The United States Pharmacopeia (USP) is a non-profit organization founded in 1820 by a group of physicians. It sets standards for identity, strength, quality, and purity of medicines and is enforced by the Food & Drug Administration (FDA).

**Background**

- The purpose of USP 797 is a general protection of sterile compounds and spaces from contamination.
- First published in 2004
- Latest revision released in 2008
- Revision will be harmonized with USP 800
  - Anticipated to be published June 1, 2019
  - Becomes official on December 1, 2019

**USP 797 - Sterile Compounding**

- USP 797 expands controls for the protection of workers and environments against hazardous drug compounds.
- Based on published reports of adverse effects in healthcare personnel from exposure to hazardous drugs, USP 800 was developed.
- First published for public comment in March 2014
- Will be harmonized with USP 797
  - Becomes official on December 1, 2019

**USP 800 - Hazardous Drug Handling**

- USP 800 expands controls for the protection of workers and environments against hazardous drug compounds.
- Based on published reports of adverse effects in healthcare personnel from exposure to hazardous drugs, USP 800 was developed.
- First published for public comment in March 2014
- Will be harmonized with USP 797
  - Becomes official on December 1, 2019
Compounding Pharmacies

Required Upgrades – USP 800 Compliance

- In containment primary engineering control devices (C-PEC) must be located in a room that will function as a secondary engineering control (C-SEC) with an ISO Class 7 rating
- Minimum room pressure differential relative to adjacent spaces
  - -0.01-0.03 in w.c. Buffer Rooms
  - +0.02 in w.c. Ante Rooms
- At least 12 air changes per hour
- Must be directly ventilated outside

Compounding Pharmacies

Required Upgrades – USP 800 Compliance

- HD storage areas are subject to the same negative air pressure requirements.
- HDs must be stored and prepared in areas separate from areas where non-HDs are similarly handled
- Exemption permitted under USP 797 that allowed small volumes of HDs to be compounded in the same areas as non-HDs has been eliminated.

Compounding Pharmacies

Concerns

- Cost
  - New equipment
  - Changes to facility design
  - Separation of HD/non-HD compounding
  - May require outside assistance/consulting
  - More frequent monitoring – more $ if performed by outside entity
- Time
  - More frequent environmental sampling
  - More frequent personnel assessment
  - More documentation/record-keeping
Compounding Pharmacies

Applications

• Considerations
  – Type of isolation (Airflow direction)
    • Buffer Rooms
    • Anterooms
  – Types of Compounding
    • Sterile (require 30 ACPH)
    • Non-Sterile (require 12 ACPH)
Compounding Pharmacies

Applications

• Compounding Sterile Preparation (CSPs)
  – A substance (medication) that is not commercially available in the strength, concentration or form needed for a specific patient
• Hazardous (Harmful) Drug (HD’s)
  – Any Drug identified as hazardous or potentially hazardous on the basis of at least one of the following criteria
    • Carcinogenicity
    • Teratogenicity or developmental toxicity
    • Reproductive toxicity in humans
    • Organ Toxicity at low doses in humans or animals
    • Genotoxicity
    • New drugs that mimic existing HDs in structure or toxicity

Compounding Pharmacies

Applications

• Biological Safety Cabinet (BSC)
  – An inflow ventilated cabinet often used for preparations of hazardous drugs. Divided into 3 classes (Class 2 is divided in 4 types)
• Laminar Airflow Work Bench (LAFW)
  – An inflow or outflow work bench typically used to protect either a compounded substance, or employee
• Compounding Aseptic Containment Isolator (CACI)
  – Designed to provide worker protection from undesirable levels of airborne drugs though out the compounding and material transport process. Air exchange with the surrounding environment should not occur unless the air is first passed through a microbial retentive filter system capable of containing airborne concentrations of the physical size and state of the drug being compounded.

Compounding Pharmacies

Applications

• Non Sterile Pharmacy

Contact: Antec Controls

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Air Distribution – Fan Filter Units

- Fan Filter Units
  - Diffuser with integral filters and motor/blower assemblies
  - Ducted inlets, or open to pressurized plenum
  - Ideal for renovation and expansion projects

Advantages of FFU’s in Cleanrooms
- Smaller air handling unit (AHU)
- Redundancy
- Negative pressure plenum design
  - No ceiling by-pass leakage
  - Less expensive ceiling system
**Critical Environment Air Distribution**

**Fan Filter Units**

- Laminar Diffusers - Ducted Supply/Return

**Critical Environment Air Distribution**

**Fan Filter Units**

- Negative Pressure Plenum with Fan Filter Units

**Critical Environment Air Distribution**

**Fan Filter Units**

- Negative Pressure Plenum with Fan Filter Units
Critical Environment Air Distribution

Pharmacy and Cleanrooms

- Cleanrooms – ISO 14644
- Compounding Pharmacies – USP 797/800 – ISO 14644

ISO 14644-1 Cleanroom Standards

<table>
<thead>
<tr>
<th>Class</th>
<th>20.1 μm</th>
<th>20.2 μm</th>
<th>20.3 μm</th>
<th>20.4 μm</th>
<th>20.5 μm</th>
<th>21 μm</th>
<th>25 μm</th>
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US FED STD 209E Cleanroom Standards

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Critical Environment Air Distribution

Pharmacy and Cleanrooms

- Compounding Pharmacies (USP 797)
  - High air change requirements
  - Design strategy to minimize costs
    - Primary Environment Control – ISO Class 5
    - Buffer Areas – ISO Class 7
    - Anteroom – ISO Class 8
• ISO 5 typically not for entire room – Laminar Air Flow Workbench (LAFW) used instead.
• Buffer Area – ISO 7
• Anteroom – ISO 8

**FFU**


<table>
<thead>
<tr>
<th>ISO Cleanroom Class</th>
<th>ISO Equivalent Class</th>
<th>Air Changes per Hour</th>
<th>Ceiling Coverage</th>
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<td>5 – 15%</td>
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<tr>
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<tr>
<td>8</td>
<td>8 (Class 100)</td>
<td>5 – 20</td>
<td>5 – 15%</td>
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<tr>
<td>9</td>
<td>9 (Class 1000)</td>
<td>5 – 10</td>
<td>5 – 15%</td>
</tr>
<tr>
<td>10</td>
<td>10</td>
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<tr>
<td>100</td>
<td>100</td>
<td>5 – 1</td>
<td>5 – 15%</td>
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</table>

**FFU**

• Used as recirculation device
Critical Environment Air Distribution

FFU
• Used as recirculation device, mixed w/ primary air

Air Distribution – Fan Filter Units
• Mixing plenum on FFU inlet (blend supply and return)
  – Non-Hazardous pharmacies

Compounding Pharmacies

Air Distribution – Fan Filter Units
• LED Indicators
  – All is normal, green light
  – Filter pressure drop exceeds limit (FL), orange light
  – Motor has stopped working (ML), red light
Air Distribution – Fan Filter Units

• Aerosol Test System (ATS)
  – Room-side challenge to validate filter integrity
  – Eliminates the need to enter plenum space
  – Integrated 3/8” NPT fitting

• BACnet Control and Monitoring
  – Simple daisy chain connections
  – New benchmark for control and visibility
    • Airflow monitoring and control
    • Filter pressure drop and runtime
    • Motor status and runtime
Airflow Control Valves

Compounding Pharmacies

- Considerations
  - Mechanical Operation
  - Flow and Pressure Ranges
  - Control Methods
  - Control Accuracies
  - Speed of Response
  - Maintenance
  - Sound
  - Coatings

- Mechanically Pressure Dependent
  - Terminal Unit (VAV)
  - High Accuracy Terminal (HAT)

- Mechanically Pressure Independent
  - Venturi Valve (VV)
### Compounding Pharmacies

**Airflow Control Valves**

- **Standard Accuracy Damper Control Valve**
  - Direct airflow measurement using in-stream flow sensors that utilize velocity pressure.
  - Typical 6:1 turndown ratios.
  - Typically require three duct diameters of straight duct leading into and out of the valve.

- **High Accuracy Damper Control Valve**
  - Direct airflow measurement using velocity pressure, vortex shedding sensors, or thermal dispersion.
  - Typical 10:1 turndown ratios.
  - Typically require one duct diameters of straight duct leading into and out of the valve.

- **Venturi Valves**
  - Electronic flow feedback.
  - Mechanical pressure independent control valves.
  - Typical 16:1 turndown ratio.
  - No straight inlet/outlet duct run requirements.
Compounding Pharmacies

Room Pressure Control Strategies

- Air movement from clean to less clean spaces
- Offset between supply and exhaust
- Tightly sealed room

Airflow Offset Control
- Maintains a constant CFM offset between supply and exhaust valves
- Independent of room pressure
- Most common solution
Compounding Pharmacies

Room Pressure Control Strategies

Pressure Control
• Airflow control setpoint based on room pressure
• Less common approach

Room Pressure Control Strategies

Hard Balance Exhaust
• Simple and stable method of achieving temperature control, offset, and air change rate
• Cannot manage changes in duct pressure or fan operation
• Uncommon approach in modern pharmacies

Compounding Pharmacies

Summary

• USP 797 - standard for sterile compounding
• USP 800 - standards for handling of hazardous drugs in healthcare settings
• Enforceable on December 1, 2019