IV Room Do’s and Don’t’s

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Disclosure
The views and opinions expressed are those of the speaker and are not endorsed by or affiliated with USP.

Conflict of Interest
I have no financial relationships with any commercial sponsor with a vested interest in this presentation.

Technician Learning Objectives
1. Describe proper hand hygiene and garbing.
2. Explain aseptic technique.

Pharmacist Learning Objectives
1. List requirements for environmental monitoring.
2. Define essential aspects of cleanroom certification.
Do...

1. Comply with state and federal law, and national standards.

2. Comply with accreditation and credentialing standards (as applicable).
Do...Understand
**Shall or Must** – Requirement
**Should** - Recommendation

CSP – Compounded sterile preparation
HD – Hazardous Drug (as defined by NIOSH)
BUD – Beyond-use date

Ante-Room – ISO-7 or ISO-8 classified room where hand hygiene and garbing occur.

Do...Understand
PEC - Primary engineering control is where CSPs are compounded.
Examples: LAFW and CAI
LAFW – Laminar Airflow Workbench
CAI – Compounding Aseptic Isolator

SEC – Secondary engineering control is where PEC is located.
Examples: Positive pressure ISO-7 buffer room or segregated compounding area (SCA).

Do...Consider the design of the cleanroom.

- **BSC or CACI** - Biological Safety Cabinet
- **CACI** - Compounding Aseptic Containment Isolator

- **LAFW or CAI** - Laminar Airflow Workbench

Buffer ISO 7
negative for HDs

Ante ISO 7
positive

LAFW or CAI
Buffer ISO 7
positive
define non-HDs

C-PEC - Containment primary engineering control is where hazardous CSPs are compounded.
Examples: BSC and CACI.

C-SEC - Containment secondary engineering control is where C-PEC is located.
Examples: Negative pressure ISO-7 buffer room or containment segregated compounding area (C-SCA).
Do... Consider the environment outside of the cleanroom.

Don’t... Enter sterile compounding areas with

- Rashes
- Sunburn
- Weeping sores
- Conjunctivitis
- Active respiratory infection

Do... Consider the people entering the cleanroom.

Don’t... Enter sterile compounding areas with

- Outer garments
- Cosmetics
- Hand, wrist, visible jewelry and piercings (e.g., earrings, lip or eyebrow piercings)
- Nail polish
- Artificial nails

Natural nails shall be kept neat and trimmed.
**Do... Don garb dirtiest to cleanest**

- Dedicated shoes or shoe covers on clean side of line of demarcation. Dirty shoes should never touch clean side.
- Head and facial hair covers (e.g., beard covers)
- Face masks
- Eye shields.

Eye shields are optional unless working with irritants such as germicidal disinfecting agents or when preparing hazardous drugs.

**Don’t... Forget beard covers.**

**Do... Perform hand hygiene by**

Removing debris from underneath fingernails using a nail cleaner under running warm water followed by vigorous hand washing. Hands and forearms shall be washed to the elbows for at least 30 seconds with soap (either nonantimicrobial or antimicrobial) and water while in the ante-room. Dry hands and forearms to the elbows using lint-free disposable towels.

**Do... Don**

A nonshedding gown with sleeves that fit snugly around the wrists and enclosed at the neck.

Once inside the buffer room or segregated compounding area, and prior to donning sterile powder-free gloves, antiseptic hand cleansing shall be performed using a waterless alcohol-based surgical hand scrub with persistent activity. Hands are allowed to dry thoroughly before donning sterile gloves. Sterile gloves shall be the last item donned before compounding begins.
Do... Disinfect
Contaminated gloved hands by wiping or rubbing sterile 70% IPA to all contact surface areas of the gloves and letting the gloved hands dry thoroughly.

Routine application of sterile 70% IPA to sterile gloves shall occur throughout the compounding process and whenever nonsterile surfaces (e.g. vials, counter tops, chairs, carts) are touched.

Don’t... Leave
ISO Class 7 area without reperforming hand-hygiene and garbing before reentering the ISO Class 7 buffer room.

Don’t... Reuse
Shoe covers, hair and facial hair covers, face masks/eye shields, or gloves.

Gown used in non-HD areas may be removed and retained in the ante-room or segregated compounding area if not visibly soiled, to be re-donned during that same work shift only.

Do... Doff garb
On the clean side of line of demarcation in ante-room or segregated compounding area.

- Remove gloves and perform hand hygiene.
- Remove gown and discard it, or hang it on hook if it is to be reused within the same work shift.
- Remove and discard mask, head/beard cover.
- Remove and discard shoe covers one at a time, ensuring that uncovered foot is placed on the dirty side of the line of demarcation and perform hand hygiene again.
Do... Don additional PPE for hazardous compounding
• Second set of shoe covers.
• Chemo gown (may not be re-used)
  Change per manufacturer or every 2-3 hours or after splash/spill
• Two pairs of chemotherapy gloves.
  Change per manufacturer or every 30 minutes or after tear. Remove and discard outer glove while in BSC or CACI.

Do... Know
LAFW – Laminar Airflow Workbench (PEC)
Protects the product or preparation. No personnel protection.
May be either horizontal or vertical air flow.
• BSC – Biological Safety Cabinet (C-PEC)
  Protects personnel. Used for hazardous drugs.
  Vertical air flow.
  Class II Type A2, B1, or B2
  Class III
Best to run PEC (LAFW) continuously. C-PEC (BSC) must run continuously (per <800>). LAFW/BSC must run 30 minutes before use after being off.

Do... Know
RABS – Restricted Access Barrier System
• CAI – Compounding Aseptic Isolator (PEC)
  Protects the product or preparation. No personnel protection.
  Vertical air flow, positive pressure.
• CACI – Compounding Aseptic Containment Isolator (C-PEC)
  Protects personnel. Used for hazardous drugs.
  Vertical air flow, negative pressure.
Isolator
Contains an internal system to decontaminate interior with sporicidal agent.

DO... Clean and disinfect the PEC
At the beginning of each shift, before each batch, not longer than 30 minutes following the previous surface disinfection when ongoing compounding activities are occurring, after spills, and when surface contamination is known or suspected.
Remove items from areas to be cleaned, and clean surfaces by removing loose material and residue from spills; e.g., remove water-soluble residues with sterile water (for injection or irrigation) using low shedding wipes then wipe with a residue-free disinfecting agent such as sterile 70% IPA, and allow to dry before compounding begins.
Do...Clean and disinfect PEC
From cleanest to dirtiest using overlapping strokes and a new side of the cloth for each location. Start by carefully cleaning the grid covering the HEPA filter.

LAFW (horizontal air flow)
Clean top then sides then work surface.

BSC and LAFW (vertical air flow)
Clean back then then work surface.

CAI and CACI with the front panel closed:
Follow manufacturer’s instructions or if not stated start with the work chamber then move to the ante chamber. Start by carefully cleaning the grid covering the HEPA filter being careful not to let any liquid enter. Clean back wall, sides, front wall and work surface.

Clean the gauntlet sleeves. Apply sterile gloves over gauntlet gloves. Sanitize gloves frequently with sterile 70% isopropyl alcohol.

CAI with the front panel open:
Follow manufacturer’s instructions or if not stated open front panel and start with the work chamber then move to the ante chamber. Start by carefully cleaning the grid covering the HEPA filter being careful not to let any liquid enter. Clean back wall, sides, areas under the work surface (if applicable), work surface, and front wall.

Clean the gauntlet sleeves. Apply sterile gloves over gauntlet gloves. Sanitize gloves frequently with sterile 70% isopropyl alcohol.

Reminder: do not open the front panel on CACI.

Do... Follow manufacturer’s recommendations
For changing gauntlet sleeves and gauntlet gloves.

Know recovery time to return to ISO 5 after CAI is turned off. CACI should never be turned off.

Know purge time before moving items from ante chamber to work chamber.
Do... Use a sporicidal agent
On ISO-5 surfaces (including under the work surface) at least monthly. Document cleaning and disinfecting agents (and contact time as applicable).

Do... Understand
Deactivation renders a compound inactive. If no specific information is available on SDS then use sodium hypochlorite or other EPA registered oxidizer.

Decontamination removes inactivated substances. May use sodium hypochlorite, peroxide, 70% IPA, or water.

Do... Deactivate, decontaminate, clean, and disinfect
C-PEC at least daily and area under the work surface at least monthly.

Decontaminated, clean, and disinfect between compounding of different HDs, any time a spill occurs, before and after certification, any time voluntary interruption occurs, and if moved.

Document agents used and contact times.

Do... Clean and disinfect
Ante-Room and Buffer Room and Segregated Compounding Area
Work surfaces at least daily.
Floors daily at a time when no aseptic operations are in progress.

Use mop labeled ‘floor’ start at area furthest from door (cleanest) moving to door (dirtiest). Buffer room first then ante-room. Floor mops may be used in both the buffer room and ante-room, but only in that order.
Do...Clean and disinfect

Ceiling, walls, carts, equipment exteriors, storage and anything not covered in daily cleaning monthly. Ceiling first then walls, area furthest from door (cleanest) moving to door (dirtiest). Buffer room first then ante-room. Clean and disinfect equipment exteriors, storage and any other areas not covered in daily cleaning/disinfection. Must be done all in one day when no aseptic operations are in progress.

Document date, time, cleaning agent, disinfectant and contact time. Use sporicidal agent on all surfaces at least monthly.

Do...Perform

Monthly cleaning any time the clean room is compromised including

- Inappropriate garbing or staging
- When HEPA fans are off (for any reason including maintenance and power outages)
- Walls/ceiling have been opened

Do...Understand additional requirements for C-SEC (per <800>).

All areas where hazardous drugs are handled and all reusable equipment and devices must be deactivated, decontaminated, cleaned and disinfected.

It is incumbent on compounding personnel to ensure that such cleaning is performed properly. Schedules of use and methods of application shall be in accordance with written SOPs and followed by custodial or compounding personnel.

Do...Perform and document environmental monitoring.

Daily

- Temperature (< or equal to 77F ideally < 68F)
- Humidity (recommend < 60%)
- Pressures
  - Positive (non-HD rooms) at least 0.02
  - Negative (HD rooms) -0.01 to -0.03
- Refrigerator/Freezer temperatures
  - Refrigerators 2 to 8C (36 to 46F)
  - Freezers -25 to -10C (-13 to 14F)
Each day of use

- Incubator temperature and checking of contents

Periodic

- Surface testing in all ISO-classified and segregated compounding areas.
- Use TSA with lecithin and polysorbate 80. Incubate 30-35°C for 48 to 72 hours.
- Recommended action levels
  - ISO 5 > 3 cfu
  - ISO 7 > 5 cfu
  - ISO 8 > 100 cfu

Every 6 months

- Nonviable air counts under dynamic conditions.
- Viable air counts (400-1000L volumetric air sample) using TSA (and MEA for high-risk) under dynamic conditions with growth identified.reported as CFU per cubic meter.
- Recommended action levels
  - ISO 5 > 1 cfu
  - ISO 7 > 10 cfu
  - ISO 8 > 100 cfu
- ACPH
- Pressure
- HEPA Integrity

Do... Identify

Any microbial bioburden captured as a cfu using an impaction air sampler to at least the genus level. Using an appropriate credentialed laboratory.

Regardless of the number of cfu further corrective actions will be dictated by the identification of microorganisms.

Do... Immediately remediate

Highly pathogenic microorganisms (e.g., Gram-negative rods, coagulase positive staphylococcus, molds and yeasts) with the assistance of a competent microbiologist, infection control professional, or industrial hygienist.
Do... Re-evaluate
Adequacy of personnel work practices, cleaning procedures, operational procedures, and air filtration efficiency within the aseptic compounding location if any cfu count exceeds its respective action level.

An investigation into the source of the contamination shall be conducted. Sources could include HVAC systems, damaged HEPA filters, and changes in personnel garbing or working practices. The source of the problem shall be eliminated, the affected area cleaned, and resampling performed.

Do... Ensure equipment is
• Clean
• Used appropriately
• Properly maintained, verified, calibrated, certified.

• Hood
• Balance
• Repeater pump
• Compounder

Do... Stage equipment and supplies
By first removing from shipping cartons. No shipping or other external cartons may be taken into the buffer room or segregated compounding area (or C-SCA).

Stage equipment and supplies by wiping with sterile 70% IPA and a low lint wipe before entering buffer room and again into PEC.

Do... Open
Sealed sterile pouches as the supplies are introduced into the ISO Class 5 PEC without disinfecting the individual items.
Aseptic Technique Do’s and Don’t’s

- Do... Ensure first air touches critical points of vials, syringes, needles, etc.
- Don’t shadow. Hands/objects should never come between critical point and HEPA filter.
- Don’t touch critical points or allow critical points to touch nonsterile surfaces.

Where’s the first air?

- LAFW
- BSC

DCA 6 inches from front above work surface

Aseptic Technique Do’s and Don’t’s

- Do work in the direct compounding area (DCA).
- Do keep trash out of direct compounding area (DCA).
- Don’t rest hands/arms on DCA.
- Don’t allow head to enter PEC.
- Do disinfect gloves every time they leave the PEC.
- Do use slow purposeful movements.
- Don’t sneeze, cough, or talk excessively.
- Do compound one preparation or batch at a time.

Critical Points

Vial
- Stoppers
- Syringes
- Needles

Syringes
- Tip, Piston Plunger, Inner Shaft
- Hub, Bevel, Tip, Heel, Shaft, Lumen

Taking apart vials or syringes adds risk.
Do... **Disinfect**

Vials, injection ports, etc. by wiping with sterile 70% IPA swabs and allowing to dry.

The surface of the sterile 70% IPA swabs used for disinfecting entry points of sterile packages and devices shall not contact any other object before contacting the surface of the entry point.

Sterile 70% IPA wetted gauze pads or other particle-generating material shall not be used to disinfect the sterile entry points of packages and devices.

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Do... **Understand HD requirements**

- Wipe down HD containers to reduce the amount of contamination introduced into the C-PEC.
- Supplemental engineering controls [CSTD] should be used when the dosage form allows. CSTDs must be used when administering antineoplastic HDs when the dosage form allows.
- When CSTD not available, use negative pressure technique to withdraw liquid from vials.
- Seal in impervious plastic bags with cautionary label.
- Transport in impact-resistant and/or water-tight containers. Do not use pneumatic tubes for hazardous liquids or antineoplastic drugs.

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Do... **Understand**

- Single dose containers opened outside ISO 5 may be used up to ONE hour.
- Single dose containers opened inside ISO 5 may be used up to SIX hours.
- Open ampules must be filtered and used immediately.
- Multi-dose containers may be used up to 28 days unless specified otherwise by manufacturer.
- Stored containers must be labeled.

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Do... **Know USP <797> storage**

**Low-Risk** compounding involves not more than three commercially manufactured packages of sterile products and not more than two entries into any one sterile container or package.

- Controlled Room Temp 20-25C or 68-77F <= 48 hrs
- Cold Temp 2-8C or 36-46F <= 14 days
- Frozen -25 to -10C or -13 to 14F <= 45 days
**Medium-Risk** compounding involves more than three commercially manufactured packages of sterile products, more than two entries into any one sterile container or package, complex manipulations or unusually long duration.

- Controlled Room Temp 20-25°C or 68-77°F <= 30 hrs
- Cold Temp 2-8°C or 36-46°F <= 9 days
- Frozen -25 to -10°C or -13 to 14°F <= 45 days

**High-Risk** (1) compounding involves nonsterile components or devices or (2) compounding personnel are improperly garbed or gloved or (3) any of the following are exposed to air quality worse than ISO Class 5 for more than 1 hour: sterile contents of commercially manufactured products, CSPs that lack effective antimicrobial preservatives, and sterile surfaces of devices and containers for the preparation, transfer, sterilization, and packaging of CSPs.

- Controlled Room Temp 20-25°C or 68-77°F <= 24 hrs
- Cold Temp 2-8°C or 36-46°F <= 3 days
- Frozen -25 to -10°C or -13 to 14°F <= 45 days.

**Note:** Repackaging and biologics have their own rules.

**Immediate-use** is for emergency or immediate patient administration of a CSP where patient is subject to risk from delays in therapy.

- Nonhazardous low risk only.
- No batch compounding.
- No Storage. Under continuous supervision.
- Must follow aseptic technique
- Prepared & administration started within one hour.
- Must be discarded if administration has not begun within 1 hour from the start of preparation.
- If not prepared/witnessed by administrator, must be labeled with names/amounts of ingredients, initials of the preparer and the exact 1-hour BUD and time.
Low-risk with 12-hour BUD if the PEC is a CAI/CACI that does not meet the exception requirements or LAFW/BSC that is not located within an ISO Class 7 buffer room.
- Low-risk nonhazardous and radiopharmaceutical only.
- Pursuant to a physician’s order for a specific patient.
- PEC located in segregated compounding area restricted to sterile compounding activities that minimize the risk of contamination.
- Segregated compounding area shall be located away from unsealed windows or doors that connect to the outdoors, high traffic areas, construction sites, warehouses, food preparation areas.

Low-risk with 12-hour BUD
Personnel shall follow <797>
- Hand hygiene and garbing
- Cleaning and disinfection
- Aseptic technique
- Environmental monitoring
- Training and competency

CAI/CACI Exception Requirements
CAI/CACI outside of an ISO 7 buffer room needs documentation from manufacturer and certification company (every six months):
1) CAI shall provide isolation from the room and maintain ISO Class 5 during dynamic operating conditions, including transferring ingredients, components, and devices into and out of the isolator and during preparation of CSPs.
2) Particle counts sampled approximately 6 to 12 inches upstream of the critical exposure site shall maintain ISO Class 5 levels during compounding operations.
3) Not more than 3520 particles (0.5 mm and larger) per m3 shall be counted during material transfer, with the particle counter probe located as near to the transfer door as possible without obstructing the transfer.

Make sure documentation from manufacturer is for your specific model.
CAI/CACI Exception Requirements
• Only authorized personnel and materials in the compounding area.
• Presterilization procedures for high-risk, such as weighing & mixing, shall be completed in no worse than an ISO Class 8 environment.
• PECs located out of traffic patterns/air currents.
• CACIs for hazardous must be in a compounding area that maintains a minimum negative pressure of 0.01-inch water column and have a minimum of 12 ACPHs.
• Appropriate personnel protective equipment (PPE) shall be worn.

Do...Know
When is a sterility test needed?
• All risk levels require a sterility test when exceeding USP <797> storage limits.
• All high-risk level prepared in groups of more than 25 identical individual single-dose packages or in multiple-dose vials for administration to multiple patients or that are exposed longer than 12 hours at 2° to 8° and longer than 6 hours at warmer than 8° before they are sterilized.
• [NOTE—Sterility tests for autoclaved CSPs are not required unless they are prepared in batches >25]

Sterility Tests must be comply with USP <71>

Do... Understand
• Extending BUD requires sterility AND stability assurance.
• Stability is not the same as potency.
• BUDs and expiration dates are not the same.
  -Expiration dates for the chemical and physical stability of manufactured products are determined from rigorous testing.
  -BUDs for compounded preparations are assigned on the basis of direct testing or extrapolation from reliable literature sources and other documentation.
Do... Perform Quality Control

- Double-check on technicians.
  - Drug
  - Quantity
- Visual examination for clarity, particulates, and leaking.
- pH (if needed).
- Accuracy of label

Do... Select

Packing containers and materials that are expected to maintain physical integrity, sterility, and stability of CSPs during transit.

Packing should be selected that simultaneously protects CSPs from damage, leakage, contamination, and degradation, and protects personnel who transport packed CSPs from harm.

Do... Perform training/competency

Initially: GFS x 3 with zero cfus
Initially & Annually for Low-, Medium-risk
Initially & Q6mo for High-risk
- Didactic review/test and media-fill
- GFS after garbing and after completing media-fill. (One plate for each hand. Total of 3 or fewer cfus.)
- Visual observation
  - Hand Hygiene and Garbing (Appendix III)
  - Aseptic Technique (Appendix IV)
  - Cleaning and Disinfection (Appendix V)
- Post media fill surface test (3 or fewer cfus) to validate staging and disinfection process.

Media-fill tests represent the most challenging or stressful conditions actually encountered by the personnel being evaluated when they prepare particular risk level CSPs and when sterilizing high-risk level CSPs.

Compounding personnel who fail written tests or whose media-fill test vials result in gross microbial colonization shall be immediately re-instructed and re-evaluated by expert compounding personnel to ensure correction of all aseptic practice deficiencies.
Do Perform HD training/competency

• All personnel who handle HDs or who perform custodial waste removal or cleaning activities must be trained based on job functions.
• Personnel must be trained prior to the introduction of a new HD or new equipment and prior to a new or significant change in process or SOP.
• Effectiveness of training must be demonstrated.
• Competency must be reassessed at least annually.
• All training and competency assessments must be documented according to OSHA standards and other applicable laws and regulations.

Do... Understand HD requirements

Must maintain a list of HDs, which must include any items on the current NIOSH list. List must be reviewed at least every 12 months.

Drugs on the NIOSH list that must follow the requirements of USP <800> include:
— Any HD API
— Any antineoplastic requiring HD manipulation

Drugs on the NIOSH list that do not have to follow all the containment requirements of USP <800> if an assessment of risk is performed and implemented include:
— Final dosage forms of compounded HD preparations and conventionally manufactured HD products, including antineoplastic dosage forms that do not require any further manipulation other than counting or repackaging (unless required by the manufacturer).

For dosage forms of other HDs on the NIOSH list, the entity may perform an assessment of risk to determine alternative containment strategies and/work practices.

Training/Competency requirements for HDs

• Overview of HDs in use and their risks
• Use of Safety Data Sheets
• Storage
• Review of SOPs related to handling of HDs
• Use of equipment and devices
• Use of PPE including use of NIOSH respirators
• Prevention of HD contamination
• Labeling and transport
• Disposal of HDs and trace-contaminated materials
• Spill management and use of a spill kit
• Response to known or suspected HD exposure
The assessment of risk must consider the following:

- Type of HD
- Dosage form
- Risk of exposure
- Packaging
- Manipulation

If an assessment of risk approach is taken, the entity must document what alternative containment strategies and/or work practices are being employed for specific dosage forms to minimize occupational exposure. If used, the assessment of risk must be reviewed at least every 12 months and the review documented.

EPA provides information on environmental hazards. P- and U-listed drugs must be segregated and disposed of as hazardous waste to comply with EPA regulations. Note that these drugs are different than the drugs on the NIOSH list. EPA defines hazardous as related to the disposal of hazardous drugs so aims to protect the environment. Section 13 of the Safety Data Sheet lists disposal considerations. Keep in mind that state and local laws may be even more restrictive.

DOT defines hazardous from a shipping perspective. Section 14 of the Safety Data Sheet lists transport information. Also check vendor requirements.

**Technician Learning Assessment**

Shoe covers may be re-used during the same shift.

A. True
B. False

**Technician Learning Assessment**

Shoe covers may be re-used during the same shift.

B. False
Technician Learning Assessment

In a horizontal LAFW, shadowing occurs when hands or objects are placed

A. behind critical sites
B. in front of critical sites
C. to the side of critical sites
D. over the top of critical sites

Pharmacist Learning Assessment

Growth is expected when surface testing.

A. True
B. False

A. True
Pharmacist Learning Assessment

Certification must be performed under __________ conditions

A. static
B. stagnant
C. dynamic
D. passive

C. dynamic

Reference
United States Pharmacopeia USP 39 - NF 34

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