PHARMACEUTICAL COMPOUNDING:

COMPLYING WITH USP <797& 800>

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Focus on what is good for the patient!!!

Compliance will follow.....

COMPOUNDED PHARMACEUTICAL

- Compounded by pharmacists, doctors, etc., for millions yearly
- Meets needs of patients with no access to required medicine
- Provides correct concentration or dosage
- Minimizes risks by following USP standards

COMPOUNDED PHARMACEUTICALS

- USP Compounding Standards
  - USP <795, 797, 800, 825>
- Containment Risk Assessment
  - Gap Analysis
- Physical Requirements
  - USP <797 & 800>

COMPOUNDED PHARMACEUTICALS

Compounding Standards

WHAT IS USP

United States Pharmacopeia (USP):

- Founded in 1820, as science-driven organization
- Publishes pharmacopeia annually
- Convenes experts for standard-setting
- Provides referenced standards & quality verification services
- Headquartered in North Bethesda, MD

COMPOUNDING STANDARDS

- USP <795> - Compounding Quality

  Non-sterile Preparations
- USP <797> - Compounding

  Sterile Preparations
- USP <800> - Safe Handling of

  Hazardous Drugs
- USP <825> - Preparation, Compounding, Dispensing, and Repackaging

  Radiopharmaceuticals (Req 60 & 61)

USP <795> NON-STERILE PREPARATIONS

- Provides standards for non-sterile products
- Reduces contamination, infection, dosing risks
- Describes processing requirements:
  - facilities
  - equipment & components
  - quality controls & training
- Implement revisions in Dec 1, 2019

USP <797> STERILE PREPARATIONS

- Quality preparations free from contaminants
- Consistent in identity, strength & potency
- Requirements for compounding;
  - personnel & training
  - environmental monitoring
  - storage
  - testing of finished preparations
- 2008 Chapter official, update Dec 2019

USP <800> HAZARDOUS DRUGS

Applies to all healthcare personnel in all environments conducting activities:

- Receiving
- Preparing
- Administering
- Transporting
- Other activities

USP <800> HAZARDOUS DRUGS

- Provides safe handling procedures to minimize risk:
  - deactivating, decontaminating & cleaning
  - spill control
  - documentation
- Defines facility & engineering controls

USP <800> HAZARDOUS DRUGS

- Procedures for activities involving:
  - deactivating
  - decontaminating & cleaning
  - spill control
- Documentation of usage
- Implement on December, 2019

USP <825> RADIOPHARMACEUTICALS

- Sterile & non-sterile compounding
- Preparing, dispensing & repackaging
- Radiation protection measures (T, D, S)
- Ancillary supplies (e.g., radiation shields)
- Special equipment (e.g., radioactivity measuring devices & monitors)

COMPOUNDED PHARMACEUTICALS

Risk Assessment

or

"Gap Analysis"

RISK ASSESSMENT

- Category of Compounded Sterile Product (CSP)
- Sterile vs Non-sterile Products
- Hazardous vs Non-hazardous Drugs
- Radioactive vs Non-radioactive Drugs

GAP ANALYSIS???

- Compliance with current USP <797>
- Appropriate Containment Space
  - Cleanroom Suite
  - Segregated Containment Area
- Proper Containment Equipment
  - Laminar Airflow Workbench
  - Biological Safety Cabinet
  - Glove Box

COMPOUNDED STERILE PRODUCT (CSP)

Criteria

- Processing conditions
  - room temperature, refrigerated, clean air
- Microbial growth probability
  - single or multiple sterile items
- Time period to be used
  - **B**eyond-**U**se-**D**ate (BUD)

COMPOUNDED STERILE PRODUCT (CSP)

Category CSP-NA

- Only sterile materials
- BUD < 1 hour

Category CSP 1

- BUD =/< 12 hrs - controlled room temperature
- BUD =/< 24 hrs or less - refrigerated

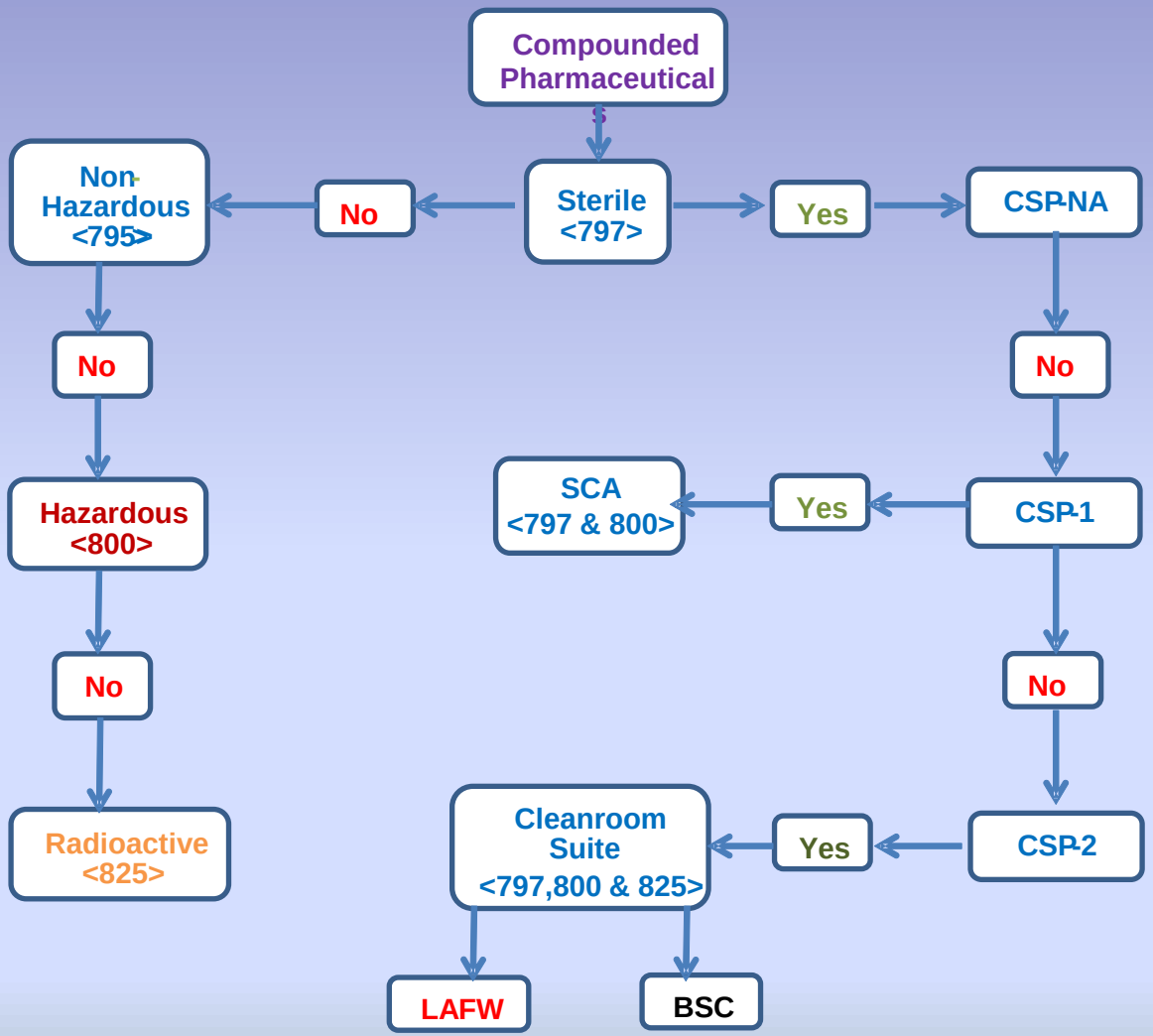
COMPOUNDED STERILE PRODUCT (CSP)

Category CSP 2

- BUD > 12 hrs - controlled room temperature

- BUD > 24 hrs - refrigerated

RISK ASSESSMENT



COMPOUNDED PHARMACEUTICALS

Physical Requirements

COMPOUNDED PHARMACEUTICALS

USP <797>

Non-Hazardous

Drugs

Compounding

USP <797> PHYSICAL REQUIREMENT

Air Quality - Particulate Matter

Containment Space

Containment Equipment

Work Space

AIR QUALITY

Filtered Air

- HEPA filtered air in compounding device
- HEPA filtered air from ceiling in compounding space

Conditioned Air

- *Comfortable* for personnel in PPE
- Temp =/<20 degree C (68 degrees F)
- Humidity =/<60%

ISO CLASSIFIED AIR QUALITY

"air quality improves moving to the PEC"

ISO Class	Particle Count/m ^{3}
3	35.2
4	352
5	3520
6	35,200
7	352,000
8	3,520,000

CONTAINMENT SPACE

Required for all Sterile Compounding:

Direct Compounding Area (DCA)

- Direct HEPA Filtered "first air"
- ISO Class 5

Primary Engineering Control (PEC)

- Device or room containing DCA
- HEPA filtered air
- ISO Class 5

CONTAINMENT SPACE

Required for all Sterile Compounding:

Secondary Engineering Control (SEC)

- Room containing PEC
- Buffer Room & Ante-room
- Cleanroom Suite
- ISO Class 7 & 8

HIGH RISK CONTAINMENT

CONTAINMENT SPACE

Segregated Compounding Area (SCA)

- *CSP-1 compounding only!!!!!!!!!!*
- Space, area, or room contains PEC
- Defined, visible perimeter to establish the boundaries
- Provides “Unclassified” air quality
- Without an ante-room or buffer room

LOW RISK CONTAINMENT

ISO CLASSIFIED AREAS

- PEC = ISO Class 5
- Buffer Room = ISO Class 7
- Ante-room:
  - Non-hazardous drugs = ISO Class 8
  - Hazardous Drugs = ISO Class 7

CONTAINMENT EQUIPMENT

Laminar Airflow Work Bench

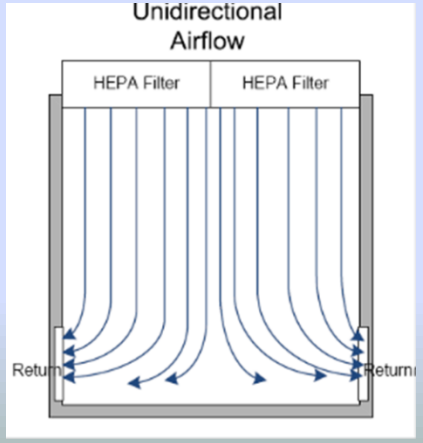
- (LAFW)

Biological Safety Cabinet

- (BSC)

Restricted-access Barrier System

- (RABS)



LAMINAR AIR FLOW WORKBENCH (LAFW)

- ISO Class 5 or better for sterile compounding
- Horizontal or vertical
  - "unidirectional" HEPA-filtered airflow
- Not for anti-neoplastic or active pharmaceutical ingredient

BIOLOGICAL SAFETY CABINET (BSC)

- Open front with inward & downward, "unidirectional" airflow
- HEPA-filtered airflow & exhaust
- Personnel protection from airborne drugs
- ISO Class 5 for CSP-2
- Air exhausted externally for anti-neoplastic drugs

RESTRICTED-ACCESS BARRIER SYSTEM (RABS)

- HEPA-filtered, “unidirectional” airflow, ISO Class 5
- Ingress &/or egress through defined openings
- Prevents transfer of contamination
- Buffer Room may not be needed

COMPOUNDING ASEPTIC CONTAINMENT ISOLATOR (CACI)

- RABS "style" Containment Equipment
- Glove Box design
- Compounding **sterile HDs**
- External exhaust
- *First air exchange must first pass through HEPA filter*

WORK SPACE

- Buffer Room
- Ante-room
- Cleanroom Suite

BUFFER ROOM

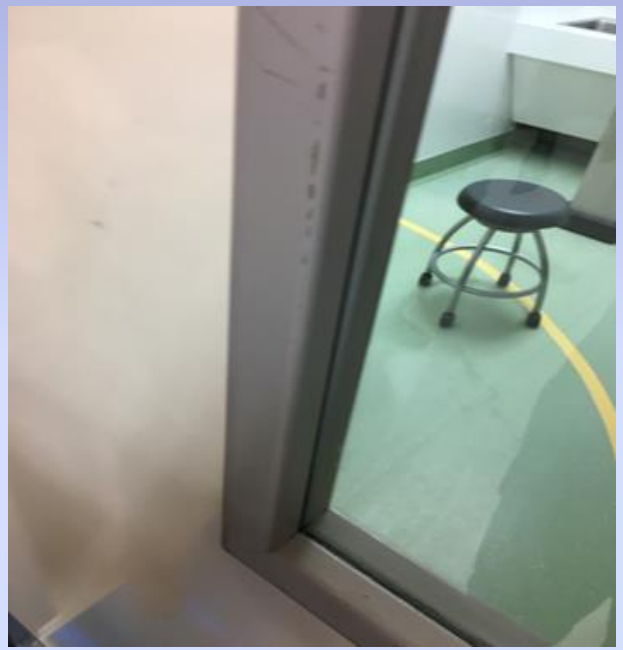
- Contains PEC
- ISO Class 7 or cleaner
- Fixed walls & doors
- Accessed through the Ante-room

ANTE-ROOM

- ISO Class 8 or cleaner
- Transition between the "unclassified" area & Buffer Room
- Personnel hand hygiene, garbing, etc., procedures

ANTE-ROOM

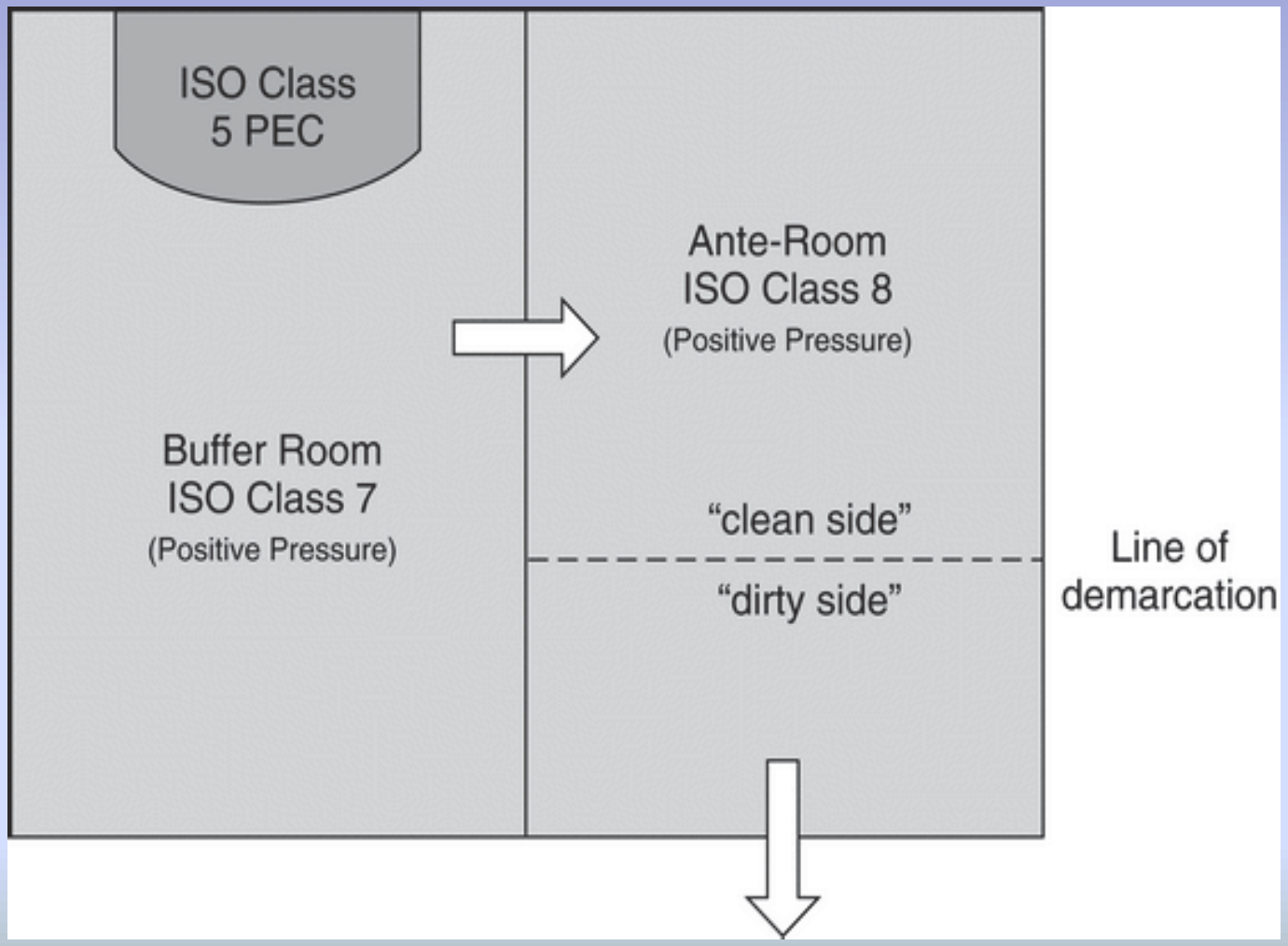
- High particulate level activities
- Demarcation Line clean/dirty side
- Entered through the dirty side
- Clean side closest to the Buffer Room



CLEANROOM SUITE

- Ante-room & Buffer Room
- Classified Area
- Contains PEC
- Ceiling supplied, HEPA air
- Returns low on the wall
- Pressure-differential monitoring systems

CLEANROOM SUITE



CLEANROOM SUITE

- Well-lighted & comfortable working environment
- Surfaces:
  - smooth & impervious
  - free from cracks & crevices
  - easily cleaned & disinfected
- Eliminate dirt or accumulation in cracks and crevices

CEILINGS

- Caulked, inlaid ceilings panels
- Or sealed & secured around support frame
- Washable, scrubbable, & soil resistant
- Designed for use in a Cleanroom environment (IFU Sheet)
- Ceiling light fixtures, smooth, flush & sealed

WALLS & FLOORS

- Walls-epoxy painted or heavy-gauge polymer
- Panels joined together & sealed
- Floors smooth, sealed, welded seams
- Impervious with coving to the sidewall
- Sealed penetrations in surfaces

OVERHANGS & LEDGES

- Dust-collecting overhangs minimized, such as utility pipes, ledges & windowsills
- Overhangs or ***ledges*** easily cleanable
- Sprinkler systems recessed & covered, easily cleanable

AIR EXCHANGE RATES

If the PEC ventilation is used to meet the minimum total ACPH requirements:

- PEC must **not** be turned off except for maintenance
- ACPH from HVAC must be **documented** on certification report
- Emergency power supply is supplied

Note: ACPH assists ISO Classification, not differential pressure

AIR CHANGES RATES

Compounding Area*	ACPH
Unclassified SCA	No requirement
ISO Class 7 space	≥30
ISO Class 8 space	≥20

**HEPA-filtered air for ISO Classification*

DIFFERENTIAL AIR PRESSURE

- Continuously monitoring:
  - Ante-room to Buffer Room
  - Ante-room to general environment outside the "Classified Area"
- Documented at least daily when compounding – logs!!!
- Results reviewed – periodically!!

DIFFERENTIAL AIR PRESSURE

Non-Hazardous Drug Compounding

- Positive pressure =/> 0.02” wc
- Between the Buffer Room & Ante-room
- Between Ante-room & “unclassified” area
- Pressure monitor must be tested for accuracy & performance every 6 months – ***document!!!***

VENTILATION VERIFICATION

CSP Category	Category CSP-1	Category CSP-2
Placement of the PEC	Not required to be placed in a ISO Classified area (SCA)	Required to be placed in a ISO classified area; SEC
Recertification of Ventilation	Every 6 months for the PEC	Every 6 months for the PEC and SEC
Nonviable airborne monitoring: ISO Levels	Every 6 months in Classified area	Every 6 months in Classified area

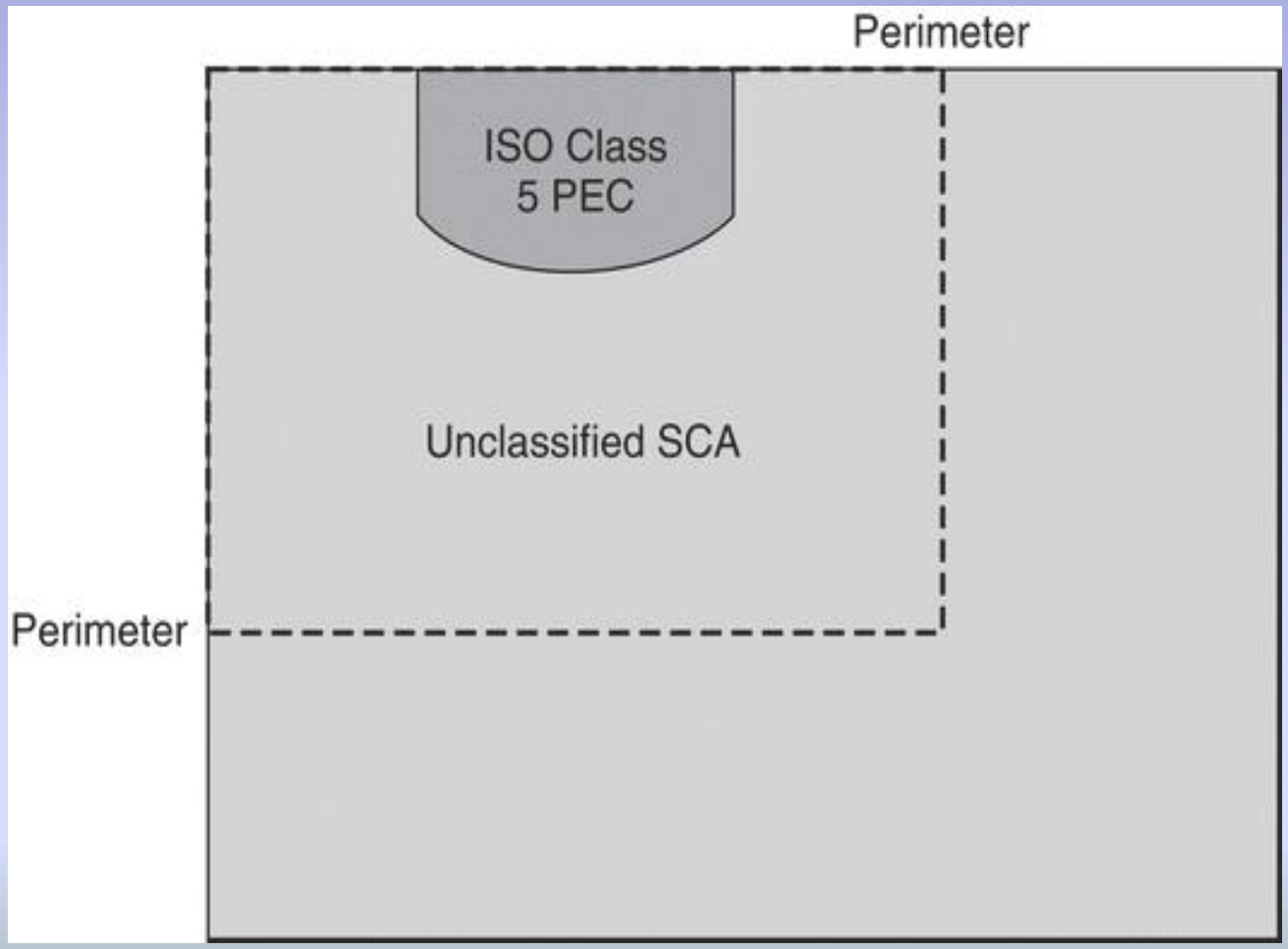
WATER SOURCES

- Hand hygiene sink inside or outside Ante-room
- Hand hygiene sink on dirty side in Ante-room
- Ante-room must not contain floor drain
- Buffer Room must **not** contain sink, eyewash, shower or floor drain**!**

SEGREGATED COMPOUNDING AREA (SCA)

- Not located adjacent to environmental control challenges (e.g., *food preparation areas*, restrooms, warehouses)
- Located away from unsealed windows, doors to the outdoors, traffic flow
- Surrounding activities should not impact compounding activities

SEGREGATED COMPOUNDING AREA (SCA)



WATER SOURCES (SCA)

- Sink must be accessible
- Located at least 1 meter away from the PEC
- Not be located inside the perimeter of the SCA

COMPOUNDED PHARMACEUTICALS

USP <800>

Hazardous

Drugs

Compounding

USP <800> FOCUS

- Personnel responsibilities for handling hazardous drugs
- Facilities & engineering controls
- Environmental quality & control
- Personal protective equipment
- Hazard communication program
- Personnel training

USP <800> REQUIREMENTS

- Containment Designation
- Major Activities
- Environmental Controls

CONTAINMENT DESIGNATION

- Containment Primary Engineering Control (C-PEC)
- Containment Secondary Engineering Control (C-SEC)
- Containment Segregated Compounding Area (C-SCA)

CONTAINMENT PRIMARY ENGINEERING CONTROL (C-PEC)

- Ventilated device – minimizes exposure when directly handling HDs
- Operates continuously if supplies C-SEC space negative pressure or sterile area for compounding
- Activities suspended if electrical power is lost

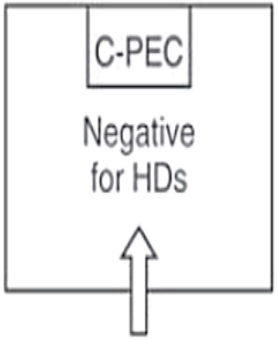
CONTAINMENT PRIMARY ENGINEERING CONTROL (C-PEC)

- Externally vented if used for sterile HDs
- LAFW must not be used HDs
- ISO Class 5 or better air quality
- Class II BSC or CACI
- Cleanroom Suite = ISO Class 7
- C-SCA only if CSP-1

SECONDARY ENGINEERING CONTROL (C-SEC)

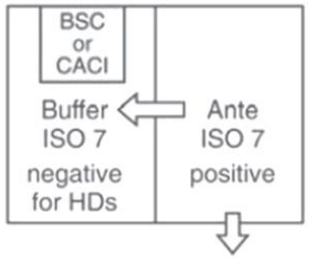
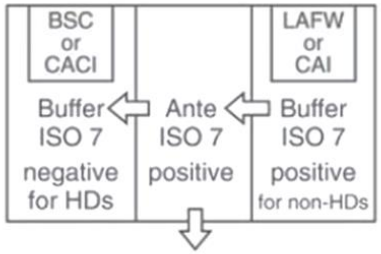
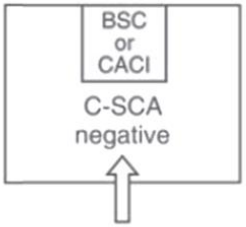
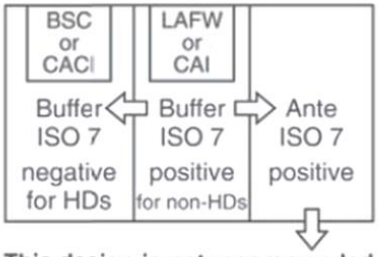
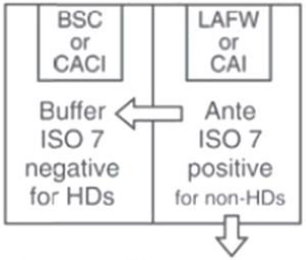
- Room contains the C-PEC
- Sterile & non-sterile compounding is externally vented
- Physically separated, different room, other preparation areas
- Negative pressure to all adjacent areas is between 0.01 - 0.03 “ wc

NON-STERILE HD COMPOUNDING

Use	Optimal Primary and Secondary Control	Minimum ACPH	Limitations Primary and Secondary Control	Minimum ACPH	Notes for limitations
Nonsterile HD compounding		12			

*Arrow indicates direction of airflow

STERILE HD COMPOUNDING

Use	Optimal Primary and Secondary Control	Minimum ACPH	Limitations Primary and Secondary Control	Minimum ACPH	Notes for limitations
Sterile HD compounding	 OR 	30	 OR  **This design is not recommended** OR  Typically used in oncology clinic settings.	12 30 30	Maximum BUD as described in <797> for segregated compounding area. If this design is in place, measures must be taken to avoid contamination of the positive-pressure buffer room. Maximum BUD as described in <797>.

*Arrows indicate direction of airflow

MAJOR ACTIVITIES

- Receipt
- Storage
- Compounding

RECEIPT

- Unpack HDs in an area:
  - pressure = neutral/normal or negative
  - relative to the surrounding areas
- Unpack HDs from external shipping containers:
  - not in sterile compounding areas
  - not in positive pressure areas

STORAGE

- Externally ventilated
- Negative-pressure room
  - HD storage room
  - HD Buffer Room
  - Containment Segregated Compounding Area (C-SCA)
- At least 12 ACPH

STORAGE

- Dedicated refrigerator
- Located in negative pressure Buffer Room
- Exhaust behind refrigerator adjacent to compressor
- Sterile & non-sterile products may be stored together
- Non-sterile products not stored in sterile compounding areas

ENVIRONMENTAL CONTROLS

Designated areas must have capacity for:

- Receipt & unpacking
- Storage
- Compounding Sterile & Non-sterile HD
- Emergency power source to maintain negative pressure for power loss

ENVIRONMENTAL CONTROLS

- Hazard signs prominently displayed
- Sign at entrance to the HD handling areas
- Restricted access – authorized personnel only involved in handling HD
- Areas remote to breakrooms & refreshment areas

UTILITY SYSTEMS

Capacity:

- Ventilation
- Electricity

Capabilities:

- Provide directional air flow
- Maintain differential pressure
- Supply quality air
- Insure emergency power supply

Who monitors performance???

SUMMARY

- Conduct Risk Assessments
- Provide “Quality” Air
- Maintain Differential Pressure & Direction Airflow
- Perform Equipment Maintenance
- Document Ventilation Verification
- Review *Life Safety* Requirements

THANK YOU!

QUESTIONS

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