MEMORANDUM

Date: September 12, 2013

To: CCA Clients

From: Tim Loughran

Re: Sterile Compounding Pharmacies

Following is my review and opinion on regulations related to Sterile Compounding Pharmacy facility construction requirements.

FDA Guidance on Pharmacy Compounding:

FDA will generally defer to state authorities. Violations related to activities normally associated with a drug manufacturer may lead to FDA enforcement. ("Guidance for FDA Staff and Industry, Compliance Policy Guides Manual, Sec 460.200, Pharmacy Compounding," 6/7/2002)

State Licensing per CMR 247 6.0

State licensing for a pharmacy or for a compounding pharmacy occurs by application of a registered pharmacist to operate a pharmacy.

General facility requirements per CMR 247 6.0

1. A private patient consultation area that is available without traversing stockroom or dispensing area
2. A prescription area of minimum 300 sf
3. Equipment as required by USP
4. Various other paper record and related items
5. A sink near prescription filling area
6. For a "central intravenous admixture service," a clean room is required as follows:
    a. Minimum work area of 72 sf
    b. Closed on all sides except for a door and a passage opening
    c. Laminar flow hood
    d. Continual positive pressure except if hood is self-venting
    e. Located directly adjacent to prescription area

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Some states require performance in accordance with USP 795 for non-sterile compounding, and 797 for sterile compounding per the recent Advisory. The Board recommends use of the "Gap Analysis Survey," a checklist.

Agencies strongly advised need for touch free doors and touch free hand sink, doors not made of wood, and an airlock for doors into negative pressure areas. The "airlock" could just mean an anteroom.

USP 797 for sterile compounding facility requirement are as follows:

Client Risk Determination

Client is to determine compounding risk: immediate, low, low with 12 hour use, medium, or high. These categories relate to length and temperature of storage. The "risk" is risk of contamination.

Client also is to determine if hazardous drugs such as for chemotherapy are to be used, and if radiopharmaceuticals are to be used.

Non-hazardous drugs

Ante room:

1. ISO 8 (Class 100,000) for non-hazardous drugs. See below for hazardous drugs, ISO 7.

Buffer area:

2. ISO 7 (Class 10,000).
3. Typically temperature 20 degrees C or cooler for comfort.
4. Physical separation—wall and door—between buffer and ante areas needed for high risk areas. Also recommended in any case, since HVAC requirements are otherwise difficult to achieve.
5. Non hazardous buffer area: positive pressure relative to ante area, .02-.05" water. See below for hazardous drugs with negative pressure.
6. Minimum 30 air changes per hour through HEPAs for buffer area and ante room. 15 of those may be through the PEC below.
7. HEPA supply to be in ceiling, returns low on wall.
8. HEPAs to be leak tested in situ.
9. No equipment allowed in buffer area except as required for compounding.
10. No sinks or floor drains in buffer area.

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11. Ceilings to wall to be coved or caulked. Ceiling panels to be impregnated with a polymer, and sealed to support frame.
12. Walls may be polymer sealed panels or epoxy GWB.
13. Floors to be coved to walls, preferably wide sheet vinyl with heat welded seams.
14. Lighting lenses to be sealed.

Primary Engineering Control (PEC) is to be a BSC (biological safety cabinet), laminar airflow workbench, or CAI/CACI (compounding aseptic containment isolator) where the compounding is performed:

1. It is located in the buffer area.
2. The work chamber is to be ISO 5, HEPA filtered, confirmed with in situ smoke studies.
3. Needs to be out of traffic flow and in manner to avoid disruption from HVAC and room cross-drafts.
4. Certain exceptions allow CAI/CACI not in a buffer area.
5. Additionally, low level risk compounding with 12 hour Before Use Date (BUD) may be in a segregated compounding area that is not in a buffer area.

Hazardous Drugs

1. Storage: shall be stored separately from other inventory, preferably under negative pressure with 12 air changes per hour.
2. Ante room: ISO Class 7, and can be common to non-hazardous drug buffer area.
3. Hazardous buffer area: negative pressure relative to ante area, .01" water, with pressure indicator.
4. Buffer area to be separated from other prep areas.
5. Hazardous primary engineering control (PEC): To be a BSC or CACI in a buffer area. Preferably 100% exhausted directly to exterior through HEPA filtered exhaust.
6. Use of closed-system vial-transfer devices (CSTDs) is preferred in the BSC or CACI.
7. Under certain exceptions, CACI may be outside a buffer area.
8. NIOSH hazardous drugs guidelines ("Alert: Preventing Occupational Exposure to Antineoplastic and Other Hazardous Drugs in Health Care Settings," 2004) are to protect personnel. It includes a recommendation for storage to have a dedicated emergency exhaust fan (p. 12).

Radiopharmaceuticals

Radiopharmaceuticals are addressed in USP 823, except that 797 applies to further handling once released as a finished product.

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