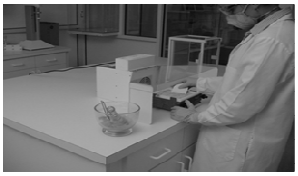
Pharmaceutical Compounding Sterile Preparations

-USP 797-



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GOALS

- To know the rules and regulations outlining USP 797
- To know the proper protocols that detail hood cleanliness, item placement, aseptic technique and all the details in order to compound sterile products under the USP 797 requirements
- To have a solid foundation of USP 797
- To be comfortable enough to implement such regulations in the work force

ROAD MAP

- Define USP 797
- Review the Risk Level Classifications
- Understand Standard Operating Procedures
- Know how to properly garbing up including chemotherapy biohazard compounding
- Review the proper steps to clean the hood
- Know the difference between Horizontal vs Vertical hoods
- Understand the importance of "item placement"
- Review Aseptic Technique
- Revisit the details

WHAT IS USP <797>?

- USP stands for United States Pharmacopeia
  - Non-government, non-profit organization
  - Designed to create standards on patient safety, healthcare information, and verification of products
- <797> specifically refers to sterile compounding of pharmaceuticals (i.e. IV admixtures) in order to prevent patient harm

RISK LEVEL CLASSIFICATIONS

- Divided into low, medium, and high
- Barring exemptions for immediate-use (<3) CSPs for non-hazardous sterile drugs only, which must have administration begun within 1 hr. after start of preparation, the levels break down as follows:
- Low-risk level: (ISO Class 5 environment)
  - Involves only a few basic, steps (reconstituting single-dose vials of antibiotics, simple transfers of sterile products or preparing hydration solutions). There is also a subsection of low risk designed for facilities with no ISO 7 secondary control clean room the low-risk level with 12 hour or less Beyond Use Date (BUD). This category is for those products that are low risk and will be administered within 12 hours of compounding.

RISK LEVEL CLASSIFICATION, CONT.

- Medium-risk level: (ISO Class 5 environment)
  - involves complex procedures: ie…bulk compounding
  - could occur over an extended period
  - Includes using pooled sterile commercial products for multiple patients or for one patient multiple times, as in chemotherapy or pain management administered by an infusion device

Risk Level Classification, cont.

- High-risk level:
  - Measuring or mixing sterile ingredients in non-sterile devices before sterilization is performed
  - Dissolving non-sterile bulk drug and nutrient powders to make solutions, which will be sterilized
  - i.e. Cardioplegia drips
  - OR from sterile ingredients but the environment is below ISO Class 5.
  - It also occurs if > 6 hours passes between compounding and sterilization and/or the purity of compounds are not verified by documentation.

Hazardous Drugs as CSPs

- When compounding hazardous drugs, a biological safety cabinet (BSC) or compounding aseptic containment isolator (CACI) must be used.
- All hazardous drugs must be stored and prepared in a negative pressure ISO 7 with an ISO 7 ante area.
- BSCs or CACIs should be vented to the outside.
- Waste disposal should be according to state and federal regulations.

Radiopharmaceuticals as CSPs

- Highly particulate generating materials, like lead containers, are required to be used for the protection of handlers. ISO Class 8 air is permitted because it is hard to maintain air cleanliness with all of the lead shielding being used.
- Therefore, when preparing these CSPs the guidelines are:
  - Must be prepared in an ISO 5 containment device in an ISO 8 environment or cleaner
  - Principals of ALARA followed (as low as reasonably achievable)
  - Allowance for preparation of radiopharmaceuticals under the Low-Risk Level with 12 hr BUD – hot labs in hospitals have better chance of compliance as long as they have ISO Class 5 PEC

ALLERGEN EXTRACTS AS CSPS

- Unpreserved allergen extracts must fully comply with 797, but most allergen extracts are highly preserved. Preparations using preserved allergen extracts are exempt from certain aspects of USP 797 under certain conditions involving:
  - Hand hygiene
  - PPE used
  - Simple aseptic transfer
  - Contain effective amount of preservative
  - Single patient only
  - Gloves are disinfected with IPA
  - Vial stoppers disinfected
  - Labeling requirements

ENVIRONMENTAL SAMPLING

- Designed to demonstrate a suitable environment for aseptic compounding
- Electronic measurement of the total number of airborne particles
- Certification of ISO 5, 7, and 8 environments
- Volumetric air sampling of viable microorganisms
- Glove fingertip monitoring
- Surface sampling

STANDARD OPERATING PROCEDURES

- Prior to entering the IV room:
  - Remove outer jackets, and jewelry (watches/rings)
  - Long-sleeved shirts may NOT be worn
- Personnel must comply to the cleaning and gowning policy (hair bonnet, mask, gown, gloves, shoe covers, no: makeup, lotions, perfume, chapstick, etc)
- All additive containers must be swabbed with 70% isopropyl alcohol
- Blowers of the laminar air hoods must operate continuously, or be turned with appropriate time period prior to procedures
- Supplies must be arranged aseptically within the hood to minimize air flow turbulence
- At the end of compounding, discard all syringes and needles in the sharps container
- All compounded products will be labeled properly

Initial Garbing

- Mask
  - Masks must cover the nose and mouth
- Hair bonnet
  - All hair must be contained within the hair cover
- Shoe covers

Hand Washing

- Thoroughly wash hands, nails, and arms up to the elbow with antiseptic cleansing agent and water for 30 seconds
- Dry hands with a non-shedding towel, from fingertips to elbow discarding after each swipe

Gowning for Sterile Compounding

- Cover gown must be donned

After Gowning . . .

- Wear protective gloves
- Gloves extend over the gown cuffs
- Gloves should be sprayed with isopropyl alcohol 70% and rubbed thoroughly
- Allow gloves to air dry before proceeding with sterile preparations

All the Details

- Remove outer garments and jewelry, makeup, including earbuds and headsets
- Garb from dirtiest to cleanest parts of body
- Shoe covers, hair covers, beard covers and face masks, even if have no hair
- Hand/arm hygiene
- Disposable non-shedding gowns
- Sterile powder-free gloves compatible w/ IPA
- Repeatedly apply IPA to contact areas of gloves
- Immediate use provision (emergency situation) does not have garbing requirements
- Disinfectant and Cleaning
- Maintenance of compounding areas is overlooked and this was an extensively updated portion of USP 797.
- Designed to reduce bioburden in compounding areas
- Use sterile 70% IPA and germicidal detergent
- To be performed in ISO 5 environment very frequently
- Clean from cleanest to dirtiest
- Use dedicated mops and cleaners

Gloves

- Intermittently sterilize gloves with isopropyl alcohol 70%
- Change glove when torn, punctured, or contaminated

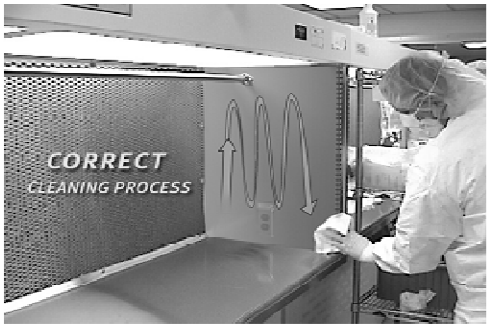
Chemotherapy/Biohazard

- Prior to Compounding:
  - disposable chemo gown and chemo gloves when compounding a chemotherapeutic or biohazard agent
  - Make sure that the gloves extend over the cuff of the gown

Cleaning of Compounding Area

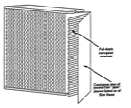
- Before each shift:
  - Use isopropyl alcohol 70% to clean the compounding area prior to the next shift
- Allow alcohol to remain for at least 30 seconds
- Clean from back to front and top to bottom and avoid contact and contamination of the HEPA filter

Correct Hood Cleaning



Incorrect Hood Cleaning

HEPA FILTER

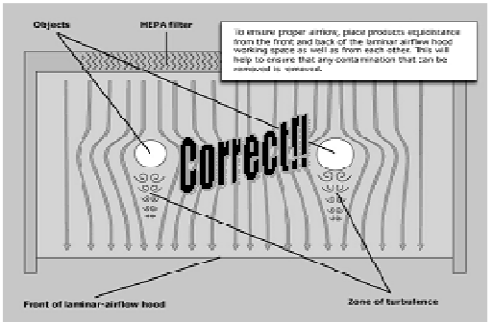


- High Efficiency Particulate Air (HEPA) filter removes 99.97% of all air particles 0.3microns or larger
- It flows at a constant rate and physically sweeps the work area and prevents the entry of contaminated air
- Nothing should be permitted to come in contact with the HEPA filter
  - Including: cleaning solutions, aspirate from syringes, sterile fluids, needles
  - Break ampules away from the HEPA filter

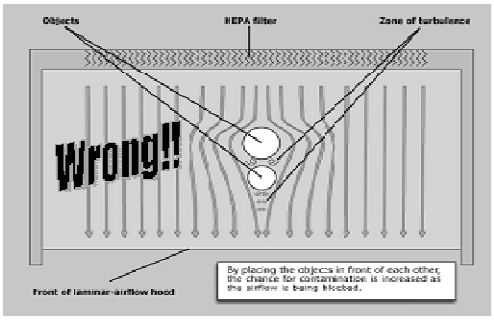
AIR FLOW HOODS

- Horizontal Flow (Laminar Flow Hood)
  - Air blows towards personnel
  - Should be left operating continuously
  - If it is turned off, it must be run for **30 minutes** to re-establish air flow and be cleaned before use
- Vertical Flow (Chemotherapy Hood)
  - Air blows from top down
  - Should be left operating continuously
  - If it is turned off, it must be run for **4 hours** to re-establish air flow and be cleaned before use

LAMINAR FLOW HOOD CORRECT ITEM PLACEMENT



Laminar Flow Hood Incorrect Item Placement



Aseptic Technique

- A technique for manipulations of compounded sterile products and parenteral preparations that prevents contamination
- Contamination sources:
  - People – touch and airflow contamination
  - Air (via ventilation or air conditioning)
  - Infiltration (via adjacent rooms)
  - Internal generation (via walls, floors, ceilings)

Aseptic Technique, Cont.

- Hand placement during aseptic manipulation should be such that laminar airflow is not interrupted around any of the critical sterile surface pathways
- Talking or coughing should be directed away from the hood to minimize contamination
- No food or drink is allowed in the clean room

ASEPTIC TECHNIQUE, CONT.

- All sterile compounding inside the hood should take place at least six inches into the hood to prevent contamination from the room air
- Only essential products should be in the hood
  - No paper, cardboard, pens, calculators, or labels in the hood

BREAKING DOWN THE DETAILS

- Vials
- Syringes
- Needles
- Ampules
- Finally, THE FINAL PRODUCT

VIALS

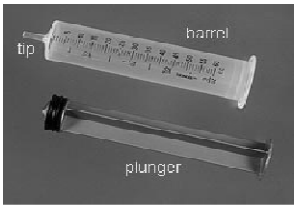
- Swab the rubber top of the vial with an alcohol prep pad using firm strokes in a unidirectional sweeping motion at least once
- Allow the alcohol to air dry
- Inject an equal amount of air for the volume of fluid to be removed to prevent vacuum formation

Single-Dose vs. Multiple Dose Containers

- Single dose vials (SDV), if opened or punctured in > ISO 5 area, may be used for ≤ 6 hours.
- SDV, punctured in < ISO 5 air quality, must be used within one hour and remaining contents discarded.
- Opened single-dose ampules must be discarded and may not be stored for any time period.
- The BUD for opened or entered multiple-dose containers is 28 days, unless otherwise specified by the manufacturer.
- Additionally, in Multiple-dose and single-dose sterile products or CSPs for use as multiple-dose applications, **combining is forbidden**.

Syringes

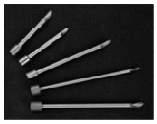
- Never touch the tip or plunger of the syringe for this could lead to touch contamination



Syringes, cont.

- Syringes are available in sizes ranging from 0.5 to 60 mL
- In most cases, you should use the smallest syringe possible to draw up your complete volume; exception: chemotherapy

NEEDLES



- Needle size is determined by gauge and length
- Never touch any part of the needle
- Open needle packages within hood to maintain sterility
  - Peel open the needle wrapper
  - Tearing the paper introduces paper particles into the hood, leading to contamination
- Needles and syringes must be disposed of in the sharps container

NEEDLES, CONT.

- Coring: A core or hole in the rubber top of the vial
- To prevent coring, insert the needle as shown
- Insert the bevel tip first, then press downward and toward the bevel so that the bevel tip and heel enter at the same point

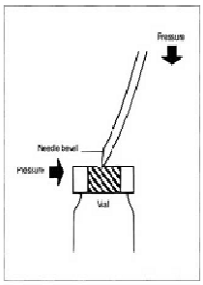


Figure 15-5 A noncoring method of piercing a vial with a needle.

AMPULES

- Clean the ampule neck with an alcohol swab
- Leave swab in place and grasp the ampule neck
- Use quick, firm, snapping motion away from the body towards the side wall of the hood
- Do NOT break ampule towards HEPA filter

AMPULES, CONT.

- To withdraw medication from the ampule:
  - Tilt ampule
  - Place needle bevel near opening of ampule
    - No need to withdraw air first
  - Pull back on syringe plunger
  - ALWAYS use a filter needle to remove ampule contents
  - Filter needles can only be used in one direction, otherwise glass particles originally filtered are reintroduced.

FINAL PRODUCT

- Inspect final product after admixing to look for precipitation, cores, or other particulate matter

LABELING REQUIREMENTS

- Patient name
- Patient location (room #, address)
- Drug name, strength, and quantity
- Diluent and volume
- Route of administration
- Beyond use date and final time
- Infusion rate
- Compounder's initials
- Pharmacist's initials
- Auxiliary label(s)
- Bar code (whenever possible)

SUMMARY

- USP <797> can be complicated
- There are many details to consider while maintaining compliance with USP <797> such as Risk Level Assessment, proper garbing, different hoods, item placement, sterile aseptic technique, and all the details with vials, syringes, needles, and disposal.
- Lastly, the labeling requirements are extensive, and uniformly so, but necessary to prevent errors.

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QUESTIONS?