

Between \$800,000 and \$800 Million: The True Cost of USP <800> Compliance

Ryan A. Forrey, Pharm.D., M.S., FASHP

Director of Pharmacy

Emory University Hospital Midtown

March 1, 2017



Faculty Disclosures

I **currently have or have had** the following relevant financial relations to disclose:

- Consultant- Amgen
- Honorarium/Fees Paid- Becton Dickinson, InfuSystem



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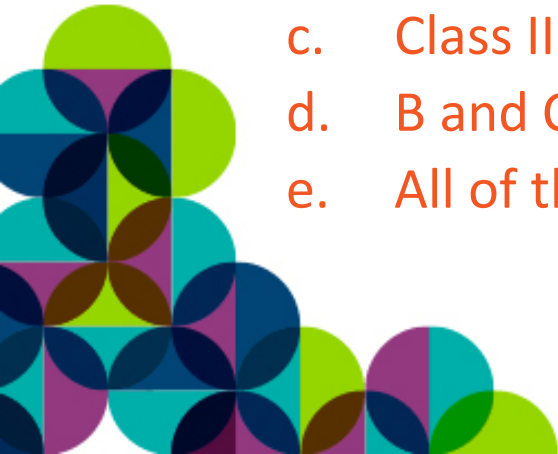
Objectives

- Identify the key facility requirements of USP <800> for antineoplastic hazardous drug (HD) compounding
- Describe steps that must be taken to ensure thorough evaluation of sterile i.v. compounding's financial and operational needs in an oncology setting
- Outline steps that contribute to successful construction/renovation of hazardous drug sterile i.v. compounding spaces in an oncology setting



Pre-Test Questions

1. According to USP <800>, all antineoplastic HD compounding MUST occur in a physically separated room with ISO Class 7 or better air quality.
 - a. True
 - b. False
2. Which of the following is an appropriate containment primary engineering control (C-PEC) for sterile antineoplastic HD compounding?
 - a. CVE (Containment Ventilated Enclosure)
 - b. Class II B2 BSC (Biological Safety Cabinet)
 - c. Class II A2 BSC (Biological Safety Cabinet)
 - d. B and C
 - e. All of the above



Pre-Test Questions

3. According to USP <800>, which of the following types of air need not be passed through a High-Efficiency Particulate Air (HEPA) filter?
- a. C-SEC exhaust air
 - b. C-SEC supply air
 - c. Anteroom supply air
 - d. C-PEC air
 - e. All of the above



USP <800> Facilities and Engineering Controls

- 5.1 Receipt

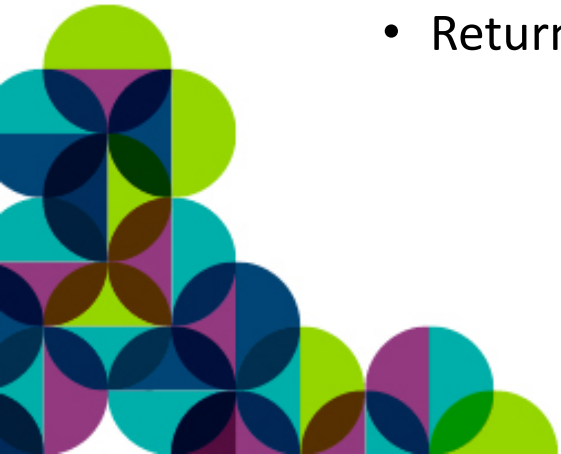
- Antineoplastic HDs and HD active pharmaceutical ingredients (APIs) must be unpacked in neutral/negative pressure
- HDs must not be unpacked from external shipping containers in sterile compounding areas



USP <800> Facilities and Engineering Controls

- 5.2 Storage

- Antineoplastic HDs requiring manipulation or HD APIs must be stored separately from non-HDs
- Externally ventilated
- Negative pressure
- At least 12 air changes per hour (ACPH)
- Refrigerated HDs must be stored in a separate refrigerator
 - May be located in the HD buffer room
 - Return air vent near refrigerator compressor



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- 5.3 Compounding

- Containment Secondary Engineering Control (C-SEC)

- Be externally ventilated ~~through high efficiency particulate air (HEPA) filtration~~
 - Errata published on May 27, 2016
 - Official June 1, 2016
 - Be physically separated (i.e., different room from other preparation areas)
 - Have an appropriate air exchange (e.g. ACPH)
 - Have a negative pressure between 0.01 and 0.03 inches water column relative to all adjacent areas

- Sink must be available for hand washing

- Eyewash station must be readily available

- Not in room if a classified space
 - At least 1 meter from C-PEC if unclassified space



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- 5.3.1 Nonsterile Compounding

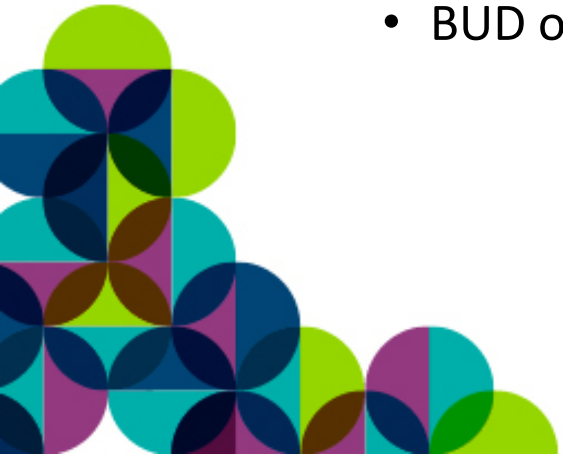
- C-PEC must be externally vented (preferred) OR
- Have redundant-HEPA filters in series
- C-PEC for nonsterile compounding must be
 - Containment ventilated enclosure (CVE) OR
 - Class I biological safety cabinet (BSC) or higher

| C-PEC | C-SEC Requirements |
|---|--|
| <ul style="list-style-type: none">• Externally vented (preferred) or redundant-HEPA filtered in series• Examples: CVE, Class I or II BSC, CACI | <ul style="list-style-type: none">• Externally vented• 12 ACPH• Negative pressure between 0.01 and 0.03 inches water column relative to adjacent areas |



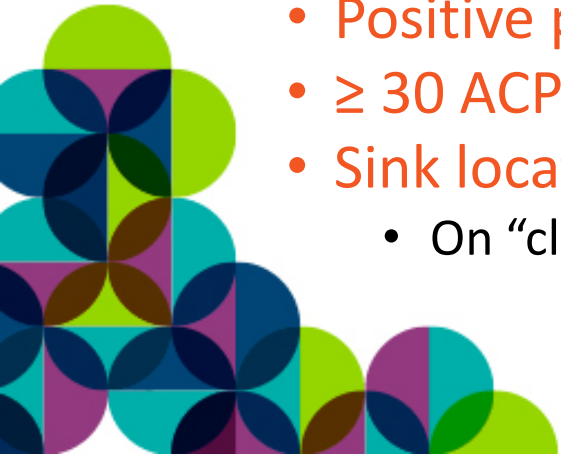
USP <800> Facilities and Engineering Controls

- 5.3.2 Sterile Compounding
 - C-PEC must be externally vented
 - C-PEC must provide ISO Class 5 or better air quality
 - Class II BSC types A2, B1, or B2
 - Class II BSC
 - Compounding aseptic containment isolator (CACI)
 - C-PEC located in ISO 7 buffer room with ISO 7 anteroom OR
 - C-PEC located in containment segregated compounding area (C-SCA)
 - BUD of CSPs limited to 12 hours or less



USP <800> Facilities and Engineering Controls

- ISO Class 7 Buffer Room with an ISO Class 7 Ante-room
 - Fixed walls
 - HEPA-filtered supply air
 - Negative pressure between 0.01 and 0.03 inches water column
 - ≥ 30 ACPH
 - Externally ventilated
- Ante-room
 - HEPA-filtered supply air (ISO Class 7)
 - Positive pressure > 0.02 inches water column
 - ≥ 30 ACPH
 - Sink located ≥ 1 meter from entrance to buffer room
 - On “clean” side of ante-room



USP <800> Facilities and Engineering Controls

- If HD buffer room entered from non-HD buffer room
 - Line of demarcation in HD buffer room for donning and doffing PPE
 - Method to pass materials through without spreading HD contamination
 - Pass-through chamber
 - Pass-through refrigerator must not be used
- This is not the preferred design
- C-SCA
 - Fixed walls
 - Negative pressure between 0.01 and 0.03 inches water column
 - ≥ 12 ACPH
 - Externally ventilated
 - Sink at least 1 meter from C-PEC

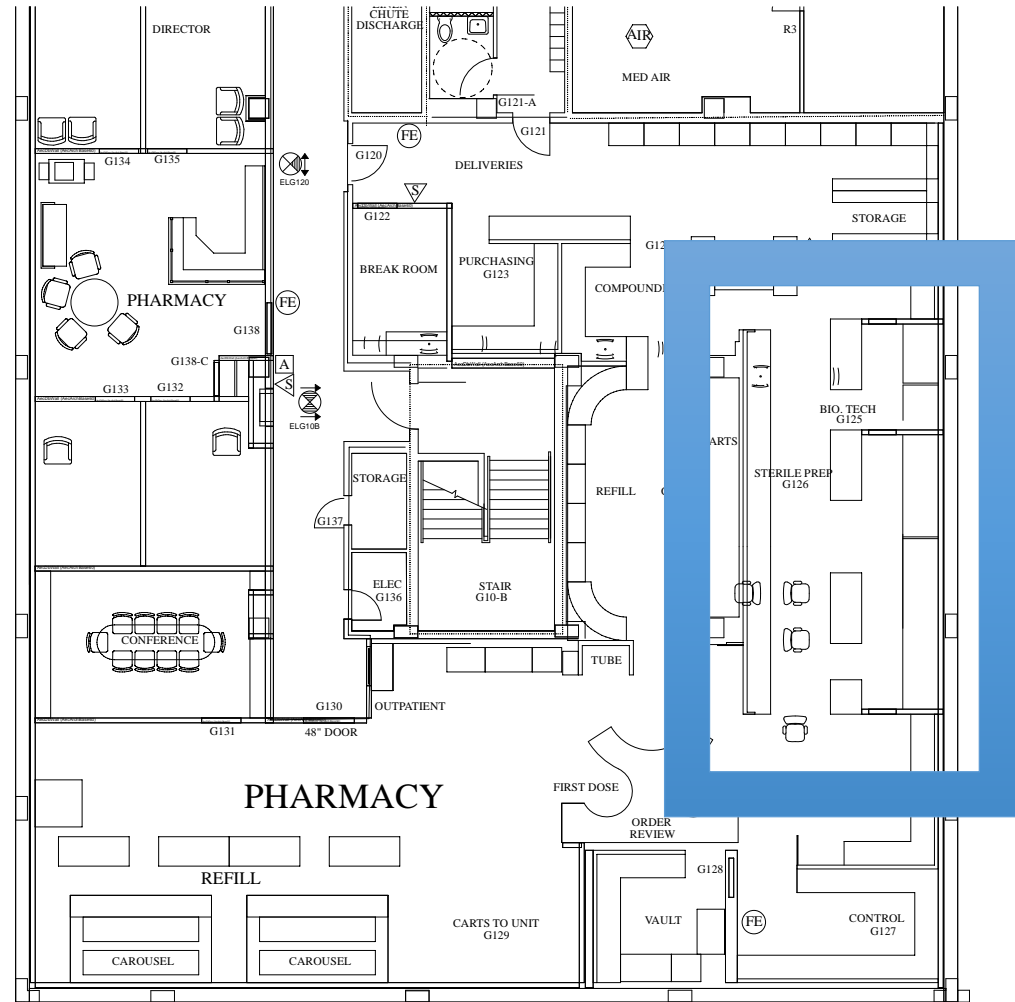


USP <800> Facilities and Engineering Controls

| Configuration | C-PEC | C-SEC |
|---|--|---|
| ISO Class 7 buffer room with an ISO Class 7 ante-room | <ul style="list-style-type: none">Externally ventedExamples: Class II BSC or CACI | <ul style="list-style-type: none">Externally vented30 ACPHNegative pressure between 0.01 and 0.03 inches of water column relative to adjacent areas |
| Unclassified C-SCA | <ul style="list-style-type: none">Externally ventedExamples: Class II BSC or CACI | <ul style="list-style-type: none">Externally vented12 ACPHNegative pressure between 0.01 and 0.03 inches of water column relative to adjacent areas |



Case Study 1: Pre-Renovation



Case Study 1: Pre-Renovation

- Sterile products area renovated in 2004, shortly after release of first version of USP Chapter <797>
- Uses the displacement airflow concept of facility design
 - No ability to compound high risk compounded sterile products (CSPs)
 - Hazardous drugs are compounded in a compounding aseptic containment isolator (CACI)
 - No dedicated ante-room with fixed walls



Planning for Renovations

- A program of requirements (POR) should be developed in advance of any facility planning
 - Determines the services to be provided and identifies future needs
 - Allows standardized planning for adequate space
 - Does not assume that current space is sufficient
 - Can be reproduced for multiple sites
- POR planning should involve internal and external stakeholders
 - What are we currently lacking?
 - What would you like pharmacy to provide (e.g. OR syringes, etc.)?
 - What do our peers provide?



POR Space Requirements

- Primary Engineering Control (PEC)
 - 50 - 100 square feet (SF) of clean room per PEC
- Ante-room (for garbing)
 - 100 SF of clean room per facility
 - Two ante-rooms (HD and non-HD) or one
- Workroom
 - 80 - 120 SF of “office space” per PEC



Budgeting Costs of Renovation

| Example 1,100 SF Renovation (2 HD PECs, 5 non-HD PECs) | Buffer Room Space (per SF) | Office Space (per SF) |
|---|-------------------------------|-----------------------|
| Construction | \$ 800 | \$ 108 |
| Professional Services (11%) | \$ 88 | \$ 11.88 |
| Furniture, Fixtures & Equipment (FF&E) (18%) | \$ 144 | \$ 19.44 |
| Miscellaneous (3%) | \$ 24 | \$ 3.24 |
| Contingency (8%) | \$ 64 | \$ 11.40 |
| Total | \$ 1120 | \$ 153.96 |

- **Construction cost and FF&E per SF decrease with increasing size**
 - **Much of the cost is due to heating, ventilation, and air conditioning (HVAC) equipment**



Example Renovation #1

| Item | Quantity | Space per Unit (in SF) | Total Space (in SF) |
|------------|----------|------------------------|---------------------|
| HD PEC | 2 | 100 | 200 |
| Non-HD PEC | 5 | 50 | 250 |
| Anteroom | 1 | 100 | 100 |
| Workroom | 1 | 550 | 550 |
| Total | | | 1100 |

| Example 1,100 SF Renovation (2 HD PECs, 5 non-HD PECs) | Buffer Room Space (per SF) | Office Space (per SF) |
|---|----------------------------|-----------------------|
| Construction | \$ 800 | \$ 108 |
| Professional Services (11%) | \$ 88 | \$ 11.88 |
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Example Renovation #1

- Clean room space = 550 SF
 - Budget is \$616,000
- Office space = 550 SF
 - Budget is \$84,678
- Total cost
 - Budget is \$700,678



Example Renovation #2

| Item | Quantity | Space per Unit (in SF) | Total Space (in SF) |
|------------|----------|------------------------|---------------------|
| HD PEC | 1 | 120 | 120 |
| Non-HD PEC | 2 | 100 | 200 |
| Anteroom | 1 | 100 | 100 |
| Workroom | 1 | 420 | 420 |
| Total | | | 840 |

| Example 840 SF Renovation (1 HD PEC, 2 non-HD PECs) | Buffer Room Space (per SF) | Office Space (per SF) |
|---|----------------------------|-----------------------|
| Construction | \$ 800 | \$ 108 |
| Professional Services (11%) | \$ 88 | \$ 11.88 |
| FF&E (18%) | \$ 144 | \$ 19.44 |
| Miscellaneous (3%) | \$ 24 | \$ 3.24 |
| Contingency (8%) | \$ 64 | \$ 11.40 |
| Total | \$ 1120 | \$ 153.96 |

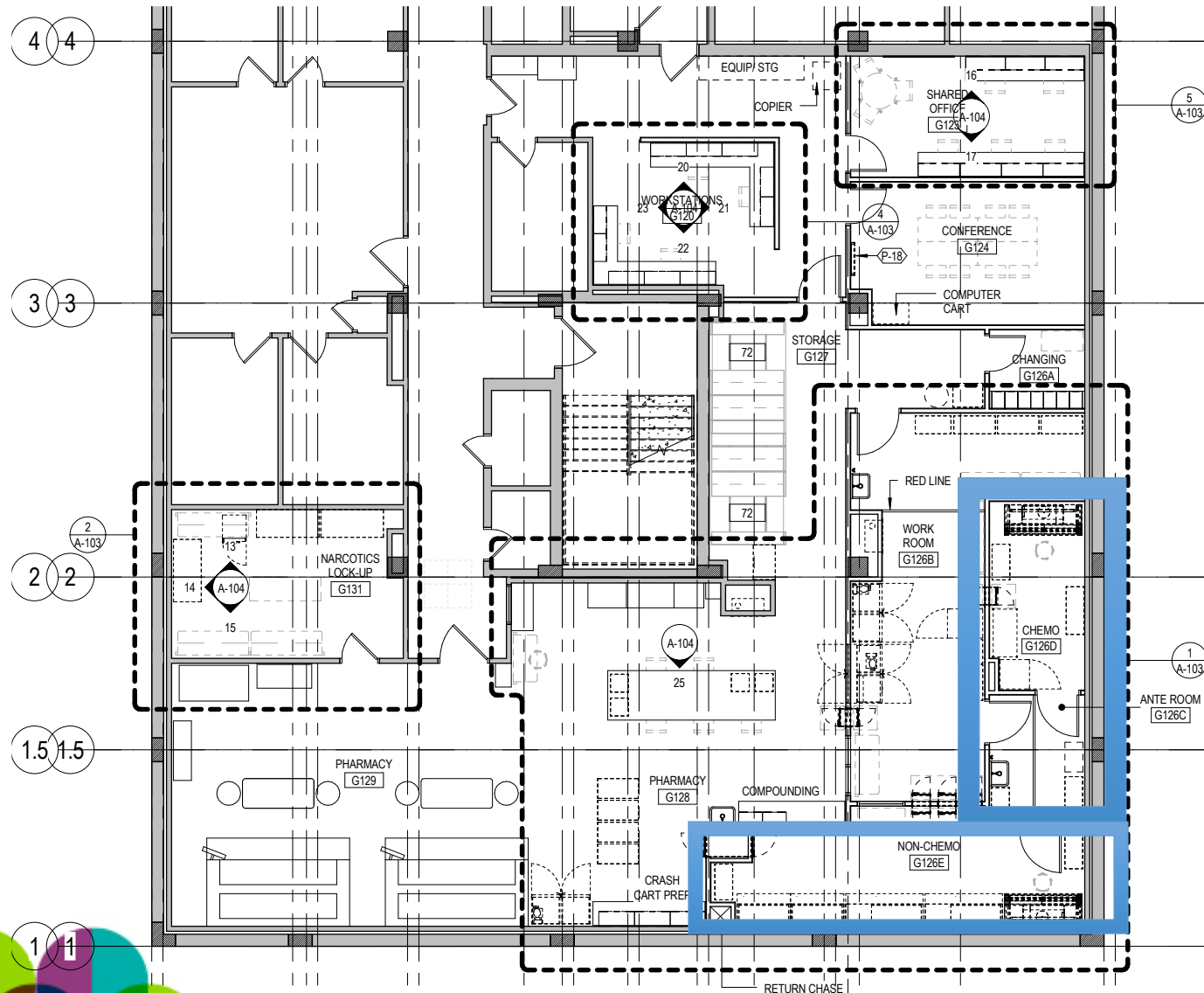


Example Renovation #2

- Clean room space = 420 SF
 - Budget is \$470,400
- Office space = 420 SF
 - Budget is \$64,663
- Total cost
 - Budget is \$535,063



Case Study 1: Future State



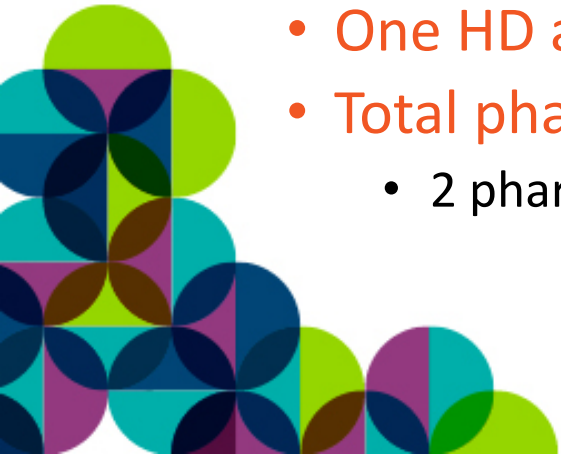
Case Study 1: Future State

- Total project budget initially came in at nearly \$1.2 million
 - Additional scope creep within pharmacy
- Only \$650,000 plus \$80,000 in equipment had been budgeted
- Reclassified the workroom air from ISO Class 7 to ISO Class 8 or even cleaner, not classified (CNC)
 - Reduced the HVAC supply air requirements
- Single exhaust fan for all HD PECs
- Final budget at \$1.04 million
 - \$826,000 construction
 - \$81,000 in additional equipment and IT resources
 - \$133,000 in design and professional fees



Case Study 2: Pre-Renovation

- Outpatient oncology infusion center
 - 18 infusion chairs
- Infusion pharmacy not USP Chapter <797> compliant
 - CACI in use, not externally vented
 - HD and non-HD sterile preparations compounded in same space
 - Not ISO classified, HEPA-filtered air
- Space insufficient for capacity needed
 - One HD and one non-HD PEC
 - Total pharmacy space ~250 square feet
 - 2 pharmacy technicians, 2 pharmacists



Case Study 2: Future State

- New infusion center to grow to 24 infusion chairs
- Relocated to the 16th floor of a 19-story Medical Office Tower (MOT)
- Separate HVAC system for the pharmacy
- POR included:
 - 2 HD C-PECs
 - 1 non-HD PEC
 - Shared (with nursing) storage space
 - Workstations for 2 pharmacists and 2 technicians
 - New location ~515 square feet



Case Study 2: Budgeting

| Item | Quantity | Space per Unit (in SF) | Total Space (in SF) |
|------------|----------|------------------------|---------------------|
| HD PEC | 2 | 120 | 240 |
| Non-HD PEC | 1 | 100 | 100 |
| Anteroom | 1 | 100 | 100 |
| Workroom | 1 | 150 | 150 |
| Total | | | 590 |

| Example 840 SF Renovation (1 HD PEC, 2 non-HD PECs) | Buffer Room Space (per SF) | Office Space (per SF) |
|---|----------------------------|-----------------------|
| Construction | \$ 800 | \$ 108 |
| Professional Services (11%) | \$ 88 | \$ 11.88 |
| FF&E (18%) | \$ 144 | \$ 19.44 |
| Miscellaneous (3%) | \$ 24 | \$ 3.24 |
| Contingency (8%) | \$ 64 | \$ 11.40 |
| Total | \$ 1120 | \$ 153.96 |



Case Study 2: Budgeting

- Clean Room Space: 440 square feet
 $440 \times \$1120 = \$492,800$
- Non-Clean Room Space: 150 square feet
 $150 \times \$154 = \$23,100$
- Total Estimated Budget: \$516,000
 - Pharmacy-only
- Total Project Budget: \$960,884*
*Pre-USP <800> budget was \$660,250



Case Study 2: Value Engineering

- Original planning included:
 - HEPA filtration for C-SEC exhaust
 - Removal
 - Stainless steel exhaust ducts
 - Change to galvanized sheet metal
 - HVAC changes saved ~\$50,000
 - Two pass-through chambers to HD compounding
 - Removed one to save \$7,000
 - No emergency power
 - 1-hour UPS purchased for \$4000
 - Saved thousands in generator costs or electrical work



Case Study 2: Budget Comparison

| Category | Budget 11.05.2014 | Const 06.19.2015 | Difference |
|---------------------------|-------------------|------------------|------------|
| General Conditions | 54305 | 54305 | 0 |
| Design (Arch/MEP) | 62550 | 62550 | 0 |
| Demolition | 15825 | 15825 | 0 |
| Concrete | 1000 | 1000 | 0 |
| Carpentry/Millwork | 98343 | 69500 | -28843 |
| Doors/Windows | 21075 | 38844 | 17769 |
| Drywall/Acoustical | 30320 | 65134 | 34814 |
| Flooring | 34750 | 23450 | -11300 |
| Wall Finishes | 17375 | 8650 | -8725 |
| Miscellaneous Specialties | 29619 | 29851 | 232 |
| Equipment | 0 | 14787 | 14787 |
| Conveying Systems | 0 | 35000 | 35000 |
| Fire Protection | 6950 | 5694 | -1256 |
| Plumbing | 55600 | 82500 | 26900 |
| HVAC | 99400 | 297963 | 198563 |
| Electrical | 76450 | 102400 | 25950 |
| Building Permits | 4250 | 7575 | 3325 |
| | | | |
| Subtotal | 628810 | 915128 | 286318 |
| Fee | 3140 | 45756 | 14316 |
| Total | 660250 | 960884 | 300634 |



Renovation and Construction Pearls

- Identify C-PECs and PECs at the beginning of the project and specify in POR
 - Class II B2 vs. Class II A2 C-PEC makes a significant difference in HVAC requirements
- Review construction documents in detail, especially:
 - Reflected ceiling plans (ceiling tile type, gasketed grid)
 - Electrical plan (lighting fixtures in clean room, emergency power, outlet placement for equipment)
 - Finish plan (flooring material, wall paint specifications)
 - HVAC plan (location of variable air velocity (VAV) valves outside of clean room ceiling spaces, number and location of exhaust fans)



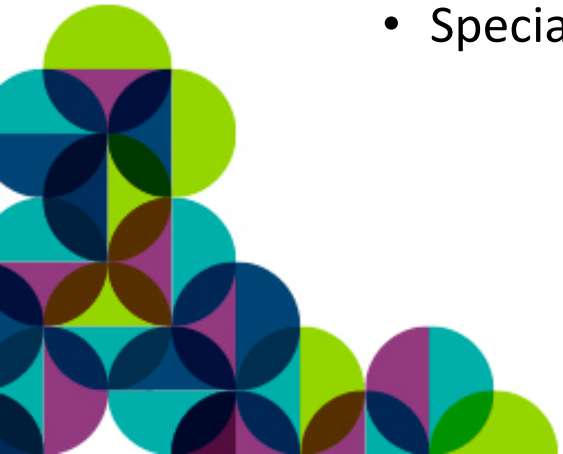
Renovation and Construction Pearls

- Review construction documents in detail, especially (cont'd):
 - Life safety plan (clean room sprinklers)
 - Door plan (borrowed light (aka windows), door width (40" or 42"))
 - Floor plan elevations (workstation configuration)
 - Floor plan (ensure large equipment has a path in and out)
- Important equipment list:
 - Refrigerators
 - Pass-through chambers (interlocking, with shelves)
 - C-PECs, PECs
 - Storage shelving



Renovation and Construction Pearls

- Visit the site often to oversee construction
 - The extra effort will be invaluable to prevent costly mistakes and delays
- Order equipment early and understand lead time
 - Some equipment may take 8-12 weeks
- Understand if “Inside” or “White Glove” delivery is needed
 - If no loading dock, inside delivery is needed
 - Determine if contractor/facilities have equipment needed to move C-PECs
 - Special lifts/cranes required due to size and weight



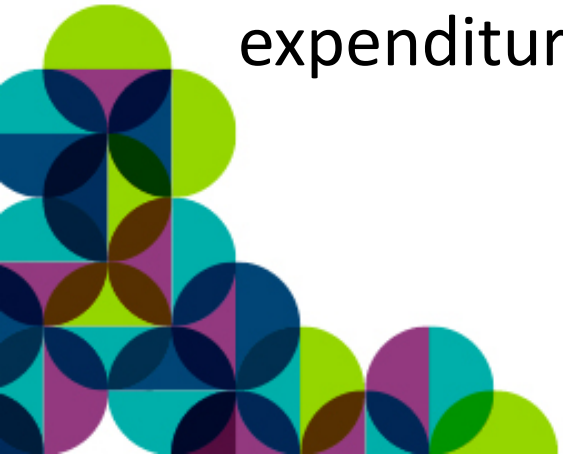
Renovation and Construction Pearls

- Work closely with contractors and architects
- Trust, but verify every decision on the project
 - Do not be fooled into thinking that the architects and engineers will know USP <797> and/or <800>
- Develop (or have the engineer) develop a commissioning plan for the space
 - Test all of the key systems to ensure proper functioning
- Plan for about 6 months of fine tuning and system failures until everything works as expected



Conclusion

- The cost of constructing a USP <800> compliant clean room can be significant
- Planning should include a POR that will meet the needs of all of the stakeholders and provide for future capacity
- Some value engineering may be needed to reduce construction costs while still maintaining compliance with USP <800> standards
- Careful planning and oversight of the details can prevent additional expenditures during and after the construction is complete

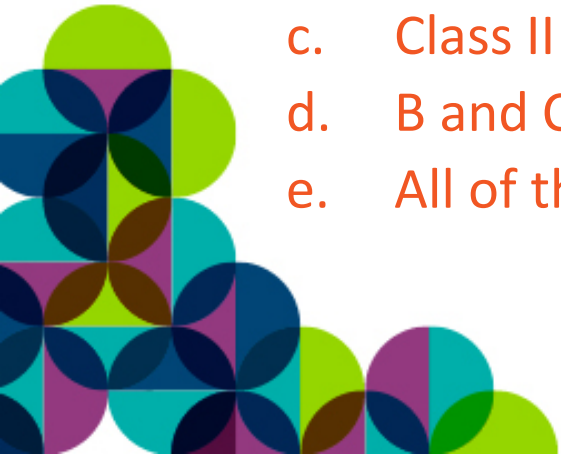


Questions



Post-Test Questions

1. According to USP <800>, all antineoplastic HD compounding MUST occur in a physically separated room with ISO Class 7 or better air quality.
 - a. True
 - b. False
2. Which of the following is an appropriate containment primary engineering control (C-PEC) for sterile antineoplastic HD compounding?
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 - b. Class II B2 BSC (Biological Safety Cabinet)
 - c. Class II A2 BSC (Biological Safety Cabinet)
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 - b. C-SEC supply air
 - c. Anteroom supply air
 - d. C-PEC air
 - e. All of the above

