Illinois Pharmacists Association
The Voice for Pharmacy in Illinois℠

Safe Handling of Hazardous Drugs in Community Pharmacy

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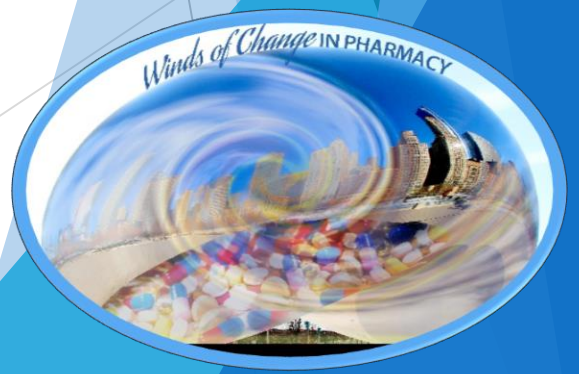
Disclosures and Conflict of Interest for Christine Roussel:

- Consultant, Medisca
- Facilitator and Content Author, LP 3 Network
- Speaker Bureau ICU Medical

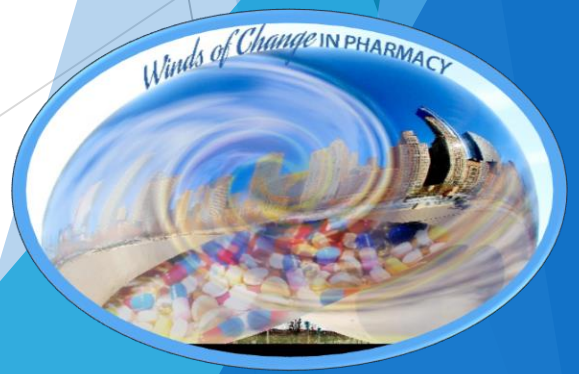
- Not speaking on any products or services offered by their company.



Pharmacist Objectives

At the conclusion of the program, the pharmacists will be able to:

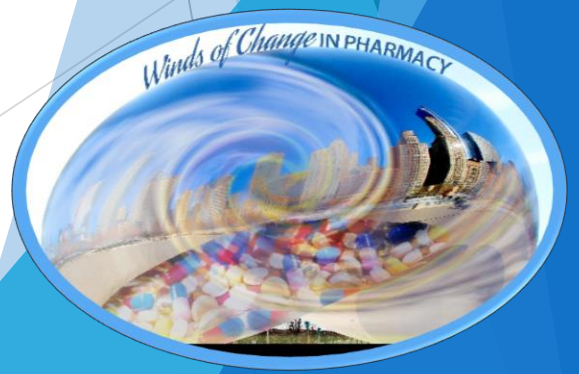
1. Identify hazardous drugs and determine appropriate handling procedures to minimize contamination
2. Perform the steps in an assessment of risk to plan alternate containment strategies
3. Facilitate safe compounding by identifying activities with them including all manipulation, crushing and splitting
4. Create procedures for disposal and decontamination of hazardous drugs



Technician Objectives

At the conclusion of this program, the pharmacy technician will be able to:

1. Recognize vectors of hazardous drug contamination and be able to review the risks to their safety and the safety of others
2. Facilitate safe compounding by identifying activities with them including all manipulation, crushing and splitting
3. Assist the pharmacist in creating procedures for disposal and decontamination of hazardous drugs

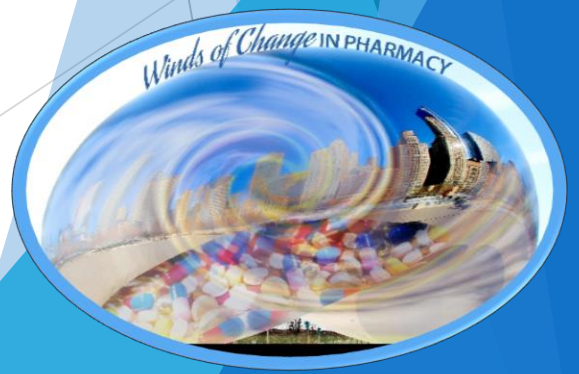


Pre-Test Question

Which one of these medications are hazardous drugs?

a. Estradiol
b. Tamoxifen
c. Phenytoin
d. Tacrolimus
e. Cyclosporine
f. All of the above

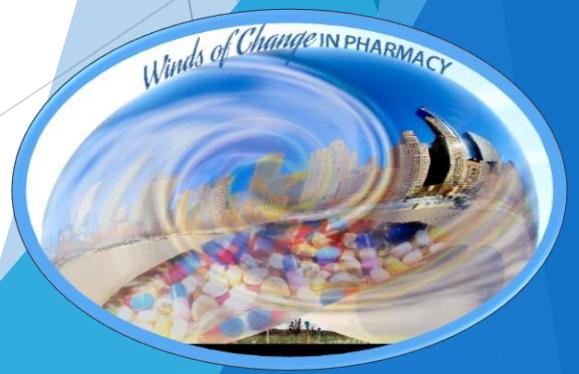
All These are Drugs are Hazardous



Pre-Test Question

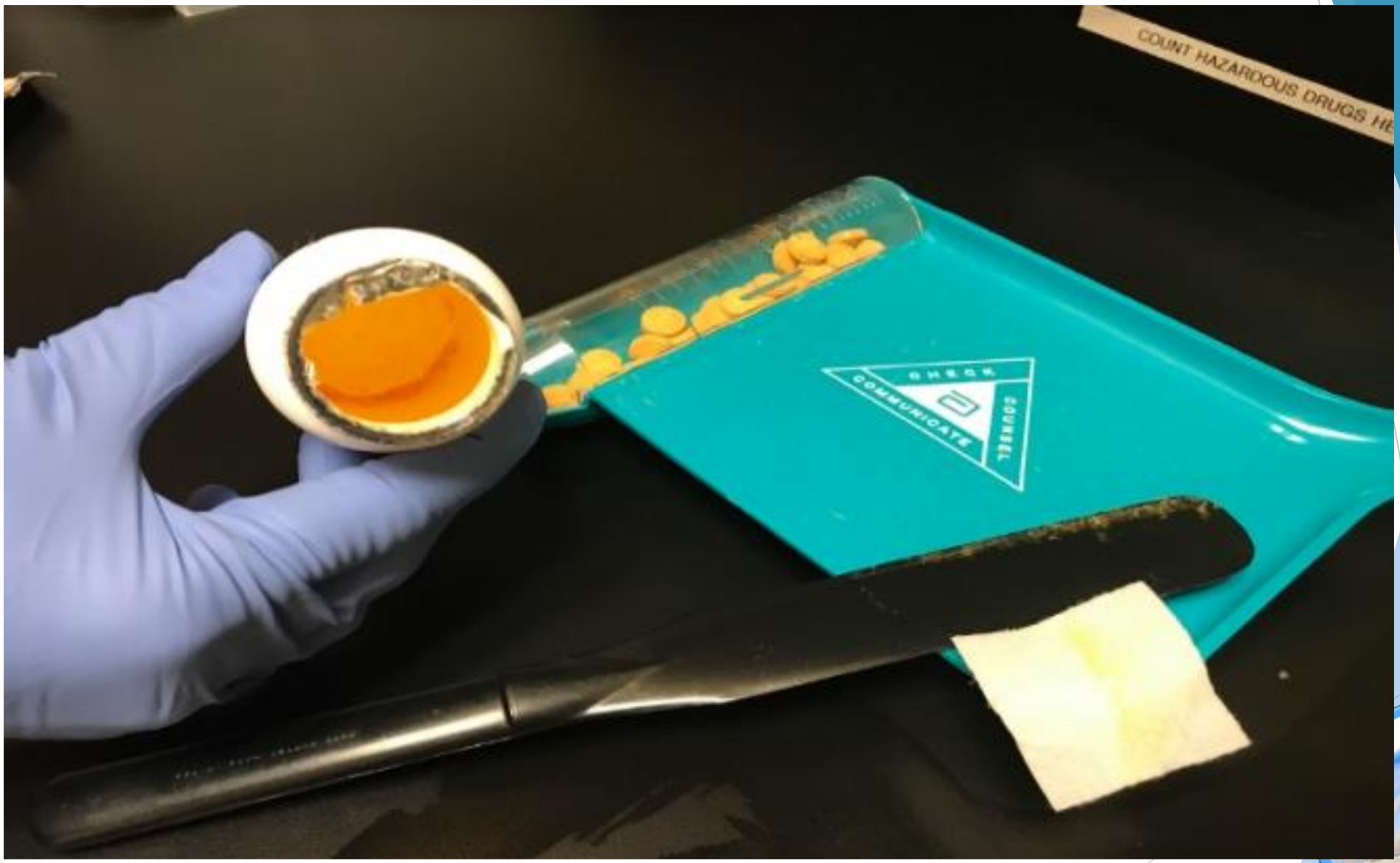
True or False: Has the dust of hazardous drugs been found in the air in retail pharmacies?

TRUE



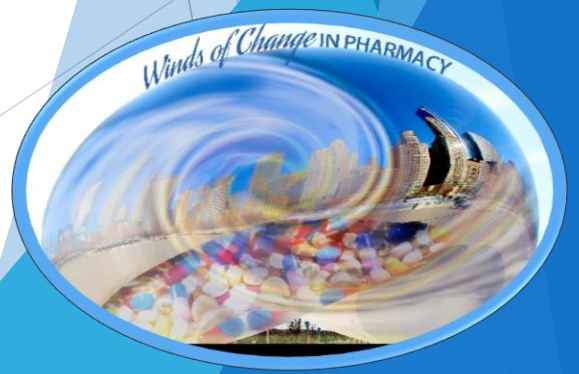
Pre - Test Question

True or False: Women who are actively trying to conceive, and women who are pregnant or breast feeding must notify co-workers to maintain safe hazardous drug handling.


COUNT HAZARDOUS DRUGS
CHECK
COMMUNICATE
COUNSEL

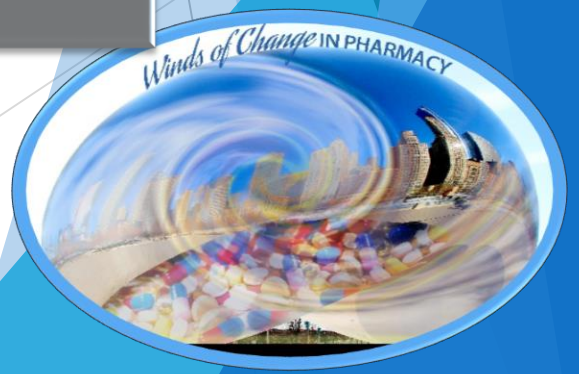
OUTLINE

1. Risks
2. Regulations and standards of practice
3. Facility Controls
4. Personnel protective equipment
5. Administrative Controls



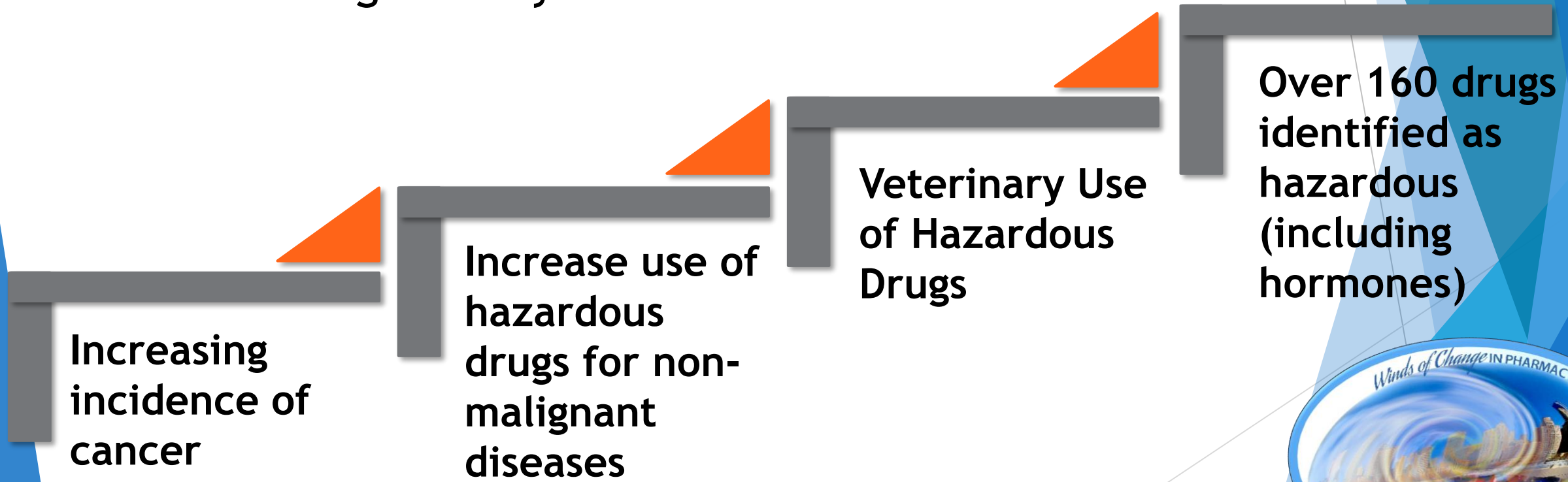
HAZARDOUS DRUG CHARACTERISTICS

- Carcinogenic
- Genotoxic
- Teratogenic
- Reproductive toxicity
- Organ toxicity at low doses
- Similar drugs



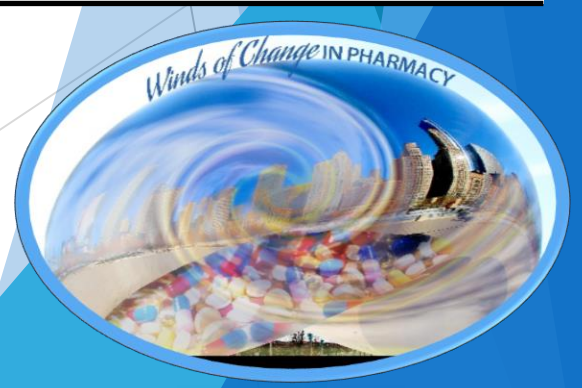
GROWING CONCERN

- 12% of US workers are employed by healthcare.
- 8 million healthcare workers are potentially exposed to hazardous drugs each year



DRUGS – IT'S NOT JUST ONCOLOGY!

Therapy	Hazardous drug
Hormone Replacement Therapy	Estrogen, progesterone, diethylstibestrol, Testosterone
Veterinary	Propylthiouracil, trilostane, methimazole, chemotherapy
Ophthalmology	Mitomycin, fluorouracil, tacrolimus, cyclosporine, retinoic acid
Pediatric Compounding	Suspensions of chemotherapy, immunosuppression
Community Pharmacy	Methotrexate, estrogen, cyclosporine, tacrolimus, mycophenolate
Home Infusion	Ganciclovir, fluorouracil, mycophenolate
Specialty Pharmacy	Oral and Injectable Chemotherapy, Immunomodulators



- Workplace occupational exposure to low levels of HDs over a long time can result in negative health consequences.

- Contamination throughout the healthcare continuum.

WARNING!

Working with or near hazardous drugs in health care settings may cause skin rashes, infertility, miscarriage, birth defects, and possibly leukemia or other cancers

OPPORTUNITIES AND ROUTES OF EXPOSURE

Receipt
Inventory control
Dispensing
Compounding
Disposal
Spills
Cleaning
Transport

Dermal contact

- Direct contact with drugs and drug packaging
- Indirect contact touching contaminated surfaces

Inhalation

- Breathing contaminated air
- Drug particulates, aerosols and vapors

Ingestion

- Hand to mouth contact (eating, drinking, gum chewing)

Injection

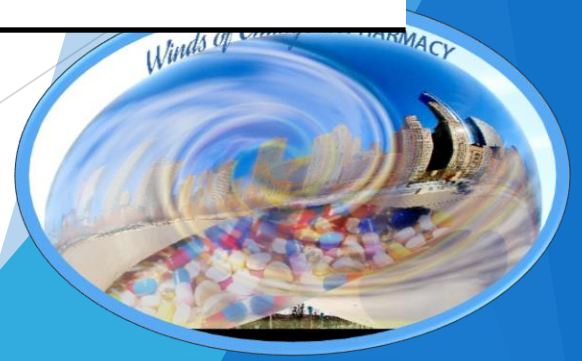
- Finger sticks
- Vial breakage

NIOSH – Hazardous Drug Alert 2004

Minimizing potential adverse effects requires a multifaceted approach

TOXICITY

Short Term Toxicity	Long Term Toxicity
Skin reactions	Reproductive issues
Ocular reactions	Chronic cough
Allergic asthma	End-organ damage
Flu-like symptoms	Leukemia
Headache	Lymphoma
Dizziness	Myelodysplastic Syndrome (MDS)
Increased infections	Bladder and liver cancer



NIOSH – Hazardous Drug Alert 2004

NIOSH HAZARDOUS DRUG LIST

Group 1	• **Antineoplastic drugs**: May also pose a reproductive risk in susceptible populations • *Examples*: ***anastrazole, cyclophosphamide, fluorouracil, hydroxyurea, leuprolide, megestrol, mitotane, tamoxifen***
Group 2	• **Non-antineoplastic drugs** that meet one or more of the HD NIOSH criteria: may also pose a reproductive risk in susceptible populations • *Examples*: ***chloramphenicol, diethylstilbesterol, estradiol, progesterone (all forms), phenytoin, tacrolimus, carbamazepine***
Group 3	• Drugs that primarily pose a **reproductive risk** to men and women who are actively trying to conceive and women who are pregnant or breast feeding • *Examples*: ***finasteride, fluconazole, oxytocin, valproate, tretinoin, colchicine***

NIOSH HAZARDOUS DRUG LIST

NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings, 2016

- International Agency for Research on Cancer (IARC)
- Human studies
- *In vitro* and *in vivo* genotoxicity studies
- Drug manufacturer (Package insert & Safety Data Sheets)
- Special Warnings from FDA and professional organizations
- Reports and case studies published in profession journals
- Animal studies

- **Veterinary medications and non-FDA treatments used in compounding pharmacies may not be included but are significant human health hazards**

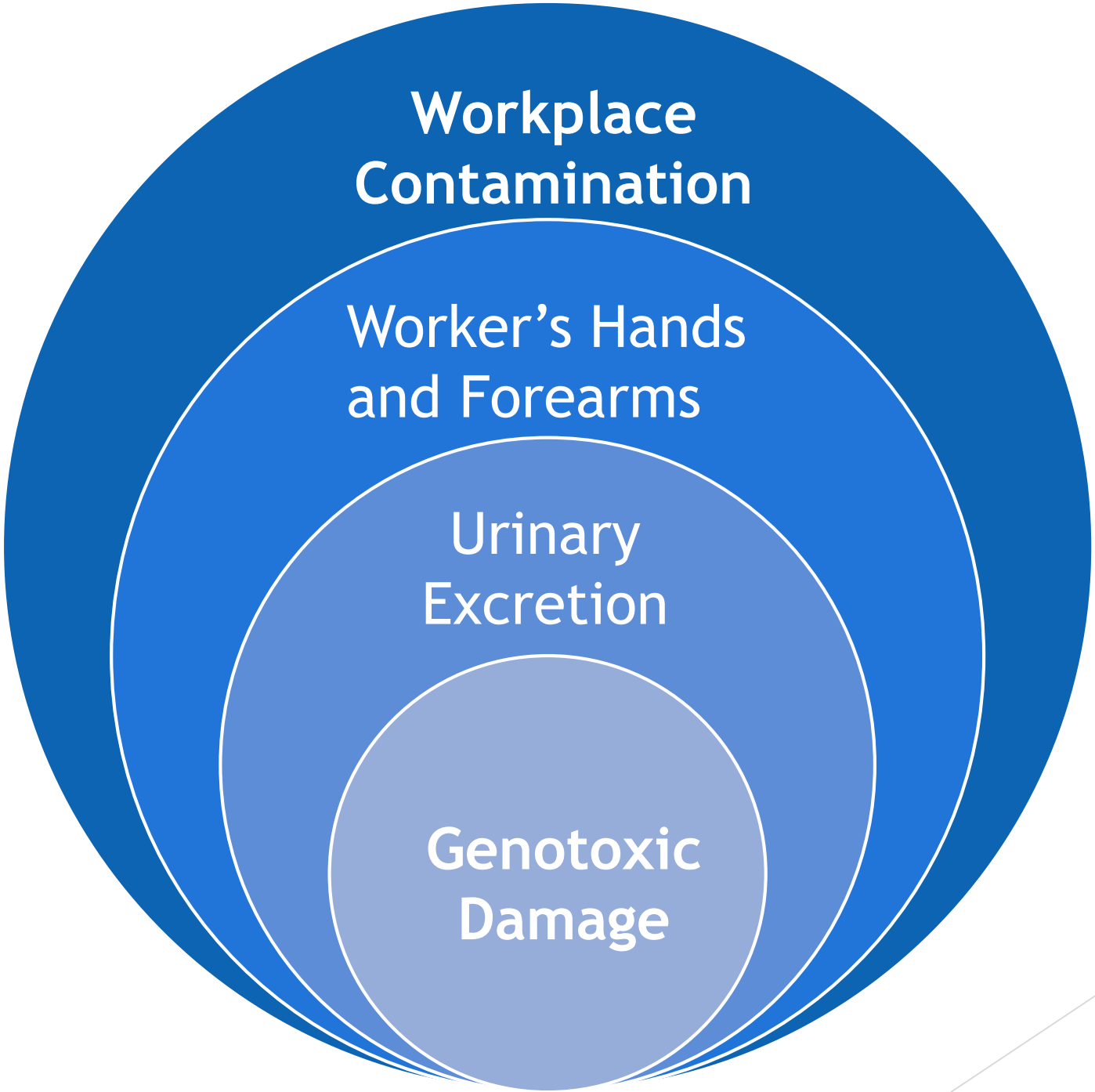
CREATE A LIST OF HAZARDOUS DRUGS LIST AND TYPES OF EXPOSURE

Multi-disciplinary team to:

- Review the NIOSH list
- Identify other HDs
- Identify the dosage forms handled
- Identify activities with them, including all manipulation, crushing, splitting

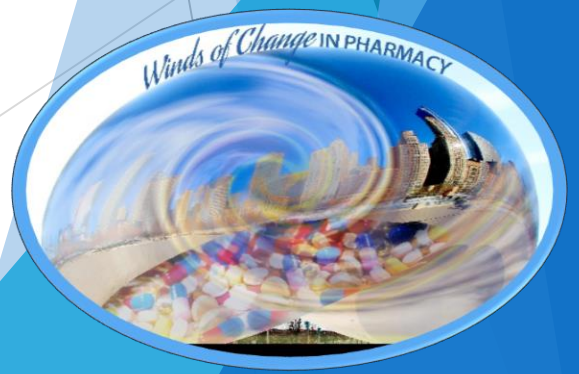
HD risk as a permutation

- **Drug characteristics**
- **Dosage form**
- **Packaging**
- **Type of handling / exposure**


Workplace Contamination
Worker's Hands and Forearms
Urinary Excretion
Genotoxic Damage

OCCUPATIONAL EXPOSURE – BY THE EVIDENCE

- Contamination of external drug packaging
- Surface contamination throughout pharmacy
- Contamination on workers hands and clothing
- Systemic drug exposure: direct and indirect
- Biomarkers of exposure in urine samples
- Biomarkers of effect (showing genetic damage)



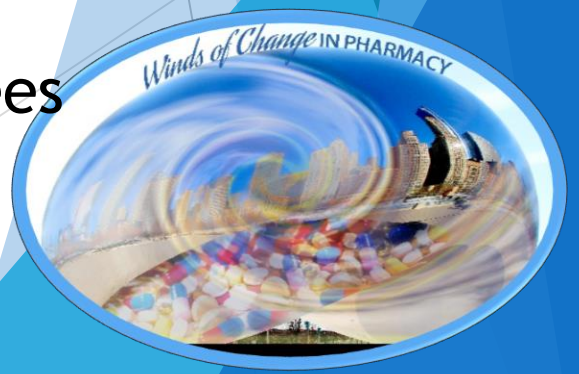
COMMON LOCATIONS OF CONTAMINATION

High levels of contamination

- Work Surfaces for Compounding
- Counting Trays
- Working surfaces of Biologic Safety Cabinets and “Hoods: used for compounding
- Floor in front of the compounding area

Lower levels of contamination

- Floor in pharmacy
- Countertops
- Storage bins and trays
- Storage shelves
- Inside and outside pass-through windows
- Waste containers
- Keyboards
- Door handles
- Shoes of pharmacy employees
- Employee telephones



Exposure

Occupational Risk

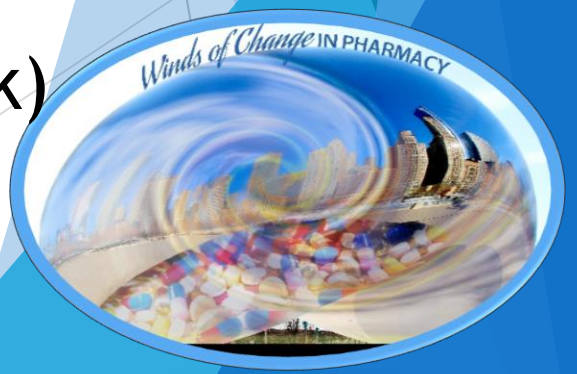
Compounding with Bulk Product
(API = Active Pharmaceutical Ingredients)

Manipulating Solid Dosage Forms
(breaking or cutting tablets)

Pouring Bulk Liquids

Counting Solid Dosage Forms
(pressed powder uncoated tablets = ↑ risk)

Unit Dose Oral Solids / Dispensing Whole Bottle



CDC / NIOSH. Evaluation of Pharmaceutical Dust Exposures at an Outpatient Pharmacy. April 2013

Figure 1. Optifill machine.

Lisinopril – while not hazardous, air samples exceeded the manufacturer recommended Occupational Exposure Limit (OEL 1 ug/m3)

Levothyroxine – air samples when cleaning and refilling canisters (OEL < 1ug/m3)

PHARMACEUTICAL DUST EXPOSURE

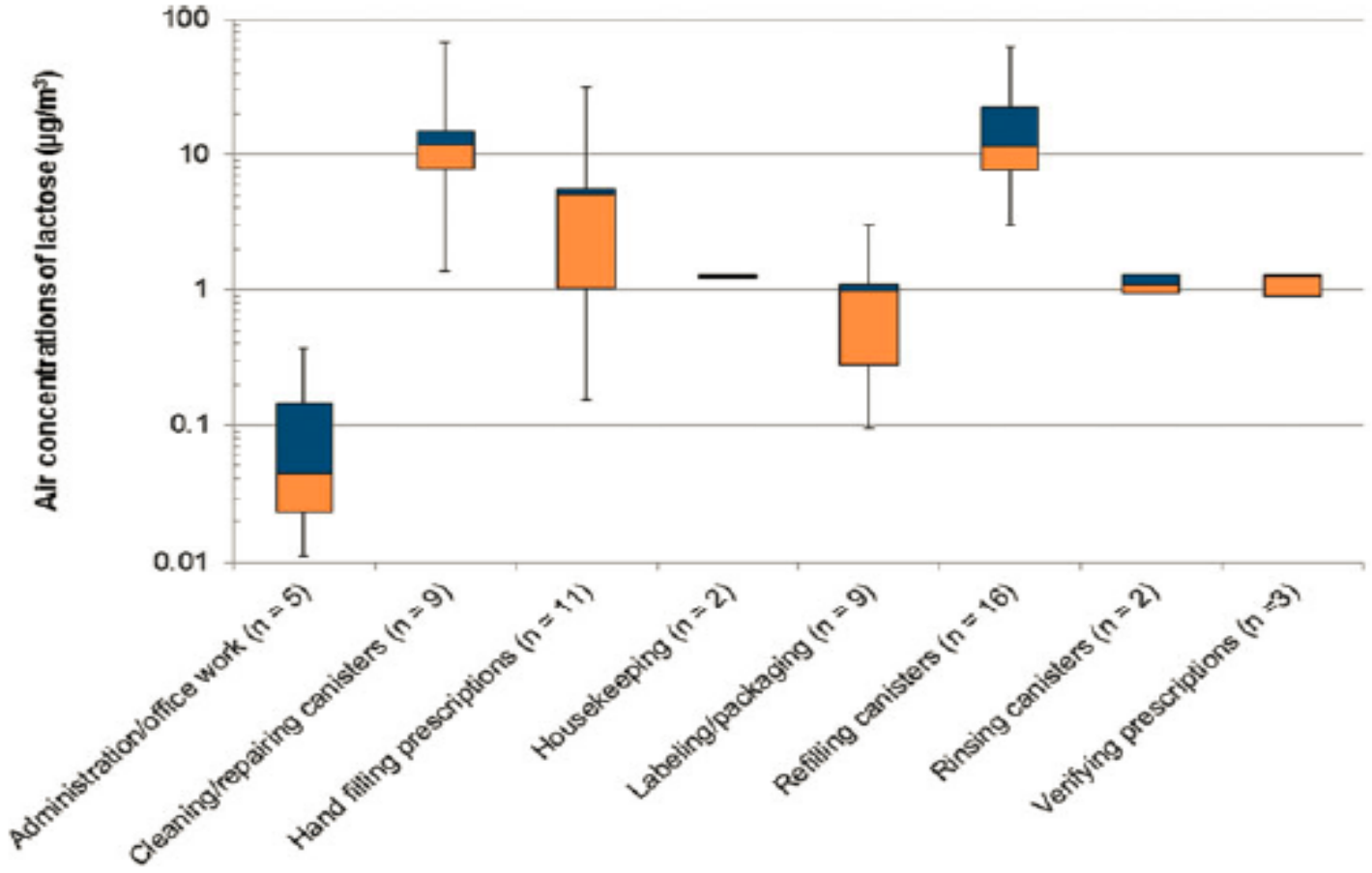


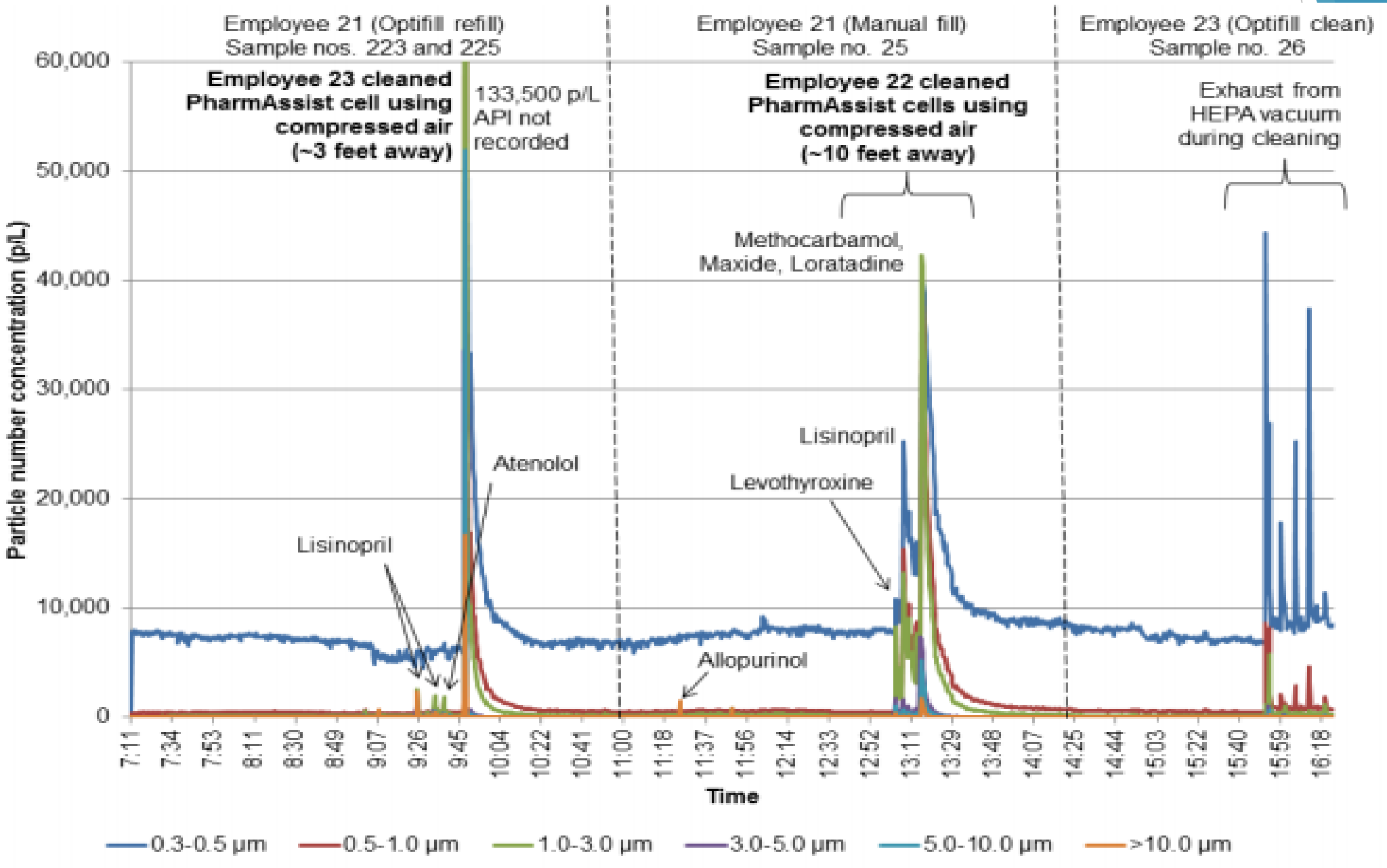
FIGURE 2. Lactose air concentrations (minimum, maximum, and 25th, 50th, and 75th percentiles) by job. (Color figure available online).

→ Lactose was only present in 77 of 200 tablets sampled

Work Surface Contamination with Lactose detected in 14 / 18 samples

Max level found [25] - 19 µg/cm2 .

PERSONAL BREATHING SPACE

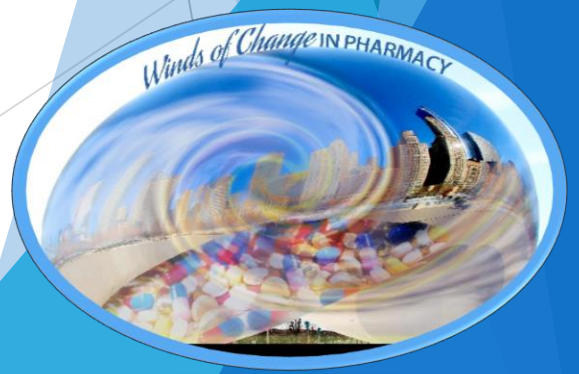


SAFE PRACTICES OF AUTOMATED DISPENSING MACHINES

- Do not put Hazardous Drugs in Automated Dispensing Machines
- Consider use of hood when refilling canisters
- Clean machines with HEPA filtered vacuum and change filter often per manufacturer guidelines
- Do not use compressed air to clean canisters
- Wear nitrile gloves when handling pharmaceuticals
- Clean pharmacy surfaces every 2-4 hours *
- Wash hands before eating, drinking or using tobacco products

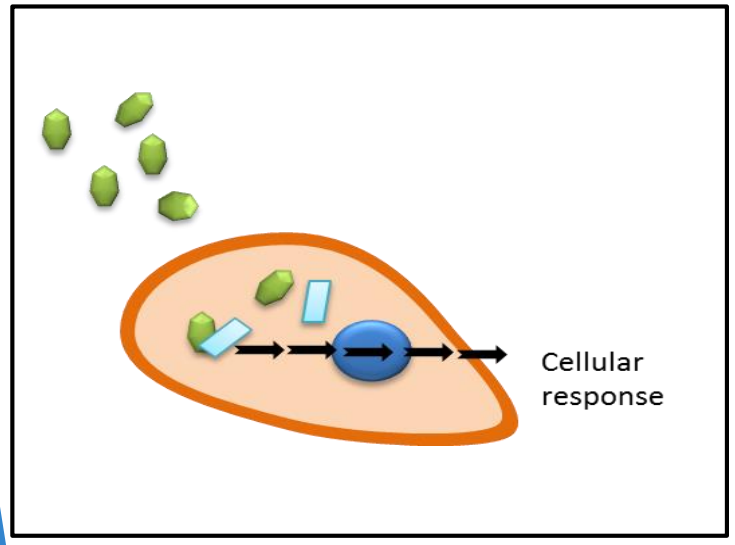
- *** Hand count hazardous drugs in segregated area – assessment of risk for determining required personal protective equipment

* Alcohol - puts drugs into solution and can further spread contamination

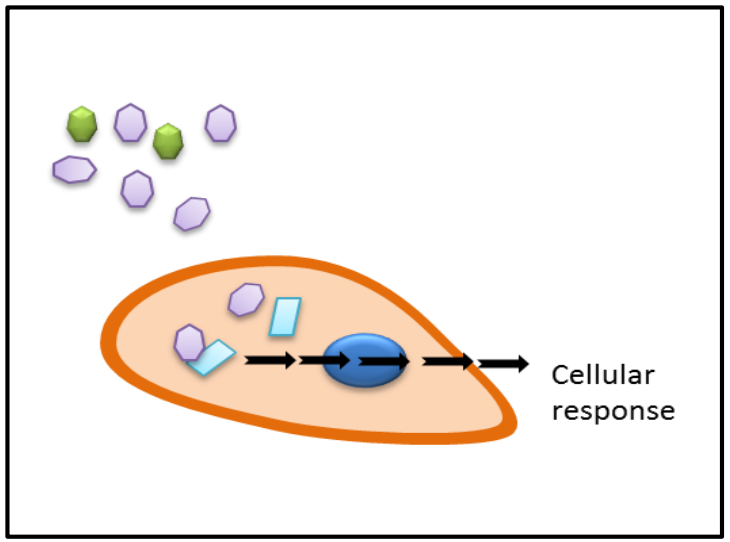


ENDOCRINE DISRUPTERS

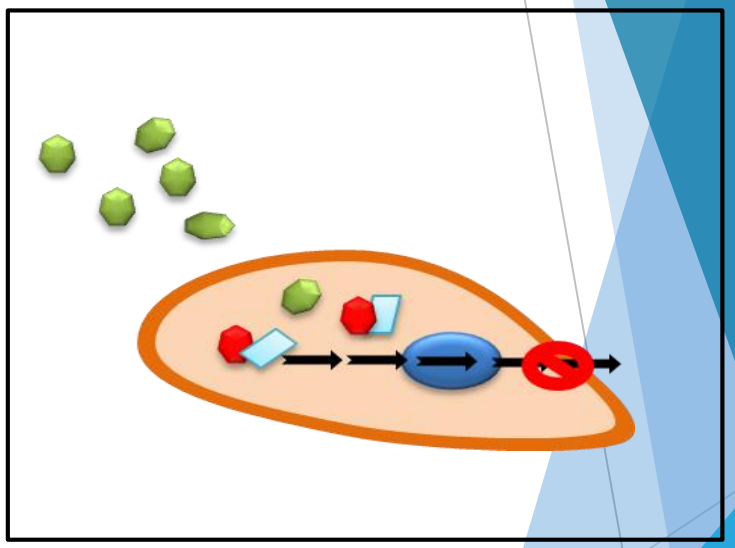
Body's natural hormone system

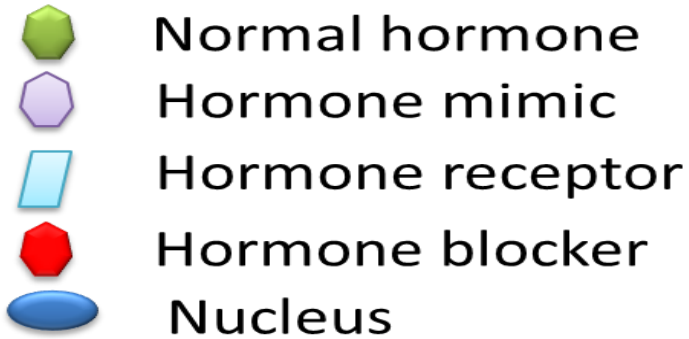


Hormone mimics
Increases normal cellular response

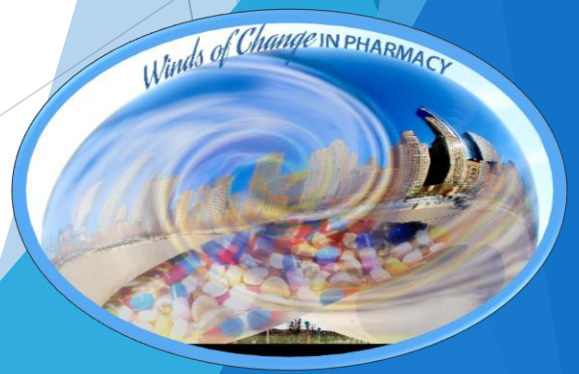


Hormone antagonists
Inhibits normal cellular response





NIESH – National Institute of Environmental Safety and Health



POTENTIAL HEALTH HAZARDS

Health problems reported among healthcare workers exposed to hormones

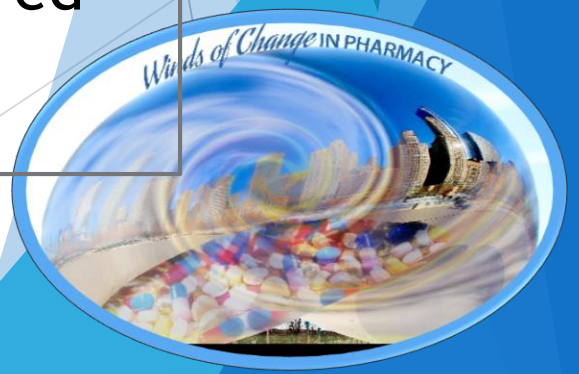
Acute

- Menstruation anomalies (e.g., irregular bleeding)
- Testicular dysfunction
- Unwanted changes in physical appearance:
  - Masculinization of female workers
  - Breast development in males

Long-term

- Increase in breast cancer (may be attributed to inhalation and skin absorption of estrogen during work)
- Impaired fertility
- Further information required

Risk communication:
Personnel have the right to know the risks!



It is chemotherapy!

- **Methotrexate** – air samples tested positive during and after hand filling a prescription for MTX (OEL 0.03 ug/m3)

- **MTX** is generally purchased in pressed powder uncoated tablets that freely liberate dust

C. Roussel counting Folic Acid. 2017

CDC / NIOSH. Evaluation of Pharmaceutical Dust Exposures at an Outpatient Pharmacy. April 2013

CHEMOTHERAPY DOES NOT DISCRIMINATE

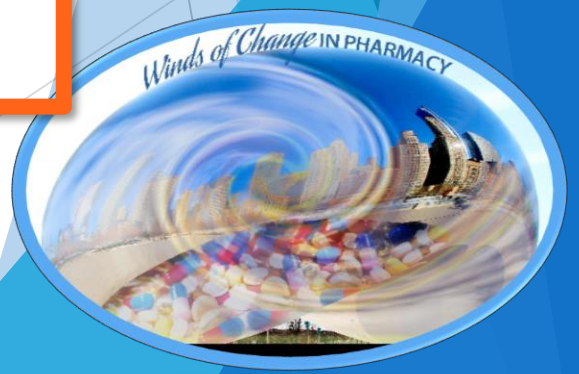
- Genotoxic
- Carcinogenic
- Damage DNA in both diseased and healthy cells

Why are we concerned about exposure in healthcare workers?

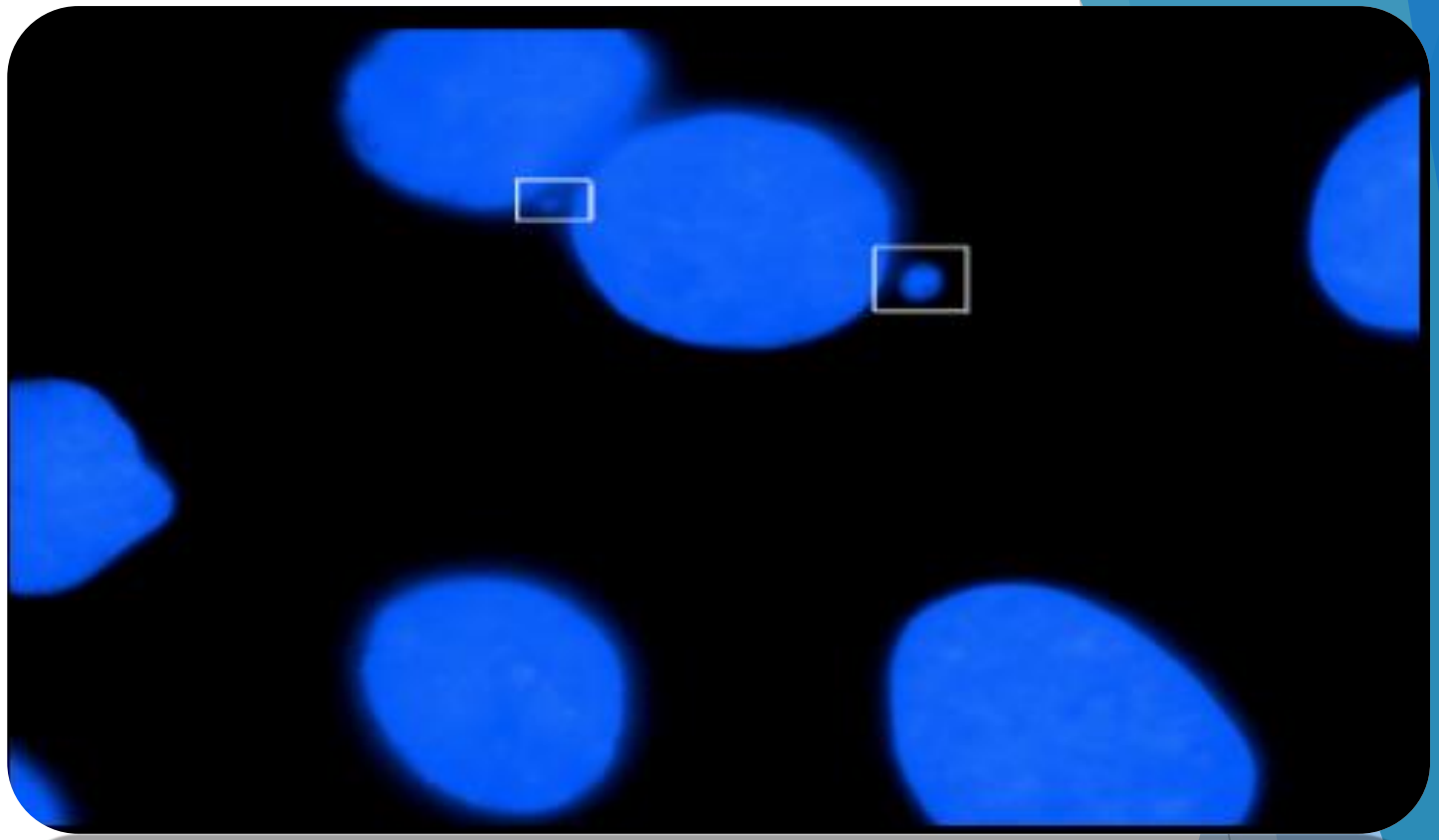
Based on long term side effects in treated patients, it became obvious that there are risks for the occupational exposed

Patients receive concentrated doses of a limited number of agents for a defined period of time.

Healthcare workers are exposed to small doses of a broad range of hazardous medications over decades



MARKERS OF DNA DAMAGE - MICRONUCLEI



Micronuclei is the name given to the small nucleus that forms whenever a chromosome or a fragment of a chromosome is not incorporated into one of the daughter nuclei during cell division

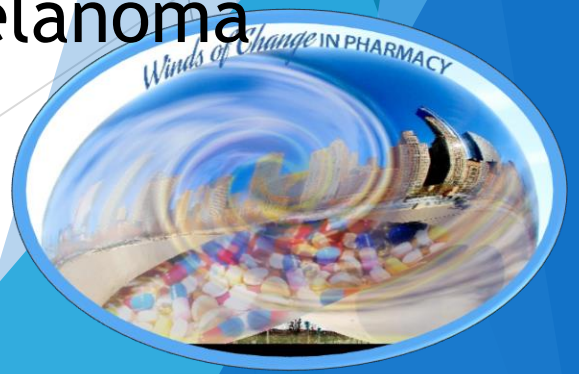
Meta-Analysis Data shows that healthcare workers exposed to Hazardous Drugs have significantly more micronuclei than the general population

EPIDEMIOLOOGY IN HEALTHCARE WORKERS

Cancer mortality study of HCWs in 24 states

- Nurses: 30% ↑ mortality due to liver cancer and myeloid leukemia among nurses
- Pharmacists: two-fold ↑ of mortality from myeloid leukemia in pharmacists
- Occupation and Leukemia Study in two mid-western US states Nursing and healthcare workers: ↑ in Leukemia
- Danish Female Pharmacy Technicians: ↑ risk of non-melanoma skin cancer and non-Hodgkin's lymphomas

Petralia et al. 1999; Blair et al. 2001, Hansen and Olsen 1994



Add the following:

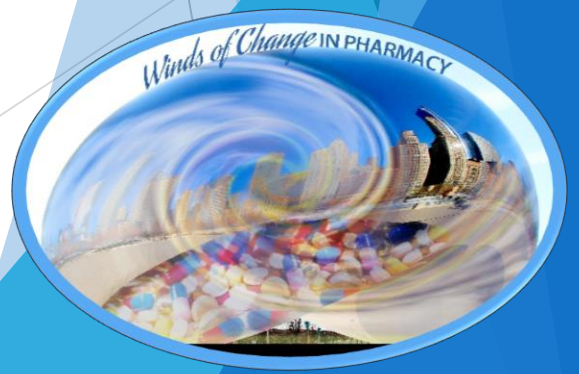
▪⟨800⟩ HAZARDOUS DRUGS—HANDLING IN HEALTHCARE SETTINGS

preparations and all entities that store, prepare, transport, or administer HDs (e.g., pharmacies, hospitals and other healthcare institutions, patient treatment clinics, physicians' practice facilities, or veterinarians' offices)."

Download a free copy of USP 800
http://www.usp.org/compounding/general-chapter-hazardous-drugs-handling-healthcare

TOPIC SECTIONS IN USP 800

- List of Hazardous Drugs and Types of Exposure
- Responsibilities of Personnel Handling Hazardous Drugs
- Facilities
- Environmental Quality and Control
- Personal Protective Equipment
- Hazard Communication Program and Personnel Training
- Receiving
- Labeling, Packaging, and Transport
- Dispensing Final Dosage Forms
- Compounding
- Administration
- Deactivation/Decontamination, Cleaning, and Disinfection
- Spill Control
- Disposal
- Documentation and Standard Operating Procedures
- Medical Surveillance



USP <800> LIST OF HAZARDOUS DRUGS

- Every facility must maintain their own list of hazardous drugs
- Must consider the type of HD, risk of exposure, packaging, and manipulation
- Review annually or when a new drug or dosage form is used; be sure to document

Box 1: Containment Requirements

- Drugs on the NIOSH list that must follow the requirements in this chapter 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 this chapter 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

- All Active Pharmaceutical Ingredients (API) and compounding activities must be stored and conducted in the appropriate negative pressure, externally exhausted room.

USP <800> FACILITY SPECIFIC ASSESSMENT OF RISK

"Some dosage forms of drugs defined as hazardous may not pose a significant risk of direct occupational exposure because of their dosage formulation"

"An assessment of risk may be performed for the dosage forms to determine alternative containment strategies and / or work practices."

"If an assessment of risk is not performed, all HDs must be handled with all containment strategies defined in this chapter."

”ASSESSMENT OF RISK”

- Identification
- Hazard Assessment
- Risk Evaluation
- Plan
- Risk Control Implementation
- Monitoring

Define alternate containment strategies

Define alternative work practices

Review process and document handling and risk ≤ Q 12 months

USP <800> FACILITY SPECIFIC ASSESSMENT OF RISK

Some dosage forms of drugs defined as hazardous may not pose a significant risk of direct occupational exposure because of their dosage formulation (e.g., tablets or capsules—solid, intact medications that are administered to patients without modifying the formulation). However, dust from tablets and capsules may present a risk of exposure by skin contact and/or inhalation. An assessment of risk may be performed for these dosage forms to determine alternative containment strategies and/or work practices. If an assessment of risk is not performed, all HDs must be handled with all containment strategies defined in this chapter.

The assessment of risk must, at a minimum, consider the following:

- Type of HD (e.g., antineoplastic, non-antineoplastic, reproductive risk only)
- 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.

Allows for an internal assessment of risk with regards to final dosage forms

- (ie. Filled capsules of non-antineoplastics, such as progesterone capsules) to be stored in main area and counted in main area with PPE and process to be determined such as gloves, a dedicated tray and counting area through facility specific assessment of risk

Example: “Assessment of Risk”

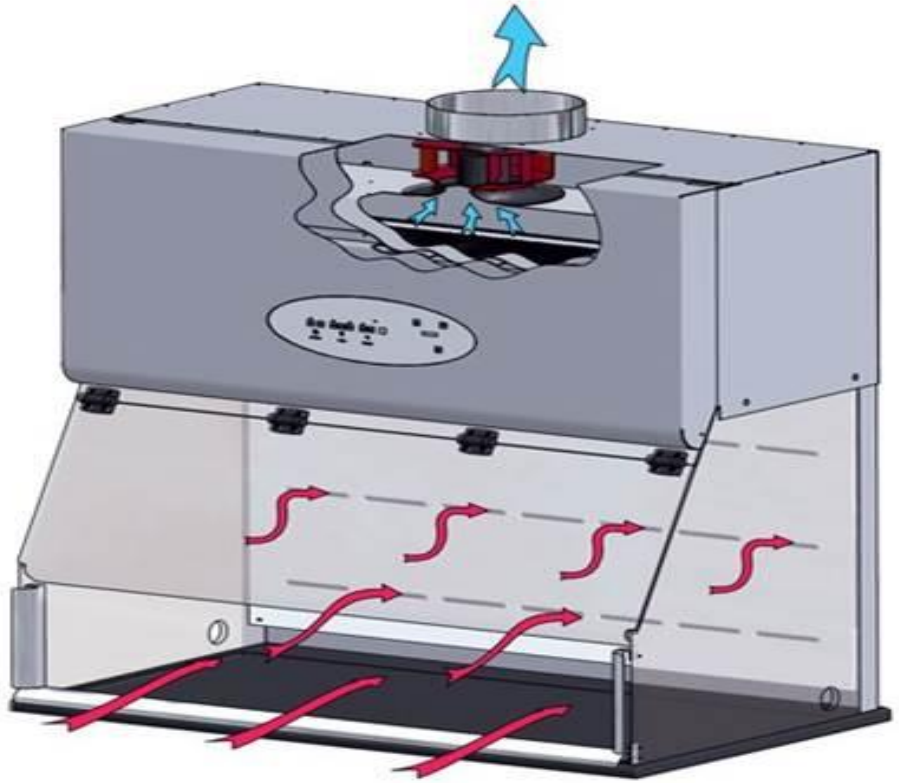
Steps	Drug Specific Discussion
Identification of HDs	NIOSH List - Tacrolimus
Hazard Assessment (Type of HD, dosage form)	Group 2 Risk for all employees Risk for pregnant, lactating and those activity trying to conceive
Risk Evaluation (Risk of exposure)	Counting capsules Activities performed include opening capsules and collecting powder for compounding or working API
Plan (be specific to type of handling or manipulation, packaging, ect)	Reproductive Risk population can not perform handling. Capsule Dosage Forms – minimal risk for counting. All employees wear gloves. Compounding with API or solid dosage form manipulation– must be done with BSC with full PPE and safe handling work processes
Risk Control Implementation	Staff Education on HD Program, Labelling HD’s, signs on how and where to handle, inventory segregation
Monitoring	Observe staff filling these orders, competency assessment

FACILITY

1. USP <797> (Sterile Compounding)
2. USP <795> (Non-Sterile Compounding)
3. Containment-primary engineering controls (aka “the Hood”)
4. Containment-secondary engineering controls (aka “the Room”)
5. Workflow
6. Facility design layout
7. Storage and Receiving areas for HDs

CLASS I BSC – NON-STERILE COMPOUNDING

- Negative Pressure
- Appropriate for HD powder containment
- **Must be Contained within a negative pressure room (the C-SEC)**
- **For NON-STERILE COMPOUNDING: Externally vented (preferred) OR Double HEPA Filtration**



C-PEC SELECTION

Type of HD Compounding Today and Future growth

- Will the C-PEC be externally Exhausted
- How does the C-PEC effect Air Changes Per Hour and the Pressure Gradient of the Room
- Location for the C-PEC: airflow, location of the HEPA filters within the cabinet & technician access
- Cost considerations:
  - Cost of device
  - Installation costs
  - Operational costs (energy saving considerations)

C-PEC SELECTION

If you already have a hood:

- Ask your manufacturer if your powder containment hood meets the definition of a Class! BSC or if it is a Containment Ventilated Enclosure
- Are their kits available to externally Exhaust it
- Are their kits available to add an additional HEPA filter
- If retrofitting the hood is not an option, it is time to go shopping

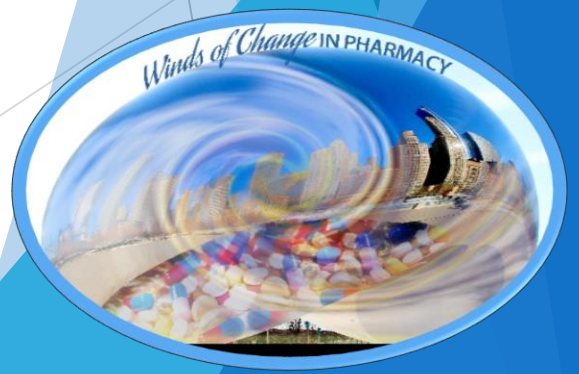
NON-STERILE HAZARDOUS DRUG COMPOUNDING FACILITY DESIGN

Externally vented

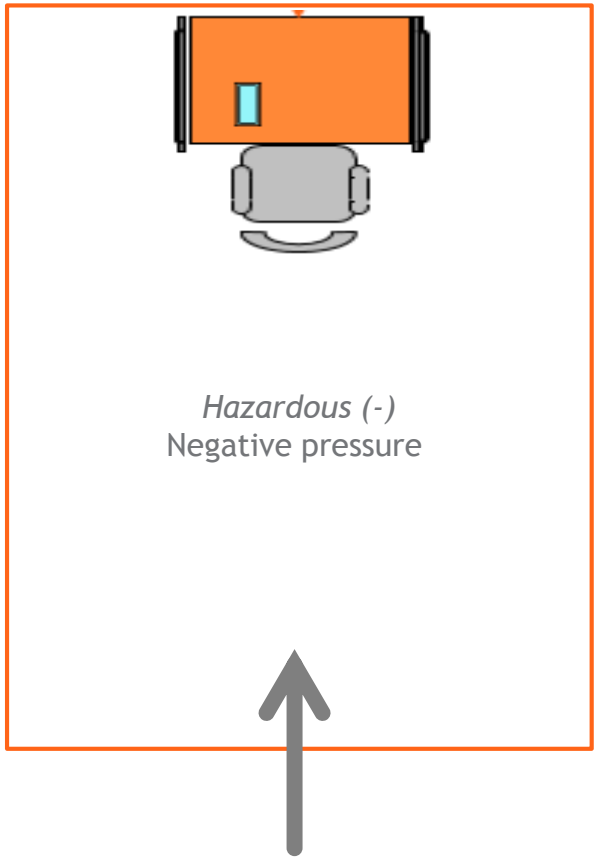
≥ 12 ACPH (non-sterile)

0.01–0.03”of water column negative pressure

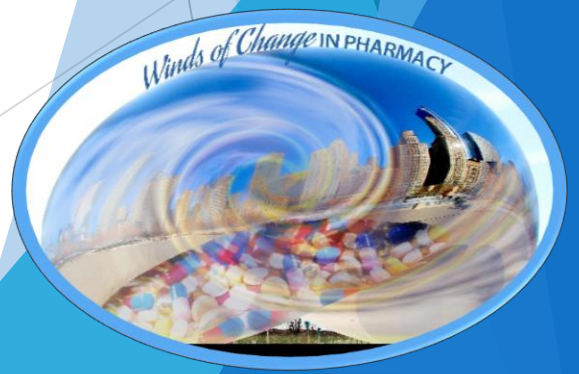
Physically Separate
(a different room from other preparation areas)



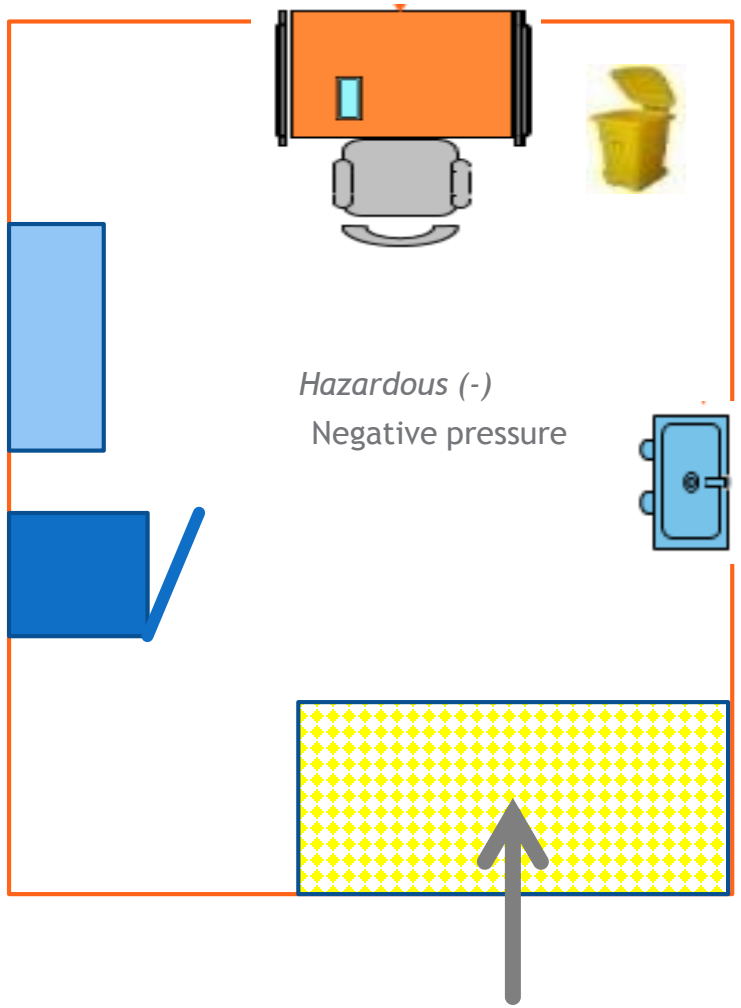
OPTIMAL FACILITY DESIGN – HD NON-STERILE COMPOUNDING



- No ISO classification required
- Minimum 12 ACPH
- 0.01–0.03”of water column negative pressure
- C-SEC (room) externally vented
- C-PEC (hood) externally vented or internally vented through at least two HEPA filters in series



OPTIMAL FACILITY DESIGN – HD NON-STERILE COMPOUNDING



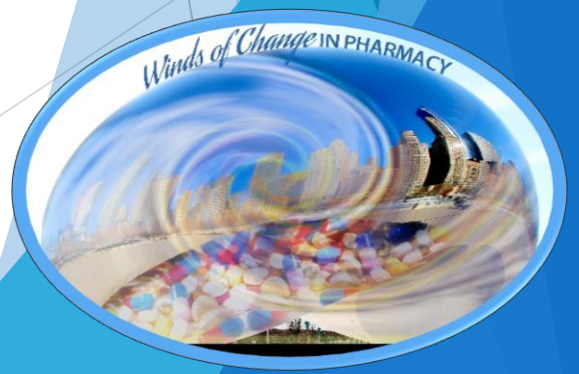
Class 1 Biological Safety Cabinet (BSC) or Containment Ventilated Enclosure (CVE)

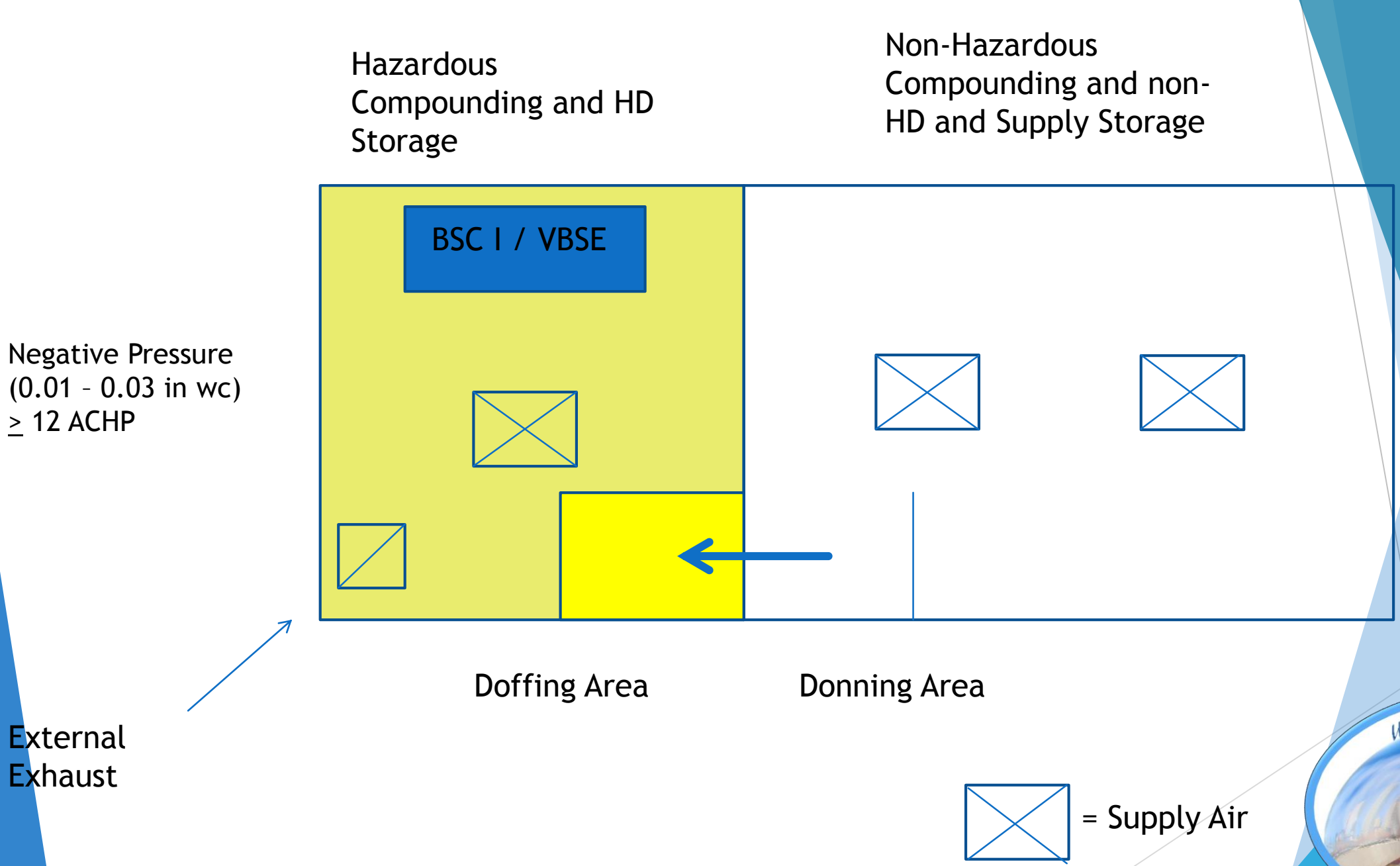
A Sink is recommended but not required

HD Storage Area, possibly including a Refrigerator for HD storage

Proper HD Waste Disposal Receptacle

Area for Donning and Doffing HD Personal Protective Equipment




Hazardous
Compounding and HD
Storage
Non-Hazardous
Compounding and non-
HD and Supply Storage
BSC I / VBSE
Negative Pressure
(0.01 – 0.03 in wc)
≥ 12 ACHP
Doffing Area
Donning Area
External
Exhaust
= Supply Air

WORKFLOW AND LAYOUT FOR NON-STERILE HD COMPOUNDING

- Where will you wash your hands when garbing?
  - If you are gowned up and forget something outside the room how will you get it?
- Where will you wash your HD contaminated equipment?
  - Is there risk for exposure when transporting dirty equipment
- Where will you remove your contaminated PPE?
  - Even for non-sterile there must be dedicated space for Donning and Doffing
- Where will you discard HD contaminated waste?

SEGREGATED COUNTING AREA FOR SPECIFIC HD

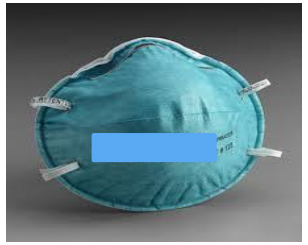
RECEIVING

- Must be in negative pressure or neutral/normal pressure area
- Can NOT be in positive pressure area

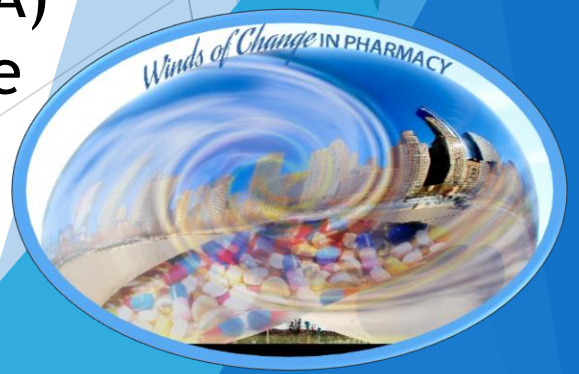
- Have wholesalers designate the HD containing packages
  - Separate colored totes
  - Separate account for ordering or separate POs

PPE – RESPIRATORY PROTECTION

- Respiratory Protection
- Gown
- Foot Protection
- Eye & Face Protection
- Gloves

- Select respiratory protection based on risk assessment
- NIOSH certified N-95 and N-100 masks
- Powered Air Purifying Respirators (PAPRs)
- Rating of filter cartridge
- Self-Contained Breathing Apparatus (SCBA)
- Respirators require fit testing prior to use



RESPIRATOR FIT TEST

“The employer shall ensure that an employee using a tight-fitting face-piece respirator is fit tested prior to initial use of the respirator, whenever a different respirator face-piece (size, style, model, or make) is used, and at least annually thereafter.”
- OSHA 1910.134(f) s

Associates must be trained on the importance of the respirator

How improper fit, usage, or maintenance can compromise the protective effect of the respirator

The limitations and capabilities of the respirator

How to inspect, put on and remove, use, and check the seals of the respirator

RESPIRATORY PROTECTION - TESTING

Qualitative Testing

- Aerosol protocol: sweet tasting
- (i.e. saccharin) or bitter tasting
- Irritant smoke protocol
- Test the user's ability to detect the agent
- Meets OSHA requirements for particulate or gas/vapor respirator performance
- Reliable pass/fail results
- Kit includes hood and collar assembly, 2 nebulizers and fit test solutions

GOWN

- Hair Cover
- Respiratory Protection
- Gown
- Foot Protection
- Eye & Face Protection
- Gloves

- Designed for chemotherapy
- Change based on permeation data or every 2-3 hours, whichever is shorter
- Closed in the back, long sleeves, and closed cuffs that are elastic or knit, Splash resistant
- Polyethylene-coated polypropylene / laminate
- Optional disposable sleeve protectors

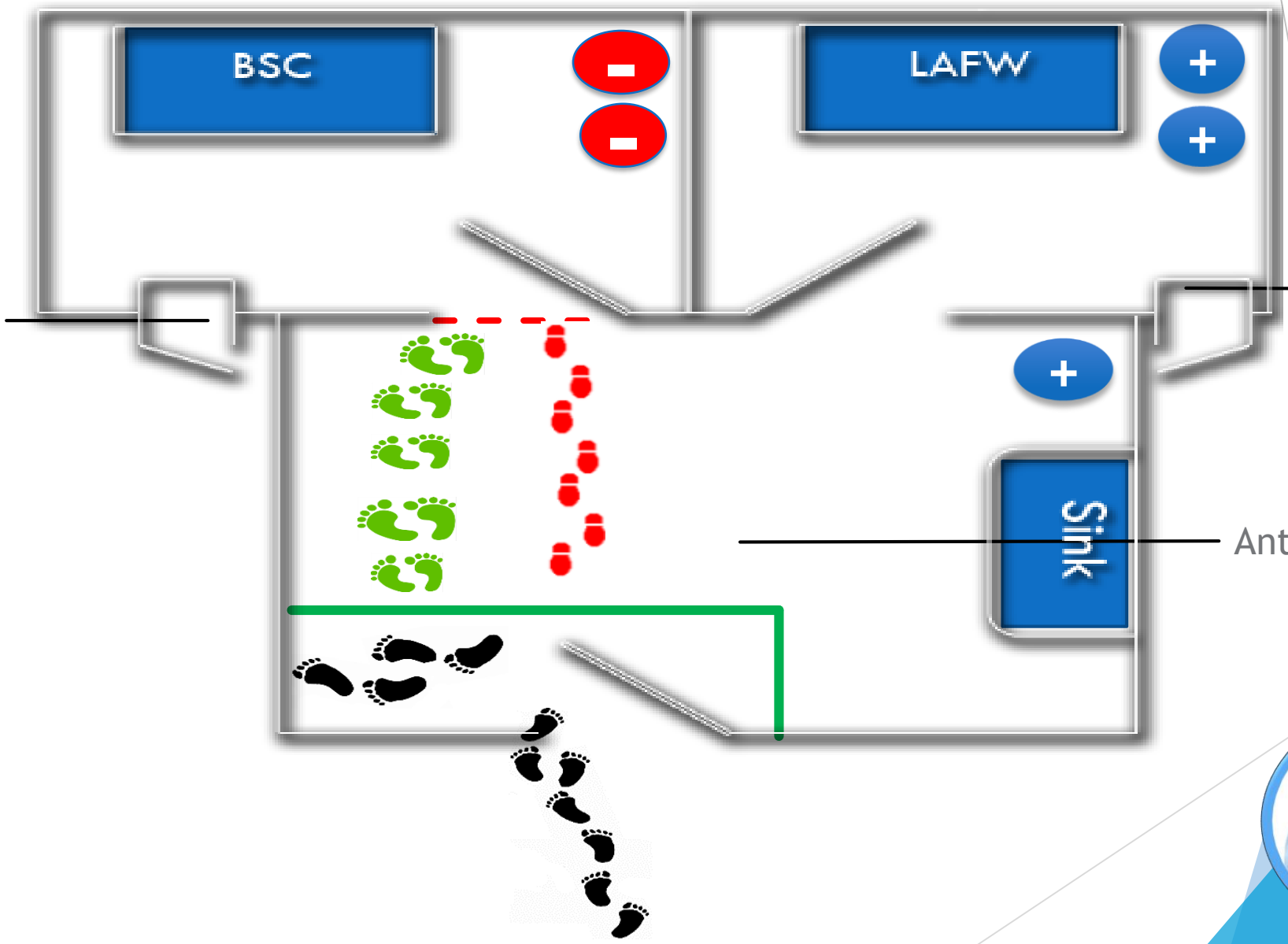
- To Avoid Spreading Contamination:
  - Do not wear gowns outside the compounding area
  - Dispose of gown after each use

FOOT PROTECTION

- Hair Cover
- Respiratory Protection
- Gown
- Foot Protection
- Eye & Face Protection
- Gloves

- Closed toe shoes that cover the foot
- Double shoe covers
  - First pair put on as the compounder crosses the line of demarcation in the ante room
  - Second pair is for use in the hazardous drug compounding area

FOOT TRAFFIC AND DOUBLE BOOTIES



Buffer Area

Buffer Area

Ante Room

EYE & FACE PROTECTION

- Hair Cover
- Respiratory Protection
- Gown
- Foot Protection
- Eye & Face Protection
- Gloves

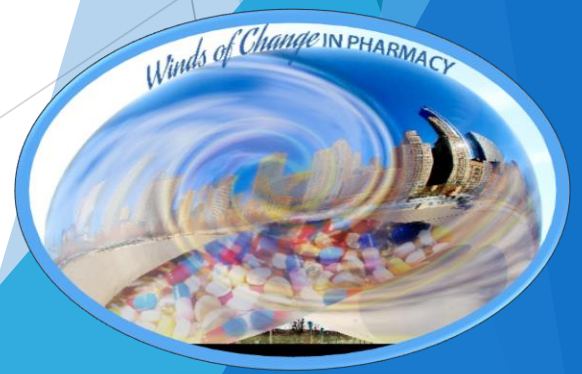
- Safety goggles
- Protection: splashes, irritation, broken glass/objects

GLOVES

- Hair Cover
- Respiratory Protection
- Gown
- Foot Protection
- Eye & Face Protection
- Gloves

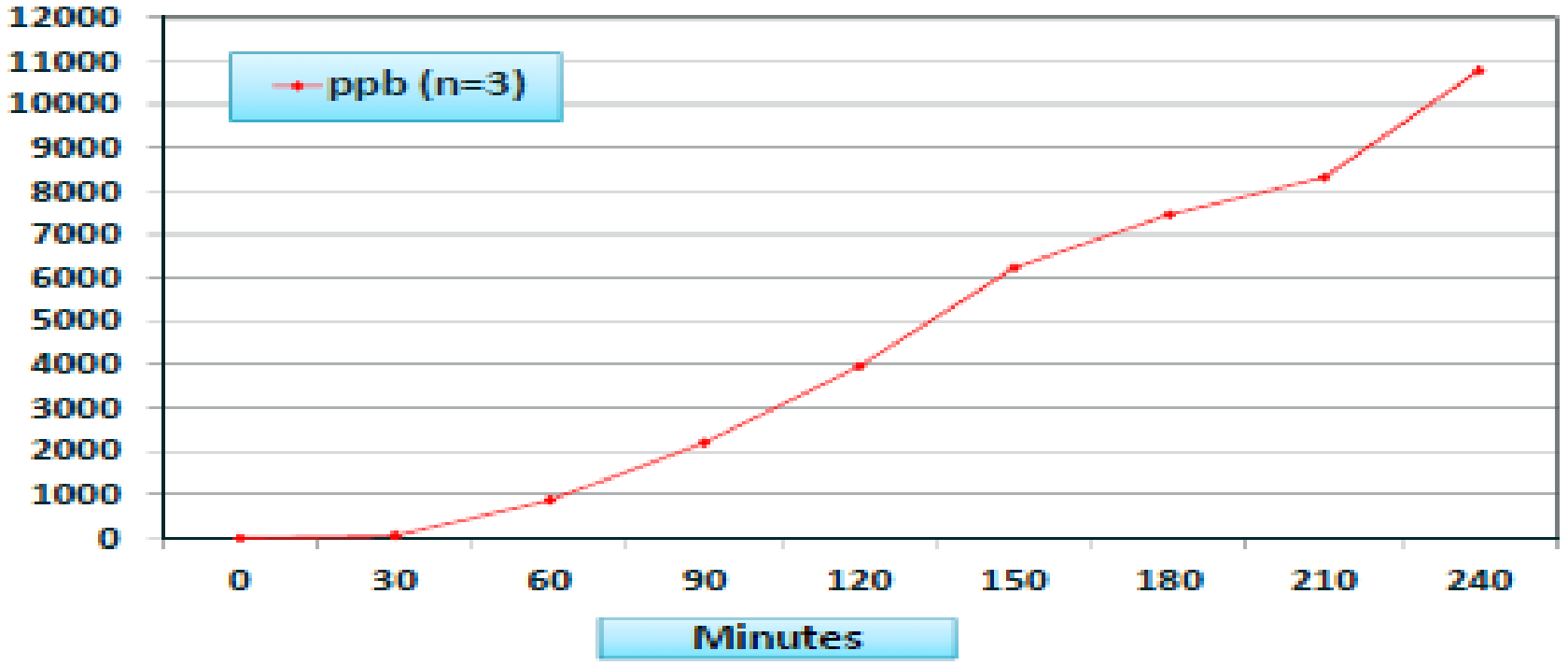
- Wear 2 gloves when compounding with HD drugs
- Gloves are required when handling reproductive risk HDs, non-antineoplastic and chemotherapy HDs

- Materials: latex, nitrile, neoprene
- Change based on permeation data or every 30 minutes, whichever is shorter
- Change gloves anytime HD contamination is known or suspected; if torn or punctured
- Inner glove in worn under gown cuff
- Outer glove is worn over gown cuff
- Gloves must be powder-free



GLOVES

Cyclophosphamide Permeation at 37 °C with Polyvinyl Chloride Gloves*



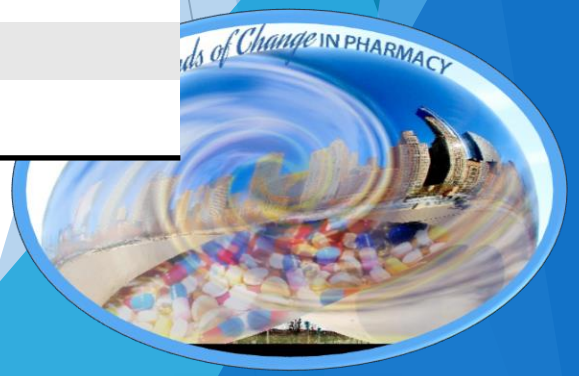
*Connor, TH: Unpublished data

ppb = parts per billion

GLOVES

Know the value of your gloves…

Chemotherapy Drugs Listed on the Package		
Product (Test Method)	### Gloves 1 (ASTM DC978-05)	### Gloves 2 (ASTM DC978-05)
Bleomycin Sulfate (15.0 mg/ml)	X	
Busulfan (6.0 mg/ml)	X	
Carboplatin/paraplatin (10.0 mg/ml)	X	
Carmustine (3.3 mg/ml)	X	
Cisplatin (1.0 mg/ml)	X	X
Cyclophosphamide (20.0 mg/ml)	X	X
Cytarabine HCl (100.0 mg/ml)	X	
Dacarbazine (10 mg/ml)	X	X
Daunorubicin HCL (5.0 mg/ml)	X	
Docetaxel (10.0. mg/ml)	X	
Doxurobicin HCl (Adriamycin) (2.0 mg/ml)	X	X
Ellence (Epirubicin) (2.0 mg/ml)	X	



GLOVES

ASTM Permeation Standard

ASTM Standard	Permeation Rate	Drugs	Temperature
F739 Standard Test Method for Permeation of Liguids and Gases Through Protective Clothing Materials Under Conditions of Continuous Contact	0.1 mcg/cm2/min	No specific drugs	25 C (Room temperature)
D6978 Standard Practice for Assessment of Resistance of Medical Gloves to Permeation by Chemotherapy Drugs	0.01 mcg/cm2/min	Cermustine Cyclophosphamide Doxorubicin Etoposide Fluorouracil Paclitaxel Thiotepa + 2 others	35 C (Temperature gloves reach after wearing them for 5 minutes)

NIOSH TIERED APPROACH

Formulation	Activity	Double gloves	Protective gown	Eye protection	Respiratory protection	Ventilated engineering controls
Intact tablet or capsule	Administration from unit-dose package	No (single gloves should be used)	No	No	No	N/A
Tablets or capsules	Cutting, crushing, or manipulating tablets or capsules	Yes	Yes	No	Yes, if not done in a control device	Yes
Tablets or capsules	Administration	Yes	Yes	No	Yes, if powder generated	N/A
Oral liquid drug	Compounding	Yes	Yes	Yes, if not done in a control device	Yes, if not done in a control device	Yes
Oral liquid drug	Administration	Yes	Yes	No	No	N/A
Topical drug	Compounding	Yes	Yes	Yes	Yes, if not done in a control device	Yes
Topical drug	Administration	Yes	Yes	Yes, if liquid that could splash	Yes, if inhalation potential	N/A
Ampoule	Opening	Yes	Yes	Yes, if not done in a control device	Yes, if not done in a control device	Yes, BSC of CACI

NIOSH TIERED APPROACH

Formulation	Activity	Double gloves	Protective gown	Eye protection	Respiratory protection	Ventilated engineering controls
Subcutaneous intramuscular injection	Preparation (withdrawing from vial or ampoule)	Yes	Yes	Yes, if not done in a control device	Yes, if not done in a control device	Yes, BSC or CACI
Subcutaneous intramuscular injection	Administration from prepared syringe	Yes	Yes	Yes, if liquid that could splash	Yes, if inhalation potential	N/A
Intravenous solution	Compounding	Yes	Yes	Yes, if not done in a control device	Yes, if not done in a control device	Yes, BSC or CACI; recommended for CSTD
Intravenous solution	Administration of prepared solution	Yes	Yes	Yes	Yes	N/A
Solution for irrigation	Compounding	Yes	Yes	Yes, if not done in a control device	Yes, if not done in a control device	Yes, BSC or CACI; recommended for CSTD
Solution for irrigation	Administration (bladder, HIPEC, limb, perfusion, etc.)	Yes	Yes	Yes	Yes	N/A
Powder/ solution for inhalation	Inhalation	Yes	Yes	Yes	Yes	Yes, when applicable

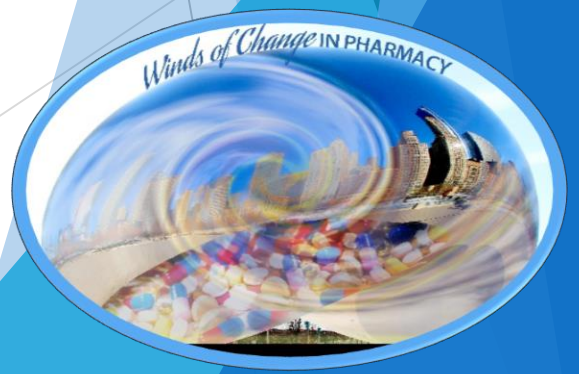
DISPENSING DRUGS TO NURSING FACILITIES

Labelling the Product so the healthcare professional administering the product:

- **is aware of the risks of handling**
- **Alerted to wear personal protective equipment appropriate for administration**

Consider additional alert for each HD administered for each patient.

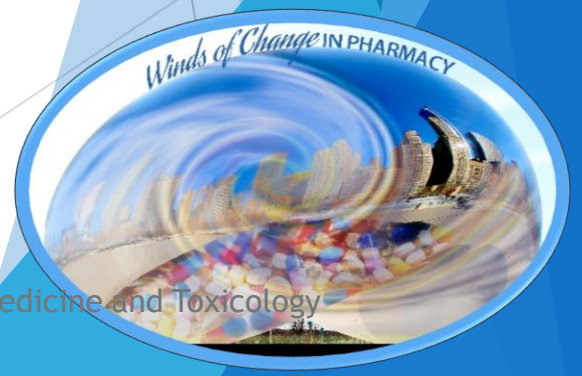
- colored stickers/labels
- MAR info



COMPLIANCE WITH GLOVE PROCEDURES

	Nurses	Micronuclei	Chromosomal Abnormalities
< 100% Compliance	29	9.5 (+/-5.2)	2.6 (+/-2.6)
100% Compliance	33	4.3 (+/-3.7)	0.9 (+/-1.9)

For both markers of genetic damage there were statistically significant differences between staff with 100% compliance and staff non-compliant with recommended personal protective equipment.



1992 Harris and Connor, Journal of Occupational Medicine and Toxicology

COMMON HD MISHANDLING DURING NON-STERILE COMPOUNDING

Contamination

- Mishandling API Containers
  - Only Open containers inside the C-PEC
  - Clean off Containers prior to/during removal from C-PEC

Contamination

- Breach of C-PEC's air-curtain during active powder manipulation
- Meaning moving hands in and out of hood for supplies or documentation
- Need: all supplies in C-PEC, documentation process

Contamination

- Contaminated products for disposal removed from C-PEC uncontained (and even left in open disposal receptacles)
- Powder clings to used weigh boats, gloves, etc and must be contained prior to removal from the hood Contamination

Contamination

- Reusable lab equipment should be minimized as cleaning and transport to cleaning locations are risk points
- Contaminated lab equipment in need of cleaning must be contained in sealed plastic within the C-PEC, for transport to area for cleaning

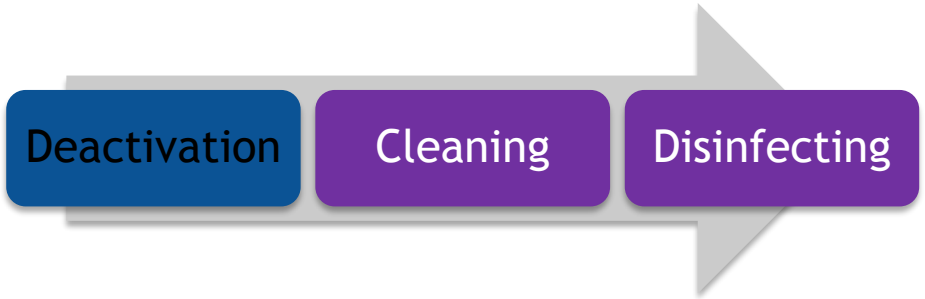
Decontamination

Deactivation: the treatment of a HD with another chemical, heat, ultraviolet light, or other agent to create a less hazardous agent

Decontamination: Inactivation, neutralization, and removal of HD contaminants (usually by chemical means).

Cleaning: Removal of dirt and particulate contamination

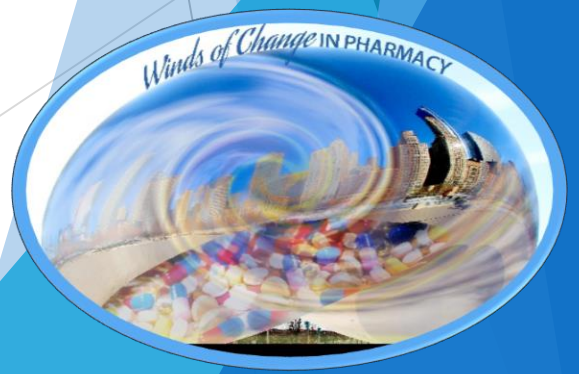
Disinfecting: Destroy or inhibit microbial growth



Deactivation | Cleaning | Disinfecting

- Commercially available multi-component chemical deactivation systems that provide more than one chemical degradation mechanism, whenever possible
- Bleach followed by sodium thiosulfate or a germicidal detergent
- **Alcohol is not a deactivation agent!**

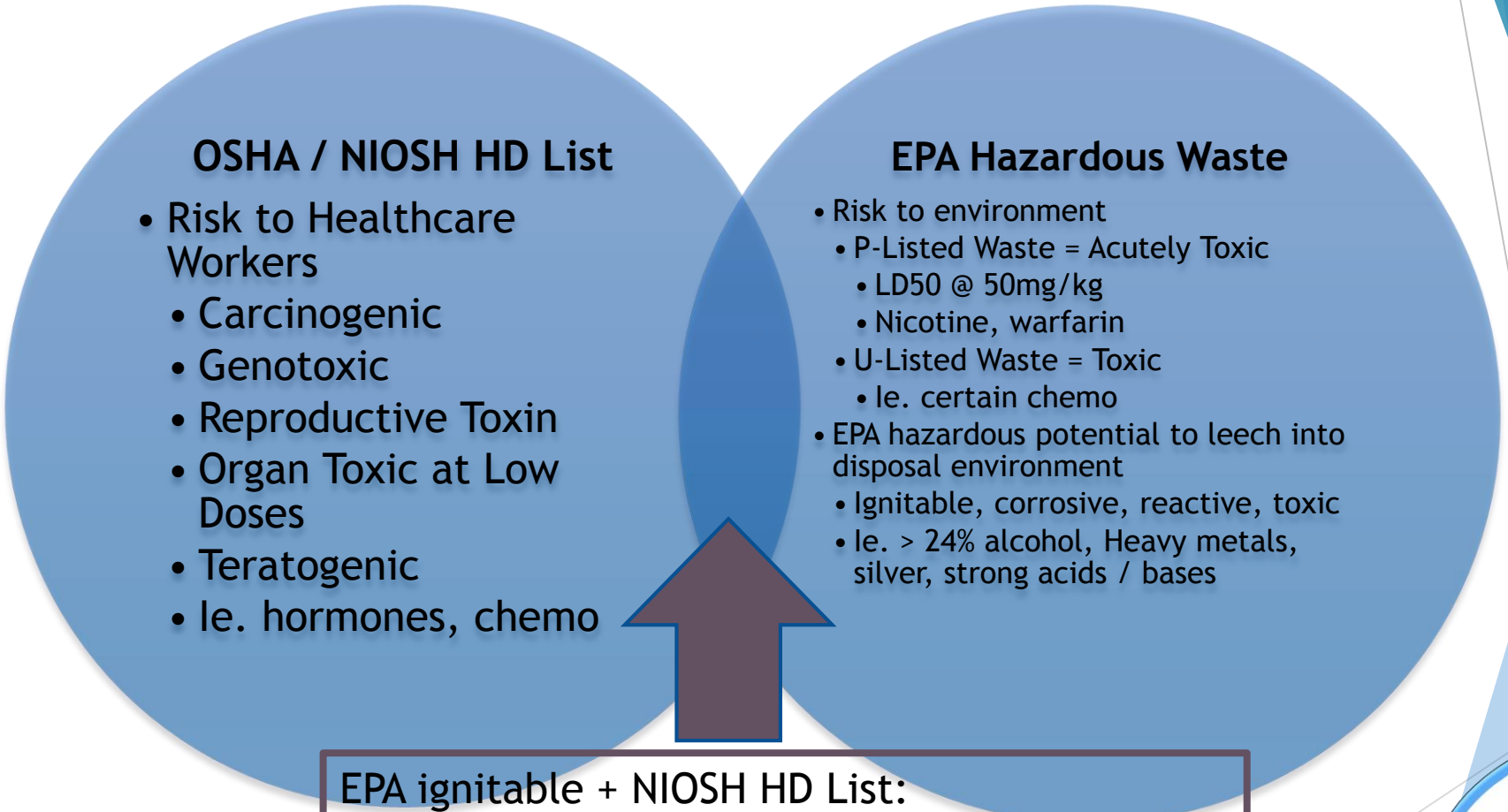
  - Cleaning supplies should be single-use
  - Changing the mop and cleaning solutions frequently
  - Clean in the order of cleanest to dirtiest
  - Environmental testing data
  - Used cleaning supplies should be considered hazardous contaminated waste



Spill Kits

- Must have appropriate spill kits available in case of accidents
- Place Spill Kit where:
  - HD Receiving
  - HD Storage
  - HD Compounding
  - HD Transportation
- Staff need proper training on spill clean-up annually
- Videos and competency tests are available free on line from some spill kit manufacturers ☑

Hazardous Drug vs Hazardous Pharmaceutical Waste



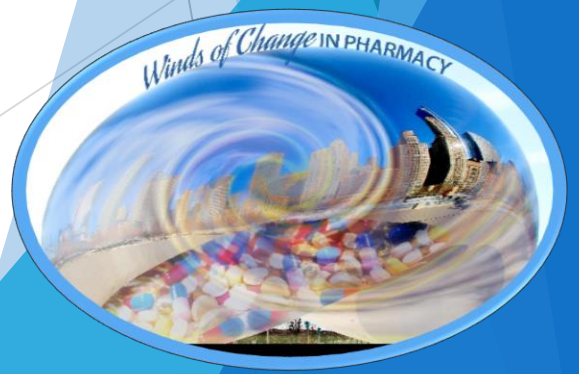
EPA ignitable + NIOSH HD List:
Paclitaxel, Etoposide

EPA P and U Listed + NIOSH HD List:
Cyclophosphamide, Mitomycin, Mephalan, Arensic Trioxide

STAFF TRAINING & COMPETENCY ASSESSMENT

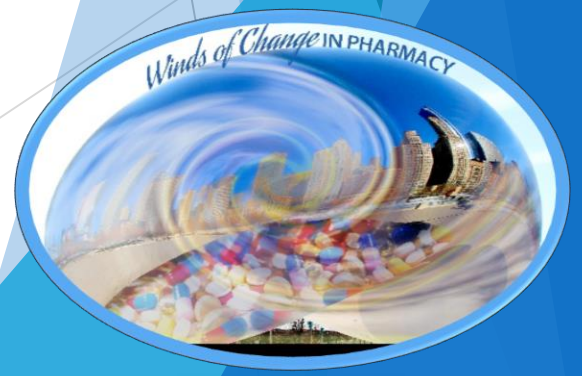
- Train staff to….

- *What are the sources of exposure and risk related to their handling*
- *How can they find more information on these agents?*
- *How will these Hazardous Drugs be identified in the Pharmacy?*
- *How will these drugs be compounded?*
- *Procedures for handling and cleaning to minimize contamination*
- *How to properly clean and decontaminate*



NON-STERILE HD COMPOUNDING STEPS TO COMPLIANCE

Facility Design	• Most Costly • But even without this, must implement all other steps
PPE	• Identifying and Obtaining Proper Supplies • Donning and Doffing
Good Lab Practices	• Prospective review of steps in compounding • Identification of risk points for HD contamination • HD SOPs integrated in Master Formulation and Compounding records
Staging of Facility	• Supplies Identified prior to initiating compounding • Eliminate / Reduce interruptions during compounding • Clean and Dirty Areas
Training and Competency	• Didactic Education • Observation of technique

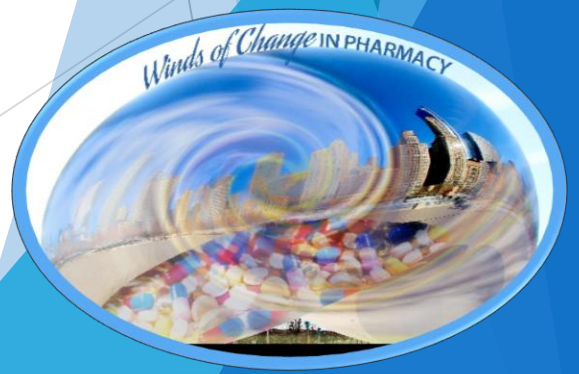


Understanding Air flow in C-PEC

- Breach of C-PEC's air-curtain during active powder manipulation causes contamination!
- Slow purposeful movements – minimize significant movements along the opening
- Completely avoid moving hands in and out of hood for supplies or documentation
- Breach of C-PEC's air-curtain during active powder manipulation
- Proper Staging and Workflow avoids this
- Include HD handling practices on Master Formulation Record / Compounding Record so compounder can think of proper handling during the prep steps

Removal

- Through out prep collect HD waste into Sealable plastic bag. Seal bag prior to removal from hood and dispose of directly into appropriate waste receptacle.
- Final Compounded product will have external contamination and should be properly contained when removed from the hood
- Contaminated, reusable lab equipment shall be contaminated in sealed plastic within the C-PEC, then transported to the area for cleaning



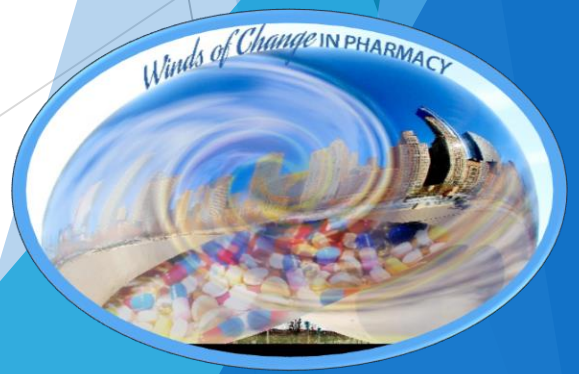
Post Test Question #1

1. Which one of these medications are hazardous drugs?
    a. Finasteride
    b. Estradiol
    c. Tamoxifen
    d. Phenytoin
    e. Tacrolimus
    f. All of the above

Post-Test Question

True or False: Has the dust of hazardous drugs been found in the air in retail pharmacies?

TRUE



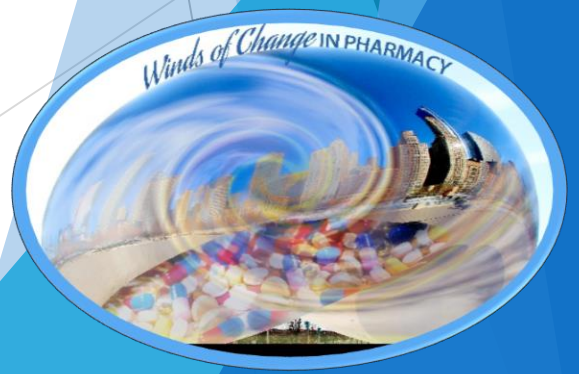
Post-Test Question

True or False: Women who are actively trying to conceive, and women who are pregnant or breast feeding must notify co-workers to maintain safe hazardous drug handling.

FALSE: Women do not have to reveal their private health information. The work environment should allow for proper identification of occupational risks without have to ask their supervisor.

TAKE HOME POINTS

- *What are the sources of exposure and risk related to he drugs you handle?*
- *How can you find more information on these agents?*
- *How will these Hazardous Drugs be identified in the Pharmacy?*
- *How will these drugs be compounded?*
- *Procedures for handling and cleaning to minimize contamination*
- *How to properly clean and decontaminate*



Resources & References

OSHA Occupational Safety and Health Administration

- Technical Manual: Controlling Occupational Exposure to Hazardous Drugs 1999
- Newly published Document in 2016, harmonized with USP 800

NIOSH National Institute for Occupational Safety and Health

- Maintain Hazardous Drug List, updated Q 2 Years, use 2018 Drug List!
- Bulletin on Medical Surveillance – 2012
- Hazardous Drug Handling – 2004

US Pharmacopoeia Chapter <800>

- Federally enforceable standard
- Finalize Publication printed on February 1, 2016
- Original Implementation Date July 1, 2018;
- Delayed Implementation December 2019

State Law

- Ex California, Washington

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