

DRAFT

NOTE TO STAKEHOLDERS:

- **The provisions in 247 CMR 17.00 will apply to resident and non-resident sterile compounding pharmacies.**
- **Specific regulatory provisions pertaining to hazardous drugs and radiopharmaceuticals have not yet been proposed, but will be the subject of future meetings.**

- 17.01: Authority and Purpose
- 17.02: Sterile Compounding Licensure
- 17.03: Commercially Available Single and Multiple Dose Vials and Containers
- 17.04: Immediate-Use CSPs
- 17.05: Low Risk Level 12 Hour BUD CSPs
- 17.06: High Risk Level CSPs
- 17.07: Implantable Infusion Pumps
- 17.08: CSPs as Stock Solutions
- 17.09: CSPs made with Blood-Derived or Biological Material
- 17.10: Allergen Extracts as CSPs
- 17.11: Sterile Compounding for Veterinary Patients
- 17.12: Sterile Compounding Facility; General
- 17.13: Sterile Compounding Facility; HVAC Systems
- 17.14: Sterile Compounding Facility; HEPA Filters
- 17.15: Sterile Compounding Facility; Airflows and Pressure Differential Monitoring
- 17.16: Sterile Compounding Facility; ISO Classified Areas
- 17.17: Sterile Compounding Facility; ISO Class 5 Primary Engineering Controls
- 17.18: Sterile Compounding Facility; Secondary Engineering Controls; Buffer Rooms; Ante Rooms; **Dedicated Compounding Rooms**; and Other Classified Areas
- 17.19: Sterile Compounding Facility; Compounding Aseptic Isolators (“CAI”)
- 17.20: Sterile Compounding Facility; Laminar Air Flow Workbench (“LAFW”)
- 17.21: Sterile Compounding Facility; Temperature and Humidity Monitoring
- 17.22: Sterile Compounding Facility; Certification of Classified Areas
- 17.23: Sterile Compounding Facility; Smoke Studies
- 17.24: Environmental Monitoring
- 17.25: Environmental Monitoring; Non-Viable and Viable Air Sampling
- 17.26: Environmental Monitoring; Surface Sampling
- 17.27: Environmental Monitoring; Action Levels
- 17.28: Environmental Monitoring; Remediation of Above Action Level Environmental Monitoring Results
- 17.29: Cleaning and Disinfecting
- 17.30: Sterile Compounding Process; Handwashing and Garbing

DRAFT

- 17.31: Sterile Compounding Process; Aseptic Technique
- 17.32: Sterile Compounding Process; Miscellaneous
- 17.33: Sterile Compounding Personnel Training; General
- 17.34: Sterile Compounding Personnel Training; Gloved Fingertip/Thumb Sampling
- 17.35: Sterile Compounding Personnel Training; Media Fill Challenge Testing
- 17.36: Sterile Compounding Equipment
- 17.37: Sterile Compounding Robotics
- 17.38: Sterile Compounding Ingredient and Component Selection
- 17.39: Sterilization and Depyrogenation
- 17.40: Sterility and Endotoxin Testing
- 17.41: Storage and Beyond-Use-Dating (“BUD”)
- 17.42: Packaging and Preparation Containers
- 17.43: Master Formulation Records
- 17.44: Compounding Record
- 17.45: Verification of Compounding Accuracy; Release Checks
- 17.46: Labeling
- 17.47: Inventory Storage and Handling; Delivery of CSPs
- 17.48: Drug Utilization Review and Patient Counseling
- 17.49: Quality Assurance (“QA”) Program
- 17.50: Sterile Compounding Policies and Procedures
- 17.51: Defective Products

17.01 Authority and Purpose

247 CMR 17.00 applies to pharmacies that hold a sterile compounding pharmacy license, non-resident sterile compounding pharmacy license, or institutional sterile compounding pharmacy license.

17.02 Sterile Compounding Licensure

(1) A pharmacy licensed by the Board shall comply with 21 U.S.C. § 353a, M.G.L. c. 94C, §§ 17 & 22, and M.G.L. c. 112, § 39F. A pharmacy may not dispense a CSP prior to receipt of a patient-specific prescription.

(2) A pharmacy licensed by the Board may not simultaneously hold an outsourcing facility registration issued by the federal Food and Drug Administration (“FDA”) pursuant to 21 U.S.C. § 353b. Massachusetts.

Comment [1]: For BOARD Discuss 11.24: physical address requirements

DRAFT

(3) The Board or its designee(s) may visit each pharmacy licensed by the Board under M.G.L. c. 112, §§ 39G, 39I, or 39J at any time without prior notice and inspect the sterile compounding pharmacy staff, activities, and records to determine compliance with 247 CMR 2.00 *et seq.* and inspectional criteria described in the Board’s Sterile Compounding Audit Tools.

17.03 Commercially Available Single and Multiple Dose Vials and Containers

(1) A licensee shall discard a **commercially available** single dose vial punctured within ISO Class 5 air within 6 hours after puncture.

Comment [2]: Prior Board Discussion: Fensky
Added commercially available to add clarity

(2) A pharmacy may not pool or prepare stock solutions utilizing single dose vials to extend a BUD beyond 6 hours after puncture within ISO Class 5.

(3) A licensee shall discard a **commercially available** multiple dose vial within 28 days after initial puncture or as directed by the manufacturer, whichever period is shorter.

Comment [3]: Prior Board Discussion: Fensky
Added commercially available to add clarity

17.04 Immediate-Use CSPs

A pharmacy may prepare a CSP outside of a classified area only if the CSP is intended for immediate use in an emergent or urgent situations in accordance with USP <797>.

17.05 Low Risk Level 12 hour BUD CSPs

A licensee shall prepare a non-hazardous, non-radiopharmaceutical, low risk level CSP with a 12 hour BUD at room temperature or 24 hour BUD refrigerated in an ISO Class 7 buffer room or an ISO Class 8 dedicated compounding room (“DCR”) equipped with a commercially manufactured PEC such as a LAFW or BSC and shall comply with all other provisions of 247 CMR 17.00, unless otherwise provided.

17.06 High Risk Level CSPs

(1) A pharmacy may not engage in high risk level sterile compounding until and unless:

(a) it submits an attestation of intent to engage in high risk level sterile compounding that is signed by the manager of record, pharmacist in charge of sterile compounding, and licensee, as applicable; and

(b) it receives notification from the Board that it achieved a satisfactory Board inspection specifically pertaining to high risk level sterile compounding. All costs

DRAFT

associated with inspections of non-resident sterile compounding pharmacies shall be paid by the non-resident pharmacy or applicant.

Comment [HAE4]: New

- (2) A pharmacy may not prepare high risk level CSPs in suspension, emulsion, pellet, or depot form.
- (3) A pharmacy may not prepare high risk level CSPs with components that are sterilized by different sterilization methods.
- (4) A pharmacy shall verify the antimicrobial effectiveness of each high risk level CSP prepared in a multiple-dose vial or container.
- (5) A pharmacy shall only utilize FDA-approved commercially available lyophilized ingredients to prepare CSPs.
- (6) A pharmacy may not utilize lyophilization equipment to prepare lyophilized drug substances or ingredients used in CSPs or final patient CSPs.
- (7) A pharmacy may not compound a component of a CSP from API when a version of that component is commercially available.
- (8) Pre-sterilization procedures for high risk level CSPs, such as weighing and mixing, shall be completed in an ISO Class 8 or cleaner environment.
- (9) A pharmacy shall sterilize the final preparation of a high risk level CSP.
- (10) A pharmacy may not dispense a high risk level CSP without preservatives unless the CSP is dispensed in a single use container and labeled as “single use only.”

Comment [B5]: Prior Board Meeting: Fensky

Comment [6]: Stakeholder Feedback

17.07 Implantable Infusion Pumps

- (1) A BUD must include the time a drug will reside inside an implantable infusion pump reservoir.
- (2) In addition to standard prescription labeling requirements, a pharmacy shall include the date of compounding on the label for CSPs prepared for administration by an implantable pump administration.

17.08 CSPs as Stock Solutions

DRAFT

- (1) A pharmacy that prepares low or medium risk level intermediate or stock solutions shall maintain a master formulation record for, and assign a BUD in accordance with 247 CMR 17.XX, to each intermediate or stock solution.
- (2) A pharmacy that prepares high risk level intermediate or stock solutions shall perform sterilization procedures immediately upon compounding the intermediate or stock solution and may not store non-sterilized solutions for future sterilization.

17.09 CSPs made with Blood-Derived or Biological Material

- (1) A pharmacy shall maintain a policy and procedure pertaining to compounding that involves blood-derived or other biological material.
- (2) The procedures for compounding CSPs using blood-derived or other biological material shall require compounding to be separate from routine material-handling procedures and must define cleaning of PEC and other equipment used in CSP preparation in order to avoid cross-contamination.
- (3) After compounding CSPs with blood-derived or other biological material, compounding personnel shall:
 - (a) thoroughly clean the PEC, equipment, and materials according to the pharmacy's daily cleaning protocol;
 - (b) repeat all hand washing and garbing activities; and
 - (c) change garbing.
- (4) A pharmacy shall immediately respond to and remediate any broken, damaged, or spilled container involving blood-derived or other biological material.
- (5) A pharmacy shall maintain a policy and procedure for the immediate and systematic response (i.e. spill kit) to broken, damaged, or spilled container involving blood-derived or other biological material.

17.10: Allergen Extracts as CSPs

- (1) A pharmacy shall prepare allergen extracts in accordance with 247 CMR 17.00.
- (2) A pharmacy shall prepare allergen extracts in an ISO 5 Classified Area located within an ISO 7 buffer room or ISO 8 DCR.

DRAFT

(3) In addition to general aseptic technique training, compounding personnel preparing allergen extract CSPs shall be trained by an accredited program, such as Joint Council of Allergy, Asthma and Immunology (JCAAI). A pharmacy shall maintain documentation of the training and competency for all personnel compounding CSPs with allergen extracts.

(4) A pharmacy shall maintain policy and procedures for proper preparation and assignment of BUD and storage of CSPs with allergen extracts.

17.11: Sterile Compounding for Veterinary Patients

(1) The preparation of CSPs for veterinary patients shall meet the same standards that apply to CSPs for human patients and shall comply with all laws and regulations governing the practice of pharmacy.

(2) A pharmacist may not compound CSPs for veterinary patients unless he/she has undergone training and demonstrates competency in veterinary sterile compounding.

(3) A licensee shall separate drugs, ingredients, and components intended for animal use only from drugs, ingredients, and components intended for human use. A licensee shall handle and clean compounding supplies and equipment in a manner that prevents cross contamination of animal use only and human drugs, ingredients, and components.

17.12: Sterile Compounding Facility; General

(1) A Licensee may not conduct sterile compounding in a segregated compounding area that is not ISO classified.

(2) Each ISO Classified area built after January 1, 2016, shall allow for visual observation of the classified space from outside the classified space.

17.13: Sterile Compounding Facility; HVAC Systems

(1) A pharmacy shall have a dedicated air handling unit (“AHU”) for HVAC systems that supplies HEPA-filtered air to each ISO classified areas, **except an ISO Class 8 DCR.**

(2) A pharmacy shall maintain a detailed HVAC design plan that includes air flow diagrams.

(3) A pharmacy shall utilize a closed loop ducted system, a sealed plenum system, **or other similar contamination control system approved by the Executive Director or his/her designee** for HVAC systems supplying HEPA-filtered air to ISO-classified spaces.

DRAFT

- (4) Conditioned supply air provided to classified area(s) shall be provided exclusively through ceiling HEPA filters.
- (5) A pharmacy shall ensure all pre-filters and HVAC components are maintained in accordance with manufacturer specifications.
- (6) A pharmacy shall conduct engineering control performance verification in accordance with USP <797> in the event of a planned or unplanned interruption of HVAC operations.
- (7) A pharmacy shall operate and monitor the HVAC systems that supply conditioned air to the non-classified areas of the pharmacy 24 hours per day, seven days per week.
- (8) A pharmacy shall operate and monitor the HVAC systems that supply HEPA filtered air to ISO classified areas 24 hours per day, seven days per week.
- (9) A pharmacy shall immediately assess the impact on the classified environment for any HVAC failure and implement a CAPA.
- (10) Each secondary engineering control shall have ducted air returns mounted low on the wall in order to create a general top-down dilution of room air with HEPA-filtered make-up air.
- (11) Relief air vents shall be mounted low on the wall and designed to prevent the ingress of less clean air or contaminants from adjacent ISO classified space or ambient air.

Comment [7]: Prior Board: Gannon
Add monitoring

17.14: Sterile Compounding Facility; HEPA Filters

- (1) A pharmacy shall utilize HEPA filters that have been tested to achieve a minimum of 99.97% efficiency rating using 0.3 µm micron particle size.
- (2) Each HEPA filter shall be leak tested using the most penetrating particle size according to the most current CETA guidelines at the factory and then leak tested again in situ after installation as part of initial certification and recertification (every 6 months) and any time a HEPA filter is repaired / replaced.
- (3) A pharmacy shall immediately remediate a failed HEPA filter by properly repairing or replacing the HEPA filter, recertifying the affected ISO classified area, and performing environmental monitoring (air and surface, bacterial and fungal) in all classified areas according to the full environmental monitoring sampling map.
- (4) A pharmacy shall ensure nothing comes in contact with the HEPA filters, including cleaning and sanitizing agents, aspirate from syringes or compounding equipment, or glass from ampules.
- (5) A pharmacy shall inspect PEC filters at least daily.

DRAFT

17.15: Sterile Compounding Facility; Airflows and Pressure Differential Monitoring

- (1) *Non-hazardous CSPs*: There shall be a minimum differential positive pressure of 0.02 inches water column (~~range of 0.02 to 0.05~~) between:
 - (a) the buffer room and ante room;
 - (b) the ante room and unclassified space; and
 - (c) ISO Class 8 area and unclassified space.
- (2) ISO Class 5 Primary Engineering Controls (PEC) shall include a pressure differential gauge and/or a low flow device displaying the positive pressure differential between the upstream and downstream air flow. The pressure shall be logged daily prior to compounding. Should the PEC display a loss of pressure exceeding 0.01" water column (gauge) compounding in the PEC shall be suspended until remediated.
- (3) A pharmacy shall measure the differential pressure between each ISO-classified area with a gauge and shall document the differential pressure at each location 24 hours per day, seven days per week, by a continuous recording device.
- (4) Beginning January 1, 2017, a pharmacy shall mount all pressure differential gauges for secondary engineering controls in the non-classified area adjacent to the classified areas.
- (5) A pharmacy shall review differential pressure logs and continuous monitoring device reports daily and shall document the review.

17.16: Sterile Compounding Facility; ISO Classified Areas

- (1) An ISO Class 7 buffer room and ante room shall maintain a minimum of 30 air changes per hour.
- (2) An ISO Class 8 room shall maintain a minimum of 20 air changes per hour.
- (3) The air changes shall come from the HEPA filtered air. HEPA filtered air shall be introduced at the ceiling. Any air exchanges supplied to buffer room from the PEC must be in addition to the 30 ACPH.
- (4) A pharmacy may not utilize any ISO classified area for both sterile and non-sterile compounding.
- (5) A pharmacy shall limit access to all ISO Classified areas to authorized individuals only.

DRAFT

- (6) The doors to DCRs, ante rooms, and buffer rooms shall be:
- (a) constructed of a nonporous, smooth, non-shedding, impermeable material such as acrylic, polycarbonate or similar fiberglass-reinforced plastic, glass, or stainless steel;
 - (b) free from cracks and crevices; and
 - (c) cleanable and resistant to degradation by cleaning agents.
- (7) Beginning July 1, 2017, the ~~The~~ doors to ante rooms and buffer rooms shall be constructed with an interlocking design to prevent the ante room door and buffer room door from opening at the same time.
- (8) A DCR, buffer room, ante room, and other ISO Classified areas shall be well lit.
- (9) Beginning January 1, 2017, a pass-through shall:
- (a) be constructed of a nonporous, smooth, non-shedding, impermeable material such as acrylic, polycarbonate or similar fiberglass-reinforced plastic, glass, or stainless steel;
 - (b) have a double interlocking door design;
 - (c) **not have an opening larger than 4 square feet;**
 - (d) be located between:
 - 1. ISO Class 7 buffer room and ISO Class 8 **area** or better;
 - 2. ISO Class 8 **area** to unclassified space or better; or
 - 3. ISO Class 7 ante room to unclassified space or better;
 - (e) **not be through a refrigerator unit.**
- (10) A licensee shall operate each ISO Class 5 PEC 24 hours per day, 7 days per week.
- (11) If there is an interruption in the operation of the ISO Class 5 PEC, a licensee may not resume compounding until the PEC operates for at least 30 minutes, in accordance with manufacturer specifications, or in accordance with the PEC's validated recovery time.
- (12) A pharmacy shall validate **at least once per year** with direct testing the recovery time of each primary and secondary engineering controls for particle count, temperature, and humidity following activities including personnel entering and exiting, gowning, staging, material transfer, compounding, labeling, cleaning, and testing.
- (13) A pharmacy shall limit furniture, equipment, supplies, and activities in a DCR, ante room, and buffer room to those essential for sterile compounding related activities.
- (14) A pharmacy may not locate a refrigerator, dishwasher, **incubator**, or other appliance in an ISO Classified area.

Comment [8]: Stakeholder Feedback

DRAFT

(15) All equipment in a DCR, ante room, and buffer room shall be nonporous, non-shedding, impermeable, cleanable, and resistant to degradation by cleaning agents.

Comment [9]: Stakeholder Feedback: removed "smooth, free from cracks and crevices"

(16) All counter tops, work surfaces, ~~and~~ racks, ~~and~~ shall be constructed of all stainless steel.

Comment [HAE10]: Removed "carts"

(17) A pharmacy may only utilize stainless steel or non-porous molded plastic carts that are cleanable and resistant to degradation by cleaning agents in ISO classified areas.

Comment [B11]: Stakeholder Feedback

(18) An ISO classified area constructed or renovated after January 1, 2017 may not contain dust-collecting overhangs or ledges.

Comment [12]: Stakeholder Feedback

(19) A pharmacy shall utilize cleanroom grade lights in all classified areas.

(20) The exterior surface of ceiling lighting fixtures shall be smooth, mounted flush with the ceiling surface, and sealed.

(21) Ceiling surfaces in ISO classified areas shall be impervious and hydrophobic.

(22) Ceilings panels, fixtures, and other penetrations through the ceiling (e.g. sprinkler heads) shall be smooth, mounted flush with ceiling tiles, and sealed around the perimeter.

(23) Beginning January 1, 2017, sprinkler heads in all ISO classified areas shall be specifically designed for clean rooms and installed in such a manner to withstand weight-bearing loads on the ceiling.

(24) Walls shall be made of solid surface, locking sealed panels, or epoxy-coated gypsum board and impervious, cleanable, and non-shedding.

(25) Floors shall be cleanable and composed of wide sheet vinyl that is heat sealed at seams or other solid, smooth surface. Floors shall be coved at the wall or appropriately sealed.

Comment [13]: Stakeholder Feedback

17.17: Sterile Compounding Facility; ISO Class 5 Primary Engineering Controls

(1) A pharmacy shall locate an ISO Class 5 PEC for non-hazardous drug compounding within a positive pressure ISO Class 7 buffer room or ISO Class 8 DCR.

(2) A pharmacy may only use compounding equipment in a PEC with vertical laminar airflow.

(3) The supporting base of a PEC shall be constructed of stainless steel or other non-shedding, coated metal.

Comment [14]: Stakeholder feedback

DRAFT

(4) Unless the pharmacy ~~is a nuclear pharmacy or~~ is utilizing a DCR with a CAI or LAFW in accordance with 247 CMR 17.00, a pharmacy shall prepare CSPs in an ISO Class 5 environment within an ISO Class 7 buffer room that is adjacent to an ISO Class 7 or 8 ante room.

(5) A pharmacy shall prepare CSPs in a commercially manufactured ISO Class 5 PEC. A pharmacy may not prepare CSPs in a vertically integrated ISO Class 5 workbench or ISO Class 5 open buffer room design.

Comment [15]: For Board Discussion 11/24

(6) A pharmacy may not locate computer screens, keyboards, computer mouse, or printer within an ISO Class 5 area.

(7) An ISO Class 5 PEC shall provide HEPA filtered unidirectional air over the direct compounding area.

17.18: Sterile Compounding Facility; Secondary Engineering Controls; Buffer Rooms; Ante Rooms; Dedicated Compounding Room; and Other Classified Areas

(1) Buffer Room

- (a) A buffer room shall be at least 144 square feet.
- (b) A buffer room may not contain a sink, drain, or any other source of water.
- (c) Buffer room doors shall be hands-free.
- (d) A buffer room shall be supplied with HEPA filtered air.
- (e) A buffer room shall be ISO Class 7 unless the pharmacy is ~~a nuclear pharmacy or~~ is utilizing a DCR in accordance with 247 CMR 17.XX.
- (f) A buffer room shall be physically separated from the ante room by walls, doors, or pass-throughs.
- (g) Unless prohibited by local building or fire code, a buffer room may not have more than one door.

Comment [HAE16]: Board: In conflict with fire code?

(2) Ante Room

- (a) An ante room shall be supplied with HEPA filtered air.
- (b) An ante room shall be at least ISO Class 8. However, an ante room adjacent to a negative pressure buffer room shall be at least ISO Class 7.
- (c) Unless prohibited by local building or fire code, an ante room may not have more than one door between the ante room and an unclassified space.
- (d) An ante room shall be at least 100 square feet.
- (e) An ante room shall have a line of demarcation that separates the less clean area from the more clean area.

DRAFT

- (f) An ante room shall have a stainless steel sink that:
 - 1. is equipped with hands-free controls for water and soap dispensing;
 - 2. has proper depth and capacity for hand washing up to the elbows;
 - 3. is designed or installed to prevent standing water;
 - 4. is located on the clean side of the line of demarcation away from the buffer room door; and
 - 5. minimizes splashing and dripping of water on adjacent walls and floor.
- (g) An ante room sink may not have an aerator mechanism on the nozzle.
- (h) An ante room shall have lint-free, disposable towels located in proximity to sink to minimize water dripping and splashing.
- (i) An ante room may not contain automatic hand dryers.
- (j) An ante room's plumbing systems shall be maintained in a good state of repair and be free of defects that could create conditions favorable for microbial growth.
- (k) Exposed plumbing system pipes within the ante room shall be limited to the immediate drain pipe and P / S traps and shall be constructed of cleanable, non-corrosive material such as copper, PVC, or stainless steel.
- (l) A pharmacy shall place a "tacky" mat outside of the ante room door and shall replace the "tacky" mat at least once per day and when visibly soiled.
- (m) A cart used in the ante room shall be dedicated to one side of the line of demarcation. Only carts dedicated to the cleaner side of the line of demarcation may enter the buffer room after proper cleaning and disinfecting.

Comment [17]: Stakeholder Feedback:

Changed "non-shedding disposable paper towels" to "disposable towels"

Comment [HAE18]: Stakeholder Feedback:

Previously: A pharmacy shall place "tacky" mats on each side of the anteroom door and shall replace "tacky" mats at least once per day and when visibly soiled.

(3) Dedicated Compounding Room ("DCR")

- (a) A pharmacy may only prepare CSPs in a DCR if it holds an institutional sterile compounding pharmacy license, issued under M.G.L. c. 112, § 39I and the CSPs are administered on-site.
- (b) A pharmacy may not prepare the following types of CSPs in a DCR:
 - 1. high risk level CSPs;
 - 2. hazardous CSPs; or
 - 3. radiopharmaceuticals.
- (c) A pharmacy utilizing a DCR shall adhere to all sections of 247 CMR 17.00, unless otherwise provided.
- (d) A DCR shall:
 - 1. be ISO Class 8 or better;
 - 2. contain a positive pressure PEC which may only be a CAI or LAFW;
 - 3. be supplied with HEPA filtered air that is introduced at the ceiling;
 - 4. have at least 20 air changes per hour (ACPH) that are independent of the ACPH's from the PEC;
 - 5. be at least 144 square feet; and
 - 6. contain a buffer space and an ante space that are separated by a line of demarcation.

Comment [HAE19]: Removed "parenteral nutrition (TPN and/or PPN).

DRAFT

- (e) A dedicated compounding room shall have a minimum differential positive pressure of 0.02 inches water column between the ISO Class 8 DCR and the unclassified space that causes air to flow from the DCR into the unclassified space.
- (f) A buffer space in a dedicated compounding room shall include 40% of the square footage in the dedicated compounding room.
- (g) An ante space in a dedicated compounding room shall:
 - 1. include 60% of the square footage in the dedicated compounding room;
 - 2. have a stainless steel sink that:
 - A. is equipped with hands-free controls for water and soap dispensing;
 - B. has proper depth and capacity for hand washing up to the elbows;
 - C. minimizes splashing and dripping of water on adjacent walls and floor;
 - D. does not have an aerator mechanism on the nozzle; and
 - E. is located at least three feet from the line of demarcation; and
 - 3. have lint-free, disposable towels located in proximity to sink to minimize water dripping and splashing.
- (h) An ante space in a dedicated compounding room may not:
 - 1. contain automatic hand dryers; or
 - 2. have more than one door between the ante space and an unclassified space.
- (i) A DCR shall employ the principle of displacement airflow and maintain an air velocity of at least 40 feet per minute from the buffer space across the line of demarcation into the ante space.
- (j) The plumbing system in the ante space of a dedicated compounding room shall be maintained in a good state of repair and be free of defects that could create conditions favorable for microbial growth.
- (k) Exposed plumbing system pipes within the ante space of a dedicated compounding room shall be limited to the immediate drain pipe and P / S traps and shall be constructed of cleanable, non-corrosive material such as copper, PVC, or stainless steel.
- (l) A pharmacy shall place a “tacky” mat outside of the DCR door and shall replace the “tacky” mat at least once per day and when visibly soiled.
- (m) A DCR may not have a pass through.
- (n) The door to a DCR shall be located in the ante space.
- (o) Carts used in a DCR shall be dedicated to one side of the line of demarcation.
- (p) A pharmacy utilizing a DCR shall perform environmental monitoring (non-viable and viable) for “other classified areas” in accordance with 247 CMR 17.XX.

Comment [20]: Stakeholder Feedback

Changed “non-shedding disposable paper towels” to “disposable towels”

Comment [HAE21]: Stakeholder feedback:

Previously: A pharmacy shall place “tacky” mats on each side of the anteroom door and shall replace “tacky” mats at least once per day and when visibly soiled.

17.19: Sterile Compounding Facility; Compounding Aseptic Isolators (“CAI”)

- (1) A pharmacy may not locate a CAI outside of an ISO Class 7 buffer room, unless:
 - (a) the CAI is located in a DCR;

Comment [HAE22]: Removed “the CSPs are for exclusive use in an inpatient, hospital setting.”

DRAFT

- (b) the pharmacy holds an institutional sterile compounding pharmacy license issued under M.G.L. c 112, § 39I;
 - (c) the CSPs are prepared for on-site administration; and
 - (d) the pharmacy obtains documentation from the manufacturer validating that the CAI maintains positive pressure ISO Class 5 conditions during dynamic operating conditions, including transferring ingredients and components into and out of the CAI and during preparation of CSPs.
- (2) A CAI located in a dedicated compounding room shall have unidirectional air flow design.
- (3) A pharmacy may not assign a BUD to any CSP prepared in a CAI located outside of an ISO Class 7 buffer room that exceeds 36 hours at room temperature or 9 days refrigerated. A pharmacy may not freeze a CSP prepared in a CAI dedicated compounding room.
- (4) A pharmacy may not use any compounding device in a CAI located outside an ISO Class 7 buffer room.

Comment [HAE23]: New

17.20: Sterile Compounding Facility; Laminar Air Flow Workbench (“LAFW”)

- (1) A pharmacy may not locate a LAFW outside of an ISO Class 7 buffer room, unless:
- (a) the LAFW is located in a DCR;
 - (b) the pharmacy holds an institutional sterile compounding pharmacy license issued under M.G.L. c 112, § 39I; and
 - (c) the CSPs are administered on-site.
- (2) A pharmacy utilizing an LAFW located in an ISO Class 8 DCR may only prepare low risk level CSPs and may only assign a BUD not to exceed 12 hour at room temperature or 24 hour refrigerated.
- (3) A pharmacy may not use any compounding device in a LAFW located outside an ISO Class 7 buffer room.

17.21: Sterile Compounding Facility; Temperature and Humidity Monitoring

Comment [24]: Stakeholder Feedback

- (1) All ISO Classified areas shall maintain a temperature of ~~68 degrees~~ or less.
- (2) All ISO Classified areas shall maintain a relative humidity of ~~60% or less~~.
- (3) Each secondary engineering control shall have a probe or sensor to measure temperature and humidity.

Comment [HAE25]: Removed specific range.

Comment [HAE26]: Removed range.

DRAFT

- (4) A licensee shall document the temperature and humidity of each secondary engineering control 24 hours per day, seven days per week, by continuous recording device.
- (5) Drug storage areas ~~of outside the ISO classified areas of a sterile compounding pharmacy~~ shall maintain a controlled room temperature of 68-77°F (20-25°C), or more restrictive if warranted by specific drug storage requirements. A pharmacy shall document the controlled room temperature at least once every work shift or by a continuous recording device.
- (6) A sterile compounding pharmacy shall maintain a humidity of 65% or less outside the ISO Classified areas. A pharmacy shall document the humidity outside the ISO Classified areas at least daily, once per work shift, or by a continuous recording device.
- (7) A pharmacy shall respond to each out of limit temperature or humidity condition and shall document its response.

Comment [HAE27]: Stakeholder feedback

Comment [HAE28]: Stakeholder feedback

17.22: Sterile Compounding Facility; Certification of Classified Areas

- (1) Primary and secondary engineering controls shall be certified at least:
 - (a) once every 6 months;
 - (b) whenever a PEC is relocated, added, or removed;
 - (c) whenever the room is altered;
 - (d) immediately following any major repair or major servicing of the compounding facility or engineering controls; and
 - (e) ~~following any planned or unplanned interruption of HVAC operations.~~
- (2) The certification testing shall be completed in its entirety within a 24 hour time period. Certification testing includes:
 - (a) airflow and velocity test;
 - (b) airflow smoke pattern test;
 - (c) room pressurization test;
 - (d) air flow displacement test, as applicable;
 - (e) HEPA filter leak test;
 - (f) induction leak and back streaming test;
 - (g) airborne non-viable particle counting, conducted under dynamic operating conditions; and
 - (h) temperature and humidity test.
- (3) In the event a primary or secondary engineering control requires major repair or major servicing, a pharmacy shall stop compounding and may not resume compounding until:

Comment [29]: To be defined in 247 CMR 2

Comment [30]: Will be defined in 247 CMR 2

DRAFT

- (a) the repair or service is complete;
- (b) the affected engineering control has been certified; and
- (c) **environmental monitoring results in the affected engineering control within USP <797> action levels** are obtained.

(4) Certification

- (a) A pharmacy shall use CETA National Board of Testing (CNBT)-accredited certifiers and all sterile compounding facilities shall be certified to most current CAG standards.
- (b) A pharmacy shall ensure that all certification reports for all primary and secondary engineering controls indicate that the most current CAG standards have been followed.
- (c) A pharmacy shall ensure that all certification reports for all primary and secondary engineering controls list all elements of the most current CAG standards.

(5) The manager of record or his/her pharmacist designee shall review and sign the certification report.

(6) A pharmacy shall validate **the maximum number of compounding personnel capable of working in a buffer room or buffer space without disrupting ISO classification** at least once per year. The validation shall include non-viable air, **viable air, and surface sampling**.

Comment [31]: Stakeholder Feedback
Previously said: A pharmacy shall validate - at least annually - through non-viable air sampling, that each primary and secondary engineering control maintains its ISO classification when the maximum number of compounding personnel are working in the area.

17.23: Sterile Compounding Facility: Smoke Studies

(1) A pharmacy shall conduct a smoke study of primary and secondary engineering controls:

Comment [HAE32]: Removed requirement for video recording.

- (a) upon initial certification;
- (b) upon recertification; and
- (c) immediately following any major **repair** or service, movement of engineering control, or addition or permanent removal of equipment located within the primary engineering control.

Comment [HAE33]: Board: Certification v. recertification.

Comment [HAE34]: Previously: "annually as part of the certification process."

(2) A pharmacy shall conduct a smoke study:

- (a) to verify unidirectional airflow, sweeping action over and away from the critical compounding area, and interface with compounding personnel for each primary engineering control;

DRAFT

- (b) to verify a general top-down dilution of room air with HEPA-filtered make-up air and sweeping action to the low wall mounted returns for each secondary engineering control;
 - (c) around all openings, doorways, and pass-throughs to confirm positive pressure or negative pressure; and
 - (d) around compounding equipment to confirm air flow.
- (3) A smoke study shall be conducted in accordance with **CAG standards**.
- (4) A pharmacy shall conduct smoke studies during dynamic operating conditions that represent to the most challenging compounding conditions encountered by compounding personnel in order to demonstrate that compounding personnel performing manipulations and/or equipment used in the direct compounding area inside of the ISO Class 5 environment are not disrupting the flow of first air (HEPA filtered air stream) over critical sites.
- (5) A pharmacy shall video record a smoke study of each primary and secondary engineering control at least once per year.
- (6) A pharmacy shall document the results of each smoke study.
- (7) A pharmacy shall **initiate an investigation and** develop and implement a Corrective Action Preventative Action (“CAPA”) plan in response to a failed smoke study.

17.24: Environmental Monitoring

- (1) A pharmacy shall develop an environmental monitoring sampling plan in conjunction with a qualified professional such as a microbiologist, industrial hygienist, or infection control professional.
- (2) A pharmacy shall conduct viable air and surface sampling for bacterial and fungal organisms.

~~(3)~~ A pharmacy shall collect environmental monitoring samples from each primary and secondary engineering control at locations that are prone to contamination.

~~(4)~~ A pharmacy shall perform trending analysis of all environmental monitoring results.

~~(5)~~ A pharmacy shall maintain an environmental monitoring plan that clearly denotes the frequency and location of viable bacterial and fungal air and surface sampling and non-viable particulate **sampling**.

Comment [HAE35]: Previously read: “A pharmacy shall maintain an environmental monitoring sampling plan clearly denoting locations and frequency of viable bacterial and fungal air and surface sampling and non-viable particulate sampling.”

(65) A pharmacy shall maintain an environmental sampling log that states the location of each sample, sampling time, sampling methodology, and activities taking place in the respective classified areas.

(76) A pharmacy shall conduct environmental monitoring of each primary and secondary engineering control:

- (a) as part of a routine environmental monitoring program and in accordance with 247 CMR 17.XX;
- (b) as part of the commissioning and certification of new facilities and equipment;
- (c) immediately following any repairs or servicing of facilities and equipment;
- (d) immediately following any planned or unplanned interruptions of HVAC operations lasting longer than 4 hours;
- (e) immediately following addition, removal, or relocation of a PEC;
- (f) as part of the re-certification of facilities and equipment;
- (g) in response to identified problems with staff technique;
- (h) in response to an actual or suspected defect or contaminant of a CSP or potential patient infection;
- (i) in response to an above action level environmental monitoring result or adverse environmental monitoring trend; and
- (j) in response to a sudden or significant change in staffing or workload.

Comment [HAE36]: Table below.

Comment [HAE37]: Board 7/16: Need to define repair and servicing that will trigger EM.

Comment [B38]: Prior Board Discussion: Godek do contractors need to be certified to do work?
Covered in vendor assessment- MOR is required to ensure the contractors hired are appropriate
Will add guidance in audit tool

(87) At minimum, a pharmacy shall conduct routine environmental monitoring of each primary and secondary engineering control at the following intervals:

- (a) low and medium risk level CSPs that are assigned standard room or refrigerated temperature BUD(s) in accordance with 247 CMR 17.XX:

	PEC used for compounding	Buffer Room	Ante Room	Other Classified
Non-Viable Air	Once per month	Once per month	Once per month	Once per month
Viable Air	Once per month	Once per month	Once per month	Once per month
Surface	Once per month	Once per month	Once per month	Once per month

- (b) low and medium risk level CSPs with extended BUD and low and medium risk level CSPs prepared in batches that will be stored in the freezer:

Comment [39]: Stakeholder feedback

	PEC used for compounding	Buffer Room	Ante Room	Other Classified

DRAFT

Non-Viable Air	At least once per month and prior to compounding each day that these types of CSPs are prepared	At least once per month and prior to compounding each day that these types of CSPs are prepared	Once per month	Once per month
Viable Air	Once per month	Once per month	Once per month	Once per month
Surface	At least once per month and at the conclusion of compounding each day these types of CSPs are prepared	At least once per month and at the conclusion of compounding each day these types of CSPs are prepared	Once per month	Once per month

Comment [40]: Stakeholder feedback
Previously read: At least once per month and prior to compounding each day that compounding is performed

Comment [41]: Stakeholder feedback
Previously read: At least once per month and at the conclusion of compounding each day that compounding is performed

Comment [42]: Stakeholder feedback
Previously read: At least once per month and at the conclusion of compounding each day that compounding is performed

(c) high risk level CSPs:

	PEC used for compounding	Buffer Room	Ante Room	Other Classified
Non-Viable Air	At least once per month and prior to compounding each day these types of CSPs are prepared	At least once per month and prior to compounding each day these types of CSPs are prepared	Once per month	Once per month
Viable Air	Once per month	Once per month	Once per month	Once per month
Surface	At least once per month and at the conclusion of compounding each day these types of CSPs are prepared	At least once per month and at the conclusion of compounding each day these types of CSPs are prepared	Once per month	Once per month

Comment [43]: Stakeholder feedback
Previously read: At least once per month and prior to compounding each day that compounding is performed

Comment [44]: Stakeholder feedback
Previously read: At least once per month and prior to compounding each day that compounding is performed

Comment [45]: Stakeholder feedback
Previously read: At least once per month and prior to compounding each day that compounding is performed

Comment [46]: Stakeholder feedback:
Previously read: At least once per month and prior to compounding each day that compounding is performed

DRAFT

- (d) high risk level CSPs with extended BUDs, and high risk level intermediate or stock solutions prepared in batches:

	PEC used for compounding	Buffer Room	Ante Room	Other Classified
Non-Viable Air	At least once per week and prior to compounding each day these types of CSPs are prepared	At least once per week and prior to compounding each day these types of CSPs are prepared	At least once per week	At least once per week
Viable Air	At least once per week	At least once per week	At least once per week	At least once per week
Surface	At least once per week and at the conclusion of compounding each day these types of CSPs are prepared	At least once per week and at the conclusion of compounding each day these types of CSPs are prepared	At least once per week	At least once per week

Comment [47]: Stakeholder feedback

Comment [48]: Stakeholder feedback

Comment [49]: Stakeholder feedback

Comment [50]: Stakeholder feedback

- (98) Environmental monitoring samples shall be collected in the following order: ISO Class 5, then ISO Class 7, and then ISO Class 8.
- (109) Personnel that perform environmental monitoring shall be **qualified** and shall demonstrate competency and proficiency in all sampling techniques including media selection, media preparation, sample collection, incubation protocols, identification of positive results, proper handling of samples for contracted lab distribution, and proper disposal of sampling plates.
- (110) **Qualified personnel that perform environmental monitoring shall utilize proper equipment and shall demonstrate competency in the use of that equipment.**
- (124) **Equipment used for environmental monitoring shall be maintained and calibrated for use at least annually or more frequently in accordance with manufacturer's specifications.**
- (132) **A sterile compounding pharmacy shall test potable water for microorganisms at the point of use at least quarterly. If a sterile compounding pharmacy has a water purification system, it shall also test source water for microorganisms at least quarterly. A pharmacy shall ensure that potable water is maintained within local municipality limits.**

Comment [HAE51]: Will define in 247 CMR 2

DRAFT

(14) A pharmacy utilizing a water purification system shall ensure the system is properly functioning in accordance with the manufacturer specifications.

(15) A pharmacy utilizing a water filtration system shall change pre-filters and filters in accordance with manufacturer specifications.

Comment [52]: Prior BOARD discussion Godek
A pharmacy shall change water filters and pre-filters

(16) A pharmacy engaged in high risk level compounding shall have a water purification system for water supplied to sink(s) used for handwashing and equipment cleaning.

(17) A pharmacy shall incubate environmental monitoring samples at the following temperatures:

Type of Plate	Temperature	Time Required
Tryptic soy agar medium	86°F – 95°F (30°C – 35°C)	48 – 72 hours
Malt Extract Agar (MEA)	78°F – 86°F (26°C – 30°C)	5 – 7 days
Other Differentiating Fungal Media Plates	78°F – 86°F (26°C – 30°C)	5 – 7 days

(18) Environmental monitoring for viable organisms shall include positive controls and negative controls.

(19) A pharmacy is responsible for ensuring that all Staphylococcus organisms are identified as coagulase positive or negative.

(20) A pharmacy shall utilize a two-plate method for collection of viable air and surface samples. One plate shall be a general growth medium and the other plate shall be a medium that specifically supports the growth of fungus.

(21) A pharmacy that has qualified internal personnel collect environmental monitoring samples shall validate sampling procedures at least quarterly through a qualified third-party vendor.

(22) A pharmacy shall obtain a “Growth Promotion Certificate” for environmental monitoring plates- to validate that the media is able to support microbial growth.

DRAFT

(23) A pharmacy shall utilize plates intended for environmental monitoring and may not ~~use~~ utilize plates intended for research-only.

(24) Results of viable air and surface sampling shall be measured by counting the number of discrete colony forming units (CFUs) per plate.

(25) A pharmacy shall trend routine environmental monitoring results in order to facilitate decision-making for requalification of a controlled environment, remediation efforts, and for maintenance and sanitization schedules.

(26) A pharmacy shall ensure its environmental monitoring reports include at a minimum:

Comment [HAE53]: Removed: whether each sample is within or outside USP 797 action levels.

- (a) ~~date report prepared;~~
- (b) sample collection date and time;
- (c) type of sample;
- (d) date sample received by lab;
- (e) ~~date sample read by the lab~~
- (f) sampling methodology;
- (g) dates of incubation;
- (h) identification of sampling locations;
- (i) sampling conditions (i.e. dynamic);
- (h) activities taking place in the respective classified areas when samples are taken;
- (j) media type(s);
- (k) media lot number, expiration date, and growth promotion confirmation;
- (l) incubation time and temperatures;
- (l) results of each sample (raw and calculated CFU count);
- (m) the identity of each CFU to at least the genus level; and
- (n) indication that the Manager of Record or his/her pharmacist designee reviewed the environmental monitoring sample collection.

(27) Microbiology reports shall be signed by a microbiologist.

Comment [54]: Prior Board Discussion
Previously ready "qualified microbiologist"

(28) A pharmacy shall immediately remediate highly pathogenic microorganisms, including gram-negative rods, coagulase positive staphylococcus, molds, and yeasts, regardless of CFU count, with the assistance of a competent microbiologist, infection control professional, or industrial hygienist.

17.25: Environmental Monitoring: Non-Viable and Viable Air Sampling

DRAFT

- (1) A pharmacy shall collect air samples under dynamic operating conditions that mimic the pharmacy's most challenging compounding conditions.
- (2) A pharmacy shall collect viable air samples with a volumetric air sampling device.
- (3) A pharmacy shall collect non-viable air samples with an electronic particle counting air sampling device.
- (4) Non-viable air sampling for each ISO classified area shall be conducted in accordance with CAG standards.
- (5) The minimum volume of a viable air sample at each sampling location is 1000 liters.
- (6) The results of viable air samples shall be described as the number of CFU per cubic meter of air sampled. Viable air sample results shall be evaluated by a microbiologist.
- (7) A pharmacy may not utilize passive air sampling procedures (i.e. settling media) to meet environmental monitoring requirements of 247 CMR 17.XX.

Comment [HAE55]: Previously read:

CFU counts from viable air monitoring shall be transformed into CFUs per cubic meter of air and evaluated by a microbiologist

17.26: Environmental Monitoring; Surface Sampling

- (1) A pharmacy shall collect surface samples following compounding activities that mimic the pharmacy's most challenging compounding conditions and prior to cleaning.
- (2) A pharmacy shall utilize the contact plate method to collect surface samples.
- (3) Media used for surface sampling shall be supplemented with additives to neutralize the effects of disinfecting agents (e.g., TSA with lecithin and polysorbate 80).
- (4) A pharmacy shall utilize a 24-30 cm² sized plate to collect and incubate each surface sample.
- (5) A pharmacy shall clean and disinfect surfaces following collection of a surface sample.

17.27: Environmental Monitoring; Action Levels

- (1) A pharmacy shall take immediate remedial actions in the event environmental monitoring results exceed action levels.
- (2) A pharmacy shall conduct a root cause analysis in response to any above action level environmental monitoring result or adverse trend in environmental monitoring.

DRAFT

(3) Non-Viable Air Sample Action Levels:

ISO Class 5	≥ 3520 particles $0.5 \mu\text{m}$ or larger per cubic meter of air
ISO Class 7	$\geq 352,000$ particles $0.5 \mu\text{m}$ or larger per cubic meter of air
ISO Class 8	$\geq 3,520,000$ particles $0.5 \mu\text{m}$ or larger per cubic meter of air

(4) Viable Air Sample Action Levels:

ISO Class 5	≥ 1 CFU
ISO Class 7	≥ 10 CFU
ISO Class 8	≥ 100 CFU
Highly pathogenic microorganisms, including gram-negative rods, coagulase positive staphylococcus, and fungi	≥ 1 CFU

(5) Surface Sample Action Levels:

ISO Class 5	≥ 3 CFU
ISO Class 7	≥ 5 CFU
ISO Class 8	≥ 100 CFU
Highly pathogenic microorganisms, including gram-negative rods, coagulase positive staphylococcus, and fungi	≥ 1 CFU

17.28: Environmental Monitoring; Remediation of Above Action Level Environmental Monitoring Results

(1) A pharmacy shall maintain a policy and procedure for remediation of above action level environmental monitoring results in accordance with "Board Policy 2015-xx: Response to Above Action Level Environmental Monitoring Results."

Comment [56]: Approved by both Subcommittee on Abnormal Results and full Advisory Committee for ISO 5 and ISO 7

DRAFT

- (2) A pharmacist Manager of Record or his/her pharmacist designee shall notify the Board via email within 24 hours of receiving notification of above action level environmental monitoring results from the microbiologist.
- (3) A pharmacist Manager of Record or his/her designee shall submit Disclosure of Above Action Level Results and the microbiology reports associated with the above action level environmental monitoring results within seven days of receiving the reports in accordance with 247 CMR 20.00.
- (4) A Pharmacy shall immediately assess above action level environmental monitoring results and may not prepare any CSPs until a remediation plan is developed and implemented in accordance with “Board Policy 2015-xx: Response to Above Action Level Environmental Monitoring Results.”
- (5) A Pharmacy shall develop a remediation plan in accordance with “Board Policy 2015-xx: Response to Above Action Level Environmental Monitoring Results.”
- (6) A pharmacy shall engage the assistance of qualified personnel, such as a microbiologist, infection control professional, or an industrial hygienist to develop a remediation plan.
- (7) A pharmacy shall properly remediate above action level environmental monitoring results in accordance with “Board Policy 2015-xx: Response to Above Action Level Environmental Monitoring Results.”
- (8) A pharmacy shall submit the completed remediation plan including microbiology report from repeat environmental monitoring to the Board within 30 days of the pharmacy’s initial notification of the results or a timeframe agreed upon by the Executive Director or their designee.
- (9) A pharmacy shall demonstrate successful remediation by performing repeat environmental monitoring of non-viable air and viable air and surface (bacterial and fungal) as part of remediation to above action level environmental monitoring results. The pharmacy may limit the repeat environmental monitoring to the affected ISO classified space based on the pharmacy’s environmental monitoring sampling plan unless otherwise directed by the Board.
- (10) Conditions for Resuming Sterile Compounding following an above action level environmental monitoring result

- (a) **ISO 5 Classified Area**
 1. A pharmacy may not resume compounding in an ISO Class 5 PEC following an above action level environmental monitoring result until remediation is completed and proven by microbiology reports of repeat environmental monitoring demonstrating results within acceptable levels.
- (b) **ISO 7 Buffer Room:**

Comment [57]: Approved by both Subcommittee on Abnormal Results and full Advisory Committee

Comment [58]: Approved by Subcommittee on Abnormal Results. Review by full Advisory Committee TBD

DRAFT

1. Upon receipt of an above action level environmental monitoring result in ISO 7 buffer room, a pharmacy may resume compounding for low and medium risk level CSPs if:
 - A. The environmental monitoring data does not indicate 3 or more consecutive sampling reports with above action level results within the last 6 months; and
 - B. The pharmacy has immediately assessed the above action level environmental monitoring results, developed and implemented a remediation plan, and scheduled repeat monitoring.
2. Upon receipt of an above action level environmental monitoring result in ISO 7 buffer room, a pharmacy may resume compounding for high risk compounding if:
 - A. The environmental monitoring data does not indicate 2 or more consecutive sampling reports with above action level results; and
 - B. The pharmacy has immediately assessed above action level environmental monitoring results, developed and implemented a remediation plan, and scheduled repeat monitoring.
3. A pharmacy resuming compounding of CSPs during remediation of ISO 7 buffer room above action level results shall limit the BUDs for CSPs to 24 hours room temperature, 3 days refrigerated or a timeframe agreed upon by the Executive Director or his/her designee until the repeat environmental monitoring reports demonstrate results within acceptable levels.
4. A pharmacy may not resume compounding if the environmental monitoring data indicates 3 or more consecutive sampling reports with above action level results within the last 6 months.
5. A pharmacy may not freeze any CSP upon receipt of an above action level environmental monitoring result in ISO 7 buffer room until repeat monitoring reports demonstrate results within acceptable levels unless otherwise approved by the Executive Director or his/her designee

(c) ISO 7 Ante room and ISO 8 Classified Area(s)

1. Upon receipt of an above action level environmental monitoring result in ISO 7 ante room or ISO 8 classified area(s), a pharmacy may resume compounding of low and medium risk level CSPs if:
 - A. The environmental monitoring data does not indicate 3 or more consecutive sampling reports with above action level results within the last 6 months; and

Comment [59]: Review by both Subcommittee on Abnormal Results and full Advisory Committee TBD

DRAFT

- B. The pharmacy has immediately assessed above action level environmental monitoring results, developed and implemented a remediation plan, and scheduled repeat monitoring.
2. Upon receipt of an above action level environmental monitoring result in ISO 7 ante room or ISO 8 classified area(s), a pharmacy may resume compounding for high risk level CSPs if:
 - A. The environmental monitoring data does not indicate 2 or more consecutive sampling reports with above action level results; and
 - B. The pharmacy has immediately assessed above action level environmental monitoring results, developed and implemented a remediation plan, and scheduled repeat monitoring.
3. A pharmacy resuming compounding of CSPs during remediation of above action level environmental monitoring results in ISO 7 ante room or ISO 8 classified area(s) shall limit the BUDs for CSPs to 24 hours room temperature, 3 days refrigerated, or a timeframe agreed upon by the Executive Director or his/her designee until the repeat environmental monitoring reports demonstrate results within acceptable levels.
4. A pharmacy may not resume compounding if the environmental monitoring data indicates 3 or more consecutive sampling reports with above action level results within the last 6 months.
5. A pharmacy may not engage in high risk level compounding upon receipt of an above action level environmental monitoring result in ISO 7 ante room or ISO 8 classified area(s) if the environmental monitoring data indicates 2 or more consecutive sampling reports with above action level results.
6. A pharmacy may not freeze any CSP upon receipt of an above action level environmental monitoring result in ISO 7 ante room or ISO 8 classified area(s) room until repeat monitoring reports demonstrate results within acceptable levels unless otherwise approved by the Executive Director or his/her designee.

(11) A pharmacy's response to above action level environmental monitoring results shall include the following:

- (a) examination by an accredited laboratory;
- (b) identification of any growth to at least the genus level;
- (c) re-evaluation of the adequacy of personnel work practices, cleaning procedures, operational procedures, as well as air filtration efficiency;
- (d) comprehensive root cause analysis; and
- (e) development and implementation of a comprehensive remediation plan, including re-cleaning and resampling.

17.29: Cleaning and Disinfecting

DRAFT

- (1) A pharmacy shall document each cleaning in a cleaning log. The log shall include the date, time, cleaning agents utilized, and personnel who performed the cleaning.
- (2) Mops, wipes, and other cleaning equipment shall be non-shedding. If a mop or other cleaning equipment is re-usable, it shall be dedicated to the classified area(s).
- (3) Cleaning equipment used in hazardous drug compounding environments may not be utilized in non-hazardous drug compounding environments.
- (4) Personnel who perform cleaning shall be trained and successfully pass initial and annual competency assessments conducted by trained and qualified compounding personnel in both of the following areas:
 - (a) hand hygiene and garbing; and
 - (b) cleaning and disinfecting.
- (5) Only trained compounding personnel may clean inside an ISO Class 5 work area. Competency assessments on proper cleaning and disinfecting procedures shall be performed and documented at least one time per year.
- (6) A licensee shall clean and disinfect the critical areas where compounding occurs inside an ISO Class 5 environment:
 - (a) at the beginning of each work shift;
 - (b) between each batch;
 - (c) every 30 minutes during continuous compounding;
 - (d) immediately following any spill; and
 - (e) in the event of, or suspicion of, a breach in compounding procedures or aseptic technique.
- (7) A licensee shall allow sterile 70% isopropyl alcohol (“IPA”) to remain in contact with surfaces to be disinfected for 30 seconds before compounding activities are started.
- (8) A licensee shall disinfect all rubber stoppers of vials and bottles, the necks of ampules and other items by wiping with sterile 70% IPA and waiting for at least 10 seconds before they are used to prepare CSPs.
- (9) A pharmacy shall clean horizontal work surfaces daily.
- (10) A pharmacy shall clean floors daily.
- (11) A pharmacy shall sanitize the sink drain with a disinfectant at least once per day.

Comment [60]: Stakeholder Feedback

Previously read: Mops, wipes, and other cleaning equipment shall be non-shedding. If a mop or other cleaning equipment is re-usable, its use shall be limited to the dedicated compounding room, buffer room, ante room, or other classified space and it shall be labeled with its location of use.

Comment [61]: Stakeholder Feedback

Previously read: A pharmacy shall clean floors after compounding has been completed.

(12) A pharmacy shall clean walls, ceilings, storage areas, and supply bins at least once per month.

(13) A pharmacy shall not engage in compounding during daily or monthly cleaning activities.

Comment [62]: Stakeholder feedback

(14) A pharmacy shall verify its cleaning agents are appropriate and effective. A pharmacy shall maintain a certificate of analysis for each cleaning product, if available.

Comment [63]: Stakeholder Feedback

17.30: Sterile Compounding Process; Handwashing and Garbing

(1) Compounding personnel shall remove personal outer garments, jewelry, piercings, cosmetics, artificial nails, and nail polish before entering the ante room. Natural nails shall be trimmed to ¼ inch.

Comment [64]: Stakeholder feedback prefer shorter than ¼” and recommended 1/8th or 1/16th.

(2) A pharmacy shall provide clean, laundered scrubs that are dedicated to sterile compounding activities and only worn within the pharmacy. Scrubs shall be laundered following each use. A pharmacy shall have a changing area for sterile compounding personnel to change and be able to enter classified areas without traversing pharmacy common areas, stock rooms, or warehouses.

Comment [HAE65]: Board 7/16: Consider allowing employees to provide their own scrubs. T. Fensky to make a recommendation.

Comment [66]: Edited for clarity and operational feasibility

Previously read: A pharmacy shall provide clean, laundered scrubs that are dedicated to sterile compounding activities and only worn within the pharmacy. Scrubs shall be laundered following each use. A pharmacy shall have a changing room immediately adjacent to the sterile compounding area so that compounding personnel do not have to traverse pharmacy common areas, stock rooms, or warehouses prior to entering classified areas.

(3) Compounding personnel shall use dedicated shoes while in classified areas. Dedicated shoes shall be stored in a segregated storage space in an area close to the ante room and donned immediately prior to entering the ante room.

Comment [67]: Stakeholder Feedback

(4) Prior to entering an ante room, compounding personnel shall don scrubs and dedicated shoes.

Previously read: Compounding personnel shall use dedicated shoes while in classified areas. Dedicated shoes shall be stored in an area just outside the ante room adjacent to the entrance and donned immediately prior to entering the ante area.

(5) Once inside the ante room, but prior to crossing the line of demarcation, compounding personnel shall perform the following tasks in the following order: don a head cover, facial hair cover if applicable, and face mask.

Comment [68]: Struck based on dedicated shoes and disposable coveralls requirement

(6) Once on the clean side of the line of demarcation, but prior to entering the buffer room, compounding personnel shall perform the following tasks in the follow order:

don shoe covers one foot at a time while stepping over the line of demarcation in a manner that does not allow shoe covers to touch the less clean side of the ante room and does not allow non-covered shoes to touch the clean side of the ante room.

(a) wash hands and forearms to the elbows for at least 30 seconds with antimicrobial soap and water. The hand cleansing procedure shall be performed by removing debris from underneath fingernails using a nail cleaner under warm running water followed by vigorous hand washing.

(b) dry with lint-free disposable towels.

(c) don:

Comment [69]: Stakeholder Feedback

Previously read: dry with lint-free, non-shedding disposable paper towels.

DRAFT

1. a non-shedding **disposable coverall** for low and medium risk level compounding; or
2. a non-shedding sterile **disposable coverall** for high risk level compounding.

Comment [70]: Stakeholder Feedback
Changed "bunny suit" to "disposable coverall"

(7) Once garbing and hand washing procedures are completed, compounding personnel shall access the buffer room without touching hands on any surface.

(8) Once inside the buffer room, compounding personnel shall perform antiseptic hand cleansing using a waterless alcohol-based surgical hand scrub with persistent activity following manufacturers' recommendations and hands shall be allowed to dry thoroughly before donning sterile powder-free gloves.

(9) Compounding personnel shall routinely disinfect gloves with sterile 70% IPA after contacting non-sterile objects and after exposure to less than ISO Class 5 air.

(10) A compounding individual shall perform antiseptic hand cleansing using a waterless alcohol based surgical hand scrub and shall don new sterile gloves prior to reentering the buffer room if he/she exited the buffer room but did not cross the line of demarcation.

(11) Compounding personnel shall repeat all hand washing and garbing activities if personnel cross line of demarcation from the clean to the less clean side of ante-room or if exposed to less than ISO Class 8 air.

(12) The non-shedding **disposable coverall** may be removed and retained in the compounding area if not visibly soiled to be re-donned by the same personnel during that shift only. All other garb must be discarded and replaced with new garb before entering the compounding area.

(13) Sterile compounding personnel shall doff garb in the following order:

Comment [71]: Prior Board Discussion Conley and Cornacchio

- (a) Remove gloves;
- (b) Remove mask, goggles, or face shield; and
- (c) Remove disposable coveralls.

17.31: Sterile Compounding Process; Aseptic Technique

- (1) Food and drinks are not allowed in any ISO Classified area.
- (2) A pharmacy may not store cardboard boxes or other particulate producing materials in any ISO Classified area or in any area adjacent to an ISO Classified area.
- (3) A pharmacy may not use paper in an ISO Classified area unless it is lint-free **paper**.

Comment [72]: Stakeholder Feedback
Previously read "lint free paper (USP paper)"

DRAFT

- (4) Compounding personnel shall remove supplies, equipment, and other materials from shipping cartons and cardboard boxes in an unclassified area and shall wipe said supplies, equipment, and other materials with residue free disinfectant before transporting said items into the ante area and again on the less clean side of the line of demarcation prior to entering the buffer area.
- (5) Compounding personnel shall disinfect all supplies and drug components with an appropriate cleaning agent prior to moving said supplies and drug components into the ISO Class 5 compounding area.
- (6) Syringes, needles, and tubing are only removed from packaging **outer wrapper** in the ISO Class 5 area.
- (7) A licensee shall don sterile gloves for all sterile compounding, regardless of the type of PEC.
- (8) Compounding personnel shall routinely inspect sterile-gloved hands for wear and tear and replace gloves as needed.
- (9) Compounding personnel shall routinely disinfect sterile-gloved hands with sterile 70% IPA prior to entering/re-entering an ISO Class 5 area and after contacting non sterile objects.
- (10) Compounding personnel shall perform manipulations in the direct compounding area inside of the ISO Class 5 environment in such a way as to not disrupt the flow of first air (HEPA filtered air stream) over critical sites.
- (11) Compounding personnel shall inspect each component for visible particulate matter, tampering, breaks in packaging, and other changes which would render the item unacceptable for use in sterile compounding.

Comment [73]: Prior Board Discussion Gannon

17.32: Sterile Compounding Process; Miscellaneous

- (1) A pharmacy shall use **filtered needles or straws** for any compounding involving the use of glass ampules.
- (2) A pharmacy may not expose non-hazardous drug environments to hazardous drugs or components.
- (3) After compounding a highly allergenic product, such as Penicillins or Beta Lactams, compounding personnel shall:
 - (a) **thoroughly clean the PEC, equipment, and materials according to the pharmacy's daily cleaning protocol;**

Comment [74]: Stakeholder Feedback

DRAFT

- (b) dispose of all garbing, including disposable coveralls; and
- (c) wash hands.

(4) A pharmacy shall immediately respond to and remediate any broken, damaged, or spilled CSP containing a highly allergenic product such as Penicillins or Beta Lactams.

(5) A pharmacy shall maintain a hood production log that documents the CSPs and compounding personnel for each PEC.

(6) A pharmacy shall ensure all classified areas allow for the orderly placement of equipment and materials to prevent confusion among ingredients, containers, labels, in-process materials, and finished preparations and shall be designed, arranged, and used to prevent cross-contamination.

(7) A pharmacy shall maintain a written continuity of care plan that describes how patient needs will be met in the event the pharmacy is unexpectedly unable to compound or dispense CSPs.

17.33: Sterile Compounding Personnel Training; General

(1) Compounding personnel shall be free from active infection and ~~all exposed~~ skin areas shall be intact without any burns, lesions, abrasions, or cuts.

(2) A pharmacy shall ensure all compounding personnel are properly trained in sterile compounding, ~~have successfully completed gloved/thumb fingertip sampling, and have been media-fill qualified~~ for the risk level and type of compounding conducted.

(3) A pharmacy shall maintain documentation of all training activities, competency assessments, and compounding qualifications. The documentation shall be readily retrievable and retained for at least two years.

(4) A pharmacy shall maintain a written or electronic file for all sterile compounding personnel that contains that individual's job description, roles and responsibilities, documentation of initial and ongoing competency assessments, and documentation of initial and ongoing compounding qualification activities.

(5) Compounding personnel, including supervising pharmacists, shall pass didactic coursework, practical skill assessment through competency evaluation, media fill testing, and gloved fingertip/thumb sampling before being allowed to compound sterile preparations.

(6) ~~Compounding personnel shall be requalified in all core competencies if a pause in compounding exceeds three months.~~

Comment [HAE75]: Previously read:

- (a) - thoroughly clean the PEC, equipment, and materials according to the pharmacy's daily cleaning protocol;
- (b) - repeat all hand washing and garbing activities; and
- (c) - change garbing.

Comment [76]: Board Discussion on 11/24 Stakeholder Feedback

Comment [77]: Stakeholder feedback

Comment [B78]: Prior Board: Gannon ? frequency of repeating, retraining at intervals

This std is substantial requirement for documentation- frequency covered in training stds.

Comment [79]: Stakeholder Feedback

Previously read:

A pharmacy shall maintain a written or electronic personnel file for each pharmacist, pharmacy technician, and pharmacy intern that engages in or oversees sterile compounding all sterile compounding personnel that contains that individual's job description, roles and responsibilities, annual performance evaluation, documentation of initial and ongoing competency assessments, and documentation of initial and ongoing compounding qualification activities.

DRAFT

(7) A pharmacy shall ensure that all compounding personnel, including supervising pharmacists, are evaluated on hand hygiene and garbing, cleaning and disinfecting, and aseptic technique initially and at least:

- (a) once per year for compounding personnel engaged in or overseeing low and medium risk level compounding; and
- (b) semiannually for compounding personnel engaged in or overseeing high risk level compounding.

(8) A pharmacy shall document competency evaluation for all sterile compounding personnel.

(9) In the event a compounding individual fails a written sterile compounding assessment exam, gloved fingertip/thumb sampling, or media-fill test, he/she may not compound until he/she is requalified and successfully retested.

Comment [80]: Added for clarity

Comment [HAE81]: Previously read:

In the event a compounding individual, including a supervising pharmacist, fails a written exam, gloved fingertip/thumb sampling, or media-fill test, he/she may not compound until he/she is requalified and successfully retested.

(10) Sterile compounding pharmacies shall maintain accurate and comprehensive records and reports related to environmental monitoring, certification, product testing, validation, personnel glove fingertip sampling, media fills, certificates of analysis, compounding records, and master formulation record in an organized manner and are immediately retrievable for inspection.

(11) A pharmacy shall send each failed gloved fingertip/thumb sample and media fill sample for microbial identification to the genus level. All Staphylococcus organisms must be identified as coagulase positive or negative.

(12) In the event a compounding individual fails a gloved fingertip/thumb sample or media fill sample, the pharmacy shall evaluate the CSPs prepared by that individual to detect potential contamination of the CSP.

(13) A pharmacy shall obtain a "Growth Promotion Certificate" for each lot of media for personnel monitoring to validate that the media is able to support microbial growth.

(14) Personnel monitoring gloved fingertip/thumb sampling shall include the use of positive and negative controls.

(15) Personnel monitoring media fills shall include the use of negative controls. Personnel monitoring media fills shall also include the use of positive controls if:

- (a) the pharmacy prepares growth promotion media from non-sterile powder; or
- (b) growth promotion certificates for media are not available.

Comment [82]: Stakeholder feedback

(16) Inoculation of a positive control shall occur outside of the classified areas.

Comment [83]: Stakeholder Feedback

DRAFT

17.34: Sterile Compounding Personnel Training; Gloved Fingertip/Thumb Sampling

- (1) The action level for a gloved fingertip/thumb sample is 1 CFU for ~~both~~ each gloves.
- (2) All compounding personnel shall successfully complete at least 3 gloved fingertip/thumb sampling procedures before initially being allowed to prepare CSPs.
- (3) During the initial gloved fingertip/thumb sampling, fingertip/thumb samples shall be 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.
- (4) All gloved fingertip/thumb sampling performed after the initial qualification shall be performed at the conclusion of compounding.
- (5) Frequency of gloved fingertip/thumb sampling
 - (a) Compounding personnel shall perform gloved fingertip/thumb sampling at least once per month.
 - (b) In addition to monthly gloved fingertip/thumb sampling, an individual who prepares low or medium risk level CSPs:
 1. with extended BUDs; or
 2. in batches that will be stored in the freezershall perform gloved fingertip/thumb sampling each day he/she prepares such CSPs.
 - (c) In addition to monthly gloved fingertip/thumb sampling, an individual who prepares high risk level CSPs shall perform gloved fingertip/thumb sampling each day he/she prepares such a CSP.
 - (d) Compounding personnel who prepare high risk level CSPs:
 1. with extended BUDs;
 2. in anticipation of a patient specific prescription or order; or
 3. that include high risk intermediate or stock solutionsshall perform gloved fingertip/thumb sampling at least once per week.
 - (e) In addition to weekly gloved fingertip/thumb sampling, an individual who prepares high risk level CSPs:
 1. with extended BUDs;
 2. in anticipation of a patient specific prescription or order; or
 3. that include high risk intermediate or stock solutionshall perform gloved fingertip/thumb sampling each day he/she prepares such CSPs.
- (6) A pharmacy that prepares high risk level CSPs or low and medium risk level CSPs with extended BUDs shall utilize both a general growth media and a fungal specific growth media for all gloved fingertip/thumb sampling.

Comment [HAE84]: Stakeholder Feedback
Clarified requirement to be only those performing
the compounding

DRAFT

- (7) Gloved fingertip/thumb sampling media shall be supplemented with additives to neutralize the effects of disinfecting agents (e.g., TSA with lecithin and polysorbate 80).
- (8) A pharmacy shall utilize a 24-30 cm² sized plate to collect and incubate each gloved fingertip/thumb sample.
- (9) A pharmacy shall incubate gloved fingertip/thumb samples at the following temperatures:

Type of Plate	Temperature	Time Required
Tryptic soy agar medium	86°F – 95°F (30°C – 35°C)	48 – 72 hours
Malt Extract Agar (MEA)	78°F – 86°F (26°C – 30°C)	5 – 7 days.
Other Differentiating Fungal Media Plates	78°F – 86°F (26°C – 30°C)	5 – 7 days.

17.35: Sterile Compounding Personnel Training; Media Fill Challenge Testing

(1) Compounding personnel who prepare low and medium risk level CSPs shall complete three media fills on three consecutive days before initially being allowed to prepare CSPs. Following initial qualification, compounding personnel shall complete three media fills on the same day at least semiannually. Compounding personnel shall perform gloved fingertip/thumb sampling immediately following the last media fill test procedure.

(2) Compounding personnel who prepare low and medium risk level CSPs with extended BUDs or in batches that will be stored in the freezer shall complete three media fills on three consecutive days before initially being allowed to compound. Following initial qualification, compounding personnel shall complete three media fills on the same day at least quarterly. Compounding personnel shall perform glove fingertip/thumb sampling immediately following the last media fill test procedure.

~~(3)~~ Compounding personnel who prepare high risk level CSPs shall complete three high risk level media fills for three consecutive days before initially being allowed to prepare or dispense a high risk level CSP. Following initial qualification, compounding personnel shall complete three high risk level media fills at least quarterly. The high risk level media fill procedure must simulate a high risk level CSP by producing the sterile growth media from non-sterile powder.

DRAFT

Compounding personnel shall perform gloved fingertip/thumb sampling upon completion of the last media fill test procedure.

(43) A pharmacy shall maintain a master formulation record for the media fill procedure that includes all equipment and steps of the media fill process for each risk level.

(54) Media fill challenge testing shall be performed under conditions that closely simulate the most challenging or stressful conditions encountered during compounding.

~~(5) A pharmacy shall utilize microbial growth promotion media, such as Soybean-Casein Digest. A pharmacy that prepares and dispenses high risk level CSPs with extended BUDs or that prepares CSPs in batches shall also utilize a fungal specific growth promotion media. A pharmacy shall obtain a "Growth Promotion Certificate" for each lot of media to validate that the media is able to support microbial growth.~~

(6) A pharmacy shall utilize microbial growth promotion media, such as Soybean-Casein Digest. A pharmacy that prepares high risk level CSPs with extended BUDs, high risk level CSPs prepared in anticipation of a patient specific prescription or order, or high risk level intermediate or stock solutions shall also utilize a fungal specific growth promotion media in addition to the general microbial growth promotion media.

(7) A pharmacy shall incubate media fill units utilizing general microbial growth promotion media at 30-35°C (86-95 °F) for a minimum of 7 days, followed by an incubation at 20-25°C (68-77 °F) for 7 days.

Comment [85]: Board Discussion on 11/24

17.36: Sterile Compounding Equipment

(1) A pharmacy shall clean, maintain, calibrate, and service equipment associated with compounding or used to monitor controlled environments in accordance with manufacturer's specifications.

(2) A pharmacy shall ensure personnel who use equipment received training, demonstrated the ability to use the equipment properly, and are able to appropriately respond to an equipment malfunction. Competency assessments shall be performed and documented at least one time per year.

(3) A pharmacy shall test Automated Compounding Devices ("ACD") used for parenteral nutrition, such as PPN or TPN, or dialysis compounding for volumetric and gravimetric accuracy at least daily or more frequently in accordance with manufacturer specifications.

Comment [86]: Stakeholder Feedback

(4) A pharmacy shall ensure balances and scales used to prepare CSPs are calibrated and qualified for performance and tolerances at least annually or more frequently in accordance with manufacturer specifications.

DRAFT

- (5) A pharmacy shall ensure incubators are calibrated and certified to NSIT standards at least annually or more frequently in accordance with manufacturer specifications.
- (6) A pharmacy shall maintain incubators in accordance with manufacturer specifications.
- (7) A pharmacy shall record temperatures of incubator daily.

17.37: Sterile Compounding Robotics

- (1) Robotic compounding equipment shall be constructed with a hard solid cleanable surface that are resistant to degradation by cleaning agents.
- (2) A sterile compounding robot utilized to prepare CSPs shall be considered a primary engineering control and shall maintain ISO Class 5 conditions during dynamic operating conditions.
- (3) A sterile compounding robot shall only utilize commercially manufactured ingredients and components and may not be utilized in the preparation of high risk level CSP.
- (4) A sterile compounding robot shall be located in an ISO Class 7 buffer area.
- (5) A pharmacy shall perform routine maintenance and calibration of the aseptic filling robot at least twice per year or more often if required by the device manufacturer.
- (6) A pharmacy shall maintain a daily record of the accuracy of the sterile compounding robot. The pharmacist MOR shall ensure the precision of the sterile compounding robot is maintained and all records are reviewed and any out of specifications are responded to immediately.
- (7) A sterile compounding robot shall utilize two separate verifications, such as bar code verification, electronic verification, weight verification, radio frequency identification (RFID), or another similar process, to identify ingredients and components during set up and replacement of components.
- (8) A sterile compounding robot shall be equipped with the capability to identify all ingredients, components, and volumes to ensure CSPs are accurately prepared and labeled.
- (9) A pharmacy shall validate the sterile compounding robot maintains sterility of final CSPs through media fill challenges, in accordance with 247 CMR 17.XX, Personnel Media-Fill Challenge Testing.

DRAFT

(10) A pharmacy shall assure that tubing set(s) used for the sterile compounding robot are traced from the source container to the port where it is attached during the initial daily set up and with each change in the source container.

Comment [87]: Prior Board Discussion: Conley
? labeling
Not required due to design.

(11) Compounding personnel shall be trained and shall demonstrate competency in the use of the aseptic filling robot. A pharmacy shall document initial training, as well as annual competency assessments.

(12) ~~Only~~ The pharmacist in charge or his/her designee shall ~~maintain or~~ validate changes to the sterile compounding robot product database.

Comment [88]: Prior Board discussion Gannon:
? if done by other qualified individual and RPh verification

(13) Only a pharmacist may perform overrides to alerts from the sterile compounding robot.

(14) A pharmacy shall adhere to manufacturer recommendations pertaining to the maximum time ingredients or components may be stored in the sterile compounding robot. A pharmacy shall document each instance an ingredient or component is added or replaced.

(15) A licensee shall clean and disinfect the critical areas where compounding occurs inside the ISO Class 5 environment of the aseptic filling robot:

Comment [HAE89]: Removed requirement for cleaning every 30 minutes during continuous compounding.

- (a) at the beginning of each work shift;
- (b) between each batch;
- (c) immediately following any spill;
- (d) in the event of, or suspicion of, a breach in compounding procedures or aseptic process; and
- (e) in accordance with manufacturer's specifications.

(16) A pharmacy shall properly disinfect all ingredients and components prior to placement in the sterile compounding robot.

17.38: Sterile Compounding Ingredient and Component Selection

(1) A pharmacy shall store compounding ingredients and components according to manufacturer specifications or USP standards.

(2) A pharmacy may not obtain components from a facility that is not registered by the FDA unless said components are not available from any FDA registered facility. In the event a pharmacy obtains components from a facility that is not registered by the FDA, the pharmacist shall evaluate the Certificate of Analysis, manufacturer reputation, and the reliability of the source.

(3) Active Pharmaceutical Ingredients (APIs) used in high risk level sterile compounding shall be parenteral grade. If API is not parenteral grade, the pharmacy shall obtain documentation from the supplier confirming that final processes for API production utilized Sterile Water for Injection (SWFI).

DRAFT

- (4) A pharmacy shall utilize API intended for human-use in compounding CSPs for human patients.
- (5) A pharmacy shall obtain components utilized in high risk level sterile compounding, including buffers, diluents, excipients, preservatives, and vehicles from commercially available sources if available in the marketplace. A pharmacy may not compound or produce high risk level sterile compounding components, including buffers, diluents, excipients, preservatives, and vehicles, if said products are commercially available.
- (6) A pharmacy shall use commercially available sterile containers and sterile container closure systems if available in the marketplace.

Comment [90]: Stakeholder Feedback

17.39: Sterilization and Depyrogenation

- (1) A pharmacy may not utilize ethylene oxide gas or irradiation to sterilize components, equipment, ingredients, or CSPs.
- (2) A pharmacy may not utilize steam sterilization or dry heat sterilization if the CSP can be sterilized using filtration.
- (3) A pharmacy shall sterilize the final preparation of a high risk level CSP, even if intermediate or stock solutions were previously sterilized.
- (4) A pharmacy shall depyrogenate all glassware and containers, able to withstand dry heat, utilized for sterile compounding with dry heat.
- (5) Sterilization by filtration
 - (a) A pharmacy shall perform sterilization by filtration in an ISO Class 5 environment using sterilizing (pharmaceutical) grade, pyrogen-free, 0.2 micron sterile filters.
 - (b) A pharmacy shall perform and document a filter integrity test (such as bubble point) at the conclusion of the compounding procedure.
 - (c) A pharmacy shall utilize sterile filters that are intended for human-use applications in sterilizing CSPs and suitable for the intended use.
- (6) Sterilization by Dry Heat and Steam
 - (a) A pharmacy may not utilize dry heat sterilization if the materials can be sterilized using steam.

DRAFT

- (b) A pharmacy shall pass CSPs through a filter with a nominal pore size not larger than 1.2 µm immediately prior to filling containers that will undergo terminal dry heat sterilization or steam sterilization.
- (c) Prior to steam sterilization, a pharmacy shall tightly wrap plastic and glass in low particle shedding paper or sealed in envelopes that prevent post sterilization microbial penetration.

(7) Dry Heat Ovens and Steam Sterilizers

- (a) A pharmacy shall locate a dry heat oven or steam sterilizer in a separate ISO Class 8 area which is adjacent to the ante room but does not have access to the buffer room. A pharmacy may not locate a dry heat oven or steam sterilizer in an ante room or buffer room.
- (b) A pharmacy shall ensure each dry heat oven and steam sterilizer operates properly and in accordance with manufacturer specifications pertaining to required temperatures, sterilizing cycle time, depyrogenation cycle time, loading patterns, loading capacity, temperature monitoring, placement of thermocouplers **or other temperature sensing device**, use of biological indicators and endotoxin challenge vials, and filter integrity testing, as applicable.
- (c) A pharmacy shall verify the effectiveness of each dry heat sterilization, dry heat depyrogenation, and steam sterilization process using appropriate Biologic Indicators or Endotoxin Challenge Vials in accordance with USP Chapter <1035>.
- (d) A pharmacy shall ensure dry heat ovens and steam sterilizers are equipped with a system for controlling and recording temperature and exposure time.
- (e) A pharmacy shall maintain a log of temperature and exposure time for each use of the dry heat oven or steam sterilizer. The log shall be readily retrievable and maintained for at least 2 years.

17.40 Sterility and Endotoxin Testing

- (1) A pharmacy shall conduct sterility testing on the following types of CSPs:
 - (a) CSPs with extended BUDs, **regardless of risk level**;
 - (b) **high risk** CSPs prepared in anticipation of a patient specific prescription or order;
 - (c) **high risk intermediate or stock solutions**;
 - (d) high risk level CSPs exposed longer than 12 hours **at refrigerated temperature 2-8 °C (36-46 °F)** before being sterilized; and

Comment [HAE91]: Previously:

Intermediate CSPs that include an intermediate, pooled, or stock solution prepared in anticipation of a patient specific prescription or order **or in a batch**;

DRAFT

(e) high risk level CSPs exposed longer than 6 hours at room temperature 8 °C (46 °F) before being sterilized.

(2) A pharmacy may not dispense a CSP that requires sterility testing until and unless it receives negative sterility testing results.

(3) A pharmacy shall utilize both a general growth media for bacteria and a fungal specific media for all high risk level CSP sterility tests.

(4) A pharmacy shall conduct sterility testing and test the proper number of articles in accordance with USP Chapter <71>.

(5) A pharmacy shall send each failed sterility test specimen for microbial identification to at least the genus level. All Staphylococcus organisms must be identified as coagulase positive or negative.

(6) A pharmacy shall conduct endotoxin testing on the following types of CSPs:

- (a) high risk level CSPs with extended BUDs;
- (b) high risk level CSPs prepared in anticipation of a patient specific prescription or order
- (c) high risk intermediate or stock solutions;
- (d) high risk level CSPs exposed longer than 12 hours at 2-8 °C (36-46 °F) before being sterilized; and
- (e) high risk level CSPs exposed longer than 6 hours at 8 °C (46 °F) before being sterilized.

(7) A pharmacy may not dispense a CSP ~~the-that~~ requires endotoxin testing until it receives endotoxin testing results within limits in accordance with USP <85>.

(8) A pharmacy shall conduct bacterial endotoxin testing in accordance with USP Chapter <85> and pyrogen testing per USP <151>.

(9) A pharmacy may conduct sterility and endotoxin testing internally, provided that personnel are trained through an accredited certificate program and the pharmacy utilizes an accredited laboratory to conduct sterility and endotoxin testing at least once per quarter.

(10) A pharmacy shall initiate an investigation and document a Corrective Action Preventative Action (CAPA) for any out of specification product testing results.

Comment [HAE92]: Prior board discussion

Comment [HAE93]: Removed requirement for third-party laboratory.

17.41: Storage and Beyond-Use-Dating (“BUD”)

(1) Unless otherwise prescribed in 247 CMR 17.00, a pharmacy may not exceed the following BUDs:

BUDs	Room Temp	Refrigerated	Freezer (Frozen Solid)
Low Risk*	48 hours	14 days	45 days
Medium Risk*	30 hours	9 days	45 days
High Risk	24 hours	3 days	45 days

(2) A pharmacy that prepares CSPs in a DCR shall apply BUDs in accordance with 247 CMR 17.18~~XX~~.

(3) The BUD assignment shall begin on the date the pharmacy prepared the CSP.

(4) A pharmacy may not exceed BUDs unless it has scientific evidence that the CSP remains potent, stable, and sterile under specified storage conditions for the duration of the BUD. Such evidence may be from relevant and reliable sources or direct testing.

(5) A pharmacy may not assign a BUD to a low or medium risk level CSP that is greater than 90 days from the date of compounding.

(6) A pharmacy may not assign a BUD to a high risk level CSP that is greater than 45 days from the date of compounding.

Comment [HAE94]: Stakeholder feedback

(7) In the event the storage condition of a CSP is changed, a pharmacy shall assign a new BUD that does not exceed the original BUD or the maximum BUD for the new storage temperature, whichever period is shorter.

(8) A pharmacy may not assign a BUD to a CSP that exceeds the expiration date of any component or BUD of any intermediate or stock solution CSP used to produce the final patient CSP.

(9) A pharmacy shall utilize freezer units that freeze CSPs to a frozen solid state and validate that microbial growth has been suspended for frozen CSP's.

17.42: Packaging and Preparation Containers

DRAFT

A pharmacy shall validate through direct testing at least annually, the impact on product sterility, stability, potency, container/vial membrane, and container closure systems when freezing and thawing CSPs.

17.43: Master Formulation Records

(1) A licensee shall maintain and follow a master formulation record for the following types of CSPs:

- (a) high risk CSPs;
- (b) CSPs with extended BUDs;
- (c) CSPs compounded in anticipation of a patient specific prescription or order;
- (d) allergen extracts as CSPs;
- (e) media fill challenge testing; and
- (f) CSPs prepared by a sterile compounding robot.

(2) A pharmacy shall validate each master formulation record to ensure CSPs compounded pursuant to that master formulation record are stable and sterile and have the correct potency. A pharmacy shall conduct the validation:

- (a) upon the first use of the master formulation record;
- (b) at least annually for low and medium risk CSPs;
- (c) at least quarterly for high risk CSPs; and
- (d) upon any change in product, process, equipment, or supplies.

(3) A pharmacy shall utilize a qualified professional to conduct the stability, sterility, and potency tests.

Comment [95]: Stakeholder feedback

Comment [96]: Stakeholder Feedback
Changed "vendor" to "professional"

(4) A master formulation record shall include:

- (a) the risk level of compounding;
- (b) all ingredients;
- (c) detailed compounding processes;
- (d) BUD assignment;
- (e) all equipment;
- (f) the primary and secondary engineering controls utilized;
- (g) product testing including sterility, stability, and potency, as applicable;
- (h) quality control procedures including final release checks;
- (i) depyrogenation and sterility procedures and validations, as applicable;

DRAFT

- (j) compounding personnel;
- (k) garbing protocol;
- (l) endotoxin limit, **as applicable**;
- (m) storage conditions; and
- (n) container closure system.

17.44: Compounding Record

(1) A compounding record shall include:

- (a) official or assigned name, strength, and dosage of the preparation;
- (b) reference to the master formulation record, if applicable;
- (c) any deviation to the master formulation record, if applicable;
- (d) names and quantities of all ingredients;
- (e) all calculations;
- (f) sources, lot numbers, and expiration dates of all ingredients and components;
- (g) total quantity compounded;
- (h) name of the person who prepared the preparation and name of the pharmacist who verified the preparation;
- (i) identity of any automated compounding device, if applicable;
- (j) date and time of preparation;
- (k) lot number, if applicable;
- (l) prescription or order number;
- (m) assigned BUD; and
- (n) duplicate patient prescription label;

(2) The compounding record shall serve as the accountability documentation described in M.G.L. c. 112, §§ 39D & 39F.

(3) A licensee shall complete a compounding record each time he/she prepares a CSP. The licensee shall review the compounding record for accuracy and completeness. A pharmacist shall verify the compounding record prior to releasing to inventory or dispensing the CSP

(4) A pharmacist shall verify the compounding record followed the master formulation record, if applicable, to ensure that errors did not occur in the compounding process and that the preparation is suitable for use.

Comment [HAE97]: New

17.45: Verification of Compounding Accuracy; Release Checks

(1) A pharmacist shall perform a release check and shall verify:

- (a) correct fill volume and quantity;
- (b) drug identity and strength;

DRAFT

- (c) the CSP matches the compounding record, master formulation record, and prescription or order, **as applicable**;
 - (d) the ingredients measured during compounding;
 - (e) packaging;
 - (f) labeling; and
 - (g) expected physical appearance.
- (2) After compounding is completed, a pharmacist shall visually examine each CSP for the presence of particulate matter with a lighted white and black background or high intensity LED light, unless the CSP is light sensitive.
- (3) A pharmacist shall visually inspect CSPs for container closure integrity and any other potential defect.
- (4) If CSPs are not distributed immediately after compounding and are stored in the pharmacy, a pharmacist shall perform a pre-release check prior to dispensing to ascertain container defects, damage, particulates, or other unexpected and undesirable circumstance.
- (5) In the event a CSP does not pass a release check, the pharmacy shall:
- (a) **quarantine the CSP**;
 - (b) perform a root cause analysis; and
 - (c) document the results of the root cause analysis and remediation plan.

Comment [B98]: Prior Board: Comacchio
Add remediation plan Board

17.46: Labeling

In addition to standard prescription labeling requirements, a pharmacy shall include the following information on the label or container of each CSP:

- (1) **Beyond Use Date (“BUD”);**
- (2) **batch or lot number of anticipatorily prepared CSPs;**
- (3) **storage and handling information; and**
- (4) **the statement, “this is a sterile compounded drug preparation.”**

17.47: Inventory Storage and Handling; Delivery of CSPs

- (1) A pharmacy shall **ensure** the methods used to transport CSPs from the pharmacy to the patient do not damage the CSP and maintain appropriate temperatures during transit.
- (2) A pharmacy shall store finished CSPs and drug components separate from food or specimens.

Comment [99]: Stakeholder Feedback

DRAFT

(3) A pharmacy shall verify that packaging, containers, and materials maintain physical integrity, sterility, stability, and purity of CSPs.

17.48: Drug Utilization Review and Patient Counseling

(1) A pharmacist or pharmacy intern shall perform a Drug Utilization Review in accordance with 247 CMR 9.XX.

(2) In addition to the counseling described in M.G.L. c. 94C, § 21A, counseling on a CSP shall include the proper use, possible side effects, storage, handling, and disposal of the medication, as applicable.

Comment [100]: Hospitals are exempt from counseling inpatients - MGL 94C

(3) A pharmacist or pharmacy intern shall instruct the patient or the patient's agent to report any adverse event related to the CSP to the compounding pharmacy.

(4) A pharmacist or pharmacy intern shall instruct the patient or patient's agent to observe and report any changes in the physical characteristics of the CSP to the pharmacy.

Comment [HAE101]: Previously below in defective product section.

17.49: Quality Assurance ("QA") Program

A pharmacy shall maintain a formal, written Quality Assurance Program in accordance with USP <1163> and 247 CMR 15.00.

17.50: Sterile Compounding Policies and Procedures

A pharmacy shall maintain a written policy and procedure pertaining to the following:

- (1) personnel monitoring, including gloved fingertip/thumb sampling and media fill challenge testing;
- (2) environmental monitoring, including non-viable air and viable air and surface testing;
- (3) ISO classified area monitoring, including airflows and pressure differential monitoring and temperature and humidity monitoring;
- (4) proper storage, handling, shipping, packaging, transportation, and delivery of CSPs;
- (5) final release checks and verification of all CSPs;
- (6) Quality Assurance Program, including RCA and CAPA;
- (7) change control, including planning, implementation, and validation of new or changed facilities, equipment, or processes;

DRAFT

- (8) hand hygiene and garbing processes;
- (9) aseptic technique;
- (10) patient monitoring in response to suspected or identified problems with CSPs or reported adverse events;
- (11) maintenance, calibration, and cleaning intervals for all pieces of equipment;
- (12) patient monitoring and adverse event reporting;
- (13) response (i.e. spill kit) to broken, damaged, or spilled CSPs;
- (14) compounding procedures specific to each risk level;
- (15) sterilization and depyrogenation processes, as applicable;
- (16) sterility and endotoxin testing, as applicable; ~~and~~
- (17) assignment of BUD;
- ~~(18) proper waste handling and disposal.~~

17.51: Defective Products

- (1) A pharmacy shall immediately recall any CSP that is contaminated or defective or suspected to be contaminated or defective.
- ~~(2) A pharmacist or pharmacy intern shall instruct the patient or the patient's agent to observe and report any changes in the physical characteristics of the CSP to the compounding pharmacy.~~