 77 degrees Fahrenheit.
(7) Freezer means a place in which a the temperature is maintained between -11 degrees and 14 degrees Fahrenheit
(8) Refrigerator means a cold place in which the temperature is maintained between 36 degrees and 46 degrees Fahrenheit
(9) Stability means the extent to which a compounded preparation retains, within specified limits and throughout its period of storage and use, the same properties and characteristics that it possessed at the time of compounding.

(a) Chemical stability means each active pharmaceutical ingredient retains its chemical integrity and labeled potency, within specified limits.

(b) Physical stability means the original physical properties, including appearance, palatability, uniformity, dissolution, and suspendability, are retained.

(c) Microbiological stability means sterility or resistance to microbial growth is retained according to specified requirements and antimicrobial agents that are present retain effectiveness within specified limits.
(d) Therapeutic stability means the therapeutic effect remains unchanged.
(e) Toxicological stability means no significant increase in toxicity occurs.

SUBCHAPTER I – General

15.10 Facilities. A pharmacist engaged in compounding shall ensure all of the following:
(1) An area designated for compounding.
(2) Orderly placement of compounding equipment, materials, and components in order to minimize the potential for compounding errors.
(3) The compounding area is well-lighted.
(4) The compounding area is maintained in a clean and sanitary condition.
(5) The compounding area is easily accessible to all of the following:
(a) Hot and cold running water, exclusive of the bathroom sink.
(b) Soap or detergent.
(c) Single-use towels.
(6) All compounding equipment, materials and components shall be stored off the floor and in a manner to prevent contamination and permit inspection and cleaning of the compounding and storage areas

15.11 Equipment and Drug Preparation Containers.
(1) A pharmacy shall possess equipment and drug preparation containers or packaging appropriate to the type of compounding performed at the pharmacy.
(2) Equipment and drug preparation containers or packaging used in compounding shall be of appropriate design and capacity, and shall be suitably stored in a manner to facilitate use, cleaning, maintenance, and protect it from contamination.
(3) Equipment and drug preparation containers/packaging used in compounding drug products shall be of suitable composition. Equipment surfaces that contact components may not be reactive, additive or adsorptive so as to alter the stability of the compounded preparation.
(4) Equipment used in compounding shall be thoroughly cleaned and sanitized after each use, and when necessary, prior to use, according to written policies and procedures, in order to reduce bioburden and reduce the opportunity for cross-contamination.
(5) All equipment utilized in compounding preparations shall be inspected, maintained, calibrated and validated at appropriate intervals, consistent with manufacturer's recommendations, to ensure the accuracy and reliability of equipment performance. Records shall be kept indicating the equipment was inspected, maintained, calibrated and validated.

15.12 Records. The managing pharmacist shall ensure written or electronic compounding documentation to systematically trace, evaluate, and replicate the compounding steps throughout the process of a preparation. The compounding documentation shall be maintained for a period of 5 years after the date of the last refill. The compounding documentation shall include all of the following:
(1) Master Formulation Record including all of the following:
(a) Official or assigned name, strength, and dosage form of the preparation.

(b) Calculations needed to determine and verify quantities of components and doses of active pharmaceutical ingredients.
(c) Description of all ingredients and their quantities.
(d) Compatibility and stability information, including references or laboratory testing
(e) Equipment needed to prepare the preparation.
(f) Mixing instructions including all of the following:
1. Order of mixing.
2. Mixing temperatures or other environmental controls.
3. Duration of mixing.
4. Other factors pertinent to the replication of the preparation as compounded.
(f) Sample labeling information, including all of the following:
1. Name and quantity or concentration of each active ingredient.
2. Assigned BUD.
3. Storage conditions.
4. Prescription or control number.
(g) Container used in dispensing.
(h) Packaging and storage requirements.
(i) Description of final preparation.
(j) Quality control procedures, if applicable, and expected results.

(2) Compounding Record including all of the following:
(a) Official or assigned name, strength, and dosage of the preparation.
(b) Master Formulation Record reference for the preparation.
(c) Names and quantities of all components.
(d) Sources, lot numbers and expiration dates of all components.
(e) Total quantity compounded.
(f) Name of the person who prepared the preparation.
(g) Name of the person who performed the quality control procedures.
(h) Name of the person who approved the preparation.
(i) Date of preparation.
(j) Assigned control or prescription number.
(k) Assigned BUD.
(L) Copy of the label to dispense final product.
(m) Description of the final preparation.
(n) Results of quality control procedures.
(o) Documentation of any quality control issues and any adverse reactions or preparation problems reported by the patient or caregiver.

15.13 Quality control.

(1) The pharmacist shall do a final check and review each procedure in the compounding process. A final check shall include verification of all the following:
(a) The master formulation record, compounding record and written procedures were followed in the execution of the compounding process. Any deviation in procedures shall be documented.
(b) There was a check and recheck of each procedure at each stage of the process.
(c) The tests or examinations conducted on the compounded preparation to ensure their uniformity and integrity followed established written procedures.

(d) The performance of compounding processes and equipment that may be responsible for causing variability in the final compounded preparations.

(2) The pharmacist shall observe the finished preparation to ensure that it appears as expected.

(3) The pharmacist shall investigate any discrepancies and take appropriate corrective action before the prescription is dispensed to the patient.

(4) The pharmacist completing the final check is solely responsible for the finished preparation.

15.14 Training. All personnel involved in the compounding, evaluation, packaging, and dispensing of compounded preparations shall be properly trained and competency is assessed for the type of compounding conducted. It is the responsibility of the managing pharmacist to ensure and document all training and competency assessments.

SUBCHAPTER II – Non-sterile Compounding

15.20 Definitions. In this subchapter:

(1) Office use means

15.21 Component Selection.

(1) A pharmacist shall use components manufactured in a FDA registered facility. If a component is unavailable from a FDA registered facility, the pharmacist may utilize a component that has been tested by a FDA approved vendor and the component has been determined to be pure and safe documented by a Certificate of Analysis.

(2) Components with an expiration date from the manufacturer or distributor may be used before the expiration date provided all of the following:

(a) The component is stored in its original container under conditions to avoid decomposition

(b) There is minimal exposure of the remaining component each time component is withdrawn from the container.

(c) When any withdrawals from the container are performed by those trained in the proper handling of the component.

(3) Components without an expiration date assigned by the manufacturer or supplier, shall be labeled with the date of receipt and assigned a conservative expiration date, not to exceed three years after receipt, based upon the nature of the component and its degradation mechanism, the container in which it is packaged and the storage conditions.

(4) Components transferred to another container which shall provide integrity that is minimally equivalent to the original container and shall be identified with all of the following:

(a) Component name.

(b) Original supplier.

(c) Lot or control number.

(d) Transfer date.

(e) Expiration date.

(5) Manufactured drug products utilized as the source of active pharmaceutical ingredients shall be manufactured in an FDA registered facility and the manufacturer's product container shall be labeled with a lot number and expiration date.

(6) A pharmacist compounding for human use may not use components that have been withdrawn or removed from the market for safety or efficacy reasons by the FDA. A pharmacist compounding for food producing animal use may not use components prohibited for use in food producing animals.

15.21 Assigning BUD.
(1) The BUD shall not be later than the expiration date on the container of any component.
(2) In the absence of stability information that is applicable to a specific drug product and preparation, the maximum BUD for a non-sterile compounded drug preparation that is packaged in a tight, light-resistant container as follows:

(a) For nonaqueous formulations stored at controlled room temperature, the BUD shall not be later than the time remaining until the earliest expiration date of any active pharmaceutical ingredient or 6 months, whichever is earlier.

(b) For water-containing oral formulations, the BUD shall not be later than 14 days when stored at in a refrigerator

(c) For water-containing semisolid, mucosal liquid, topical or dermal formulations, stored at controlled room temperature, the BUD shall not be later than 30 days.

(3) Assignment of BUD shall include an assessment of the need for antimicrobial agents and or storage in a refrigerator to protect against bacteria, yeast, and mold contamination introduced during or after the compounding process.

SUBCHAPTER III – Sterile Compounding

15.30 Definitions. In this subchapter:

(1) Ante area means an ISO class 8 or better area where personnel hand hygiene and garbing procedures, staging of components, order entry, labeling and other high particulate generating activities are performed. The ante area is also a transition area that provides assurance that pressure relationships are constantly maintained so that air flows from clean to dirty areas and reduces the need for the heating, ventilating, and air-conditioning control system to respond to large disturbances.

(2) Buffer area means an area where the primary engineering control is physically located. Activities that occur in this area include the preparation and staging of components and supplies used when compounding compounded sterile preparations.

(3) CACI means compounding aseptic isolator. A form of isolator designed to provide worker protection from exposure to undesirable levels of airborne hazardous drugs throughout the compounding and material transfer processes and to provide an aseptic environment for compounding sterile preparations. Air exchange with the surrounding environment may not occur unless the air is first passed through a microbial retentive filter system capable of containing airborne concentrations of the physical size and state of the drug being compounded.

(4) CAI means compounding aseptic isolator. A form of isolator specifically designed for compounding pharmaceutical ingredients or preparations. It is designed to maintain an aseptic compounding environment within the isolator throughout the compounding and material transfer

process. Air exchanges into the isolator from the surrounding environment may not occur unless the air has first passed through a microbially retentive filter.

(5) Cleanroom means a room in which the concentration of airborne particles is controlled to meet a specified airborne particulate cleanliness (ISO) class. Microorganisms in the environment ware monitored so that microbial level for air, surface, and personnel gear are not exceeded for a specified cleanliness class. A cleanroom includes a buffer area or room and an ante area or room.

(6) Compounded sterile preparation means the aseptic processing in a clean air environment of any pharmaceutical preparations that are required to be sterile when they are administered into patient body cavities, central nervous and vascular systems, eyes, and joints and when used as baths for live organs and tissues, including injections, aqueous bronchial and nasal inhalations, irrigations for wounds and body cavities, ophthalmic drops and ointments and tissue implants

(7) High-risk level compounded sterile preparations means preparations compounded from non-sterile ingredients or from ingredients that are incorporated using non-sterile equipment before terminal sterilization, or from commercially manufactured sterile products that lack effective antimicrobial preservatives and whose preparation, transfer, sterilization, and packaging is performed in air quality worse than ISO class 5 for more than one hour. Water-containing preparations that are stored for more than six hours before terminal sterilization are also classified as high-risk level compounded sterile preparations.

(8) Immediate use compounded sterile preparations means preparations intended for emergency patient care and involve only simple aseptic measuring and transfer manipulations of no more than three sterile non-hazardous commercial drug and diagnostic radiopharmaceutical drug products, including an infusion or diluent solution.

(9) ISO class 5 air quality conditions means conditions in which the air particle count is no greater than a total of 3,520 particles of 0.5 micrometers and larger per cubic meter of air that is supplied by high-efficiency particulate air (HEPA) or HEPA-filtered air.

(10) ISO class 7 air quality conditions means conditions in which the air particle count is no greater than a total of 352,000 particles of 0.5 micrometers and larger per cubic meter of air that is supplied by high-efficiency particulate air (HEPA) or HEPA-filtered air.

(11) ISO class 8 air quality conditions means conditions in which the air particle count is no greater than a total of 3,520,000 particles of 0.5 micrometers and larger per cubic meter of air that is supplied by high-efficiency particulate air (HEPA) or HEPA-filtered air.

(12) Low-risk level compounded sterile preparations means preparations compounded with aseptic manipulations entirely within ISO class 5 or better air quality using only sterile ingredients, products, components, and devices. The compounding process involves only assembling, transferring, measuring, and mixing, using no more than three commercially manufactured sterile products, and not more than two entries into one sterile container or package to make the compounded sterile preparations. The compounding process is limited to

aseptically opening ampules, penetrating sterile 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.

(13) Medium-risk level compounded sterile preparations means preparations compounded under low-risk level conditions but which require multiple individual or small doses of sterile products to be combined or pooled to prepare compounded sterile preparations that will be administered either to multiple patients or to one patient on multiple occasions. The compounding process includes complex aseptic manipulations other than single volume transfer, and requires and unusually long duration, such as that required to complete dissolution or homogeneous mixing.

(14) Stability means the extent to which a preparation retains, within specified limits and throughout its period of storage and use, the same properties and characteristics that it possessed at the time of compounding.

15.31 General. All personnel who compound sterile preparation shall be responsible for understanding the fundamental practices and precautions, for developing and implementing appropriate procedures and for continually evaluating the procedures and the quality of the final compounded sterile preparation.

15.32 Responsibility of compounding personnel. The managing pharmacist is responsible for ensuring that compounded sterile preparations are accurately identified, measured, diluted, and mixed and are correctly purified, sterilized, packaged, sealed, labeled, stored, dispensed, and distributed. The responsibilities include maintaining appropriate cleanliness conditions and providing labeling and supplementary instructions for the proper clinical administration of compounded sterile preparations.

15.33 Facility Design and Environmental Controls. (1) CLEANROOM. A cleanroom shall be physically designed and environmentally controlled to minimize airborne contamination from contacting critical sites. Critical sites are locations that include any component or fluid pathway surfaces, openings, exposed and at risk of direct contact with air, moisture or touch contamination. A cleanroom shall include a buffer area and an ante area. The buffer area shall contain an ISO class 5 or better primary engineering control unless the buffer area has ISO class 5 or better air quality. A cleanroom shall be all of the following:

(a) Accessible only to designated personnel.

(b) Used only for the compounding of sterile preparations or other tasks that require a cleanroom.

(c) Structurally isolated from other areas within the pharmacy by means of restricted entry or access.

(d) Maintained at a temperature of 59 to 77 degrees Fahrenheit.

(g) Maintained free of chewing gum, drinks, candy or food items.

(2) CLEANROOM REQUIREMENTS. A cleanroom shall meet all of the following:

(a) The surfaces of ceilings, walls, floors, fixtures, shelving, counters and cabinets in the cleanroom shall be smooth, impervious, free from cracks and crevices and nonshedding, thereby minimizing spaces in which microorganisms and other contaminants may accumulate.

(b) Work surfaces shall be constructed of smooth, impervious materials so that the work surfaces may be readily cleaned and sanitized. All work surfaces shall be resistant to damage from cleaning and sanitizing agents.

(c) Junctures where ceilings meet walls shall be covered, caulked, or sealed to avoid cracks and crevices in which microorganisms and other contaminate can accumulate. All areas in ceilings and walls where the surface has been penetrated shall be sealed.

(d) Ceilings that consist of inlaid panels shall be impregnated with a polymer to render them impervious and hydrophobic and shall either be caulked or weighted and clipped.

(e) Walls shall be constructed of flexible material, panels locked together and sealed or of epoxy-coated gypsum board.

(f) Floors shall have a covering that shall be seamless or have teat-welded seams and coving to the sidewall. There shall be no floor drains.

(g) There shall be no dust –collection overhangs and ledges should be avoided. All sprinkler heads shall be flush with the ceiling.

(h) Ceiling lighting fixtures shall have exterior lens surfaces which are smooth, mounted flush and air tight.

(i) Carts shall be of stainless steel wire, nonporous plastic or sheet metal construction with good quality, cleanable casters to promote mobility.

(j) Refrigerators shall be within, or reasonably accessible to, the cleanroom in order to ensure the integrity of compounded sterile preparations.

(3) ANTE AREA REQUIREMENTS. The ante area shall meet all of the following:

(a) Appropriate environmental control devices capable of maintaining ISO class 8 air quality conditions for non-hazardous drug compounding activities and ISO class 7 air quality conditions for hazardous drug compounding activities.

(b) Contain all of the following equipment:

1. A sink with hot and cold running water with an integrated and closed plumbing system.
2. Waste containers for all personal protective equipment.
3. An eyewash station.
4. A hazardous waste spill kit.

(4) BUFFER AREA REQUIREMENTS. The buffer area shall meet all of the following:

(a) The buffer area shall have appropriate environment control devices capable of maintaining ISO class 7 air quality conditions during normal activity.

(b) The buffer area shall contain only the following:

1. Items, including furniture, equipment, and supplies, that are required for the tasks to be performed in the buffer area.
2. Items that are nonpermeable, nonshedding, cleanable, and resistant to disinfectants.
3. Items that have been cleaned and disinfected immediately prior to their being placed in the buffer area.

(c) Equipment and other items used in the buffer area shall not be taken from these areas except for calibration, servicing, or other activities associated with the proper maintenance of the item.

(d) The buffer area shall be kept clean and arranged in an orderly fashion. All required equipment shall be maintained in good operating condition.

(e) The buffer area shall not be used for bulk storage, warehousing or clerical functions.

(f) The buffer area shall not contain any sinks.

(g) The buffer area shall be a minimum of 100 square feet in size and shall be compatible with the volume of compounding being conducted.

(h) The buffer area shall contain waste containers in compliance with Occupational Safety and Health Administration standards for disposal of used needles and syringes and for disposal of chemotherapy waste.

(5) USE OF CAI AND CACI LOCATED OUTSIDE OF A CLEANROOM. A pharmacy may utilize a CAI or CACI not located in a cleanroom to prepare compounded sterile preparations, provided all of the following:

(a) The CAI or CACI can provide isolation from the room and maintain ISO class 5 air quality during dynamic operating conditions, including transferring ingredients, components, and devices into and out of the isolator and during preparation of compounded sterile preparations. Particle counts sampled approximate 6 to 12 inches upstream of the critical exposure site must maintain ISO class 5 air quality levels during compounding operations.

(b) Compounding personnel shall obtain documentation from the manufacturer that the CAI or CACI will meet this standard when located in worse than ISO class 7 environments.

(c) A CAI or CACI not located in a buffer area shall be located in an area that is maintained under sanitary conditions and such area shall only be traveled by persons engaging in the compounding of sterile preparations.

15.34 Personnel cleansing and garbing requirements. (1) All personnel who engage in compounding sterile preparations shall comply with all of the following requirements before entering the buffer area:

(a) Remove personal outer garments, all cosmetics, visible jewelry and piercings.

(b) The wearing of artificial nails or extenders is prohibited while working in the compounding area. Natural nails shall be kept neat and trimmed.

(c) Personnel protective equipment shall be put on in the following order:

1. Dedicated shoes or shoe covers.
2. Head and facial hair covers.
3. Face masks.
4. Eye shields, if required due to working with irritants or hazardous drugs.

(d) A hand and forearm cleansing procedure shall be performed. Personnel shall remove debris from underneath fingernails using a nail cleaner under running warm water followed by vigorous hand washing for at least 30 seconds. Hands and forearms to the elbows shall be completely dried using either lint-free disposable towels or an electronic hand dryer.

(e) Personnel shall wear non-shedding gowns with sleeves that fit snugly around the wrists and enclosed at the neck that are designed for buffer area use.

(2) Following the completion of all the steps in sub. (1) and once inside the buffer area, personnel shall perform antiseptic hand cleansing, using a waterless alcohol based surgical hand scrub with persistent activity following manufacturer's recommendations. Once hands are dried thoroughly, personnel shall don sterile gloves. Gloves shall be routinely inspected for holes, punctures, or tears and shall be replaced immediately if any are detected.

(3) Gloves become contaminated when they make contact with non-sterile surfaces during compounding activities. Disinfection of contaminated gloved hands may be accomplished by wiping or rubbing sterile 70% isopropyl alcohol on all contact surface areas of the gloves and letting the gloved hands dry thoroughly. Routine application of sterile 70% isopropyl alcohol shall occur throughout the compounding process and whenever non-sterile surfaces, including vials, counter tops, chairs and carts, are touched.
(4) When compounding personnel exit the cleanroom during a work shift, the exterior gown may be removed and retained in the cleanroom if not visibly soiled and may be re put on during that same work shift only. Shoe covers, hair and facial hair covers, face masks, eye shields and gloves shall be replaced with new ones before re-entering the buffer area and proper hand hygiene shall be performed.

15.35 Cleaning and Disinfecting the Compounding Area. (1) Compounding personnel are responsible determining the cleaning and disinfecting products to be used and for ensuring that the frequency of cleaning and disinfecting compounding area is done in accordance with the following frequency:

(a) ISO Class 5 primary engineering control at the beginning of each shift or before each batch, but not longer than 30 minutes following the previous surface disinfection when ongoing compounding activities are occurring.
(b) Counters and easily cleanable work surfaces daily.
(c) Floors daily.
(d) Walls, ceilings and storage shelving monthly.

(2) All cleaning and disinfecting practices and policies for the compounding of compounding sterile preparations shall be included in written standard operating procedures and shall be followed by all compounding personnel.
(3) Disinfecting sterile compounding areas shall occur on a regular basis at the intervals in sub. (1) or when any of the following occurs:

(a) Spills occur.
(b) The surface is visibly soiled.
(c) Microbial contamination is known to have been or is suspected of having been introduced into the compounding area.

(4) Cleaning, using a germicidal detergent, and disinfecting shall occur before compounding is performed. Items shall be removed from all areas to be cleaned, and surfaces shall be cleaned by removing loose material and residue from spills. This shall be followed by wiping with sterile 70% isopropyl alcohol, which is allowed to dry before compounding begins.
(5) Work surfaces in the ISO Class 7 buffer areas and ISO Class 8 ante areas as well as segregated compounding areas shall be cleaned and disinfected at least daily. Dust and debris shall be removed when necessary from storage sites for compounding ingredients and supplies using a method that does not degrade the ISO Class 7 or 8 air quality.
(6) Floors in the cleanroom, buffer area and ante area are cleaned by mopping with a germicidal detergent once daily at a time when no aseptic operations are in progress. Mopping shall be performed by trained personnel using approved agents and procedures.
(7) In the cleanroom, buffer area and ante area, the walls, ceilings and shelving shall be cleaned and disinfected with a germicidal detergent with consideration of compatibilities, effectiveness and inappropriate or toxic residues.

(8) All cleaning materials shall be nonshedding and dedicated to use in the cleanroom, buffer area and ante area and shall not be removed from these areas except for disposal. If cleaning materials, including mops, are reused, procedures shall be developed based on manufacturer recommendations, that ensure that the effectiveness of the cleaning device is maintained and that repeated use does not add to the bioburden of the area being cleaned.
(9) Supplies and equipment removed from shipping cartons shall be wiped with a suitable disinfecting agent delivered from a spray bottle or other suitable delivery method. After the disinfectant is sprayed or wiped on a surface to be disinfected, the disinfectant shall be allowed to dry, during which time the item shall not be used for compounding purposes.
(10) Wiping with small sterile 70% isopropyl alcohol swabs or comparable method for disinfecting entry points on bags and vials, allowing the isopropyl alcohol to dry before piercing stoppers with sterile needles and breaking necks of ampuls. The surface of the sterile 70% isopropyl alcohol swabs used for disinfecting entry points of sterile package and devices may not contact any other object before contacting the surface of the entry point. Particle generating material may not be used to disinfect the sterile entry points of packages and devices.
(11) When sterile supplies are received in sealed pouches designed to keep them sterile until opening, the sterile supplies may be removed from the covering pouches as the supplies are introduced into the ISO Class 5 primary engineering control without the need to disinfect the individual sterile supply items.
(12) No shipping or other external cartons may be taken into the buffer or clean area or segregated compounding area.

15.36 Accuracy.
Compounding procedures and sterilization methods used for preparations require planned testing, monitoring and documentation to demonstrate adherence to environmental quality requirements, personnel practices and procedures critical to achieving and maintaining sterility. Pharmacist verification of a preparation shall include visual inspection of labeling, physical integrity and expected appearance, including final fill amount.

15.37 Immediate use compounded sterile preparations.
(1) The compounding process shall occur continuously without delays or interruptions and does not exceed one hour, unless required for the preparation,
(2) Immediate use compounded sterile preparations shall begin administration within one hour of preparation. If administration has not begun within 1 hour following the start of preparing the compounded sterile preparation, the compounded sterile preparation shall be promptly, properly and safely discarded.
(3) Unless immediately and completely administered by the person who prepared the compounded sterile preparation or immediate and complete administration is witnessed by the preparer, the compounded sterile preparation shall have a label listing patient identification information, the names and amounts of all ingredients, the name or initials of the person who prepared the compounded sterile preparation and the exact 1 hour BUD and time.
(4) Immediate use compounded sterile preparations shall not be compounded and stored for anticipated needs and shall not be compounded as batch preparations.
(5) At no time during the compounding process, nor prior to administration, are critical sites and ingredients of the compounded sterile preparation to be directly exposed to contact

contamination, including human touch, cosmetic flakes or particulates, blood, human body substances and non-sterile inanimate sources.

15.38 Stability and Sterility.

(1) Unless the manufacturer's package indicates a different stability time, the following dates and times for storage and initiation of administration of the compounded sterile preparations shall apply:

(a) For low risk level compounded sterile preparations, one of the following:

1. Administration shall begin within 48 hours when the preparation is stored at controlled room temperature.
2. Administration shall begin within 14 days when the preparation is stored in a refrigerator.
3. Administration shall begin within 45 days when the preparation is stored in a freezer.

(b) For medium risk level compounded sterile preparations, one of the following:

1. Administration shall begin within 30 hours when the preparation is stored at controlled room temperature.
2. Administration shall begin within 9 days when the preparation is stored in a refrigerator.
3. Administration shall begin within 45 days when the preparation is stored in a freezer.

(c) For high risk level compounded sterile preparations, one of the following:

1. Administration shall begin within 24 hours when the preparation is stored at controlled room temperature.
2. Administration shall begin within 3 days when the preparation is stored in a refrigerator.
3. Administration shall begin within 45 days when the preparation is stored in a freezer.

(2) The administration dates and times established in sub. (1) shall not be exceeded or extended for compounded sterile preparations without verifiable supporting valid scientific sterility and stability information that is directly applicable to the specific preparation or compound.

(3) A pharmacist shall determine the BUD for a compounded sterile preparation consistent with sub. (1) and (2) and assign an appropriate discard after date for the compounded sterile preparation. The discard after date shall appear on the label.

(4) Opened or needle-punctured single dose containers of sterile products used in the compounding of sterile preparations for immediate use in an institutional pharmacy shall be used within one hour if opened in worse than ISO Class 5 air quality and any remaining contents shall be discarded.

(5) Single dose vials used in the compounding of sterile preparations exposed to ISO Class 5 or cleaner air quality may be used up to 6 hours after initial puncture.

(6) Opened single dose ampules used in the compounding of sterile preparations may not be stored for any period of time.

(7) Opened or needle punctured multiple dose vials used in the compounding of sterile preparations shall be used within 28 days after initially entering the vial, unless otherwise specified by the manufacturer.

15.39 Sterilization methods.

(1) Sterilization methods employed shall be based on experience and appropriate information sources.

(2) Presterilization requirements for high risk preparations shall meet all of the following:

(a) During all compounding activities that precede terminal sterilization, including weighing and mixing, compounding personnel shall be garbed and gloved in the same manner as when performing compounding in an ISO Class 5 environment. All presterilization procedures shall be completed in an ISO Class 8 or superior environment.

(b) Immediately before use, all nonsterile measuring, mixing, and purifying devices used in the compounding process shall be thoroughly rinsed with sterile, pyrogen-free water and then thoroughly drained or dried.

(3) High risk preparations shall be utilize one of the following sterilization methods:

(a) Sterilization by filtration involves the passage of a fluid or solution through a sterilizing grade membrane to produce a sterile effluent. This method shall meet all of the following:

1. Sterile filters used to sterile filter preparations shall be pyrogen-free and have a nominal porosity of 0.22 microns. The filter dimensions and liquid material to be sterile filtered shall permit the sterilization process to be completed rapidly without the replacement of the filter during the filtering process.
2. Compounding personnel shall ascertain that selected filters will achieve sterilization of the specific preparation.
3. Sterilization by filtration shall be performed entirely within an ISO Class 5 or superior air quality environment.

(b) Terminal sterilization is the use of saturated steam under pressure or autoclaving. This method shall meet all of the following:

1. All materials shall be exposed to steam at 250 degrees Fahrenheit under the recommended pressure and duration, verified by testing the sterility of the finished preparation.
2. The description of steam sterilization conditions and duration for specific preparations shall be included in written documentation maintained in the compounding facility.
3. Before or during entry into final containers, all high-risk preparations in solution form that are subjected to terminal steam sterilization shall pass through a filter with nominal porosity not larger than 1.2 microns for removal of particulate matter.

(c) Dry heat sterilization shall be completed in an oven designed for sterilization and shall be used only for those materials that cannot be sterilized by steam. The effectiveness of dry heat sterilization shall be verified using appropriate biological indicators and temperature sensing devices.

(4) All high risk preparations, except those for inhalation and ophthalmic administration, that are prepared in groups of 25 or more identical single dose containers or in multiple dose vials for administration to multiple patients or that are exposed longer than 12 hours at 36 to 46 degrees Fahrenheit or longer than 6 hours at warmer than 46 degrees Fahrenheit before they are sterilized, shall be quarantined and tested to ensure that the preparations are sterile and that they do not contain excessive bacterial endotoxins before they are dispensed or administered.

(5) If a preparation may be needed before the results of sterility testing have been received, the pharmacy shall daily observe the incubating test specimens and immediately recall the dispensed preparations when there is any evidence of microbial growth in the test specimens. The patient and the physician of the patient to whom a potentially contaminated compounded sterile preparation was administered shall be notified immediately of the potential risk.

15.40 Quality Assurance. The pharmacy's quality assurance program shall meet all the following requirements:
(1) The pharmacist shall use adequate labeling and verbal or written instructions regarding proper storage and administration as set forth by the product manufacturer with each compounded sterile preparation dispensed.
(2) Encompasses all phases of sterile compounding for each unique type of compounded sterile preparation dispensed.
(3) After the preparation of every admixture, the contents of the container are thoroughly mixed and then visually inspected to ensure the absence of particulate matter in solutions, the absence of leakage from vials and bags, or any other defects, and the accuracy and thoroughness of labeling.
(4) All pharmacists, pharmacy technicians, pharmacy interns, involved in compounding sterile preparations shall have their aseptic technique tested.
(5) All high-risk level compounded sterile preparations that are prepared in groups of more than 25 identical individual single-dose packages or in multiple-dose vials for administration to multiple patients, or that are exposed longer than 12 hours at 35 degrees to 46 degrees Fahrenheit and longer than 6 hours at warmer than 46 degrees Fahrenheit before they are sterilized and all compounded sterile preparations whose beyond-use date has been exceeded, shall be tested to ensure that they are sterile before they are dispensed or administered. The USP membrane filtration method shall be used where feasible. Another method may be used if verification results demonstrate that the alternative is at least as effective and reliable as the membrane filtration method or the USP direct inoculation of the culture medium method.
(6) When high risk level compounded sterile preparations are dispensed before receiving the results of the sterility tests, the written quality assurance procedures shall require daily observation of the incubating test specimens an immediate recall of the dispensed compounded sterile preparations when there is any evidence of microbial growth in the test specimens. The patient and the physician of the patient to whom a potentially contaminated compounded sterile preparation was administered shall be notified immediately of the potential risk. Positive sterility tests shall require rapid and systematic investigation of aseptic technique, environmental control and other sterility assurance controls in order to identify sources of contamination and to take corrective action.
(7) All high-risk level compounded sterile preparations, except those for inhalation and ophthalmic administration, shall be tested to ensure that they do not contain excessive bacterial endotoxins.
(8) Air and surface sampling for microbial organisms in ISO class 5 primary engineering controls, including laminar airflow workbenches, CAI, CACI and biological safety cabinets, and in all other ISO classified areas is done once every 6 months and at any time when microbial contamination is suspected.

(9) Laminar airflow workbenches, CAI, CACI and biological safety cabinets shall be certified every 6 months and every time they are moved, by an independent certification company to ensure that these primary engineering controls meet appropriate ISO classifications.
(10) A cleanroom shall be certified by an independent certification company every 6 months and whenever the room or a primary engineering control in the room is relocated or altered, or whenever major service to the facility is performed, to ensure that the cleanroom meets appropriate ISO classifications.
(11) Whenever test results indicate that the cleanroom or any primary engineering controls do not meet the standards established in this section, the pharmacy shall immediate cease using the cleanroom or primary engineering control that is out of compliance until such time that the cleanroom or the primary engineering control meets the requisite standards. Test results indicating non-compliance with the requisite standards shall require re-evaluation of all procedures associated with the production of compounded sterile preparations in the impacted cleanroom or primary engineering control and documentation with respect to the period of time that the cleanroom or primary engineering control was out of compliance.
(12) All certification records shall be reviewed by the managing pharmacist to ensure that the controlled environments comply with the proper air cleanliness, room pressures and air change per hour.

15.41 Training and evaluation. (1) GENERAL. The managing pharmacist, all pharmacists, pharmacy technicians, pharmacy interns and pharmacy externs involved in compounding sterile preparations shall have didactic and practical training in sterile preparation compounding, including proper personnel cleaning and garbing, cleaning and disinfecting the sterile compounding areas, cleanroom technology, laminar flow technology, isolator technology, if applicable, and quality assurance techniques. This training shall be successfully completed and documented before any compounding personnel begins to prepare compounding sterile preparations and annually thereafter for all who compound sterile preparations.
(2) GLOVED FINGERTIP. All compounding personnel shall successfully complete a gloved fingertip and thumb sampling procedure prior to compounding sterile preparations. Gloved fingertip and thumb sampling shall be conducted annually for all personnel engaged in compounding low and medium risk level preparations and semi-annually for all personnel engaged in compounding high risk level preparations. When gloved fingertip sample results exceed action levels after proper incubation, a review of hand hygiene and garbing procedures, glove and surface disinfection procedures and work practices shall be performed and documented.
(3) MEDIA-FILL TESTING. The pharmacy shall develop, maintain, and implement written procedures that include appropriate media-fill testing by personnel authorized to compound preparations. The issues to consider in the development of a media-fill test are media-fill procedures, media selection, fill volume, incubation, time and temperature, inspection of filed units, documentation, interpretation of results and possible corrective actions required. Tests shall be performed without interruption in an ISO Class 5 environment under conditions that closely simulate the stressful conditions encountered during compounding of the specific risk level preparations for which the test is intended. The pharmacy shall maintain records of media-fill testing performed, and results of testing procedures shall be available to the board upon request. Compounding personnel whose media-fill test vials result in gross microbial

colonization shall be immediately reinstructed and reevaluated by expert compounding personnel to ensure correction of all aseptic practice deficiencies.
(4) RECORDS. Documentation of training, gloved fingertip tests and media-fill tests shall be maintained by the pharmacy for 5 years and made available to the Board upon request.

15.42 Policies and Procedures. (1) A written policy and procedure manual shall be prepared, implemented, maintained and adhered to for the compounding, dispensing, delivery, administration, storage and use of sterile preparations. The manual shall establish policies and procedures governing all of the following:

(a) A risk management program, including documentation of incidents, adverse drug reactions and product contamination.
(b) Security measures ensuring the premises where compounded sterile drugs are present are secured.
(c) Procedures for use of equipment and documentation of applicable certifications.
(d) Cleaning and disinfecting.
(e) Reference materials.
(f) Drug preparation, storage, handling, dispensing, labeling, delivery, destruction, recalls and returns.
(g) Handling, dispensing and documentation of investigational new drugs.
(h) Quality assurance program.
(i) Training and competency guidelines.
(j) Sterile compounding process validation.
(k) Garb and garbing.
(l) Personnel responsibilities.
(m) Patient education.
(n) Maintaining the integrity of the interior work area of the laminar airflow workbenches, compounding aseptic isolators, compounding aseptic containment isolators and biological safety cabinets.
(o) Handling small and large spills of antieoplastic agents and other hazardous substances.

(2) The policy and procedures manual shall be reviewed at least once every 24 months and shall be updated, on a continuous basis, to reflect current practice. Documentation of the review shall be made available to the board upon request.

Reaction to Chapter Phar 15 Revisions from:

Members of the Pharmacy Society of Wisconsin (PSW)

Disclosure:

Recommendations and/or points for consideration that are outlined below are meant for the purposes of generating discussion only. They are not final positions of the Pharmacy Society of Wisconsin or its members.

Summary of Approach:

In the Statement of Scope for revising Phar 15, the Pharmacy Examining Board (PEB) intends to reference the United States Pharmacopeia Chapters <95>, Pharmaceutical Compounding - Nonsterile Preparations and <797>, Pharmaceutical Compounding - Sterile Preparations. The following document provides comments and tracks suggested revisions to the draft text of Chapter Phar 15 for consideration by the PEB during the Phar 15 rule revision process. Upon reviewing this draft, PSW member compounding subject matter experts feel that the following components need to be incorporated to ensure public safety: garbing technique, facility design, quality assurance processes, and training.

DRAFT TEXT of Chapter Phar 15

[*NOTE: There are some areas which may not be contained in this draft due to my needing more input in order to address in the rule.*]

15.01 Definitions. In this chapter:
(1) Active pharmaceutical ingredient (API) means any substance or mixture of substances intended to be used in the compounding of a drug preparation and that, when used in the compounding of a drug preparation, becomes an active ingredient in the preparation intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment or prevention of disease in humans and animals or affecting the structure and function of the body.
(2) Added substances means ingredients that are necessary to compound a drug preparation that are not intended or expected to cause a pharmacologic response if administered alone in the amount or concentration contained in a single dose of the compounded preparation.
(3) Beyond Use Date (BUD) means the date after which a non-sterile compounded preparation shall not be used, or the date and time after which a sterile compounded preparation shall not be stored or transported.
(4) Component means any, active pharmaceutical ingredient, or added substances used in the compounding of a drug preparation.
(5) Compounding means the preparation, mixing, assembling, altering, packaging, and labeling of a drug, drug delivery device, or a device in accordance with a prescription, medication order or initiative. Compounding includes any of the following:

(a) Preparation of drug dosage forms for both human and animal patients.
(b) Preparation of drugs or devices in anticipation of prescription drug orders based on routine, regularly observed prescribing patterns.

(c) Reconstitution or manipulation of commercial products that may require the addition of one or more ingredients. Notwithstanding this paragraph, the reconstitution or mixing that is performed pursuant to the directions contained in approved labeling provided by the manufacturer of a commercially available product is not compounding.

(d) Preparation of drugs or devices for the purposes of, or as an incident to, research, teaching or chemical analysis.

(6) Controlled room temperature means a temperature maintained thermostatically that encompasses the usual and customary working environment of 68 degrees to 77 degrees Fahrenheit.

(7) Freezer means a place in which a the temperature is maintained between -11 degrees and 14 degrees Fahrenheit

(8) Refrigerator means a cold place in which the temperature is maintained between 36 degrees and 46 degrees Fahrenheit

(9) Stability means the extent to which a compounded preparation retains, within specified limits and throughout its period of storage and use, the same properties and characteristics ~~that it possessed at the time of compounding~~within specified limits throughout its BUD.

(a) Chemical stability means each active pharmaceutical ingredient retains its chemical integrity and labeled potency without causing harmful impurities, within specified limits.

(b) Physical stability means the original physical properties, including appearance, palatability, uniformity, dissolution, and suspendability, are retained.

(c) Microbiological stability means sterility or resistance to microbial growth is retained according to specified requirements and antimicrobial agents that are present retain effectiveness within specified limits.

(d) Therapeutic stability means the therapeutic effect remains unchanged.

(e) Toxicological stability means no significant increase in toxicity occurs.

SUBCHAPTER I – General

15.10 Facilities. A pharmacist engaged in compounding shall ensure all of the following:

(1) An area designated for compounding.

(2) Orderly placement of compounding equipment, materials, and components in order to minimize the potential for compounding errors.

(3) The compounding area is well-lighted.

(4) The compounding area is maintained in a clean and sanitary condition.

(5) The compounding area is easily accessible to all of the following:

(a) Hot and cold running water, exclusive of the bathroom sink.

(b) Soap or detergent.

(c) Single-use towels.

(6) All compounding equipment, materials and components shall be stored off the floor and in a manner to prevent contamination and permit inspection and cleaning of the compounding and storage areas

15.11 Equipment and Drug Preparation Containers.

(1) A pharmacy shall possess equipment and drug preparation containers or packaging appropriate to the type of compounding performed at the pharmacy.

(2) Equipment and drug preparation containers or packaging used in compounding shall be of appropriate design and capacity, and shall be suitably stored in a manner to facilitate use, cleaning, maintenance, and protect it from contamination.
(3) Equipment and drug preparation containers/packaging used in compounding drug products shall be of suitable composition. Equipment surfaces that contact components may not be reactive, additive or adsorptive so as to alter the stability of the compounded preparation.
(4) Equipment used in compounding shall be thoroughly cleaned and sanitized after each use, and when necessary, prior to use, according to written policies and procedures, in order to reduce bioburden and reduce the opportunity for cross-contamination.
(5) All equipment utilized in compounding preparations shall be inspected, maintained, calibrated and validated at appropriate intervals, consistent with manufacturer's recommendations, to ensure the accuracy and reliability of equipment performance. Records shall be kept indicating the equipment was inspected, maintained, calibrated and validated.

15.12 Records. The managing pharmacist shall ensure written or electronic compounding documentation to systematically trace, evaluate, and replicate the compounding steps throughout the process of a preparation. The compounding documentation shall be maintained for a period of 5 years after the date of the last refill. The compounding documentation shall include all of the following:
(1) Master Formulation Record including all of the following:
(a) Official or assigned name, strength, and dosage form of the preparation.
(b) Calculations needed to determine and verify quantities of components and doses of active pharmaceutical ingredients.
(c) Description of all ingredients and their quantities.
(d) Compatibility and stability information, including references or laboratory testing
(e) Equipment needed to prepare the preparation.
(f) Mixing instructions including all of the following:
1. Order of mixing.
2. Mixing temperatures or other environmental controls.
3. Duration of mixing.
4. Other factors pertinent to the replication of the preparation as compounded.
(f) Sample labeling information, including all of the following:
1. Name and quantity or concentration of each active ingredient.
2. Assigned BUD.
3. Storage conditions.
4. Prescription or control number.
(g) Container used in dispensing.
(h) Packaging and storage requirements.
(i) Description of final preparation.
(j) Quality control procedures, if applicable, and expected results.
(2) Compounding Record including all of the following:
(a) Official or assigned name, strength, and dosage of the preparation.
(b) Master Formulation Record reference for the preparation.
(c) Names and quantities of all components.
(d) Sources, lot numbers and expiration dates of all components.
(e) Total quantity compounded.

Comment [ALD1]: Suggest creating two separate master formulation record / compounding records for non-sterile and sterile compounding. 797 updates will specify what needs to be in compounding record.

Comment [ALD2]: This may not happen with IV products. Allow compounding record to be master formulation record.

Comment [ALD3]: Add allowance to use compounding record as master formulation record.

(f) Name of the person who prepared the preparation.
(g) Name of the person who performed the quality control procedures.
(h) Name of the person who approved the preparation.
(i) Date of preparation.
(j) Assigned control or prescription number.
(k) Assigned BUD.
(L) Copy of the label to dispense final product.
(m) Description of the final preparation.
(n) Results of quality control procedures.
(o) Documentation of any quality control issues and any adverse reactions or preparation problems reported by the patient or caregiver.

15.13 Quality control.
(1) The pharmacist shall do a final check and review each procedure in the compounding process. A final check shall include verification of all the following:
(a) The master formulation record, compounding record and written procedures were followed in the execution of the compounding process. Any deviation in procedures shall be documented.
(b) There was a check and recheck of each procedure at each stage of the process.
(c) The tests or examinations conducted on the compounded preparation to ensure their uniformity and integrity followed established written procedures.
(d) The performance of compounding processes and equipment that may be responsible for causing variability in the final compounded preparations.
(2) The pharmacist shall observe the finished preparation to ensure that it appears as expected.
(3) The pharmacist shall investigate any discrepancies and take appropriate corrective action before the prescription is dispensed to the patient.
~~**(4)** The pharmacist completing the final check is solely responsible for the finished preparation.~~

Comment [ALD4]: Not necessary. Several RPh's may be involved with the process, including the PIC

15.14 Training. All personnel involved in the compounding, evaluation, packaging, and dispensing of compounded preparations shall be properly trained and competency is assessed for the type of compounding conducted. It is the responsibility of the managing pharmacist to ensure and document all training and competency assessments.

Comment [ALD5]: New version of 797 will be prescriptive wrt: assessments. For non-sterile, add a timeframe

SUBCHAPTER II – Non-sterile Compounding

Comment [ALD6]: Non-sterile language seems to be missing components

15.20 Definitions. In this subchapter:

(1) Office use means a preparation that is provided directly to a prescriber for patient use during an in office procedure. There is no patient name associated with this preparation, only LOT# and Exp Date.

a. The pharmacist shall record the lot numbers and exp dates of all preparation provided to each individual prescriber.

b. The prescriber shall record the lot number and exp date of all preparations used in the treatment of their patients and provide that documentation to the compounding pharmacists on a quarterly basis.

c. There shall be a recall procedure established that would allow for all medication to be recalled in a timely manner from all prescribers.

d. It is prohibited for these preparations to be sold by prescribers or given to patients for at home use or post procedure care.

Comment [ALD7]: Label should say "not for resale" or "for office use only." Otherwise this may not be enforceable.

15.21 Component Selection.
(1) A pharmacist shall use components manufactured in a FDA registered facility. If a component is unavailable from a FDA registered facility, the pharmacist may utilize a component that has been tested by a FDA approved vendor and the component has been determined to be pure and safe documented by a Certificate of Analysis.

Comment [ALD8]: Clarify, is this a testing facility?

(2) Components with an expiration date from the manufacturer or distributor may be used before the expiration date provided all of the following:

(a) The component is stored in its original container under conditions to avoid decomposition
(b) There is minimal exposure of the remaining component each time component is withdrawn from the container.
(c) When any withdrawals from the container are performed by those trained in the proper handling of the component.

(3) Components without an expiration date assigned by the manufacturer or supplier, shall be labeled with the date of receipt and assigned a conservative expiration date, not to exceed three years after receipt, based upon the nature of the component and its degradation mechanism, the container in which it is packaged and the storage conditions.
(4) Components transferred to another container which shall provide integrity that is minimally equivalent to the original container and shall be identified with all of the following:

(a) Component name.
(b) Original supplier.
(c) Lot or control number.
(d) Transfer date.
(e) Expiration date.

(5) Manufactured drug products utilized as the source of active pharmaceutical ingredients shall be manufactured in an FDA registered facility and the manufacturer's product container shall be labeled with a lot number and expiration date.
(6) A pharmacist compounding for human use may not use components that have been withdrawn or removed from the market for safety or efficacy reasons by the FDA. A pharmacist compounding for food producing animal use may not use components prohibited for use in food producing animals.

15.22~~1~~ Assigning BUD.
(1) The BUD shall not be later than the expiration date on the container of any component.

(2) In the absence of stability information that is applicable to a specific drug product and preparation, the maximum BUD for a non-sterile compounded drug preparation that is packaged in a tight, light-resistant container as follows:

(a) For nonaqueous formulations stored at controlled room temperature, the BUD shall not be later than the time remaining until the earliest expiration date of any active pharmaceutical ingredient or 6 months, whichever is earlier.

(b) For water-containing oral formulations, the BUD shall not be later than 14 days when stored at in a refrigerator

(c) For water-containing semisolid, mucosal liquid, topical or dermal formulations, stored at controlled room temperature, the BUD shall not be later than 30 days.

(3) Assignment of BUD shall include an assessment of the need for antimicrobial agents and or storage in a refrigerator to protect against bacteria, yeast, and mold contamination introduced during or after the compounding process.

SUBCHAPTER III – Sterile Compounding

Comment [ALD9]: Subject matter experts will be at the Phar Rules Revision meeting when specific discussion on this section occurs. In general, PSW members have expressed concern with language this specific given that USP <797> is in the revision process. There is a desire to be able to reference some or all of USP <795> and <797>.

15.30 Definitions. In this subchapter:

(1) Ante area means an ISO class 8 or better area where personnel hand hygiene and garbing procedures, staging of components, order entry, labeling and other high particulate generating activities are performed. The ante area is also a transition area that provides assurance that pressure relationships are constantly maintained so that air flows from clean to dirty areas and reduces the need for the heating, ventilating, and air-conditioning control system to respond to large disturbances.

(2) Buffer area means an area where the primary engineering control is physically located. Activities that occur in this area include the preparation and staging of components and supplies used when compounding compounded sterile preparations.

(3) CACI means compounding aseptic isolator. A form of isolator designed to provide worker protection from exposure to undesirable levels of airborne hazardous drugs throughout the compounding and material transfer processes and to provide an aseptic environment for compounding sterile preparations. Air exchange with the surrounding environment may not occur unless the air is first passed through a microbial retentive filter system capable of containing airborne concentrations of the physical size and state of the drug being compounded.

(4) CAI means compounding aseptic isolator. A form of isolator specifically designed for compounding pharmaceutical ingredients or preparations. It is designed to maintain an aseptic compounding environment within the isolator throughout the compounding and material transfer process. Air exchanges into the isolator from the surrounding environment may not occur unless the air has first passed through a microbially retentive filter.

(5) Cleanroom means a room in which the concentration of airborne particles is controlled to meet a specified airborne particulate cleanliness (ISO) class. Microorganisms in the environment ware monitored so that microbial level for air, surface, and personnel gear are not

exceeded for a specified cleanliness class. A cleanroom includes a buffer area or room and an ante area or room.

(6) Compounded sterile preparation means the aseptic processing in a clean air environment of any pharmaceutical preparations that are required to be sterile when they are administered into patient body cavities, central nervous and vascular systems, eyes, and joints and when used as baths for live organs and tissues, including injections, aqueous bronchial and nasal inhalations, irrigations for wounds and body cavities, ophthalmic drops and ointments and tissue implants

(7) High-risk level compounded sterile preparations means preparations compounded from non-sterile ingredients or from ingredients that are incorporated using non-sterile equipment before terminal sterilization, or from commercially manufactured sterile products that lack effective antimicrobial preservatives and whose preparation, transfer, sterilization, and packaging is performed in air quality worse than ISO class 5 for more than one hour. Water-containing preparations that are stored for more than six hours before terminal sterilization are also classified as high-risk level compounded sterile preparations.

(8) Immediate use compounded sterile preparations means preparations intended for emergency patient care and involve only simple aseptic measuring and transfer manipulations of no more than three sterile non-hazardous commercial drug and diagnostic radiopharmaceutical drug products, including an infusion or diluent solution.

(9) ISO class 5 air quality conditions means conditions in which the air particle count is no greater than a total of 3,520 particles of 0.5 micrometers and larger per cubic meter of air that is supplied by high-efficiency particulate air (HEPA) or HEPA-filtered air.

(10) ISO class 7 air quality conditions means conditions in which the air particle count is no greater than a total of 352,000 particles of 0.5 micrometers and larger per cubic meter of air that is supplied by high-efficiency particulate air (HEPA) or HEPA-filtered air.

(11) ISO class 8 air quality conditions means conditions in which the air particle count is no greater than a total of 3,520,000 particles of 0.5 micrometers and larger per cubic meter of air that is supplied by high-efficiency particulate air (HEPA) or HEPA-filtered air.

(12) Low-risk level compounded sterile preparations means preparations compounded with aseptic manipulations entirely within ISO class 5 or better air quality using only sterile ingredients, products, components, and devices. The compounding process involves only assembling, transferring, measuring, and mixing, using no more than three commercially manufactured sterile products, and not more than two entries into one sterile container or package to make the compounded sterile preparations. The compounding process is limited to aseptically opening ampules, penetrating sterile 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.

(13) Medium-risk level compounded sterile preparations means preparations compounded under low-risk level conditions but which require multiple individual or small doses of sterile products

to be combined or pooled to prepare compounded sterile preparations that will be administered either to multiple patients or to one patient on multiple occasions. The compounding process includes complex aseptic manipulations other than single volume transfer, and requires and unusually long duration, such as that required to complete dissolution or homogeneous mixing.

(14) Stability means the extent to which a preparation retains, within specified limits and throughout its period of storage and use, the same properties and characteristics that it possessed at the time of compounding.

15.31 General. All personnel who compound sterile preparation shall be responsible for understanding the fundamental practices and precautions, for developing and implementing appropriate procedures and for continually evaluating the procedures and the quality of the final compounded sterile preparation.

15.32 Responsibility of compounding personnel. The managing pharmacist is responsible for ensuring that compounded sterile preparations are accurately identified, measured, diluted, and mixed and are correctly purified, sterilized, packaged, sealed, labeled, stored, dispensed, and distributed. The responsibilities include maintaining appropriate cleanliness conditions and providing labeling and supplementary instructions for the proper clinical administration of compounded sterile preparations.

15.33 Facility Design and Environmental Controls. (1) CLEANROOM. A cleanroom shall be physically designed and environmentally controlled to minimize airborne contamination from contacting critical sites. Critical sites are locations that include any component or fluid pathway surfaces, openings, exposed and at risk of direct contact with air, moisture or touch contamination. A cleanroom shall include a buffer area and an ante area. The buffer area shall contain an ISO class 5 or better primary engineering control unless the buffer area has ISO class 5 or better air quality. A cleanroom shall be all of the following:

(a) Accessible only to designated personnel.

(b) Used only for the compounding of sterile preparations or other tasks that require a cleanroom.

(c) Structurally isolated from other areas within the pharmacy by means of restricted entry or access.

(d) Maintained at a temperature of 59 to 77 degrees Fahrenheit.

(g) Maintained free of chewing gum, drinks, candy or food items.

(2) CLEANROOM REQUIREMENTS. A cleanroom shall meet all of the following:

(a) The surfaces of ceilings, walls, floors, fixtures, shelving, counters and cabinets in the cleanroom shall be smooth, impervious, free from cracks and crevices and nonshedding, thereby minimizing spaces in which microorganisms and other contaminants may accumulate.

(b) Work surfaces shall be constructed of smooth, impervious materials so that the work surfaces may be readily cleaned and sanitized. All work surfaces shall be resistant to damage from cleaning and sanitizing agents.

(c) Junctures where ceilings meet walls shall be covered, caulked, or sealed to avoid cracks and crevices in which microorganisms and other contaminate can accumulate. All areas in ceilings and walls where the surface has been penetrated shall be sealed.

(d) Ceilings that consist of inlaid panels shall be impregnated with a polymer to render them impervious and hydrophobic and shall either be caulked or weighted and clipped.
(e) Walls shall be constructed of flexible material, panels locked together and sealed or of epoxy-coated gypsum board.
(f) Floors shall have a covering that shall be seamless or have teat-welded seams and coving to the sidewall. There shall be no floor drains.
(g) There shall be no dust –collection overhangs and ledges should be avoided. All sprinkler heads shall be flush with the ceiling.
(h) Ceiling lighting fixtures shall have exterior lens surfaces which are smooth, mounted flush and air tight.
(i) Carts shall be of stainless steel wire, nonporous plastic or sheet metal construction with good quality, cleanable casters to promote mobility.
(j) Refrigerators shall be within, or reasonably accessible to, the cleanroom in order to ensure the integrity of compounded sterile preparations.

(3) ANTE AREA REQUIREMENTS. The ante area shall meet all of the following:
(a) Appropriate environmental control devices capable of maintaining ISO class 8 air quality conditions for non-hazardous drug compounding activities and ISO class 7 air quality conditions for hazardous drug compounding activities.
(b) Contain all of the following equipment:
1. A sink with hot and cold running water with an integrated and closed plumbing system.
2. Waste containers for all personal protective equipment.
3. An eyewash station.
4. A hazardous waste spill kit.

(4) BUFFER AREA REQUIREMENTS. The buffer area shall meet all of the following:
(a) The buffer area shall have appropriate environment control devices capable of maintaining ISO class 7 air quality conditions during normal activity.
(b) The buffer area shall contain only the following:
1. Items, including furniture, equipment, and supplies, that are required for the tasks to be performed in the buffer area.
2. Items that are nonpermeable, nonshedding, cleanable, and resistant to disinfectants.
3. Items that have been cleaned and disinfected immediately prior to their being placed in the buffer area.
(c) Equipment and other items used in the buffer area shall not be taken from these areas except for calibration, servicing, or other activities associated with the proper maintenance of the item.
(d) The buffer area shall be kept clean and arranged in an orderly fashion. All required equipment shall be maintained in good operating condition.
(e) The buffer area shall not be used for bulk storage, warehousing or clerical functions.
(f) The buffer area shall not contain any sinks.
(g) The buffer area shall be a minimum of 100 square feet in size and shall be compatible with the volume of compounding being conducted.
(h) The buffer area shall contain waste containers in compliance with Occupational Safety and Health Administration standards for disposal of used needles and syringes and for disposal of chemotherapy waste.

Comment [ALD10]: There doesn't need to be a specific size listed

Comment [ALD11]: Standards for pharmacy are DNR based, not OSHA.

(5) USE OF CAI AND CACI LOCATED OUTSIDE OF A CLEANROOM. A pharmacy may utilize a CAI or CACI not located in a cleanroom to prepare compounded sterile preparations, provided all of the following:

(a) The CAI or CACI can provide isolation from the room and maintain ISO class 5 air quality during dynamic operating conditions, including transferring ingredients, components, and devices into and out of the isolator and during preparation of compounded sterile preparations. Particle counts sampled approximate 6 to 12 inches upstream of the critical exposure site must maintain ISO class 5 air quality levels during compounding operations.

(b) Compounding personnel shall obtain documentation from the manufacturer that the CAI or CACI will meet this standard when located in worse than ISO class 7 environments.

(c) A CAI or CACI not located in a buffer area shall be located in an area that is maintained under sanitary conditions and such area shall only be traveled by persons engaging in the compounding of sterile preparations.

15.34 Personnel cleansing and garbing requirements. (1) All personnel who engage in compounding sterile preparations shall comply with all of the following requirements before entering the buffer area:

(a) Remove personal outer garments, all cosmetics, makeup, visible jewelry and piercings.

(b) The wearing of artificial nails or extenders is prohibited while working in the compounding area. Natural nails shall be kept neat and trimmed.

Comment [ALD12]: Nail polish is also prohibited

(c) Personnel protective equipment shall be put on in the following order:

1. Dedicated shoes or shoe covers.
2. Head and facial hair covers.
3. Face masks.
4. Eye shields, if required due to working with irritants or hazardous drugs.

(d) A hand and forearm cleansing procedure shall be performed. Personnel shall remove debris from underneath fingernails using a nail cleaner under running warm water followed by vigorous hand washing for at least 30 seconds. Hands and forearms to the elbows shall be completely dried using either lint-free disposable towels or an electronic hand dryer.

(e) Personnel shall wear non-shedding gowns with sleeves that fit snugly around the wrists and enclosed at the neck that are designed for buffer area use.

(2) Following the completion of all the steps in sub. (1) and once inside the buffer area, personnel shall perform antiseptic hand cleansing, using a waterless alcohol based surgical hand scrub with persistent activity following manufacturer's recommendations. Once hands are dried thoroughly, personnel shall don sterile gloves. Gloves shall be routinely inspected for holes, punctures, or tears and shall be replaced immediately if any are detected.

(3) Gloves become contaminated when they make contact with non-sterile surfaces during compounding activities. Disinfection of contaminated gloved hands may be accomplished by wiping or rubbing sterile 70% isopropyl alcohol on all contact surface areas of the gloves and letting the gloved hands dry thoroughly. Routine application of sterile 70% isopropyl alcohol shall occur throughout the compounding process and whenever non-sterile surfaces, including vials, counter tops, chairs and carts, are touched.

(4) When compounding personnel exit the cleanroom during a work shift, the exterior gown may be removed and retained in the cleanroom if not visibly soiled and may be re put on during that same work shift only. Shoe covers, hair and facial hair covers, face masks, eye shields and gloves shall be replaced with new ones before re-entering the buffer area and proper hand hygiene shall be performed.

15.35 Cleaning and Disinfecting the Compounding Area. (1) Compounding personnel are responsible determining the cleaning and disinfecting products to be used and for ensuring that the frequency of cleaning and disinfecting compounding area is done in accordance with the following frequency:

(a) ISO Class 5 primary engineering control at the beginning of each shift or before each batch, but not longer than 30 minutes following the previous surface disinfection when ongoing compounding activities are occurring.
(b) Counters and easily cleanable work surfaces daily.
(c) Floors daily.
(d) Walls, ceilings and storage shelving monthly.

(2) All cleaning and disinfecting practices and policies for the compounding of compounding sterile preparations shall be included in written standard operating procedures and shall be followed by all compounding personnel.
(3) Disinfecting sterile compounding areas shall occur on a regular basis at the intervals in sub. (1) or when any of the following occurs:

(a) Spills occur.
(b) The surface is visibly soiled.
(c) Microbial contamination is known to have been or is suspected of having been introduced into the compounding area.

(4) Cleaning, using a germicidal detergent, and disinfecting shall occur before compounding is performed. Items shall be removed from all areas to be cleaned, and surfaces shall be cleaned by removing loose material and residue from spills. This shall be followed by wiping with sterile 70% isopropyl alcohol, which is allowed to dry before compounding begins.
(5) Work surfaces in the ISO Class 7 buffer areas and ISO Class 8 ante areas as well as segregated compounding areas shall be cleaned and disinfected at least daily. Dust and debris shall be removed when necessary from storage sites for compounding ingredients and supplies using a method that does not degrade the ISO Class 7 or 8 air quality.

Comment [ALD13]: Dust and debris should not be there in the first place.

(6) Floors in the cleanroom, buffer area and ante area are cleaned by mopping with a germicidal detergent once daily at a time when no aseptic operations are in progress. Mopping shall be performed by trained personnel using approved agents and procedures.
(7) In the cleanroom, buffer area and ante area, the walls, ceilings and shelving shall be cleaned and disinfected with a germicidal detergent with consideration of compatibilities, effectiveness and inappropriate or toxic residues.
(8) All cleaning materials shall be nonshedding and dedicated to use in the cleanroom, buffer area and ante area and shall not be removed from these areas except for disposal. If cleaning materials, including mops, are reused, procedures shall be developed based on manufacturer recommendations, that ensure that the effectiveness of the cleaning device is maintained and that repeated use does not add to the bioburden of the area being cleaned.
(9) Supplies and equipment removed from shipping cartons shall be wiped with a suitable disinfecting agent delivered from a spray bottle or other suitable delivery method. After the

disinfectant is sprayed or wiped on a surface to be disinfected, the disinfectant shall be allowed to dry, during which time the item shall not be used for compounding purposes.
(10) Wiping with small sterile 70% isopropyl alcohol swabs or comparable method for disinfecting entry points on bags and vials, allowing the isopropyl alcohol to dry before piercing stoppers with sterile needles and breaking necks of ampuls. The surface of the sterile 70% isopropyl alcohol swabs used for disinfecting entry points of sterile package and devices may not contact any other object before contacting the surface of the entry point. Particle generating material may not be used to disinfect the sterile entry points of packages and devices.
(11) When sterile supplies are received in sealed pouches designed to keep them sterile until opening, the sterile supplies may be removed from the covering pouches as the supplies are introduced into the ISO Class 5 primary engineering control without the need to disinfect the individual sterile supply items.
(12) No shipping or other external cartons may be taken into the buffer or clean area or segregated compounding area.

15.36 Accuracy.
Compounding procedures and sterilization methods used for preparations require planned testing, monitoring and documentation to demonstrate adherence to environmental quality requirements, personnel practices and procedures critical to achieving and maintaining sterility. Pharmacist verification of a preparation shall include visual inspection of labeling, physical integrity and expected appearance, including final fill amount.

15.37 Immediate use compounded sterile preparations.
(1) The compounding process shall occur continuously without delays or interruptions and does not exceed one hour, unless required for the preparation,
(2) Immediate use compounded sterile preparations shall begin administration within one hour of preparation. If administration has not begun within 1 hour following the start of preparing the compounded sterile preparation, the compounded sterile preparation shall be promptly, properly and safely discarded.
(3) Unless immediately and completely administered by the person who prepared the compounded sterile preparation or immediate and complete administration is witnessed by the preparer, the compounded sterile preparation shall have a label listing patient identification information, the names and amounts of all ingredients, the name or initials of the person who prepared the compounded sterile preparation and the exact 1 hour BUD and time.
(4) Immediate use compounded sterile preparations shall not be compounded and stored for anticipated needs and shall not be compounded as batch preparations.
(5) At no time during the compounding process, nor prior to administration, are critical sites and ingredients of the compounded sterile preparation to be directly exposed to contact contamination, including human touch, cosmetic flakes or particulates, blood, human body substances and non-sterile inanimate sources.

15.38 Stability and Sterility.
(1) Unless the manufacturer's package indicates a different stability time, the following dates and times for storage and initiation of administration of the compounded sterile preparations shall apply:
(a) For low risk level compounded sterile preparations, one of the following:

1. Administration shall begin within 48 hours when the preparation is stored at controlled room temperature.
2. Administration shall begin within 14 days when the preparation is stored in a refrigerator.
3. Administration shall begin within 45 days when the preparation is stored in a freezer.

(b) For medium risk level compounded sterile preparations, one of the following:
1. Administration shall begin within 30 hours when the preparation is stored at controlled room temperature.
2. Administration shall begin within 9 days when the preparation is stored in a refrigerator.
3. Administration shall begin within 45 days when the preparation is stored in a freezer.

(c) For high risk level compounded sterile preparations, one of the following:
1. Administration shall begin within 24 hours when the preparation is stored at controlled room temperature.
2. Administration shall begin within 3 days when the preparation is stored in a refrigerator.
3. Administration shall begin within 45 days when the preparation is stored in a freezer.

(2) The administration dates and times established in sub. (1) shall not be exceeded or extended for compounded sterile preparations without verifiable supporting valid scientific sterility and stability information that is directly applicable to the specific preparation or compound.
(3) A pharmacist shall determine the BUD for a compounded sterile preparation consistent with sub. (1) and (2) and assign an appropriate discard after date for the compounded sterile preparation. The discard after date shall appear on the label.
(4) Opened or needle-punctured single dose containers of sterile products used in the compounding of sterile preparations for immediate use in an institutional pharmacy shall be used within one hour if opened in worse than ISO Class 5 air quality and any remaining contents shall be discarded.
(5) Single dose vials used in the compounding of sterile preparations exposed to ISO Class 5 or cleaner air quality may be used up to 6 hours after initial puncture.
(6) Opened single dose ampules used in the compounding of sterile preparations may not be stored for any period of time.
(7) Opened or needle punctured multiple dose vials used in the compounding of sterile preparations shall be used within 28 days after initially entering the vial, unless otherwise specified by the manufacturer.

15.39 Sterilization methods.
(1) Sterilization methods employed shall be based on experience and appropriate information sources.
(2) Presterilization requirements for high risk preparations shall meet all of the following:
(a) During all compounding activities that precede terminal sterilization, including weighing and mixing, compounding personnel shall be garbed and gloved in the same manner as when performing compounding in an ISO Class 5 environment. All presterilization procedures shall be completed in an ISO Class 8 or superior environment.

(b) Immediately before use, all nonsterile measuring, mixing, and purifying devices used in the compounding process shall be thoroughly rinsed with sterile, pyrogen-free water and then thoroughly drained or dried.

(3) High risk preparations shall be utilize one of the following sterilization methods:

(a) Sterilization by filtration involves the passage of a fluid or solution through a sterilizing grade membrane to produce a sterile effluent. This method shall meet all of the following:

1. Sterile filters used to sterile filter preparations shall be pyrogen-free and have a nominal porosity of 0.22 microns. The filter dimensions and liquid material to be sterile filtered shall permit the sterilization process to be completed rapidly without the replacement of the filter during the filtering process.
2. Compounding personnel shall ascertain that selected filters will achieve sterilization of the specific preparation.
3. Sterilization by filtration shall be performed entirely within an ISO Class 5 or superior air quality environment.

(b) Terminal sterilization is the use of saturated steam under pressure or autoclaving. This method shall meet all of the following:

1. All materials shall be exposed to steam at 250 degrees Fahrenheit under the recommended pressure and duration, verified by testing the sterility of the finished preparation.
2. The description of steam sterilization conditions and duration for specific preparations shall be included in written documentation maintained in the compounding facility.
3. Before or during entry into final containers, all high-risk preparations in solution form that are subjected to terminal steam sterilization shall pass through a filter with nominal porosity not larger than 1.2 microns for removal of particulate matter.

(c) Dry heat sterilization shall be completed in an oven designed for sterilization and shall be used only for those materials that cannot be sterilized by steam. The effectiveness of dry heat sterilization shall be verified using appropriate biological indicators and temperature sensing devices.

(4) All high risk preparations, except those for inhalation and ophthalmic administration, that are prepared in groups of 25 or more identical single dose containers or in multiple dose vials for administration to multiple patients or that are exposed longer than 12 hours at 36 to 46 degrees Fahrenheit or longer than 6 hours at warmer than 46 degrees Fahrenheit before they are sterilized, shall be quarantined and tested to ensure that the preparations are sterile and that they do not contain excessive bacterial endotoxins before they are dispensed or administered.

(5) If a preparation may be needed before the results of sterility testing have been received, the pharmacy shall daily observe the incubating test specimens and immediately recall the dispensed preparations when there is any evidence of microbial growth in the test specimens. The patient and the physician of the patient to whom a potentially contaminated compounded sterile preparation was administered shall be notified immediately of the potential risk.

15.40 Quality Assurance. The pharmacy's quality assurance program shall meet all the following requirements:

(1) The pharmacist shall use adequate labeling and verbal or written instructions regarding proper storage and administration as set forth by the product manufacturer with each compounded sterile preparation dispensed.
(2) Encompasses all phases of sterile compounding for each unique type of compounded sterile preparation dispensed.
(3) After the preparation of every admixture, the contents of the container are thoroughly mixed and then visually inspected to ensure the absence of particulate matter in solutions, the absence of leakage from vials and bags, or any other defects, and the accuracy and thoroughness of labeling.
(4) All pharmacists, pharmacy technicians, pharmacy interns, involved in compounding sterile preparations shall have their aseptic technique tested.
(5) All high-risk level compounded sterile preparations that are prepared in groups of more than 25 identical individual single-dose packages or in multiple-dose vials for administration to multiple patients, or that are exposed longer than 12 hours at 35 degrees to 46 degrees Fahrenheit and longer than 6 hours at warmer than 46 degrees Fahrenheit before they are sterilized and all compounded sterile preparations whose beyond-use date has been exceeded, shall be tested to ensure that they are sterile before they are dispensed or administered. The USP membrane filtration method shall be used where feasible. Another method may be used if verification results demonstrate that the alternative is at least as effective and reliable as the membrane filtration method or the USP direct inoculation of the culture medium method.
(6) When high risk level compounded sterile preparations are dispensed before receiving the results of the sterility tests, the written quality assurance procedures shall require daily observation of the incubating test specimens an immediate recall of the dispensed compounded sterile preparations when there is any evidence of microbial growth in the test specimens. The patient and the physician of the patient to whom a potentially contaminated compounded sterile preparation was administered shall be notified immediately of the potential risk. Positive sterility tests shall require rapid and systematic investigation of aseptic technique, environmental control and other sterility assurance controls in order to identify sources of contamination and to take corrective action.
(7) All high-risk level compounded sterile preparations, except those for inhalation and ophthalmic administration, shall be tested to ensure that they do not contain excessive bacterial endotoxins.
(8) Air and surface sampling for microbial organisms in ISO class 5 primary engineering controls, including laminar airflow workbenches, CAI, CACI and biological safety cabinets, and in all other ISO classified areas is done once every 6 months and at any time when microbial contamination is suspected.
(9) Laminar airflow workbenches, CAI, CACI and biological safety cabinets shall be certified every 6 months and every time they are moved, by an independent certification company to ensure that these primary engineering controls meet appropriate ISO classifications.
(10) A cleanroom shall be certified by an independent certification company every 6 months and whenever the room or a primary engineering control in the room is relocated or altered, or whenever major service to the facility is performed, to ensure that the cleanroom meets appropriate ISO classifications.
(11) Whenever test results indicate that the cleanroom or any primary engineering controls do not meet the standards established in this section, the pharmacy shall immediate cease using the cleanroom or primary engineering control that is out of compliance until such time that the

cleanroom or the primary engineering control meets the requisite standards. Test results indicating non-compliance with the requisite standards shall require re-evaluation of all procedures associated with the production of compounded sterile preparations in the impacted cleanroom or primary engineering control and documentation with respect to the period of time that the cleanroom or primary engineering control was out of compliance.
(12) All certification records shall be reviewed by the managing pharmacist to ensure that the controlled environments comply with the proper air cleanliness, room pressures and air change per hour.

15.41 Training and evaluation. (1) GENERAL. The managing pharmacist, all pharmacists, pharmacy technicians, pharmacy interns and pharmacy externs involved in compounding sterile preparations shall have didactic and practical training in sterile preparation compounding, including proper personnel cleaning and garbing, cleaning and disinfecting the sterile compounding areas, cleanroom technology, laminar flow technology, isolator technology, if applicable, and quality assurance techniques. This training shall be successfully completed and documented before any compounding personnel begins to prepare compounding sterile preparations and annually thereafter for all who compound sterile preparations.
(2) GLOVED FINGERTIP. All compounding personnel shall successfully complete a gloved fingertip and thumb sampling procedure prior to compounding sterile preparations. Gloved fingertip and thumb sampling shall be conducted annually for all personnel engaged in compounding low and medium risk level preparations and semi-annually for all personnel engaged in compounding high risk level preparations. When gloved fingertip sample results exceed action levels after proper incubation, a review of hand hygiene and garbing procedures, glove and surface disinfection procedures and work practices shall be performed and documented.
(3) MEDIA-FILL TESTING. The pharmacy shall develop, maintain, and implement written procedures that include appropriate media-fill testing by personnel authorized to compound preparations. The issues to consider in the development of a media-fill test are media-fill procedures, media selection, fill volume, incubation, time and temperature, inspection of filed units, documentation, interpretation of results and possible corrective actions required. Tests shall be performed without interruption in an ISO Class 5 environment under conditions that closely simulate the stressful conditions encountered during compounding of the specific risk level preparations for which the test is intended. The pharmacy shall maintain records of media-fill testing performed, and results of testing procedures shall be available to the board upon request. Compounding personnel whose media-fill test vials result in gross microbial colonization shall be immediately reinstructed and reevaluated by expert compounding personnel to ensure correction of all aseptic practice deficiencies.
(4) RECORDS. Documentation of training, gloved fingertip tests and media-fill tests shall be maintained by the pharmacy for 5 years and made available to the Board upon request.

15.42 Policies and Procedures. (1) A written policy and procedure manual shall be prepared, implemented, maintained and adhered to for the compounding, dispensing, delivery, administration, storage and use of sterile preparations. The manual shall establish policies and procedures governing all of the following:

(a) A risk management program, including documentation of incidents, adverse drug reactions and product contamination.

(b) Security measures ensuring the premises where compounded sterile drugs are present are secured.

Comment [ALD14]: Is this for controlled substances? Is it needed for outsourcing facilities?

(c) Procedures for use of equipment and documentation of applicable certifications.
(d) Cleaning and disinfecting.
(e) Reference materials.
(f) Drug preparation, storage, handling, dispensing, labeling, delivery, destruction, recalls and returns.
(g) Handling, dispensing and documentation of investigational new drugs, if applicable.
(h) Quality assurance program.
(i) Training and competency guidelines.
(j) Sterile compounding process validation.
(k) Garb and garbing.
(l) Personnel responsibilities.
(m) Patient education.
(n) Maintaining the integrity of the interior work area of the laminar airflow workbenches, compounding aseptic isolators, compounding aseptic containment isolators and biological safety cabinets.
(o) Handling small and large spills of antieoplastic agents and other hazardous substances.

(2) The policy and procedures manual shall be reviewed at least once every 24 months and shall be updated, on a continuous basis, to reflect current practice. Documentation of the review shall be made available to the board upon request.

Are USP <797> Compliance Rates Good Enough?

Kate Douglass, MS, RN, APN,C, CRNI, Eric S. Kastango, MBA, RPh, FASHP, Peter Cantor

With the completion of this year's study, we can now reflect on 5 years of compliance data—and the results are mixed. Certainly there has been real and measurable improvement in USP Chapter <797> scores in this study, but is it enough? We do not think it is, not nearly so. As such, we would like to take this opportunity to share our perspectives on compliance. Our thoughts are drawn from this and previous years' study results; in addition, they are informed from the hundreds of emails, telephone calls, and visits we have conducted with sterile compounding personnel and regulators over the same time period.

Following the NECC compounding tragedy that killed 64 people and permanently injured hundreds more, we expected the response would be an enduring sense of urgency driving the implementation of improved sterile compounding practices. More recently, a federal grand jury handed down a 131-count indictment in the NECC case that encompasses crimes ranging from racketeering to mail fraud, as well as 25 counts of second-degree murder. One might expect this would bolster any fading sense of complacency; however, that does not seem to be the case. As Michael Cohen of ISMP has oft been quoted, "Unfortunately, there are too many in health care who feel that if it hasn't happened to them directly, the adverse experiences of others do not apply."

The lessons learned from this preventable tragedy (including the necessity of disciplined facility cleaning and environmental and personnel sampling and the imperative to take actions based upon those results) have yet to translate into change at the rate that we had hoped. In comparing this year's compliance scores for hospitals (the largest cohort in this study) against the scores from 5 years ago, we see an overall improvement in compliance, with only a few exceptions (see **Figure 1**). Nevertheless, the 2015 data demonstrate that despite significantly greater regulatory and enforcement action (see **Table 1**), progress remains slow. Lagging compliance in what we believe are essential activities—such as aseptic technique, cleaning and disinfection, environmental sampling, staff training/competency, and quality metrics such as sterility testing, bacterial endotoxin testing, and filter integrity testing—is troubling.

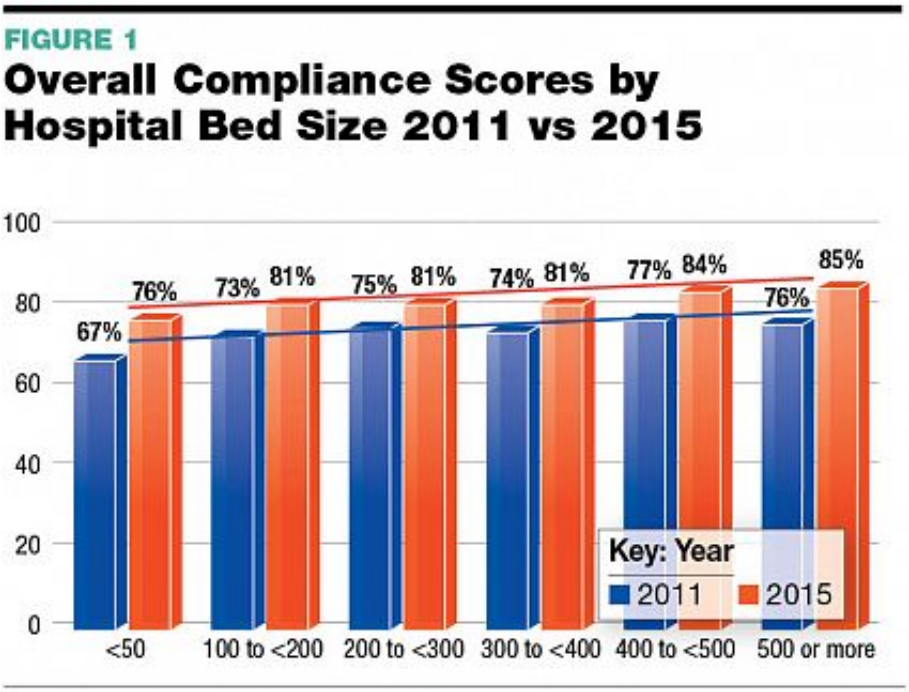
TABLE 1
Rate of Reported Negative Findings

Year	# of pharmacies reporting no negative findings	# of pharmacies reporting negative findings at 1 or more entities	Total # of pharmacies reporting	Rate of reported negative findings
2011	764	109	873	12%
2015	634	181	815	22%

Survey Bias

Though valuable, it is important to note that the data from the CriticalPoint USP <797> study contains an inherent bias. Those who participate are likely motivated to do so because they are either interested in benchmarking their organization's performance or are incentivized by the Action Plan for Compliance they receive upon completing the survey. As such, the participating locations are likely to be committed to and engaged in the pursuit of improvement in sterile compounding practice. In addition, since this is a self-report study, we are certain that respondents' answers do not always reflect their actual practice. On many occasions, we have asked pharmacies to complete a gap analysis in preparation for a visit or telephone consultation. When we follow up, we typically discover that the staff did not fully understand the gap analysis items or they indicated compliance in areas where their actual practices did not fully

comply. In every single case, when we objectively verify scores with observation, the resulting scores are lower than originally reported.



Understanding the Data

It is important to look at these data with an understanding that the scores are likely to reflect higher rates of compliance versus actual practice. Overall, hospital pharmacies report a compliance rate of 80%. Considering that this translates into a B-: we need to decide whether we should accept this as good enough. Note that the items with the lowest or lagging compliance often are practice areas that may engender the most risk to patients.

USP Chapter <797> provides minimum practice and quality standards for compounded sterile preparations of drugs and nutrients based on current scientific information and best sterile compounding practices. When the American Society of Health-System Pharmacists published its Sterile Compounding Technical Assistance Bulletin in 1993, Kenneth E. Avis, often considered to be the father of good compounding practices in pharmacy, asserted, "This is not new science, but rather old news that few bothered to heed." Similarly, many of the <797> requirements have been in place for over a decade. Even the newest requirements of the chapter have been official for 8 years. Since 2001, the Sterile Compounding Expert Committee has been hard at work revising the chapter and the resulting updates are expected to be released for public comment in late 2015 or early 2016. Our hope is that you will join us in pushing for full compliance with the current version of the chapter. We need you to actively participate in the revision process and provide thoughtful feedback to the Expert Committee once the revised chapter is available for public comment. Your participation is imperative because what we are doing now is not good enough to ensure patient safety.

Kate Douglass, MS, RN, APN,C, CRNI, is the vice president of CriticalPoint, LLC, and serves as the codirector of the annual USP <797> Compliance Survey.

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The 2015 USP <797> Compliance Study

a National Study of Sterile Compounding Practices

Pharmacy departments across the country completed the 2015 USP <797> Compliance Survey, led by Eric Kastango and Kate Douglass. This is an executive summary of the 35 sites in Wisconsin that completed the USP <797> Compliance Survey. It identifies areas Wisconsin has to improve sterile compounding practice, improve patient safety, and opportunities to comply with the proposed Chapter Phar 15.

[72%] State of Wisconsin USP <797> Compliance Survey Grand Total

Domain Results

[0%] Bacterial Endotoxin Testing

[0%] Radio Pharmaceuticals

[7%] Filter Integrity Test

[42%] Sterility Testing

[43%] Gloved Fingertip Sampling

[53%] Quality Management: General

Items - Environment

[0%] There is evidence in the form of employee-specific documentation that media fill units have been successfully completed and at least semi-annually thereafter.

[22%] Personnel who compound in ISO Class 5 environments located outside of an ISO Class 7/8 buffer area perform hand hygiene and garbing.

[33%] Filters are subject to filter integrity test at the conclusion of the compounding procedure.

[35%] There is written confirmation by each compounding employee of reproductive age that they understand the risk of handling hazardous CSPs.

[41%] Surface Sampling is performed at the conclusion of compounding.

[42%] Supplies equipment and other materials are uncartoned and wiped down with residue free disinfectant prior to entering the buffer area (cleanroom).

[50%] The organization stores hazardous CSPs in a negative pressure room such as the hazardous drug compounding room.

Items - Infrastructure

[0%] Isolators that are not placed in an ISO Class 7 buffer area and do not meet the exclusion criteria outline in Chapter <797>, so is the compounding that occurs within those isolators limited to nonhazardous and radiopharmaceutical CSPs that are given 12 hour or less BUD.

[22%] CSPs prepared in ISO Class 5 environments that are located outside ISO Class 7/8 buffer areas limited to non-hazardous CSPs.

[33%] Filters are subject to filter integrity test at the conclusion of the compounding procedure.

[42%] A line of demarcation in the ante-area or segregated compounding area separates the dirty area from the clean area.

[58%] All furniture, equipment and physical plant surfaces in the buffer, ante and segregated compounding areas is nonporous, smooth, free from cracks/crevices, nonshedding, impermeable, and cleanable resistant to degradations by cleaning agents.

State of Wisconsin
2015 Aggregated Findings
USP <797> Compliance Survey

Domain/Items	Compliance %
Allergen Extracts as CSPs	**N/A**
Aseptic Technique	**82%**
Do your compounding personnel wear sterile gloves?	75%
Supplies, equipment and other materials are uncartoned and wiped down with residue free disinfectant prior to entering the buffer area (cleanroom).	42%
The compounding location takes action to ensure that food, drinks, and contaminated supplies/equipment do not enter the ante and cleanroom (buffer) areas.	86%
All supplies and drug components are disinfected with an appropriate cleaning agent prior to being moved into the ISO Class 5 compounding area.	64%
Compounding personnel are vigilant to prevent touch contamination and if contamination is suspected, they discard the component, supply or preparation.	89%
Compounding personnel arrange items at least 6 inches inside of aseptic work area such as an LAFW.	89%
Compounding personnel do not expose critical sites to contact contamination or worse than ISO Class 5 air; stoppers, injection ports, ampoule necks are disinfected by wiping with sterile 70% IPA and allowed to dry each time they are entered.	86%
Compounding personnel inspect each component and supply for visible particulate matter, tampering, breaks in packaging and other changes which would render the item unacceptable for use in sterile compounding.	92%
Compounding personnel perform manipulations in the direct compounding area inside of the ISO Class 5 environment in such a way as not to disrupt the flow of first air (HEPA filtered air stream) over critical sites.	94%
Compounding personnel remove waste or unused supplies with minimal in-and-out motion. Partially used multi-dose vials are dated and initialed outside of the ISO Class 5 work area.	92%
Gloved hands are cleaned with sterile 70% IPA prior to entering/re-entering an ISO Class 5 area as well as regularly after touching non sterile objects.	75%
Sterile gloved hands are routinely inspected for wear and tear and replaced as needed.	86%
Syringes, needles and tubing remain in their individual packaging and are only opened in ISO Class 5 area.	94%
Bacterial Endotoxin Testing	**0%**
The specific procedure for bacterial endotoxin testing includes the description of the procedure and specific endotoxin unit limits based on USP Endotoxin Test<85> is included in the compounding location's written policies and procedures.	0%
The compounding location performs bacterial endotoxin (pyrogen) testing (or has outsourced the testing to a contract lab) on all high risk level CSPs, (except those for inhalation and ophthalmic administration) that have been prepared: - in groups >25 identical single dose packages **or** - in MDVs for administration to multiple patients that have been exposed longer than 12 hours to 2-8 degrees Celsius and longer than 6 hours to warmer than 8 degrees Celsius before they are sterilized.	0%
Beyond Use Dating	**86%**

Beyond use dates (BUDs) assigned to CSPs never exceed the limits outlined in USP <797> unless sterility testing is performed on that batch.	86%
There is evidence of the process by which BUD and storage conditions are assigned to each specific CSP type prepared by the compounding location. For example: There is evidence that the compounding location has evaluated data from the manufacturer/s or peer-reviewed literature that substantiates the stability and storage conditions for each type of CSP that is compounded.	86%
Compounding Facility Management: Airflows and Pressure Differential Monitoring	**60%**
Documentation indicates that pressures are monitored at least once daily.	67%
There is evidence that mechanisms exist to report excursions, repair defects, and document actions taken as a result of any out of limit pressure/airflow condition until resolution.	57%
Compounding Facility Management: Cleaning and Disinfecting	**65%**
Cleaning materials that are reused (mop handles, mop heads, etc.) are labeled according to their location of use AND policies and procedures have been developed regarding maintenance of the reusable items so that repeated use does not increase the bioburden of the controlled environments.	32%
Easily cleanable horizontal work surfaces in the buffer (cleanroom), ante or segregated compounding areas are cleaned daily and documented.	53%
Floors in the buffer area, ante area, or segregated compounding area are cleaned daily with the designated cleaning agent after compounding has been completed and this activity is documented.	53%
Personnel who perform cleaning receive training in and successfully pass initial and ongoing competency assessments in both of these areas: 1. Hand hygiene and garbing (which includes gloved fingertip sampling) 2. Cleaning and disinfecting	54%
Sterile 70% IPA is allowed to remain in contact with surfaces to be disinfected for 10-30 seconds before compounding activities are started.	79%
Mops, wipers, and other cleaning equipment are non-shedding and if re-usable, they are dedicated to use in the buffer area, ante-area or segregated compounding area.	68%
Only trained compounding personnel clean inside of the ISO Class 5 work areas.	92%
Supplies, components and other items required for compounding are removed from their outer packaging before entering the buffer area. (asked of the 80 who said they have a buffer room)	94%
The critical areas inside the ISO Class 5 environments are cleaned and disinfected at the beginning of each work shift; between batches; every 30 minutes during continuous compounding; when there are spills and in the event of or suspicion of procedural breach.	63%
Trained personnel use written policies and procedures which detail cleaning agents, non-shedding wipes, mop materials, procedures for cleaning, frequency of cleaning and documentation forms.	76%
Walls, ceilings, emptied shelving and supply bins are cleaned at least monthly with designated cleaning agent and documented.	67%
Compounding Facility Management: Equipment Calibration	**63%**
ACDs used for TPN or dialysis compounding are tested at least monthly for volumetric and gravimetric accuracy.	75%

Equipment associated with compounding or equipment which is used to monitor controlled environments (e.g., ACDs, temperature and humidity monitors, isolators, volumetric air samplers, freezers, refrigerators, etc.) are cleaned, maintained and calibrated in accordance with manufacturer's recommendations.	71%
Personnel who use equipment have received training and demonstrated the ability to use the equipment properly as well as troubleshoot the equipment in the event of malfunction.	79%
Written policies and procedures provide specific detail about the maintenance, calibration and cleaning intervals for all pieces of equipment.	37%
Documentation of cleaning, maintenance, calibration and service is maintained for all equipment and is readily available for review.	63%
Compounding Facility Management: Temperature and Humidity Monitoring	**81%**
The temperature of the incubator/s conform to required temperatures for both Tryptic Soy Agar (TSA) and Malt Extract Agar (MEA) or other suitable fungal media.	80%
Controlled room, controlled cold and controlled frozen environments in the pharmacy and other areas (e.g. where solutions and drugs are stored), are monitored and conform to USP temperature requirements for that storage type.	92%
Is the buffer area comfortable for garbed compounding personnel while working? (asked of those who said they have a buffer room)	100%
There is evidence that mechanisms exist to report excursions, repair defects, protect CSPs and document actions taken as a result of any out of limit temperature/humidity conditions until resolution.	70%
There is evidence that temperatures in all controlled storage areas, incubators and controlled compounding environments are monitored at least once daily and documented (manually or electronically).	73%
CSPs for Immediate Use	**78%**
At your organization are CSPs for Immediate-Use limited to those that do not include more than a simple transfer of 3 or fewer commercially manufactured packages of sterile, non-hazardous products from their manufacturer's original container?	82%
At your organization is compounding of CSPs that is performed outside of an ISO Class 5 environment completed within 1 hour? This question refers to compounding only, not administration.	89%
Does your organization have a written policy on Immediate-Use CSPs?	82%
At your organization, if CSPs compounded outside an ISO Class 5 environment are not used immediately by the person who prepared them, then they are labeled and that labeling includes all of the following elements: - identifier information; - names and amounts of the ingredients; - name or initials of the person who prepared the drug and - the exact 1 hour beyond use date and time.	61%
At your organization are Immediate-Use CSPs prepared in emergent or life-threatening situations only?	71%
At your organization CSPs compounded outside of an ISO Class 5 environment do not involve more than two entries into any single container.	79%

At your organization does policy specify and actual practice demonstrate that Immediate-Use CSPs not used within 1 hour from the time of preparation are discarded (to the best of your knowledge)?	79%
Filter Integrity Test	**7%**
Since your compounding location uses a filter in compounding to sterilize solutions, is it the policy to routinely follow its use with a filter integrity test (bubble point test)?	8%
The specific procedure for performing a filter integrity test is included in the compounding location's written policy and procedures (asked of the 6 who said they did perform bubble point testing).	0%
Final Release Checks	**87%**
After compounding is completed, CSPs are visually examined for the presence of particulate matter against a light and black background and not dispensed if particulates are observed.	58%
Regardless if compounding is performed patient-specific or in non-patient specific batches, all used containers, whether empty or partially full, are retained with the compounding worksheets/batch records and final CSPs for double checking by an authorized individual other than the compounder upon completion.	86%
There is evidence of mechanisms to ensure correct fill volume and quantities for each CSP.	86%
CSPs with observed defects are segregated from CSPs ready for use in a manner that prevents their administration.	100%
Finished CSPs are inspected for container closure integrity (e.g., holes, leakage) and any other potential defect.	94%
If CSPs are not distributed immediately after compounding and are stored in the organization for some period of time, a pre-release check is performed to ascertain container defects/damage, particulates, or other unexpected and undesirable circumstance, are not released and are segregated from other CSPs.	74%
Labels are checked for correct names, amounts and/or concentrations of ingredients, total volume; BUD; route of administration; storage conditions and other appropriate usage information before they are dispensed.	100%
The organization routinely inspects prescription orders, labels, compounding documentation, and expended materials to verify that the correct identity and amounts of ingredients, aseptic mixing and sterilization, packaging, labeling and expected physical appearance are consistent with expectations before they are dispensed.	94%
There is evidence of mechanisms to ensure that the identities, purities and amounts of ingredients are correct by comparing the original written order with the compounding record.	86%
General Facility Design	**71%**
A line of demarcation in the ante-area or segregated compounding area separates the dirty area from the clean area.	42%
Access to the buffer (cleanroom), ante or segregated compounding areas is limited to those who are performing compounding related activities.	76%
All furniture, equipment, and physical plant surfaces in the buffer, ante and segregated compounding areas is nonporous, smooth, free from cracks/crevices, nonshedding, impermeable, and cleanable and resistant to degradation by cleaning agents.	58%
The climate of the buffer (cleanroom) and ante-areas is conducive to operator comfort and compounding efficiency by being well lit with a temperature of 68°F ±2.	94%

The furniture, equipment and supplies in the buffer, ante or segregated compounding area is limited to that which is essential for compounding related activities.	82%
Ceilings are made of panels that are impervious and hydrophobic and are caulked around the perimeter of each to seal them to the frame.	67%
Floors are cleanable (wide sheet vinyl that is heat sealed or other solid surface) and molding is coved.	89%
The cleanroom (buffer area) does not contain a sink, drains or other sources of water.	89%
The sink in the ante-area is equipped with hands-free controls for water and soap dispensing.	50%
Walls are made of solid surface or locking panels provided they are imperious, cleanable and non shedding.	89%
Gloved Fingertip Sampling	**43%**
All compounding staff (and supervising pharmacists) perform ongoing Gloved Fingertip/Thumb Sampling of both hands at least annually at the time of their employee media fill testing.	48%
All compounding staff (and supervising pharmacists) perform ongoing Gloved Fingertip/Thumb Sampling of both hands at least semi-annually at the time of their employee media fill testing.	0%
All compounding personnel (including supervising pharmacists) successfully complete at least 3 gloved fingertip/thumb sampling procedures (success is 0 CFUs) all of which are documented before initially being allowed to compound CSPs.	31%
During the initial gloved fingertip/thumb sampling (that which occurs during and is part of the initial hand hygiene and gowning competency assessment), fingertip/thumb samples are taken of both gloved hands onto media plates immediately after compounders perform hand hygiene and garbing but before their gloves are cleaned with sterile 70% IPA.	54%
Hand Washing and Garbing	**69%**
At your compounding location the order of garbing is generally from dirtiest to cleanest. Dirty activities include donning hair net, beard cover, mask and shoe covers. All of these "dirty" activities occur PRIOR to washing of the fingernails, hands and forearm up to the elbow. Hands are then dried and are then cleansed with an antimicrobial scrub that has persistent activity PRIOR to the donning of sterile gloves.	72%
Personnel entering controlled areas remove personal outer garments, jewelry, piercings above the neck, cosmetics and artificial nails before crossing the line of demarcation on the way to the cleanroom (buffer area).	58%
Personnel repeat all hand washing and garbing activities if they are exposed to worse than ISO Class 8 air.	75%
Hazardous Drug Compounding	**69%**
Employees are not eligible for hazardous drug training or completion of the hazardous drug competency until they have successfully completed the three base competencies: - Hand washing and Garbing, - Cleaning and Disinfecting - Aseptic Technique	71%
The biological safety cabinet (BSC) your organization uses for the preparation of hazardous drugs (HDs) is exhausted either directly (hard ducted) or via canopy connection (thimble).	82%
The hazardous drug compounding buffer area has been certified to have at least 30 air changes per hour (ACPH) from the HEPA filtered air supplied to the room.	64%

The organization does NOT prepare hazardous CSPs in a laminar airflow workbench (e.g., LAFW) or other type of positive-pressure primary engineering control (PEC).	97%
The organization employs two tiers of containment (e.g., closed system transfer device (CSTD)) within a BSC or CACI.	100%
The compounding location prepares hazardous CSPs in a BSC that is located inside of an ISO Class 7 area that is physically separate from other areas and has not less than 0.01 inches water column negative pressure to adjacent positive pressure ISO Class 7 ante-area.	61%
Personnel who handle hazardous CSPs are fully trained in all of the following: - safe aseptic manipulation; - negative pressure techniques inside of BSC/CACI; - correct use of CSTDs; containment, cleanup and disposal procedures for spills; - treatment of exposed personnel; - storage, handling and disposal of HD as well as mutagenic, teratogenic and carcinogenic properties of existing and new CSPs prior to preparing or handling HDs.	77%
Employees who handle, dispose or compound hazardous CSPs successfully complete a Hazardous CSPs Competency Assessment (example below) prior to working with hazardous CSPs and annually thereafter.	42%
For each compounding employee, there is written documentation of training and successful completion of testing on hazardous drug preparation initially (prior to hazardous drug compounding) and annually thereafter.	55%
Hazardous CSPs and hazardous drug wastes are disposed of in a manner that complies with local, state and federal regulations.	100%
Personnel who compound hazardous CSPs use chemotherapy rated protective gowns, shoe covers (or dedicated shoes) and double gloving with sterile gloves in addition to standard garbing items and procedure.	68%
The organization stores hazardous CSPs in a negative pressure room such as the hazardous drug compounding room.	50%
The organization stores hazardous CSPs separately from other inventory in a manner that prevents contamination and personnel exposure.	87%
The storage area for hazardous CSPs has exhaust ventilation of at least 12 ACPH to dilute and remove potential airborne contaminants.	56%
There is written confirmation (example below) by each compounding employee of reproductive age (male or female) that they understand the risk of handling hazardous CSPs.	35%
Initial and Ongoing Training and Competency Measurement	**62%**
All staff who perform cleaning (whether compounding personnel or housekeeping support personnel) are trained in cleaning and disinfecting as well as hand hygiene and garbing and their competency is verified initially on an ongoing basis in keeping with written policies and procedures.	56%
Compounding personnel (and supervising pharmacists) who fail written exams or media-fill tests are immediately reinstructed and reevaluated by expert compounding personnel to ensure correction of aseptic processes as well as demonstrate the ability to pass repeated written and/or media-fill tests.	72%

There is evidence of a written description of the specific training and a performance evaluation program required for individuals involved in compounding sterile preparations. This is required for anyone who is performing sterile compounding (pharmacists, technicians, nurses, physicians, etc.) according to the activities they perform.	54%
All compounding staff (and supervising pharmacists) are required to pass specific didactic coursework; practical skill assessments through competency evaluation; and media-fill testing which is documented before being allowed to compound sterile preparations.	72%
At a minimum, written competency evaluations on Hand Hygiene and Garbing (including gloved fingertip/thumb sampling); Cleaning and Disinfecting, and Aseptic Technique as well as personnel media-fill testing are successfully completed by all compounding staff (and supervising pharmacists) initially and **semi-annually** thereafter.	33%
At a minimum, written competency evaluations on Hand Hygiene and Garbing (including gloved fingertip/thumb sampling); Cleaning and Disinfecting, and Aseptic Technique as well as personnel media-fill testing are successfully completed by all compounding staff (and supervising pharmacists) initially and **annually** thereafter.	61%
Inventory Storage and Handling/Delivery of CSPs	**93%**
Originally assigned BUD dates are not changed and CSPs are not redispensed unless changes are supported by the originally assigned BUD and there is absolute certainty that proper storage conditions have been maintained during the time they were outside of the pharmacy.	94%
Storage of finished CSPs and drug components is separate from food storage and from any specimen storage (if occurs onsite).	100%
The methods used to transport CSPs to the patient prevent damage and maintain appropriate temperatures during transit.	97%
There is evidence of a systematic process to evaluate when unopened, returned CSPs are safe to redispense.	76%
There is evidence that packaging maintains physical integrity, sterility, stability and purity of CSPs.	94%
Low Risk Level CSPs with 12 Hour or Less BUD	**56%**
Are the ISO Class 5 compounding environments outside of the ISO Class 7/8 buffer areas areas cleaned according to the requirements of USP <797>?	78%
Are the ISO Class 5 environments that are used for compounding outside of ISO Class 7/8 buffer areas placed inside of a segregated compounding area as defined by USP<797>?	67%
Is viable and non viable environmental sampling performed in ISO Class 5 compounding environments located outside of ISO Class 7/8 buffer areas? Viable sampling is testing for microbial contamination where air is drawn through a device and sampled on a plate then incubated to test for growth in the form of colony forming units. Non viable testing is when air is drawn through a device and the number of particles (dust, etc.) is measured.	78%

Are the CSPs prepared in ISO Class 5 environments that are located outside ISO Class 7/8 buffer areas limited to non-hazardous CSPs? For example, if you have a BSC in a segregated compounding area in an oncology clinic, you would answer "no" because compounding in an ISO Class 5 environment is NOT limited to non-hazardous CSPs.	22%
Do personnel who compound in ISO Class 5 environments located outside of an ISO Class 7/8 buffer area perform hand hygiene **and** garbing?	33%
Personnel Media-Fill Challenge Testing	**69%**
Media fill units are incubated at room temperature (20-25 degrees Celsius) or 30-35 degrees Celsius for a minimum of 14 days and results are documented at the conclusion of the incubation.	75%
There is a written procedure that details the steps of the personnel media fill procedure at your compounding location.	64%
There is evidence, in the form of employee-specific documentation, that media fill units have been successfully completed initially (before compounding CSPs) and at least **annually** thereafter.	64%
Compounding personnel are said to have successfully passed their media fill qualification only if all media fill units are free from turbidity (cloudiness) after all 14 days of incubation at the appropriate temperature.	78%
There is evidence in the form of employee-specific documentation that media fill units have been successfully completed initially (before compounding CSPs) and at least **semi-annually** thereafter.	0%
Using appropriate growth promotion media, all compounding personnel (including pharmacists who supervise compounding) perform a media-fill test procedure that represents the most challenging or stressful conditions that personnel actually face when they prepare (and sterilize if high risk) CSPs.	69%
Primary/Secondary Engineering Controls	**81%**
Once primary engineering controls are placed in their desired location, smoke studies have been conducted to verify unidirectional airflow and sweeping action over and away from the critical compounding area.	61%
Pressure gauges are installed between the nonhazardous buffer area and the ante-area and again between the ante-area and the general organization area which indicate a minimum differential positive pressure of 0.02 inches water column.	75%
The ante-area is supplied with HEPA filtered air and has been certified to meet at least ISO Class 8 air standards. If the ante-area is adjacent to a negative pressure ISO Class 7 buffer area, then it is supplied with HEPA filtered air and has been certified to meet at least ISO Class 7 air standards.	90%
The buffer area (cleanroom) is supplied with HEPA filtered air and has been certified to meet at least ISO Class 7 air standards for all compounding other than radiopharmaceutical preparation. The buffer area meets at least ISO Class 8 air standards when preparing radiopharmaceuticals.	100%
The nonhazardous drug compounding buffer area has been certified to have at least 30 air changes per hour (ACPH) and at least 15 of the 30 ACPH come from the HEPA filtered air supplied to the room.	83%
You have indicated that your compounding location's isolators are not placed inside ISO Class 7 buffer areas and they do not meet the exclusion criteria outline in Chapter <797>, so is the compounding that occurs within those isolators limited to nonhazardous and radiopharmaceutical CSPs that are given a 12 hour or less BUD?	0%

State of Wisconsin
2015 Aggregated Findings
USP <797> Compliance Survey

Are your Primary Engineering Controls certified according to the guidelines of the Controlled Environment Testing Association (CETA) guidelines (CAG-003-2006) or similar guidelines? A Primary Engineering Control (PEC) is a device or room that provides an ISO Class 5 environment for the exposure of critical sites during compounding CSPs. Such devices include but may not be limited to LAFWs, BSCs, CAIs and CACIs.	82%
Has your certifier verified that an airflow velocity of at least 40 feet per minute is maintained across the line of demarcation?	67%
Quality Management: Environmental Sampling Program	**75%**
The Environmental Sampling Plan includes all of the following: - sample locations, - method of collection, - frequency of sampling, - volume of air sampled (for viable air sampling), - time of day in relation to compounding and - action levels.	62%
The program ensures that viable air sampling occurs: - at the time of the initial certification of new facilities/equipment; - subsequent to servicing of the compounding facility or equipment; - as part of every 6 month facility/equipment testing and recertification; and - in response to problems with end products, staff technique, CSPs, patient related infections or other undesirable trend.	86%
There is an Environmental Sampling Program which is part of the overall quality management program that provides information about the effectiveness of primary and secondary engineering controls (physical plant) and personnel work practices in maintaining a compounding area with sufficiently low viable and non-viable particles.	78%
There is a current written Environmental Sampling Plan which documents where viable air sampling and surface sampling occurs within the controlled environments.	73%
Quality Management: General	**53%**
Adverse events and defects related to CSPs are reported through the FDA's MedWatch and/or Quantros programs.	69%
There is evidence of a consistent process which occurs any time a desired patient outcome is not achieved; an Action Limit is exceeded; or other operational variance is noted and appropriate follow up occurs to ascertain the effectiveness of actions taken to eliminate the problem.	44%
There is evidence of a formal, written Quality Assurance/Performance Improvement Plan that considers all aspects of sterile compounding including but not limited to environmental sampling and testing.	42%
Does the compounding location have written policies and procedures and corresponding documentation forms that address all of the aspects of sterile compounding?	69%
The Quality Assurance/Performance Improvement Program includes specific monitoring and evaluation activities; details on how results are reported; and delineation of the persons responsible.	31%

There are procedures in place which are followed to prevent personnel with rashes, sunburn, open sores, conjunctivitis and active respiratory infections from preparing CSPs.	64%
Quality Management: General Viable Air and Surface Sampling Considerations	**64%**
CFU Action Levels are established for viable air and surface sampling for each ISO Class initially based on data provided in USP Chapter<797> and refined over time based on CFU trends at each sampling location (may be refined down but not to exceed the limits in USP<797>).	69%
Results of viable air and surface sampling are reported by counting the number of discrete colonies forming units (CFUs) per plate.	78%
There is detailed written policy and procedure on all aspects of surface sampling and viable air sampling which includes preparation of plates, labeling of plates according to the Environmental Sampling Plan, reading plates; documentation of results as well as procedure for sending them to contracted lab (in the event that is applicable).	46%
There is evidence of a logical plan of actions to be taken in the event that results of viable air or surface sampling exceed established Action Levels which includes: - examination of samples by an accredited laboratory, - speciation of growth results, - re-evaluation of the adequacy of personnel work practices, cleaning procedures, operational procedures, as well as air filtration efficiency until resolution of the problem is found.	59%
Viable air sampling and surface sampling occur in each of the ISO Class areas as well as Segregated Compounding Areas and are sampled in the order from the cleanest to dirtiest areas (ISO Class 5, then 7 and then, if applicable, 8).	70%
Quality Management: Incubation	**68%**
Plates of Tryptic soy agar medium with polysorbate and lecithin (TSApl) are incubated @ 30-35°C for 48-72 hours, but Malt Extract Agar (MEA) plates are incubated @ 26-30°C for 5-7 days. Regardless of the type of plate, the plates are inverted for incubation (upside down). This question applies even if you do not incubate your own samples since you must verify your vendor meets these requirements.	68%
Quality Management: Non-Viable Particle Testing	**97%**
Certification of primary (LAFW, CAI, BSC, CACI) and secondary (buffer and ante areas) engineering controls which includes particle testing is performed every 6 months; whenever a primary engineering control is moved or subsequent to room repair or major service.	100%
Particle testing is performed in all ISO classified areas including: - ISO Class 5 primary engineering controls such as LAFWs, BSCs, CAIs, and CACIs; - ISO Class 7 buffer areas and - ISO Class 7/8 ante-areas.	95%
Particle testing is performed by qualified operators using certified equipment (which can be verified by selecting vendors who provide evidence of operator training and competency assessment as well as equipment calibration and certification procedures).	97%
Quality Management: Patient/Caregiver Training	**N/A**
Quality Management: Surface Sampling - A personnel metric	**59%**

A plate (size 24-30 cm2) containing tryptic soy agar medium with polysorbate and lecithin added to neutralize cleaning agents (TSApl) is used to collect and incubate each surface sample regardless of whether the method of sampling is by plate or swab.	62%
After the surface samples have been collected, the sample area is cleaned with an appropriate disinfectant.	73%
Surface sampling is performed at the conclusion of compounding (before the area is disinfected with an appropriate disinfectant).	41%
Surface sampling is performed using the contact plate and/or swab method.	73%
Surface sampling occurs regularly and the frequency, location and action levels of surface sampling are detailed within the Environmental Sampling Plan and written policies and procedures.	46%
Quality Management: Viable Air Sampling - A facility metric	**79%**
The volume of the air sample at each sampling location is 400-1000 liters.	69%
There is evidence that in the event an action level has been exceeded, the area is recleaned after investigation and resampled.	78%
Viable air sampling is collected using a volumetric air sampling device.	76%
Viable air sampling is performed at least semi-annually as part of the semi-annual physical plant recertification.	97%
Viable air sampling is performed using a general growth medium such as Soybean-Casein Digest Medium.	73%
Viable air sampling is performed using two different types of media: one is a general growth medium and the other is a media that specifically supports the growth of fungus, such as malt extract agar.	100%
Radiopharmaceuticals as CSPs	**0%**
Are garb and materials exposed in patient care and treatment areas cleaned and disinfected prior to re-entry to the segregated compounding area?	0%
Are technectium-99m/molybdenum-99 generator systems stored and eluted in an ISO Class 8 or cleaner air environment?	0%
Are these radiopharmaceuticals prepared in a segregated compounding area (a room or space whose use is restricted to the preparation of low risk level CSPs with 12 hour or less BUD that contains a device that provides unidirectional flow of ISO Class 5 air)?	0%
Are the radiopharmaceuticals compounded from closed sterile containers with volumes of 100 mL for single dose injections or not > 30 mL taken from a multidose container compounded in a properly functioning and certified primary engineering control located in ISO class 8 or cleaner air? A primary engineering control is a device or room that provides an ISO Class 5 environment for the exposure of critical sites when compounding. Examples are LAFWs, BSCs, CAIs and CACIs.	0%
Does inspection of radiopharmaceutical CSPs containing high doses of radioactivity occur but in accordance with that which is as low as reasonably possible (ALARA)?	0%
Does storage and transport of properly shielded vials of radiopharmaceutical CSPs occur only in a limited access ambient environment?	0%

Does the organization compound radiopharmaceuticals from sterile components in closed sterile containers with a volume of 100 mL for single dose injection or not > 30 mL taken from a multiple dose container?	0%
Does your organization prepare radiopharmaceuticals as low-risk level CSPs with 12 hour or less beyond use date?	0%
In the event that compounding activities required manipulation of patient or donor biological materials (e.g., blood), these compounding activities would occur with separate handling and procedures and those procedures are specifically outlined in written policies and procedures.	0%
Single and Multiple-Dose Vials	**92%**
At your organization are multiple dose vials discarded 28 days after initial puncture (or as directed by the manufacturer)?	100%
At your organization are single dose vials that have been punctured inside of air that is ISO Class 5 or better discarded after 6 hours?	87%
At your organization are single dose vials that have been punctured outside of ISO Class 5 air discarded if not used within 1 hour?	89%
Steam Sterilization	**N/A**
Sterility Testing	**42%**
Does the compounding location have a written procedure for immediate recall of the dispensed CSPs in the event of any evidence of microbial growth in the test specimens?	50%
Does the compounding location have a written procedure requiring **daily** observation of the incubating sterility test specimens and a procedure for immediate recall of the dispensed CSPs in the event of any evidence of microbial growth in the test specimens?	0%
Sterility testing is performed by membrane filtration or direct inoculation and in accordance with USP Chapter <71>.	33%
This compounding location conducts sterility testing (or has outsourced the testing to a contract lab).	50%
Does the compounding location have a policy that specifies actions to be taken in the event of a positive sterility test which may include a rapid and systematic investigation of aseptic technique as well as environmental control and other sterility assurance controls to identify potential sources of contamination and correct problems in processes or methods?	33%
Does the compounding location have a written procedure requiring notification of the physician and patient to whom a potentially contaminated CSP was administered?	0%
Even when sterility testing is performed, there is evidence that BUD dating never exceeds the maximum chemical stability of the drug/s in solution based on valid references.	100%
There are detailed policies, procedures, forms or electronic methods of documentation about all aspects of sterility testing.	33%
Sterilization by Dry Heat	**N/A**
Sterilization by Filtration	**56%**
Filters are subject to a filter integrity test (such as bubble point) at the conclusion of the compounding procedure.	33%
The compounding location performs sterilization by filtration using sterilizing grade, pyrogen free, 0.2 micron filters and the process is completed rapidly without replacement of the filter.	100%
The specific procedure for sterilization by filtration is included in the compounding location's policy and procedure.	33%

State of Wisconsin
2015 Aggregated Findings
USP <797> Compliance Survey

Sterilization Methods	**100%**
Since the compounding location performs high risk level compounding, please indicate of the following methods of sterilization are used (check all that apply).	100%
Grand Total	**72%**