

## 247 CMR BOARD OF REGISTRATION IN PHARMACY

### 247 CMR 17.00: STERILE COMPOUNDING

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#### 17.01: Authority and Purpose

247 CMR 17.00 is promulgated under the authority granted to the Board by M.G.L. c. 112, §§ 39F, 39G, 39I, 39J, and 42A. The purpose of 247 CMR 17.00 is to establish minimum professional standards for sterile compounding in order to safeguard the public health and welfare. 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: Licensure Requirements

- (1) A pharmacy that performs sterile compounding, including veterinary compounding, shall hold a separate license for sterile compounding in accordance with M.G.L. c. 112, §§ 39G, 39I, and 39J.
- (2) Any pharmacy licensed by the Board may not simultaneously hold an outsourcing facility registration issued by the U.S. Food and Drug Administration (FDA) pursuant to 21 U.S.C. § 353b.

17.03: General Requirements

- (1) A pharmacy licensed by the Board that performs sterile compounding, including veterinary compounding, shall comply with all state and federal laws and regulations and all chapters of the most current United States Pharmacopeia (USP).
- (2) A pharmacy shall maintain written policies and procedures on all aspects of the sterile compounding operation and a formal, written Quality Assurance Program in accordance with USP <1163>.
- (3) A pharmacy shall maintain a written policy and procedure requiring the immediate recall of any Compounded Sterile Preparation (CSP) that is contaminated or defective or suspected to be contaminated or defective.
- (4) A pharmacy shall maintain a written continuity of care plan that describes how patient needs will be met in the event the pharmacy is unable to compound or dispense CSPs.
- (5) A pharmacy may not prepare CSPs identified as demonstrably difficult to compound by the FDA or the Board.
- (6) A pharmacy may not utilize lyophilization equipment to prepare lyophilized drug substances or ingredients.
- (7) A pharmacy shall only utilize commercially available sterile, depyrogenated containers and container-closure systems, if available.
- (8) A pharmacy may not compound non-sterile preparations in any Primary Engineering Control (PEC) or Secondary Engineering Control (SEC) used for sterile compounding.
- (9) A pharmacy shall maintain a written policy and procedure for the immediate and systematic response (i.e., spill kit) to broken, damaged, or spilled containers involving a patient's blood-derived or other biological material.
- (10) A corrective action plan must be implemented and documented in response to any out-of-specification result associated with environmental monitoring (EM), personnel testing, or product testing.

17.04: General Facility Requirements

- (1) A pharmacy shall ensure that any pass-through chambers:
  - (a) have an interlocking door design; and
  - (b) are not refrigerator units.
- (2) A pharmacy shall have a dedicated changing area for sterile compounding personnel.

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- (3) A pharmacy may not use International Standards Organization (ISO) Classified areas for drug storage.

### 17.05: Heating, Ventilation, and Air Conditioning (HVAC) Systems

- (1) Newly constructed ISO Classified SECs shall utilize a closed loop ducted system, a sealed plenum system, or equivalent HVAC design.
- (2) Except for planned or unplanned service interruptions, a pharmacy shall ensure HVAC systems operate 24 hours per day, 7 days per week.
- (3) Supply air for each ISO Classified SEC shall be provided exclusively through ceiling mounted high-efficiency particulate air (HEPA) filters.
- (4) Air returns in ISO Classified SECs shall be mounted low on the walls.
- (5) If utilized, relief air vents shall be mounted low on the wall and designed to prevent the ingress of less clean air or contaminants from adjacent areas.
- (6) A pharmacy shall maintain a written policy and procedure describing the manner in which it investigates, responds to, and seeks to prevent temperature, humidity, and differential pressure excursions.

### 17.06: Primary Engineering Controls (PEC) including Containment Primary Engineering Controls (C-PEC)

- (1) A pharmacy shall utilize only commercially manufactured PECs.
- (2) Except for planned or unplanned service interruptions, a pharmacy shall operate each PEC 24 hours per day, 7 days per week.
- (3) A pharmacy may not locate any equipment or supplies within any PEC unless it is essential to the compounding process.

### 17.07: Secondary Engineering Controls (SEC)

- (1) Secondary Engineering Controls  
SECs include buffer rooms, anterooms, other ISO Classified areas, Segregated Compounding Areas (SCA), and Containment Segregated Compounding Areas (C-SCA)
  - (a) Each newly constructed SEC shall allow for visual observation through windows or technology.
  - (b) Unless prohibited by local building or fire code, an SEC may not have more than one door to immediately adjacent areas.

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- (c) The doors leading into and between ISO Classified SECs shall be constructed with an interlocking design or utilize an alternative method to ensure that doors are not opened simultaneously.
  - (d) A pharmacy shall limit activities in any SEC to those essential for the preparation of CSPs.
  - (e) A pharmacy may not locate a refrigerator in any ISO Classified SEC.
  - (f) SECs may not contain floor drains.
  - (g) SECs shall utilize light fixtures designed for sterile compounding areas (i.e., cleanroom grade) that have an exterior surface that is smooth, mounted flush with the ceiling, and sealed.
  - (h) Ceiling panels, fixtures, and other penetrations through the ceiling or walls shall be smooth and sealed around the perimeter.
  - (i) Sprinkler heads shall be recessed, covered, and easily cleanable.
  - (j) Walls shall be made of solid surface materials such as locking sealed panels or epoxy-coated gypsum board.
  - (k) SECs may not contain windows to the outdoors.
  - (l) Floors shall be composed of wide sheet vinyl that is heat sealed at the seams, or other solid, smooth surface, and coved at the wall or appropriately sealed.
- (2) Buffer Rooms
- (a) A newly constructed non-hazardous drug buffer room shall be at least 100 square feet.
  - (b) A newly constructed hazardous drug buffer room shall be at least 72 square feet.
  - (c) Buffer room doors shall be hands-free.
- (3) Anterooms and Other ISO Classified Areas
- (a) A newly constructed anteroom shall be at least 72 square feet.
  - (b) For hand hygiene, an anteroom shall have a stainless-steel sink that is located on the clean side of the line of demarcation at least one meter away from the buffer room door.
  - (c) The stainless-steel sink shall:
    - i. be equipped with hands-free controls for water and soap dispensing;
    - ii. have proper depth and capacity for hand washing up to the elbows;
    - iii. minimize splashing and dripping of water;
    - iv. be designed to prevent standing water; and
    - v. have a faucet that does not have an aerator mechanism on the nozzle.
  - (d) An anteroom shall have low-lint, disposable towels located in close proximity to the sink.
- (4) Segregated Compounding Areas (SCA) including Contained Segregated Compounding Areas (C-SCA)
- (a) A sterile compounding pharmacy or non-resident sterile compounding pharmacy may not use an SCA or C-SCA to prepare CSPs.
  - (b) An institutional sterile compounding pharmacy may utilize an SCA and / or C-SCA provided that only conventionally manufactured sterile starting components are used.

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- (c) An SCA and C-SCA shall:
- i. be a dedicated, closed room, with fixed walls and doors that is restricted to sterile compounding;
  - ii. be equipped with a hands-free door;
  - iii. have a stainless-steel sink meeting the requirements of 17.07(3)(c) that is dedicated for hand washing and is located immediately outside of the room or outside of a defined perimeter within the room; and
  - iv. have low-lint, disposable towels located in close proximity to the sink.

### 17.08: Certification of ISO Classified Areas

- (1) The Manager of Record or Designated Pharmacist-in-Charge shall review and sign certification reports for all ISO Classified areas and ensure completion of any identified actions.
- (2) The Manager of Record or Designated Pharmacist-in-Charge shall notify the Board, in the manner and format determined by the Board, of any certification failure.

### 17.09: Pressure Differential Monitoring

- (1) The quantitative results from the pressure-differential monitoring system shall be reviewed and documented at least once daily on all days the pharmacy is open, prior to engaging in compounding for the day, if applicable.
- (2) A pharmacy shall respond to out-of-range differential pressures in a timely manner and document the response.

### 17.10: Temperature and Humidity

- (1) SECs shall maintain a temperature of 68 degrees Fahrenheit (20 degrees Celsius) or lower.
- (2) SECs shall maintain a relative humidity of 60% or lower.
- (3) A pharmacy shall have a system to continuously measure the temperature and humidity of each SEC. The quantitative results shall be reviewed and documented at least daily on all days the pharmacy is open.
- (4) A pharmacy shall respond to out-of-range temperature or humidity levels in a timely manner and document the response.

### 17.11: Smoke Studies

- (1) A pharmacy shall conduct a smoke study of each:
  - (a) PEC and ISO Classified SEC upon initial certification;
  - (b) PEC upon recertification;

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- (c) ISO Classified SEC immediately following the remodeling or change in configuration or square footage; and
  - (d) PEC or ISO Classified SEC upon the permanent addition, relocation, or removal of any equipment.
- (2) A pharmacy shall ensure that a description and results of each smoke study are documented in a report.
- (3) A pharmacy shall investigate any failed smoke studies and document corrective actions.

### 17.12: Environmental Monitoring (EM)

- (1) A pharmacy shall develop an EM sampling plan for viable air and surface, and non-viable air testing in conjunction with a qualified professional such as a microbiologist, industrial hygienist, or infection control professional.
- (2) A pharmacy shall maintain a log for each environmental sampling occurrence.
- (3) In addition to any other circumstance as required by USP <797>, a pharmacy shall conduct routine:
- (a) viable air and surface, and non-viable air EM as part of any certification or recertification;
  - (b) viable surface EM at least once per month;
  - (c) viable surface EM at least weekly if sterile compounding involves the assignment of a Beyond Use Date (BUD) that requires sterility testing and / or terminal sterilization;
  - (d) viable and non-viable air EM at least once every three months; and
  - (e) viable and non-viable air EM at least once per month if sterile compounding includes any non-sterile starting components or involves the assignment of a BUD that requires sterility testing and / or terminal sterilization.
- (4) Personnel that perform EM sampling shall be properly trained and demonstrate competency and proficiency in all sampling techniques.
- (5) EM conducted as part of any certification or recertification shall be conducted by a qualified third-party professional.
- (6) A pharmacy shall utilize a two-plate method for collection of viable air and surface samples if sterile compounding includes any non-sterile starting components or involves the assignment of a BUD that requires sterility testing and / or terminal sterilization. One plate shall be a general growth medium, and the other plate shall be a medium that specifically supports the growth of fungus.
- (7) EM for viable organisms shall include negative controls.

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- (8) A microbiologist, or similarly qualified professional, shall identify to at least the genus level any microbial growth resulting from EM in an ISO Class 5 area or any action level growth in other ISO Classified areas.
- (9) The Manager of Record or Designated Pharmacist-in-Charge shall review and sign the documented results of each EM sampling occurrence and ensure prompt remediation when required.

### 17.13: Environmental Monitoring Action Levels

- (1) A Manager of Record or Designated Pharmacist-in-Charge shall notify the Board, in the manner and format determined by the Board, of any action level EM results.
- (2) Action levels shall be defined by USP <797> or Board policy, whichever is stricter.
- (3) A pharmacy shall immediately respond to and properly remediate action level EM results.
- (4) A pharmacy shall maintain a written policy and procedure for response and remediation of action level EM results.

### 17.14: Cleaning and Disinfecting

- (1) A pharmacy shall document each cleaning and disinfecting event in a cleaning log. The log shall include the area, location, date, time, agents utilized, and personnel who performed the cleaning and disinfecting.
- (2) Only trained compounding personnel may clean inside an ISO Class 5 PEC.

### 17.15: Hand Hygiene and Garbing

- (1) In the dedicated changing area, compounding personnel shall change into clean, laundered scrubs that may only be worn within the facility.
- (2) Prior to entering an anteroom, SCA, or C-SCA, compounding personnel shall don dedicated shoes or shoe covers.
- (3) Once inside an anteroom, compounding personnel shall don shoe covers while crossing the line of demarcation.
- (4) After hand hygiene procedures are completed, compounding personnel shall don a:
  - (a) clean low-lint coverall; or
  - (b) sterile low-lint coverall if sterile compounding includes any non-sterile starting components or involves the assignment of a BUD that requires sterility testing and / or terminal sterilization.

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- (5) Prior to reengaging in compounding activities, compounding personnel shall repeat all hand hygiene and garbing activities if crossing the line of demarcation from the clean to the less clean side of the anteroom or leaving the sterile compounding area.

### 17.16: Training and Qualification

- (1) After initial qualification, garbing competency and a media-fill test followed by gloved fingertip/thumb sampling and surface sampling of the direct compounding area shall be performed by personnel who physically compound or directly supervise compounding:
  - (a) at least once every six months; or
  - (b) at least once every three months if sterile compounding includes any non-sterile starting components or involves the assignment of a BUD that requires sterility testing and / or terminal sterilization.
- (2) In the event an individual fails a written sterile compounding assessment exam, gloved fingertip/thumb sampling, media-fill test, or surface sampling, they may not compound until retrained and requalified.
- (3) Compounding personnel shall be retrained and requalified if a pause in sterile compounding practice exceeds six months.

### 17.17: Sterility and Endotoxin Testing

- (1) A pharmacy shall conduct sterility testing in accordance with USP <71> for any CSP that requires sterility testing and / or terminal sterilization based on the BUD assignment as specified in **247 CMR 17.18**.
- (2) A pharmacy may not dispense a CSP that requires sterility testing unless it first receives negative sterility test results.
- (3) A pharmacy shall conduct bacterial endotoxin assay testing in accordance with USP <85> for injectable CSPs if sterility testing is required by **247 CMR 17.17(1)**.
- (4) A pharmacy may not dispense a CSP that requires endotoxin testing unless it first receives endotoxin test results within the limits specified in USP <85>.
- (5) A pharmacy shall utilize a qualified laboratory (e.g., accredited, licensed, etc.) to conduct sterility and endotoxin testing.

### 17.18: Beyond Use Date (BUD)

A pharmacy shall assign BUDs in accordance with USP <797> or Board policy, whichever is stricter.

### 17.19: Master Formulation Records

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- (1) In addition to the requirements of USP <797>, a pharmacy shall also maintain and follow a master formulation record for the following:
  - (a) CSPs requiring sterility testing;
  - (b) CSPs undergoing terminal sterilization; and
  - (c) allergen extracts as CSPs.
- (2) A pharmacy shall verify that master formulation records are based on USP standards, any relevant scientific data, or direct validation testing to ensure that CSPs produced according to the master formulation record are sterile, stable, and have the correct potency for the assigned BUD. This verification must be performed initially and any time there is a change to the master formulation record.

### 17.20: Compounding Records

- (1) Each time it prepares a CSP, a pharmacy shall complete and maintain a compounding record that includes all elements as specified in the most recent version of USP <797> and in M.G.L. c. 112, § 39D for “accountability documentation”.
- (2) A pharmacist shall verify the compounding record and master formulation record as applicable, to ensure that errors did not occur in the compounding process and that the CSP is suitable for its intended use.

### 17.21: Labeling

A pharmacy shall label each CSP with the prescription labeling requirements of M.G.L. c. 94C, § 21 and USP <797>.

### 17.22: Counseling

- (1) In addition to the counseling requirements in 247 CMR 9.00, a pharmacist or pharmacy intern shall instruct the patient or patient’s agent to report to the pharmacy any changes in the physical characteristics of the CSP, or any adverse event resulting from the CSP.
- (2) 247 CMR 17.22(1) does not apply to any CSP dispensed for administration in a nursing home or other inpatient or outpatient facility, unless otherwise required by law or regulation.