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Understanding the Basics of Aseptic Technique and Infection Prevention in Medication Preparation and the Pharmacy

Joseph Coyne, RPh – Director of Field Operations

Kastango Consulting Group

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- Conflict of Interest Disclosure
- The speaker is an employee of the Castango Consulting Group/CriticalPoint, LLC.



- Between January 1, 2001 and December 31, 2013 – nineteen (19) outbreaks resulting in at least 1,000 cases, including deaths.
- Many outbreaks linked to non-patient specific repackaging of sterile products and nonsterile-to-sterile compounding
- Consistently characterized findings
 - Lack of adherence to regulatory and professional standards
 - Outbreak incidents are likely highly preventable
 - Need improved oversight and adherence to standards crucial

Shehab N, Brown MN, Kallen AJ, Perz JF. U.S. compounding pharmacy-related outbreaks, 2001-2013: public health and patient safety lessons learned. J Patient Saf. May 21, 2015.


NECC Summary – 7-years since the Outbreak



New England Compounding Center (NECC) Meningitis Outbreak (updated)

| | |
|----------|---|
| Date | September 21, 2012 to present since patients are still suffering |
| Location | USA (20 States) |
| Cause | Fungal meningitis contamination of steroid medication |
| Injuries | 778 total case count; 384 meningitis and spinal infection; 7 stroke; 325 paraspinal/spinal infection; 33 peripheral joint infection; 2 spinal and peripheral joint; some patients recovering from the meningitis are falling ill again. sufferers of the new infection are now coping with epidural abscesses and infections near the injection site. |
| Deaths | 78 |
| Judicial | Cadden sentenced to 9 years, Chin sentenced to 8 years Court requires restitution from both |

National Assessment of state Oversight of Sterile Drug Compounding

- Published in 2016 
- The Pew Trusts found that only 30% of states (13 of 43 that responded) require sterile compounding pharmacies to report serious adverse events.
- Contamination of sterile preparations was the *most common compounding error*, though others were the result of pharmacists' and technicians' miscalculations and mistakes in filling prescriptions.



National Assessment of State Oversight of Sterile Drug Compounding

- CSPs not readily recognized as potential sources of contamination
- Medications involved may be commonly used in health care settings
- Pathogens involved may be common causes of HAIs
- Presentation of infectious illness can be delayed, depending on the pathogen (e.g., fungal pathogen with long incubation period) or site of exposure/infection (e.g., indwelling catheter).
- Cases present to multiple facilities and providers, owing to multifacility and/or multistate distribution of compounded sterile preparations.
- Mandatory reporting of adverse drug events from compounded sterile preparations to FDA by compounding pharmacies historically has not been required.

Shehab N, Brown MN, Kallen AJ, Perz JF. U.S. compounding pharmacy-related outbreaks, 2001-2013: public health and patient safety lessons learned. J Patient Saf. May 21, 2015.

SDCs, MDVs, PBP and Point of Care Activated



| Container Type | Preservatives | BUD |
|---------------------------------|--|---|
| Single Dose Ampule | No | N/A because not stored |
| Single Dose Vial* (SDV) | No | 6 hours if opened in ISO class 5 OR 1 hour if opened in air worse than ISO 5* |
| Multiple Dose Vial (MDV) | Yes | 28 days from initial puncture or per manufacturer's package insert |
| Pharmacy Bulk Package (PBP) | No | 6 hours or shorter if opened in ISO class 5 |
| Point-of-Care Activated Systems | <ul style="list-style-type: none">• ADD-Vantage™, MINIBAG PLUS, addEASE®• Attaching/activating these not considered compounding• Acceptable for nursing to attach and activate• Use manufacturer's instructions for storage and stability | |

The CDC advised on a more conservative approach to further safeguard patients. The CDC stipulates that the remaining contents must be discarded at the end of the procedure/case and must not be stored.



Single Dose Containers (SDC)

- Use of SDCs is strongly encouraged
 - Discard SDCs after use
- Ampules
 - must be discarded after opening
 - do not store
 - Must use filter needle/filter straw

Multiple Dose Vials (MDV)/ other

- If an MDV is used, it should be used for 1 patient.
- Each entry into an MDV must be with a new unused sterile needle and syringe.
- Keep MDVs away from patient care environments.
- Subsequent to emergency treatment, discard all opened medications, solutions and supplies.
- Dispose of needles at the point of use in an approved Sharps unit.



Drug Preparation DON'Ts

Never leave a needle, cannula or other spike device in a vial stopper as it increases the risk of contamination.

- This image was taken in an actual office practice setting. This was one inventive way the practitioner thought they were complying with proper sterile compounding practices. By leaving the needle in the vials and storing them in a non-ISO Class 5 space, these vials are at significant risk for contamination.



This is NEVER acceptable practice.



Drug Preparation DON'Ts (continued)

- Never use an IV container to obtain diluent/flush solution for more than 1 patient.
- Never use any supply (needle, syringe, tubing, etc.) on more than 1 patient.
- Don't remove sterile packaging until immediately before the item is used.
- Never combine leftover contents of vials for later use.
- Don't prepare medication in one syringe and transfer it to another syringe.
- Don't store vials in pockets.
- Food and beverages must be stored separately from drugs and supplies.





Aseptic Technique

A set of specific work practices and procedures performed under carefully controlled conditions with the goal of minimizing the introduction of contamination.¹

Notice the definition says “specific” work practices...make sure the elements of aseptic technique are defined in your SOPs



¹Kastango ES. Spread the Word: Aseptic Technique Prevents Infection. Pharmacy Purchasing and Products Magazine. April 2009. Retrieved on 2/20/18 from <https://www.pppmag.com/article/522/>.

Elements of Aseptic Technique

- Preparation before reporting to work
- General workplace rules
- Hand Hygiene and Garbing (next lecture)
- Proper Supply Staging
- General Conduct in Controlled Environments
- Organization of Work and Work Surfaces
- Methods of Critical Manipulation



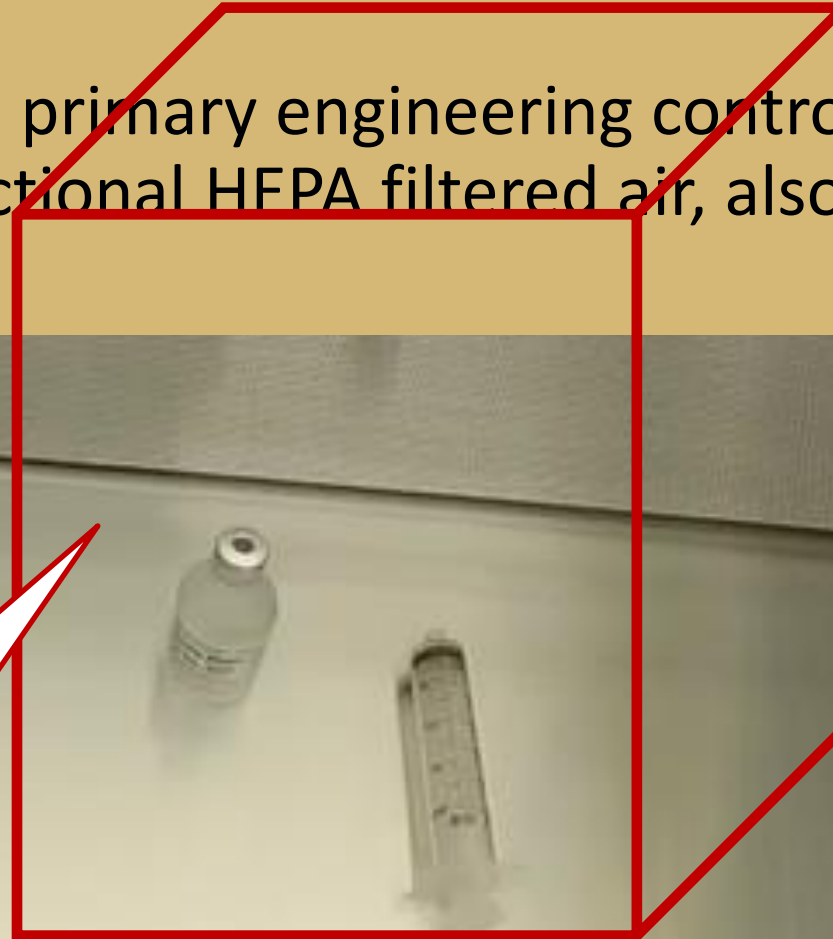
Critical Site

Locations that include any component or fluid pathway surface (via septa or injection ports) or openings (ampoules or needle hubs) exposed and at risk for direct contact with air, moisture or touch contamination.



Direct Compounding Area (DCA)

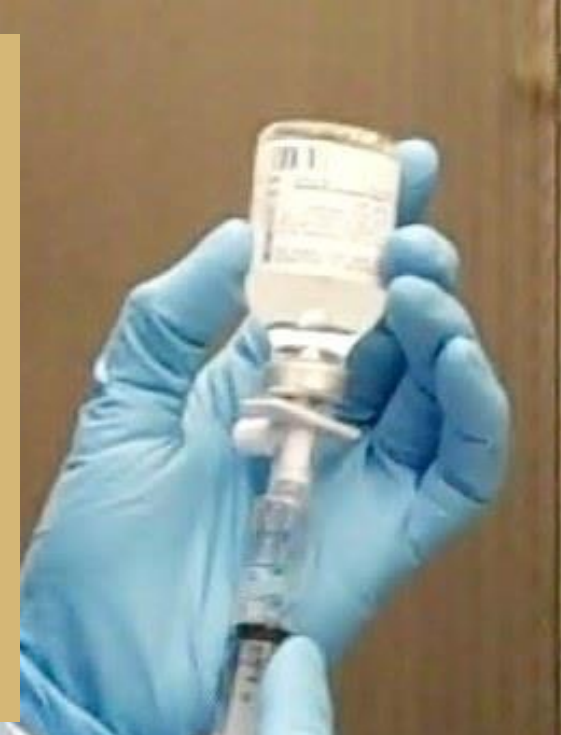
A critical area within the ISO class 5 primary engineering control (PEC) where critical sites are exposed to unidirectional HEPA filtered air, also known as First Air.



Imagine a 3-dimensional box extending from the deck to the air above the deck in the location where you will perform your critical manipulations

Aseptic Break

Result of an aseptic manipulation, whereby the manufacturer's sterile container (i.e. the solution contact surface) of medication or solution for injection, is pierced, opened, entered or exposed to an outside environment, which would allow for the introduction of microorganisms or particulate matter.



Think of a methodology that reduces the potential for contamination by reducing the number of aseptic manipulations we make while compounding.



First Air

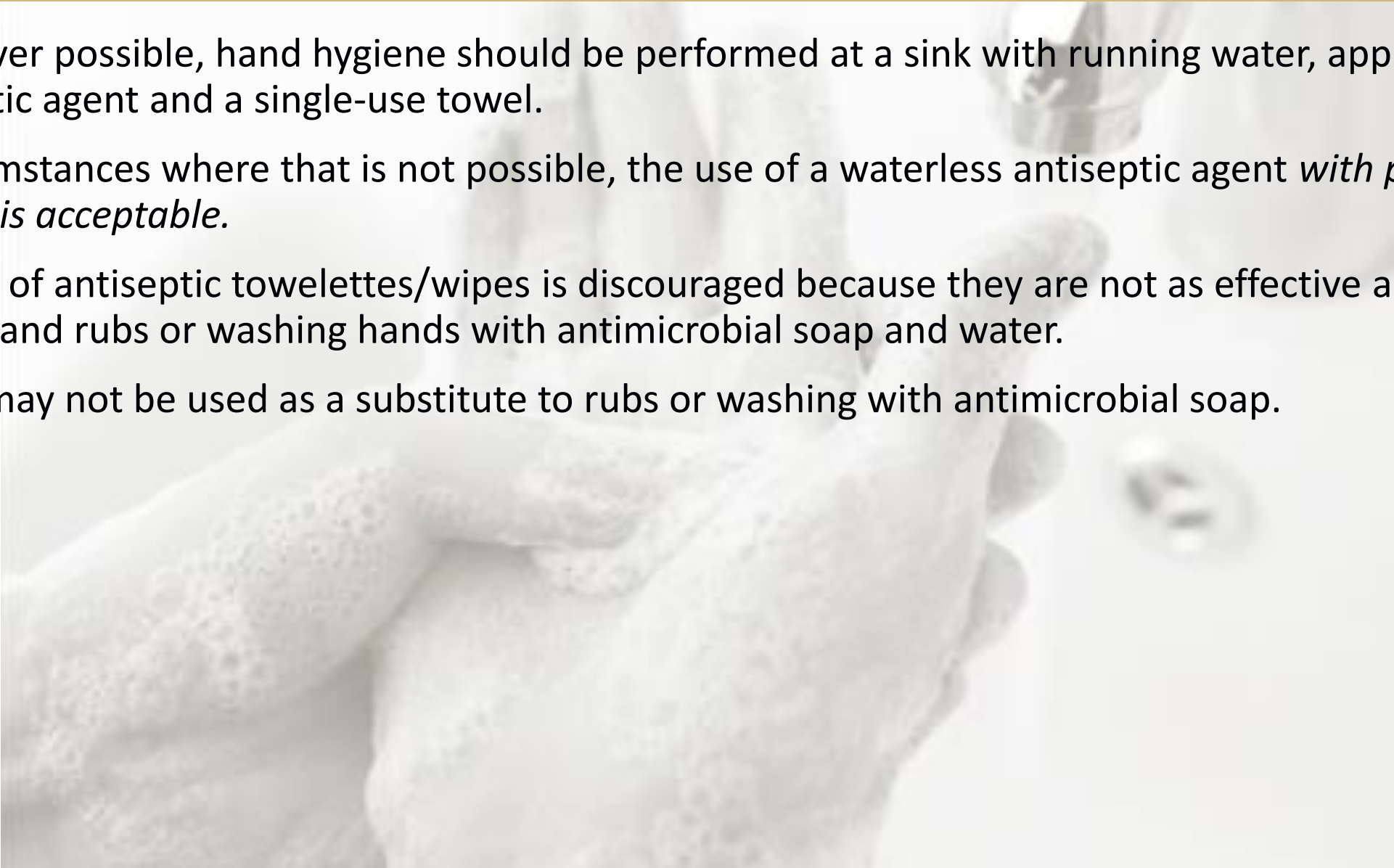
The air exiting the HEPA filter in a unidirectional air stream that is essentially particle free.



What is the problem with this technician's technique?

Perform hand hygiene and garbing

- Whenever possible, hand hygiene should be performed at a sink with running water, appropriate antiseptic agent and a single-use towel.
- In circumstances where that is not possible, the use of a waterless antiseptic agent *with persistent activity is acceptable*.
- The use of antiseptic towelettes/wipes is discouraged because they are not as effective as alcohol-based hand rubs or washing hands with antimicrobial soap and water.
- Wipes may not be used as a substitute to rubs or washing with antimicrobial soap.



- If hand hygiene was performed with antimicrobial soap and water, after drying hands thoroughly, follow with the application of an alcohol-based hand sanitizer.
- The CDC recommends choosing products that contain at least 60% alcohol.
- Apply as recommended by the manufacturer to the palm of the hand and rub hands and fingers together covering all surfaces until they are dry.



- Hair net
- Beard cover and face mask
- Gown
 - Nonsterile
- Gloves
 - Sterile
- Shoe covers



- Move slowly...it really does make a difference!

| Activity ¹ | Particles Generated |
|---------------------------------|---------------------|
| Sitting quietly | 100,000/minute |
| Walking slowly (1.9 miles/hour) | 5,000,000/minute |
| Walking medium (3 miles/hour) | 7,500,000/minute |
| Walking fast (5 miles/hour) | 10,000,000/minute |

¹Particle Measuring Systems. [Basic Guide to Particle Counters and Counting](#). 2011. Accessed on 3/15/2017 from Pharmaceutical Online.

General Conduct: Do not touch your face!

- Remember the movie, Contagion? A line from it said “the average person touches their face 2000 to 3000 times per day.” (average of 3 to 5 per waking minute)
- Students studied touched their face 16 times per hour¹
- Another study of medical students identified 23 times per hour²

26 medical students were observed to touch their face 23 times per hour.

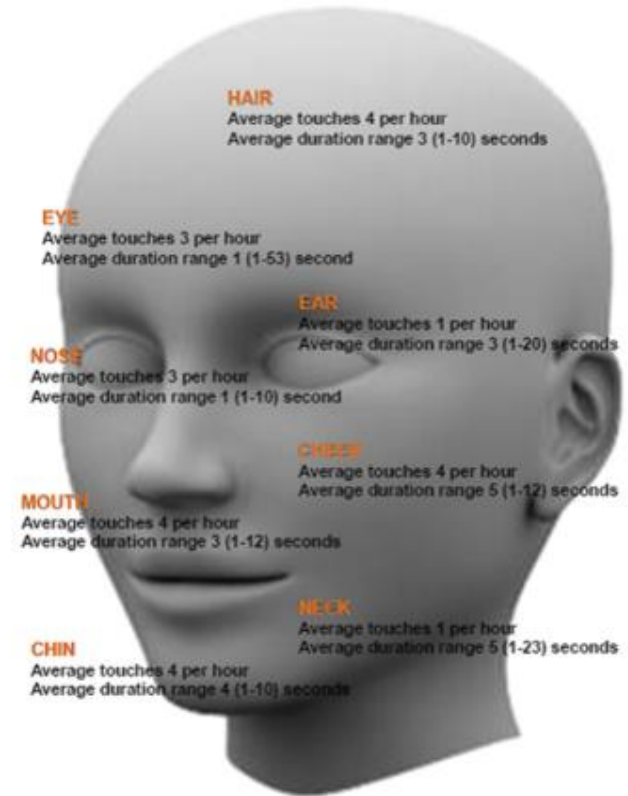


Fig 1. Average number of face touches observed in a 60-minute period.

Y.L.A. Kwok et al. / American Journal of Infection Control 43 (2015) 112-4

¹Nicas M, Best D. A study quantifying the hand-to-face contact rate and its potential application to predicting respiratory infection. J Occup Environ Hyg. 2008. 5(6): 347-52. Available for purchase at [PubMed.gov](https://pubmed.gov)

²Kwok YL, Galton J, McLaws ML. [Face touching: a frequent habit that has implications for hand hygiene](#). Am J Infect Control. 2015. 43(2):112-114

- Under NO CIRCUMSTANCES can compounding staff carry any personal electronic devices (PEDs) into the controlled environments!
 - 100% of phones contaminated with either single or mixed bacterial agents¹
 - Most prevalent methicillin-resistant *S. aureus* and coag negative staphylococci¹
 - Mean organisms per phone between 1720 to 2192¹

¹Selim HD, Abaza AF. Microbial contamination of mobile phones in a health care setting in Alexandria, Egypt. *GMS Hyg Infect Control* 2015. Retrieved on 3/15/2017 from <http://www.egms.de/static/en/journals/dgkh/2015-10/dgkh000246.shtml>.



Proper Supply Staging

#1 Wipe Components in Anteroom/Prep Area

- Chapter <797> requires drugs and components must be wiped or sprayed with an appropriate disinfectant after they are removed from cardboard packaging and before they are brought into buffer room or beyond the perimeter of the SCA
- Wipe versus spray
- Sporicide or germicidal detergent versus IPA
- Perform on dirty side of anteroom or immediately before entering anteroom (if space limitations)

#2 sIPA immediately before placing in PEC

- With the exception of syringe and needle packages, all items are wiped down with sterile 70% IPA immediately prior to their placement inside the ISO 5 space
- Must use low-linting wipe wetted with sterile IPA or preferably sterile low-linting wipes presaturated with sterile 70% IPA



Proper Supply Staging

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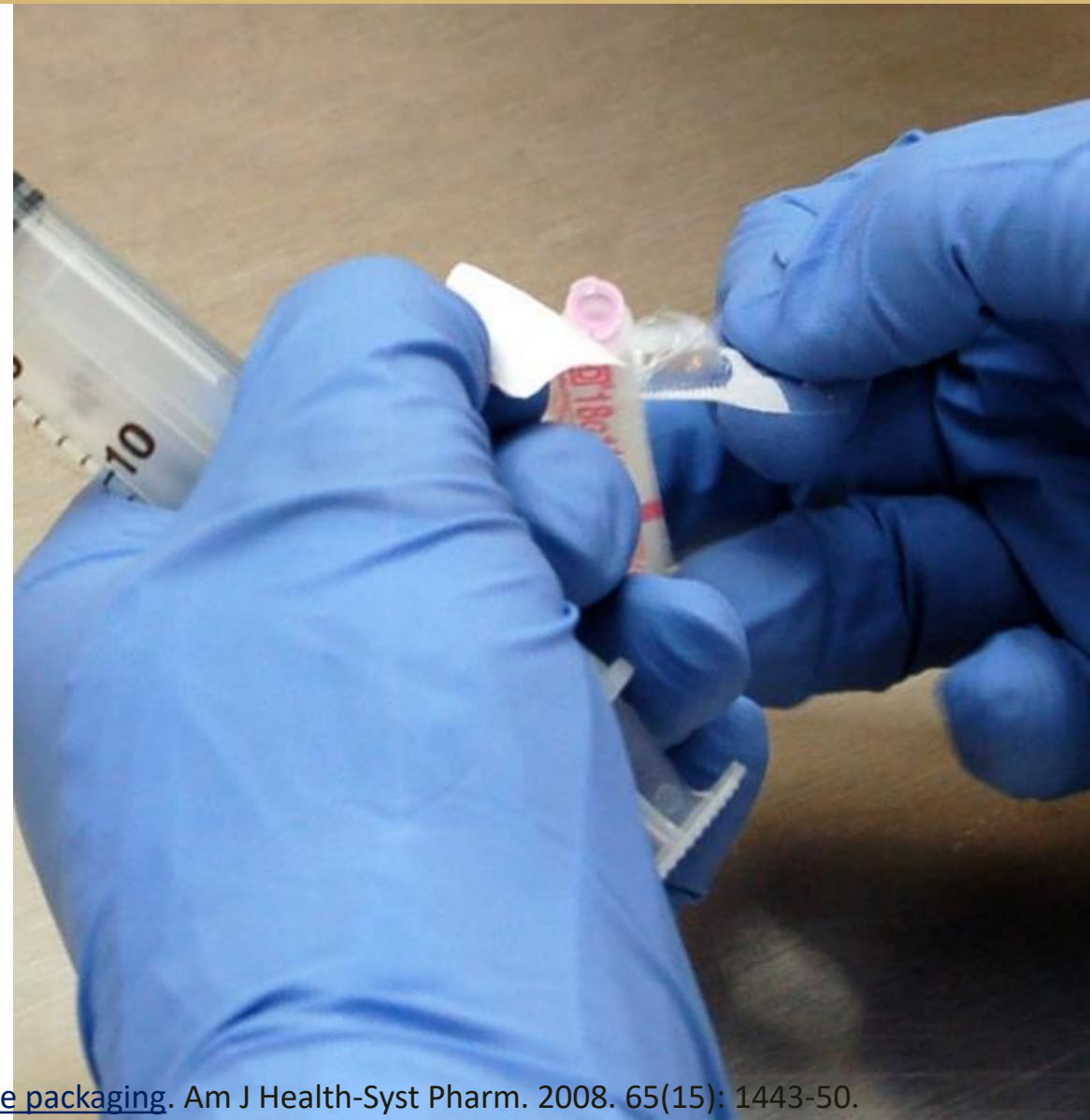


- Each patient specific CSP or batch should optimally be:
 - Staged from a Master Formulation Record or Compounding Worksheet
 - Drugs and supplies pulled by 1 person
 - Checked INDEPENDENTLY by a 2nd (different) person than the person who pulled
 - Drugs, components, supplies, labels and documentation should be contained in one bin
- Avoid entry in and out of room
- Enough staged batches for compounder to stay in room and compound for 3 hours at a time
- Sufficient space for staged batches

- Observe “area clearance” which means that you do not begin work unless the work space is first cleared of any contents from the previous batch or patient
 - Work on only 1 batch or patient CSP at a time
 - Area clearance applies to labeling patient or batch as well
- Visualize first air in your mind and remember not to block first air from bathing the critical site
- Remembering unidirectional HEPA filtered air (First Air)



- Work from left to right, keeping the DCA spartan (with minimal equipment and supplies)
- Keep a clear zone 12 inches on both sides of the DCA ensures that ISO class 5 conditions are maintained¹
- Do not open packages directly in front or over opened vials, ampules or other critical sites¹
- Open packages using the “peel and present method” versus the “pop-through” as that method generates significantly less particles¹

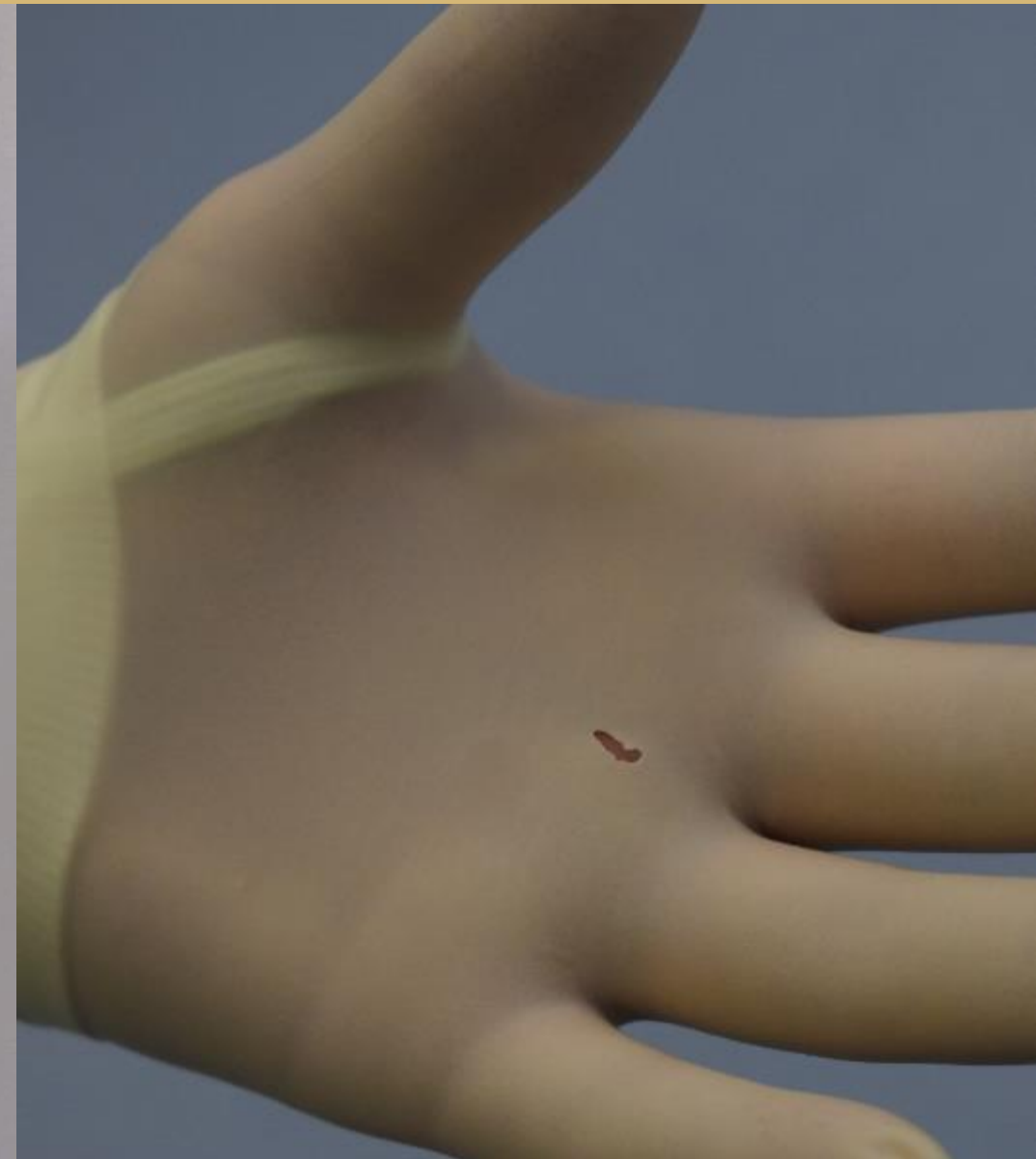


¹Kastango ES et al. [Generation of particulate matter during handling of needle and syringe packaging](#). Am J Health-Syst Pharm. 2008. 65(15): 1443-50.

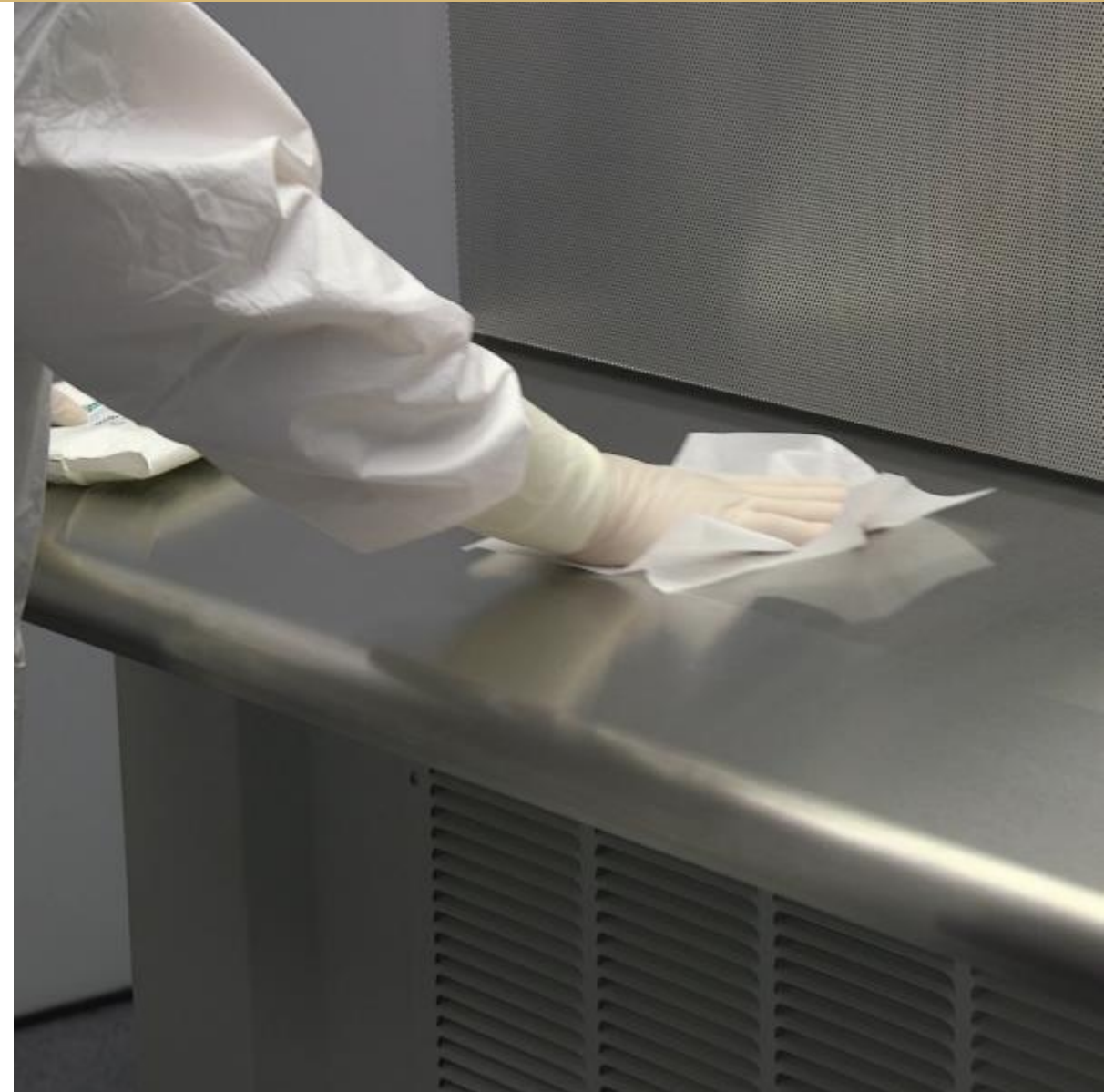
- Gloves should be disinfected routinely throughout the compounding day
- Spray gloved hands with SIPA and rub together, including in between fingers **and wrists** to ensure that the SIPA comes into contact with all surfaces of the gloves
- Allow gloves to thoroughly dry prior to beginning or continuing the preparation of CSPs
- Gloves become contaminated when they come into contact with non-sterile surfaces (e.g. phones, keyboards, vial shields) therefore, they need to be disinfected regularly
- Sanitize gloves anytime hands leave ISO Class 5 area
- Always disinfect gloves just prior to performing any aseptic procedures

Conduct in ISO 5: When to replace gloves

- Inspect gloves routinely for:
 - Holes
 - Punctures
 - Tears
- If gloves need to be replaced, remove defective gloves and perform antiseptic hand cleansing, utilizing an alcohol-based hand rub with persistent activity, prior to donning a fresh pair of gloves.
- When in doubt, if gloves are torn or worn, always replace immediately!
- You need to protect your skin from the harsh cleaning agents.



- Resanitize the deck frequently during the compounding day
- Before beginning compounding
- At least every 30 minutes
- Between batches or patient-specific
- Sanitize the deck beneath the DCA much more frequently
- Wet sufficiently with sIPA



- Sterile Alcohol Prep Pads VS Critical Site Wipes (4 x 4)?
 - Both are acceptable choices for this task
- How to use them?
 - Use once and discard? Use other side? Use until no longer wet?
 - Reality is there's no data but TJC will cite infection control failure if use more than once
 - Wipe in a single direction 3 times and allow to dry
 - Must be used on all CRITICAL SITES (vial septa, ampules neck, minibag port)

Syringes

- Syringes must be sterile (single use)
- Can be individually wrapped or in bulk sterile packaging
- Open to left of DCA
- Preferably 12" from DCA
- Do not touch critical sites
 - Piston
 - Luer lock tip

Needles

- Available in various shapes and sizes
 - Which size to use?
 - According to different references it is best to never go bigger than 19 gauge but preferable to use 20 gauge.
- Individually wrapped
- Must be careful not to touch the hub of needle while attaching to syringe
- Available with safety features (needle shielding technology, blunt needles)
- Use peel and present

- Everyone reuses needles in compounding; we need to evaluate
- Needle changes after 1st use and significantly disfigured after 6
- Most data comes from studies discouraging reuse of diabetic needles

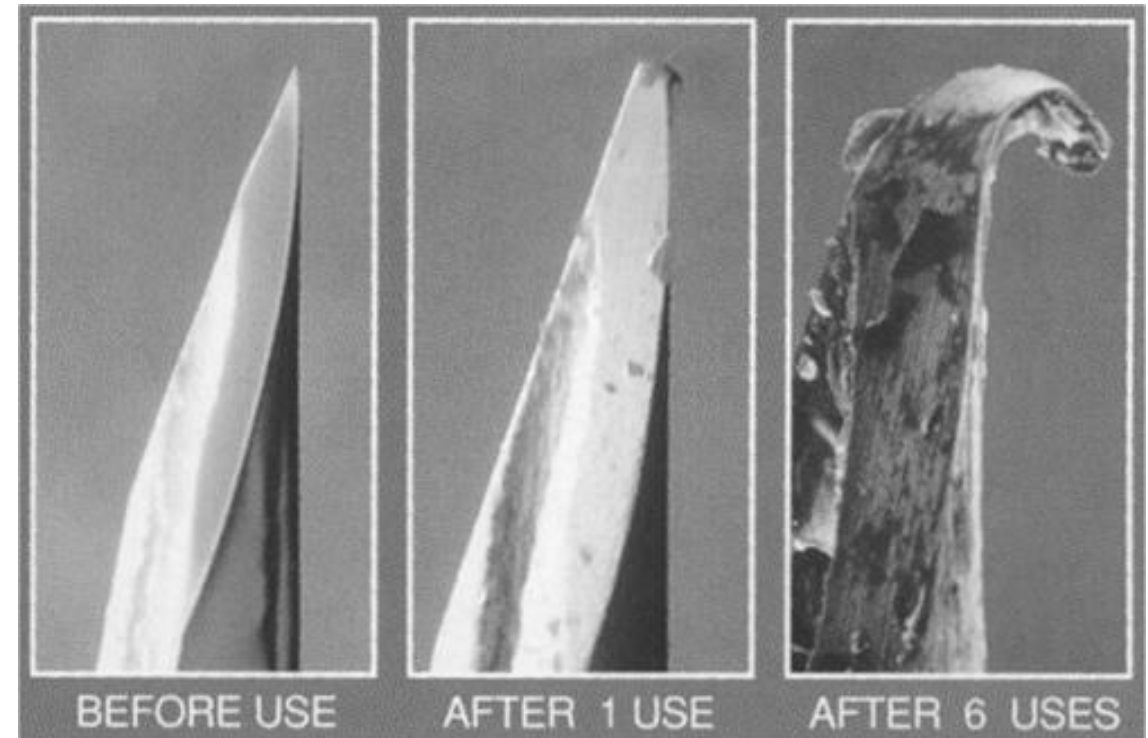


Image from [Diabetes Daily](#) retrieved on 3/16/2017

- Break towards the side wall of the PEC
- Contents must be filtered (filter straw or needle) before administration
- Filter needle can only be used to filter the contents in one direction, you can only draw up OR inject with it, not both
 - Best practice: Withdraw the contents of the ampule with a filter needle then immediately change to a regular needle
 - If you withdraw with a regular needle, change to a filter needle you can only inject (push) the contents through the filter needle
- Single use ONLY

- Can be made of glass or plastic
- Have a protective dust cover that must be removed before compounding
- A alcohol prep pad must be used to disinfect the rubber stopper
- Once needle is inserted in rubber stopper, you must never block first air as it is a critical site
- Vials are usually kept with final CSP until final verification is complete
- Can either be multidose or single use vials

- Very commonly used in making CSP
- Always contains overfill which may need to be accounted for depending on the CSP
- 2 ports available (injection port and port for infusion set for delivery to patient)
- Empty Viaflex bags are also used to mix CSPs
- A vial or injection port may be punctured up to 10 times: this is a safe estimate taking information from USP <381>

Self-Sealing Capacity

Procedure—Fill 10 suitable vials with water to the nominal volume. Fit the closures that are to be examined, and cap. Using a new hypodermic needle as described above for each closure, pierce each closure 10 times, piercing each time at a different site. Immerse the 10 vials in a solution of 0.1% (1 g per L) methylene blue, and reduce the external pressure by 27 kPa for 10 minutes. Restore to atmospheric pressure, and leave the vials immersed for 30 minutes. Rinse the outside of the vials.

Requirement—None of the vials contain any trace of blue solution.

- Conventionally manufactured 1-liter bag product
- Usually used to make electrolytes and hydration solutions for patients
- Less than 10 punctures may be made into the injection port (extrapolating from USP <381>)
- If > 10 punctures:
 - add an injection cap to the final container by attaching an injection cap onto an 18-gauge needle
 - place this “unit” into the injection cap of the final container and make all additions through the additional injection cap



- Torn glove
- Particulate matter floating in a CSP
- Needle stick injury
- Spill of medication
- Touching (manipulator touching their faces or adjusting their clothing while wearing sterile gloves, adjusting eye glasses)

26 medical students were observed to touch their face 23 times per hour.

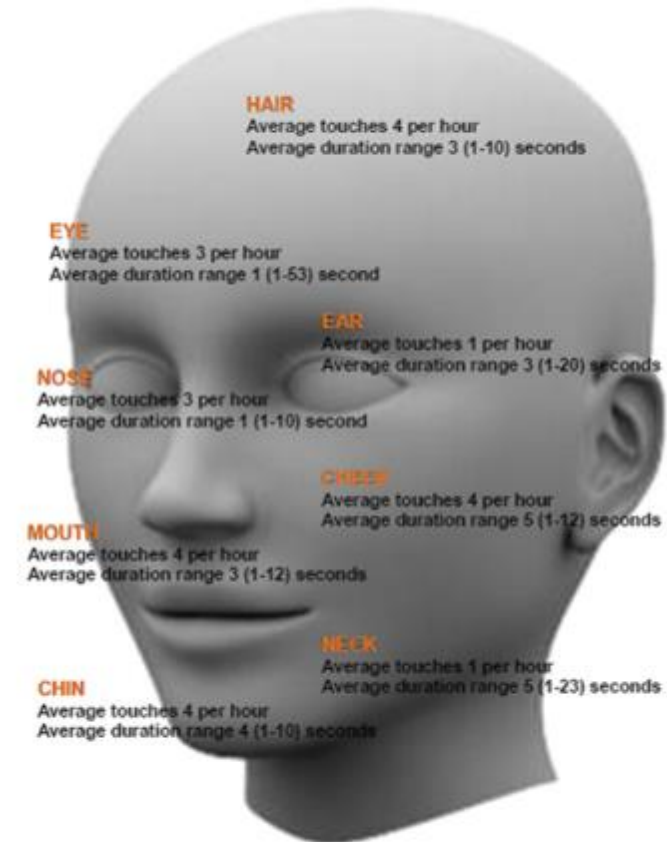


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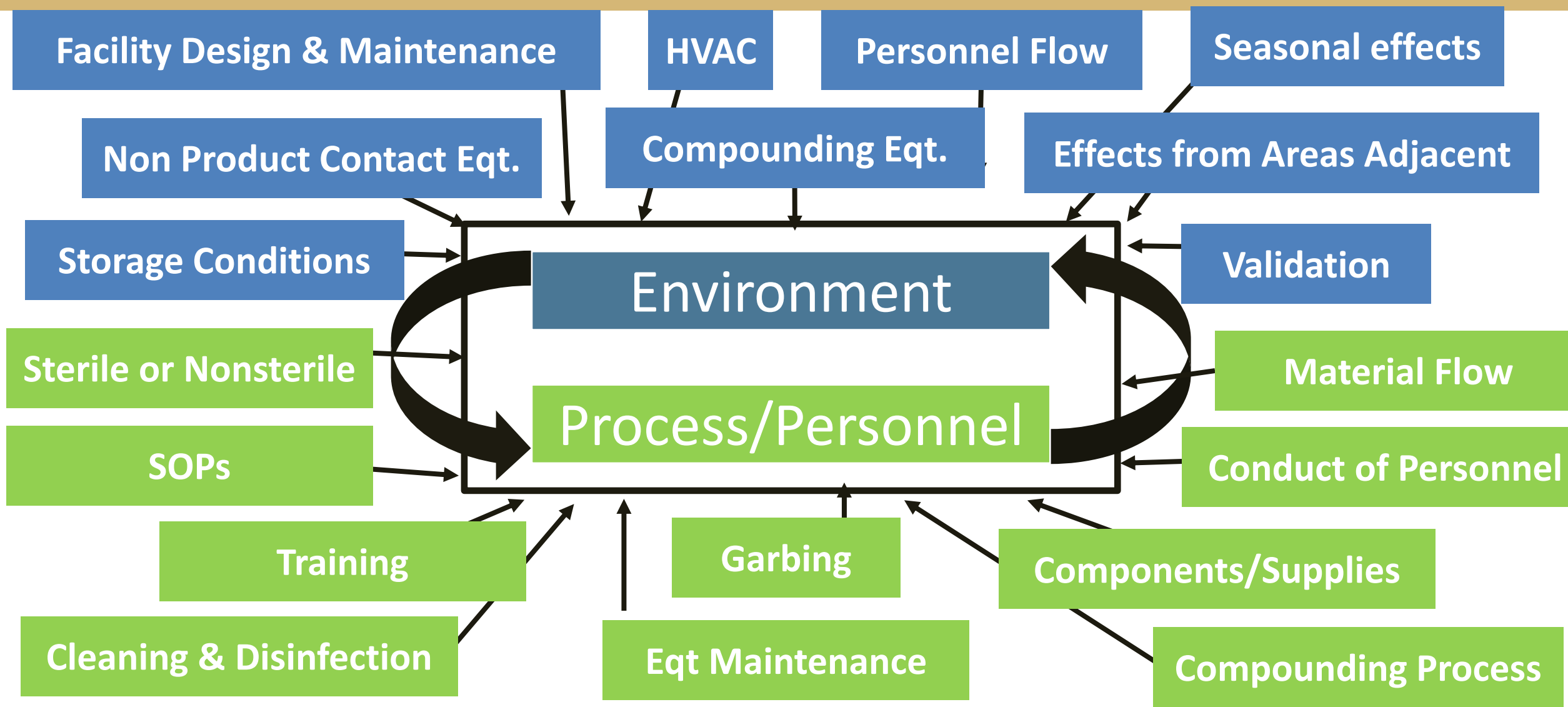
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What to do?

- Assess the severity
- Does CSP need to be discarded and restarted?
- Does PEC need to be cleaned?
- Resanitize gloves?
- Reglove?
- Re-do Hand Hygiene?

- Each compounding staff member must be vigilant at all times!
- Vigilance is:
 - Difficult
 - Takes focus
 - Constant awareness
- Suggest you perform smoke testing with all new staff as well as tenured staff to sharpen their skills
- Understanding critical sites and DCA will allow them to perform at a higher standard
- Best to perform Aseptic Technique Competency when staff does NOT know they are being observed then give immediate feedback

- Good Aseptic technique can be achieved by remembering a few basic rules
 - Limit aseptic breaks
 - Visualize first air
 - Critical Quality Assurance activities (Media Fill Units, Gloved Fingertip Sampling, and Surface Sampling)
 - Respect all SOPs
 - Leadership promotes cleanroom good practices!
 - Encourage feedback from peers and managers
 - Employee vigilance is needed and is about having robust cleanroom behaviors!



Adapted from a slide in this [presentation](#) by Jim Agalloco retrieved 3/23/2017



**“I had a miraculous dream in which
our list of questions all had answers.”**