Designing, Building, and Maintaining a Compliant Sterile Compounding Facility
Focusing on incorporating USP <800> Requirements

- NCHEA Spring Seminar
- March 2018

Presented by Leach Wallace Associates, Inc.
Outline of discussion

- Brief Introduction of Standards
- USP <800>
- Planning & Project Development
- Design requirements
- Architectural
- MEP
- Design example
- Considerations for Management
USP Compounding Compendium
USP <795>, <797>, and <800>

- Standards for preparing compounded sterile drugs to ensure patient safety
- <795> Nonsterile drugs
- <797> Sterile drugs

- Standards for safe handling of hazardous drugs to focus on worker safety
- <800> Hazardous drugs
Current Status

- USP <797> latest release which is enforceable was made official on June 1, 2008.
- Significant comments were received on the first release of a proposed revision for public comments during the Sept 2015 to Jan 2016 review.
- Revision to USP <797> is due to be published in Sept/Oct 2018 for second round of public comment.
- USP <800> was postponed to align with the next official release date of USP <797>.
- Anticipated to become “official” December 1, 2019
USP <797> Changes with Engineering Controls

- Removal of references to Hazardous Drugs
- Defined Temperature & Relative Humidity Requirements
  - $20^\circ\text{C}$ (68°F) or cooler
  - $<60\%$ RH
- No in-room humidifiers or de-humidifiers
- Defined interval for Environmental Monitoring - Monthly
USP <800> Hazardous Drugs in Healthcare Settings

- Purpose: describe practice and quality standards for handling hazardous drugs in healthcare settings
- Patient safety
- Worker safety
- Environmental protection
USP<800> History

General Chapter <800> History-

- Part of USP<797> 2004, 2008
- March 2014- 1st revision published for comment
- October 2015- 2nd revision published for comment
- Original expected date of recognition was February 1, 2016 Official grace period.
- Each State Board of Pharmacy will determine effective date-TBD
Areas of coverage

- Product transport
- Storage
- Compounding
- Preparation
- Administration
Where does it apply?

- All healthcare personnel that handle HD preparations
- Pharmacies
- Hospitals
- Other healthcare institutions
- Cancer centers
- Patient treatment clinics
- Physicians practice facilities
Enforcement

- State Pharmacy boards
- State Regulators
- FDA
- Other government authorities
- JHACO

- USP does not enforce standards
Overall Regulatory Trends

- Expectation of existing facility improvements
- Documented State of Control verified by data
- Boards of Pharmacy want self-reporting of adverse events
- Regulators expecting compliance—Pharmacies tasked with creation/maintenance of Quality Program to maintain compliance (FDA-like mentality).
- USP chapters on compounding are federally recognized as the standard of practice in the U.S.
Planning & Project Development
Planning and Project Development

- Assembling the team
- Determine project scope and goals
- Review considerations
- Program development
- Design

- Construction
- Commissioning
- Testing and Certification
- Maintenance of facility
- Compliance model
Assembling the team

- Pharmacy staff
- Pharmacy Consultant
- Safety Officer
- Infection Control
- Facilities
- EVS
- Administration
- Architect
- Engineer
- Others…..
Determine project scope and goals

- Procedures
- Maintainability
- Cost/Budget
- Standard operating modes
- Emergency plans
- Certification Standard
- Compliance methodology
- Environment
- Expectations vs results
Challenges/Considerations

- Square footage requirements and thorough analysis of personnel and material workflows critical in design/redesign process
- Renovation vs. New Construction
- Dedicated Exhaust and/or HVAC Systems
- Back Up Power
- Temperature/Relative Humidity requirements
- Pressurization
- Detailed understanding/completion of SOPs prior to facility completion - cleaning, EM
- Commissioning/As-Built verification
Other Considerations

- Risk assessment
- Personnel training
- Personal Protective Equipment (PPE)
- Facilities and Engineering Controls
- Environmental Quality and Control – Environmental monitoring (lab spaces, break rooms, retail space)
- Medical Surveillance
Design Requirements
Temperature and humidity
Positive pressure
Negative pressure (Hazardous Drugs)
Air changes
Cleanable surfaces
Sealed wall and ceiling junctures
Appropriate equipment and essential activities only
Facility Requirements - Equipment

- C-SEC – Containment Secondary Engineering Control
- Room envelope that maintains negative pressure with appropriate air changes
- C-PEC - Containment Primary Engineering Control
- Hood or Cabinet
- Hood and HEPA filter certification at 6 month intervals
- Calibration
- SOPs
- Documentation
Facility Requirements-Cleaning

- Specifies procedures for routine cleaning, decontamination, deactivation and disinfection of the room(s) and Containment-Primary Engineering Controls (C-PEC)/Hoods.
- Details location of dedicated cleaning equipment- no mop sinks!
- If EVS closet is located off anteroom-pressure monitor is highly recommended
- Must be considered when selecting floor and millwork finishes
Environmental Quality & Control

- Air Quality
- Differential Pressure
- Surface Testing
- Temperature and Humidity
- Action and Alert limits
Example: Monitoring of Temperature and Humidity

- Data logger.
- Continuous monitoring through ATC system.

- Setpoints
- Alarm points
- Trend data
What happens if the design temperature is 68 degrees and the temperature sensor says 68.2 degrees?

“These facilities shall also provide a comfortable and well lighted working environment, which typically includes a temperature of 20 degrees (68 degrees F) or cooler, to maintain comfortable conditions for compounding personnel to perform flawlessly when attired in the required aseptic compounding garb.”
- Is it due to sensor calibration?
- Duration of temperature differential?
- Causes of temperature differential?
- Alarm?
- Action?
- Report per Quality Control Plan?
Architectural Considerations
USP <800> Facility Design

- Restricted access
- Unpacking
- Storage
- Spills
- Non sterile and sterile compounding
- No Positive Pressure Areas for Hazardous Drugs
USP <800> Facility Requirements

- Compounding areas away from breakrooms, refreshment areas, staff, patients, or visitors.
- SEPARATE designated areas shall be available for:
  - Unpacking HDs*
  - Non sterile HD Compounding
  - Sterile HD Compounding
  - Storing HDs (unless buffer area is used)
USP <800> Storage

- Storage (unpacking) room must be negative pressure, 12 ACH, and vented outside.
- Cannot store on floors.
- HDs stored in manner to prevent breakage or spillage.
- Substantial challenge for most pharmacy floor plans.
- Specified PPE
Hazard Communication Program

- Required by OSHA
- Employers required to establish policies and procedures to ensure worker safety in all aspects of distribution of drugs as part of OSHA Hazardous Communication Standard (HCS)
- Specifies PPE for each activity associated with receiving, handling, stocking, compounding, administering, clean up, and spill remediation.
Cleaning

- Specifies procedures for routine cleaning, decontamination, deactivation and disinfection of the room(s) and Containment-Primary Engineering Controls (C-PEC).

- References Cleaning Section of USP <797>

- Specifies PPE

- Must be considered when selecting floor and millwork finishes
USP <800>
Challenges/Considerations

- Square footage requirements and thorough analysis of personnel and material workflows critical in design/re-design process
- Renovation vs. new construction
- Dedicated Exhaust and/or Air Handling Systems
- Temp/RH
- Segregated Storage in its own room
- External venting- hoods/rooms
- Differential Pressure requirements
- Detailed understanding/completion of SOPs prior to facility completion- cleaning, EM
- Commissioning/As-Built verification
Architectural Considerations

- Prefabricated clean rooms vs site build out
- Seamless Flooring
- Drywall Ceilings
  - Eliminate or minimize access panels
- Door Sweeps/Seals
- Pass-Throughs (Sealed)
- Sink Locations
- Eyewash Locations
- Powered Door Operators
MEP Considerations
Electrical Design Requirements

- Emergency Power
- Critical or Equipment branch
  - HEPA Fan-Powered Filter Modules
  - Chemo Hood
  - Chemo Hood Exhaust Fan
  - USP <800> Room Exhaust Fan
  - Room Pressure Monitors
  - Sealed Lighting Fixtures
  - Refrigerators
  - Security System devices
  - Pharmacy equipment
General Pharmacy Design Criteria

- 4 Air changes per hour
- 2 Outside air changes per hour
- Positive pressurization
- Negative pressurization (HD areas)
- Temperature 65°-70°F
- RH < 60%
HVAC Design Options

- ISO 7 Clean Room
  - Compounding within an ISO 5/Class 100 Clean Room
    - Room Air Change Requirements
    - Provide “House” airflow for cooling loads and pressurization requirements
    - Air Change Requirements provided by ceiling-mounted fan-powered HEPA modules
### VELOCITY & AIR CHANGE RATES FOR SELECTED CLEAN SPACE CLASSES

<table>
<thead>
<tr>
<th>Space Classification</th>
<th>Average Room Velocity (fpm)</th>
<th>Air Changes per Hour</th>
<th>Filtered Ceiling Coverage</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISO 5</td>
<td>100</td>
<td>40-80</td>
<td>240-480</td>
</tr>
<tr>
<td>7</td>
<td>10,000</td>
<td>10-15</td>
<td>30-60</td>
</tr>
<tr>
<td>8</td>
<td>100,000</td>
<td>1-8</td>
<td>5-30</td>
</tr>
</tbody>
</table>
Facility Requirements-Air

- ISO Guidelines for clean areas must be met
- ISO Class 5 Laminar Flow Hoods or BSCs
- ISO Class 7 for Buffer Area/Cleanroom
- ISO Class 8 for Anteroom (non-hazardous drugs)
- ISO Class 7 for Anteroom (hazardous drugs)
Airflow Summary

ISO 7
SA: 250 CPM (FPHM: 550 CPM (60 AC/HR))
EA: 0 CPM
TA: 100 CPM (OUT)
RA: 450 CPM

CHEMO EXHAUST HOOD

ISO 7
SA: 400 CPM (AC/HR) (FPHM: 400 CPM)
EA: 0 CPM
TA: 100 CPM (IN)
RA: 0 CPM

ISO 7
SA: 205 CPM (FPHM: 900 CPM (60 AC/HR))
EA: 0 CPM
TA: 100 CPM (OUT)
RA: 600 CPM

ISO 6
SA: 165 CPM
EA: 350 CPM
TA: 165 CPM (IN)
RA: 0 CPM

PREP
3402

+0.02" W.G.

-0.02" W.G.

AIRFLOW SUMMARY PLAN
NOT TO SCALE

SA = SUPPLY AIR FROM BLOWER COIL UNIT
EA = EXHAUST AIRFLOW
TA = TRANSFER AIRFLOW (TOTAL DESIGN THROUGH DOORS/PASS/THROUGH)
RA = RECYCLED AIRFLOW (TOTAL LOW RETURN (RECYCLED PLUS RETURN))
Cooling Loads

- Cooling Load Calculations
  - Room Envelope
    - Walls
    - Roof Load
  - Internal Loads
    - People
    - Lighting Equipment
    - Hood(s)
  - Heat Gain from Fan-Powered HEPA Module Fans
- Consider Source
  - System 24/7/365
  - Typical Outpatient Facility HVAC systems operate on occupied/unoccupied modes
### Table T-2

**PHARMACY COMPOUNDING SUITE - LOAD DESIGN PARAMETERS**

<table>
<thead>
<tr>
<th>Design Requirement or Assumption</th>
<th>IV Prep</th>
<th>Anteroom</th>
<th>Chemo Prep</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pressurization</td>
<td>Positive</td>
<td>Positive to all</td>
<td>Negative</td>
</tr>
<tr>
<td>Designation</td>
<td>Clean</td>
<td>Clean to all</td>
<td>Dirty</td>
</tr>
<tr>
<td>Space Area (SF)</td>
<td>280</td>
<td>260</td>
<td>165</td>
</tr>
<tr>
<td>Ceiling Height (Ft)</td>
<td>9</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Occupancy</td>
<td>3</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>People Load (BTUh sensible)</td>
<td>750</td>
<td>250</td>
<td>750</td>
</tr>
<tr>
<td>Lighting Load (W/SF)</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
</tr>
<tr>
<td>Equipment Load (Watts)</td>
<td>2000</td>
<td>1000</td>
<td>2000</td>
</tr>
<tr>
<td>Additional Fan Heat (BTUh)</td>
<td>5000</td>
<td>2500</td>
<td>5000</td>
</tr>
<tr>
<td>Room Design Setpoint (°F)</td>
<td>65</td>
<td>65</td>
<td>65</td>
</tr>
<tr>
<td>Sensible Cooling (BTUh)</td>
<td>14,000</td>
<td>7500</td>
<td>13,420</td>
</tr>
<tr>
<td>Supply Air at 55°F (CFM)</td>
<td>1300</td>
<td>700</td>
<td>1250</td>
</tr>
</tbody>
</table>

**Notes:**
1. Total calculated supply air volumes rounded to the nearest multiple of 50 cfm.
2. Total calculated supply air volumes are the load-driven values cooling values for the spaces. The total air within the space will actually be the air-driven values derived from the ISO Class ACH requirement.
3. Room design setpoint temperature at the low end of recommended range for conservative measure.
4. No skin load assumed to affect space.
5. Additional Fan Heat is assumed heat gained from HEPA fan modules.
HVAC Systems: Air Handling Systems

- Typical In-Hospital Systems
  - Operate 24/7/365
  - Higher Percentages of Outdoor Air
    - To accommodate Chemo Hood and Unpacking Room makeup air requirements
- Reheat Systems
  - 60% Maximum humidity threshold ok with 68°F Room Temperature
HVAC Systems: Air Handling Systems

- Typical Outpatient Facility Systems
  - DX (Direct Expansion) Rooftop Units
  - Designed for minimum outdoor air
  - Additional features/controls are needed to maintain maximum 60% space humidity due to increased outdoor air
    - Digital scroll compressor(s) for capacity control
    - Hot gas reheat/ dehumidification controls
Example Pharmacy
OPTIONAL INLET

HANGING TAB

PREFILTER FRAME

STATIC PRESSURE PORTS
REMOVE GRILLE FOR
ACCESS

BLU-JEL SEALANT

PERFORATED FLUSH GRILLE
22 GA. 316L 304 40% OPEN

BLOWER/MOTOR

SECTION VIEW
<table>
<thead>
<tr>
<th>DESIGN</th>
<th>LOCATION</th>
<th>MODULE SIZE, L x W (IN)</th>
<th>MIN HEPA EFFICIENCY (%)</th>
<th>AIR FLOW RATE (CFM) (NOTE 4)</th>
<th>MAX Ng LEVEL (NOTE 5)</th>
<th>VOLTS / PHASE / Hz</th>
<th>MODULE MOTOR SIZE (HP)</th>
<th>BASIS OF DESIGN</th>
</tr>
</thead>
<tbody>
<tr>
<td>HF-1</td>
<td>IV PREP ROOM</td>
<td>48 x 24</td>
<td>99,99</td>
<td>350</td>
<td>45</td>
<td>120/1/60</td>
<td>1/3</td>
<td>FLANDERS PUREFLO-FFM (RSR)</td>
</tr>
<tr>
<td>HF-2</td>
<td>ANTE ROOM</td>
<td>48 x 24</td>
<td>99,99</td>
<td>475</td>
<td>45</td>
<td>120/1/60</td>
<td>1/3</td>
<td>FLANDERS PUREFLO-FFM (RSR)</td>
</tr>
<tr>
<td>HF-3</td>
<td>CHEMO ROOM</td>
<td>48 x 24</td>
<td>99,99</td>
<td>450</td>
<td>45</td>
<td>120/1/60</td>
<td>1/3</td>
<td>FLANDERS PUREFLO-FFM (RSR)</td>
</tr>
</tbody>
</table>

NOTES:
1. PROVIDE ALL MODULES WITH UL LISTING, 12-INCH DUCT COLLAR, POWER CORD AND POWER INDICATOR LIGHT, REMOTE SOLID STATE FAN SPEED CONTROL, 30% EFFICIENT PLEATED PREFILTER, AND ROOM-SIDE MOTOR ACCESS.
2. ALL MODULES SHALL BE SELECTED FOR ROOM-SIDE ACCESS TO HEPA FILTER FOR REPLACEMENT, WITH LEAKTIGHT AIR SEAL BETWEEN FILTER AND MODULE.
3. PROVIDE HF-1 AND HF-3 WITH SOLID CEILING ADAPTOR FOR INSTALLATION IN GYPSUM CEILING.
4. SCHEDULED AIRFLOW IS BASED UPON 90 FPM VELOCITY ACROSS THE GROSS FACE AREA OF THE MODULE.
5. SCHEDULED SOUND PERFORMANCE IS MEASURED 30° FROM THE FACE OF THE FILTER WITH 90 FPM AVERAGE FACE VELOCITY.
SEQUENCE OF OPERATIONS (CHEMO ROOM EXHAUST FAN):

EXHAUST FAN "START-STOP" FUNCTION SHALL BE THROUGH THE BMS. THE LEAD EXHAUST FAN SHALL BE ENERGIZED AND SHALL OPERATE CONTINUOUSLY. WHENEVER INDEXED TO "STOP", THE SYSTEM SHALL BE DE-ENERGIZED AND THE CONTROLS SHALL RETURN TO THEIR NORMAL POSITION. WHENEVER SYSTEM NEGATIVE STATIC PRESSURE IS LESS THAN -1" W.G. (ADJUSTABLE) AS SENSED BY SP1, THE LEAD EXHAUST FAN SHALL BE DE-ENERGIZED, THE LAG EXHAUST FAN SHALL BE ENERGIZED, AND AN ALARM SHALL BE INITIATED THROUGH THE BMS.

THE FAN SHALL BE BALANCED DURING THE COMMISSIONING PHASE TO MAINTAIN ±0.05" W.G. (ADJUSTABLE) NEGATIVE PRESSURE WITHIN THE CHEMO ROOM. MANUAL BYPASS DAMPERS BPD-1A AND BPD-1B SHALL BE SET BY THE BALANCING CONTRACTOR TO MAINTAIN THE STATIC PRESSURE SETPOINT AT SP1.

LEAD/LAG EXHAUST FAN OPERATION SHALL BE STAGED FOR ALTERNATE FAN OPERATION EVERY 30 DAYS (ADJUSTABLE) TO EQUALIZE FAN RUN TIMES. FAN ISOLATION DAMPER ID-1A OR ID-1B SHALL BE OPEN WHENEVER ITS RESPECTIVE FAN IS INDEXED TO OPERATE. THE CURRENT SWITCH AT EACH FAN MOTOR SHALL PROVIDE PROOF OF ITS RESPECTIVE FAN THROUGH THE BMS.
Airflow Schematic 1
SEQUENCE OF OPERATIONS - PHARMACY COMPOUNDING SUITE:

GENERAL:

SUPPLY AIR TERMINAL UNITS WITH REHEAT AND RETURN AIR TERMINAL UNITS SHALL OPERATE INDEPENDENTLY, CONTROLLING FOR CONSTANT VOLUME. REFER TO THEIR RESPECTIVE SEQUENCES FOR CONSTANT VOLUME CONTROL.

ALL FAN POWERED HEPA FILTER MODULES WITHIN THE SUITE SHALL BE ENERGIZED AND SHALL OPERATE CONTINUOUSLY.

PHARMACY CHEMO ROOM EXHAUST FAN EF-IAB SHALL OPERATE CONTINUOUSLY AND SHALL BE CONTROLLED AS INDICATED IN THE "PHARMACY CHEMO ROOM EXHAUST FAN CONTROL" SEQUENCE OF OPERATIONS.

SPACE PRESSURIZATION:

IV PREP ROOM SHALL BE POSITIVE TO ANTE ROOM, AND SPACE PRESSURIZATION MONITOR PM-I SHALL MEASURE THE PRESSURE DIFFERENCE BETWEEN IV PREP AND THE ANTE ROOM. WHENEVER PRESSURE DIFFERENCE IS LESS THAN +0.02" W.G. (ADJUSTABLE), AN ALARM SHALL BE INITIATED THROUGH THE BMS. PM-I SHALL CONTROL RETURN AIR TERMINAL UNIT THROUGH THE BMS TO MAINTAIN 0.05" W.G. (ADJUSTABLE) POSITIVE PRESSURE.

CHEMO ROOM SHALL BE NEGATIVE TO ANTE ROOM, AND SPACE PRESSURIZATION MONITOR PM-2 SHALL MEASURE THE PRESSURE DIFFERENCE BETWEEN CHEMO ROOM AND THE ANTE ROOM. WHENEVER PRESSURE DIFFERENCE RISES ABOVE -0.02" W.G. (ADJUSTABLE), AN ALARM SHALL BE INITIATED THROUGH THE BMS. THE CHEMO EXHAUST FAN SHALL BE BALANCED DURING THE COMMISSIONING PHASE TO MAINTAIN -0.05" W.G. (ADJUSTABLE) NEGATIVE PRESSURE.

ANTE ROOM SHALL BE POSITIVE TO THE GENERAL PHARMACY, AND SPACE PRESSURIZATION MONITOR PM-3 SHALL MEASURE THE PRESSURE DIFFERENCE BETWEEN THE ANTE ROOM AND THE GENERAL PHARMACY. WHENEVER PRESSURE DIFFERENCE IS LESS THAN +0.01" W.G. (ADJUSTABLE), AN ALARM SHALL BE INITIATED THROUGH THE BMS. PM-3 SHALL CONTROL RETURN AIR TERMINAL UNIT THROUGH THE BMS TO MAINTAIN 0.05" W.G. (ADJUSTABLE) POSITIVE PRESSURE.

EACH SPACE PRESSURIZATION MONITOR SHALL BE INTERFACED WITH THE BMS.
Airflow Schematic II
Summary for Management Consideration
Key Questions for Pharmacy Management

- Does our facility meet requirements?
- Do our personnel and material workflows work with or against our specific facility and engineering controls?
- Do we have a documented state of control?
- Do we identify, investigate, correct and document adverse environmental events?
- Does the C-Suite understand the risk associated with non-compliance?
- What is our compliance budget/resources?
- Can small satellite/oncology practices afford compliance?
Questions?

Access updates and information at USP.org

Contact:

- Ken Frazier, PE  Leach Wallace Associates, Inc., kfrazier@leachwallace.com, 704-335-0485, 410-579-8100

Presented by Leach Wallace Associates, Inc.