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

Safe Handling of Hazardous Drugs in Community Pharmacy

Christine Roussel, PharmD, BCOP
Assistant Director of Pharmacy, Doylestown Hospital
Consultant and Facilitator, Medisca / LP 3 Network
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?
- Estradiol
- Tamoxifen
- Phenytoin
- Tacrolimus
- Cyclosporine
- 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.
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

- Increasing incidence of cancer
- Increase use of hazardous drugs for non-malignant diseases
- Veterinary Use of Hazardous Drugs
- Over 160 drugs identified as hazardous (including hormones)
DRUGS - IT’S NOT JUST ONCOLOGY!

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Hazardous drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hormone Replacement Therapy</td>
<td>Estrogen, progesterone, diethylstilbestrol, Testosterone</td>
</tr>
<tr>
<td>Veterinary</td>
<td>Propylthiouracil, triostane, methimazole, chemotherapy</td>
</tr>
<tr>
<td>Ophthalmology</td>
<td>Mitomycin, fluorouracil, tacrolimus, cyclosporine, retinoic acid</td>
</tr>
<tr>
<td>Pediatric Compounding</td>
<td>Suspensions of chemotherapy, immunosuppression</td>
</tr>
<tr>
<td>Community Pharmacy</td>
<td>Methotrexate, estrogen, cyclosporine, tacrolimus, mycophenolate</td>
</tr>
<tr>
<td>Home Infusion</td>
<td>Ganciclovir, fluorouracil, mycophenolate</td>
</tr>
<tr>
<td>Specialty Pharmacy</td>
<td>Oral and Injectable Chemotherapy, Immunomodulators</td>
</tr>
</tbody>
</table>

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 healthcare settings may cause skin rashes, infertility, miscarriage, birth defects, and possibly leukemia or other cancers.

OPPORTUNITIES AND ROUTES OF EXPOSURE

- 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

Minimizing potential adverse effects requires a multifaceted approach.

TOXICITY

<table>
<thead>
<tr>
<th>Short Term Toxicity</th>
<th>Long Term Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin reactions</td>
<td>Reproductive issues</td>
</tr>
<tr>
<td>Ocular reactions</td>
<td>Chronic cough</td>
</tr>
<tr>
<td>Allergic asthma</td>
<td>End-organ damage</td>
</tr>
<tr>
<td>Flu-like symptoms</td>
<td>Leukemia</td>
</tr>
<tr>
<td>Headache</td>
<td>Lymphoma</td>
</tr>
<tr>
<td>Dizziness</td>
<td>Myelodysplastic Syndrome (MDS)</td>
</tr>
<tr>
<td>Increased infections</td>
<td>Bladder and liver cancer</td>
</tr>
</tbody>
</table>

NIOSH - Hazardous Drug Alert 2004
NIOSH HAZARDOUS DRUG LIST

- **Group 1**
- **Antineoplastic drugs**: May also pose a reproductive risk in susceptible populations
- **Examples**: anastrozole, 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

**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

NIOSH HAZARDOUS DRUG LIST

- 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
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

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

---

Lactose was only present in 77 of 200 tablets sampled.

Work Surface Contamination with Lactose detected in 14 / 18 samples. Max level found = 19 µg/cm².

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
Health problems reported among healthcare workers exposed to hormones

**POTENTIAL HEALTH HAZARDS**

**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!

**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

**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

**CHEMOTHERAPY DOES NOT DISCRIMINATE**

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.

EPIDEMIOLOGY 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

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

First Supplement to USP 39—NF 34 / USP 800 Hazardous Drugs—Handling in Healthcare Settings

Add the following:
- (800) HAZARDOUS DRUGS—HANDLING IN HEALTHCARE SETTINGS

 préparations 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
**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 re-packing (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/or practices

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

**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"
- "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."

**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. However, due to 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 minimum, consider the following:
- Type of HD (e.g., antineoplastic, non-antineoplastic, reproductive risk only)
- Dosage form
- Risk of exposure
- Risk of dermal exposure
- 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:
- (i.e. 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”**

<table>
<thead>
<tr>
<th>Steps</th>
<th>Drug Specific Discussion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identification of HDs</td>
<td>NIOSH List - Tacrolimus</td>
</tr>
<tr>
<td>Hazard Assessment (Type of HD, dosage form)</td>
<td>Group 2 Risk for all employees Risk for pregnant, lactating and those activity trying to conceive</td>
</tr>
<tr>
<td>Risk Evaluation (Risk of exposure)</td>
<td>Counting capsules Activities performed include opening capsules and collecting powder for compounding or working API</td>
</tr>
<tr>
<td>Plan (be specific to type of handling or manipulation, packaging, etc)</td>
<td>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</td>
</tr>
<tr>
<td>Risk Control Implementation</td>
<td>Staff Education on HD Program, Labelling HD’s, signs on how and where to handle, inventory segregation</td>
</tr>
<tr>
<td>Monitoring</td>
<td>Observe staff filling these orders, competency assessment</td>
</tr>
</tbody>
</table>

**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)
If you already have a hood:

- Ask your manufacturer if your powder containment hood meets the definition of a Class I 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

**C-PEC SELECTION**

**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 I 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

Negative Pressure (0.01 – 0.03 in wc) ≥ 12 ACHP

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

CAUTION: HAZARDOUS DRUG
OBSERVE SPECIAL HANDLING, ADMINISTRATION AND DISPOSAL REQUIREMENTS
PPE - RESPIRATORY PROTECTION

- 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

- 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

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

EYE & FACE PROTECTION

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

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

<table>
<thead>
<tr>
<th>Time (Minutes)</th>
<th>Permeation Rate (p.p.b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>10000</td>
</tr>
<tr>
<td>10</td>
<td>12000</td>
</tr>
<tr>
<td>30</td>
<td>13000</td>
</tr>
<tr>
<td>60</td>
<td>14000</td>
</tr>
<tr>
<td>90</td>
<td>15000</td>
</tr>
<tr>
<td>120</td>
<td>16000</td>
</tr>
<tr>
<td>180</td>
<td>18000</td>
</tr>
<tr>
<td>210</td>
<td>20000</td>
</tr>
<tr>
<td>240</td>
<td>22000</td>
</tr>
</tbody>
</table>

*Combs, T. (Unpublished data) p.p.b = parts per billion

#### ASTM Permeation Standard

<table>
<thead>
<tr>
<th>ASTM Standard</th>
<th>Permeation Rate</th>
<th>Drugs</th>
<th>Temperature</th>
</tr>
</thead>
<tbody>
<tr>
<td>F739</td>
<td>0.1 mcg/cm2/min</td>
<td>No specific drugs</td>
<td>25 °C (Room temperature)</td>
</tr>
<tr>
<td>D6978</td>
<td>0.01 mcg/cm2/min</td>
<td>Cemustine, Cyclophosphamide, Doxorubicin, Etoposide, Fluorouracil, Paclitaxel, Thiotepa</td>
<td>25 °C (Temperature gloves reach after wearing them for 5 minutes)</td>
</tr>
</tbody>
</table>

#### NIOSH TIERED APPROACH

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

#### Chemotherapy Drugs Listed on the Package

<table>
<thead>
<tr>
<th>Product (Test Method)</th>
<th>Gloves 1 (ASTM DC978-05)</th>
<th>Gloves 2 (ASTM DC978-05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleomycin Sulfate (15.0 mg/ml)</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Busulfan (6.0 mg/ml)</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Carboplatin (paraplatin) (15.0 mg/ml)</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Carmustine (3.3 mg/ml)</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Cisplatin (1.0 mg/ml)</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Cyclophosphamide (20.0 mg/ml)</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Daunorubicin HCl (Adriamycin) (2.0 mg/ml)</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Daunorubicin HCl (Adriamycin) (5.0 mg/ml)</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Doxorubicin (2.0 mg/ml)</td>
<td></td>
<td>X</td>
</tr>
<tr>
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### NIOSH TIERED APPROACH

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Activity</th>
<th>Double gloves</th>
<th>Protective gown</th>
<th>Eye protection</th>
<th>Respiratory protection</th>
<th>Ventilated engineering controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subcutaneous Intramuscular injection</td>
<td>Preparation (withdrawal from vial or ampoule)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes, if not done in a control device</td>
<td>Yes, if not done in a control device</td>
<td>Yes, BSC or CACI</td>
</tr>
<tr>
<td>Subcutaneous Intramuscular injection</td>
<td>Administration from prepared syringe</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes, if liquid that could splash</td>
<td>Yes, if inhalation potential</td>
<td>N/A</td>
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<tr>
<td>Intravenous solution</td>
<td>Compounding</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes, if not done in a control device</td>
<td>Yes, if not done in a control device</td>
<td>Yes, BSC or CACI recommended for CSTD</td>
</tr>
<tr>
<td>Intravenous solution</td>
<td>Administration of prepared solution</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>N/A</td>
</tr>
<tr>
<td>Solution for irrigation</td>
<td>Administration (dialysis, HPPE, intrapertioneal, etc.)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>N/A</td>
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<tr>
<td>Powder/solution for inhalation</td>
<td>Inhalation</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes, when applicable</td>
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</tbody>
</table>

### 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

<table>
<thead>
<tr>
<th></th>
<th>Nurses</th>
<th>Micronuclei</th>
<th>Chromosomal Abnormalities</th>
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<tbody>
<tr>
<td>&lt; 100% Compliance</td>
<td>29</td>
<td>9.5 (+/-5.2)</td>
<td>2.6 (+/-2.6)</td>
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<tr>
<td>100% Compliance</td>
<td>33</td>
<td>4.3 (+/-3.7)</td>
<td>0.9 (+/-1.9)</td>
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</table>

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.

### COMMON HD MISHANDLING DURING NON-STERILE COMPOUNDING

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

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

OSHA / NIOSH HD List
- Risk to Healthcare Workers
  - Carcinogenic
  - Genotoxic
  - Reproductive Toxin
  - Organ Toxic at Low Doses
  - Teratogenic
  - Ie. hormones, chemo

EPA Hazardous Waste
- Risk to environment
  - P-Listed Waste = Acutely Toxic
    - LD50 @ 50mg/kg
    - Microliter, milliliter
  - U-Listed Waste = Toxic
    - Ie. certain chemo
  - EPA hazardous potential to leech into disposal environment
  - Ignitable, corrosive, reactive, toxic
  - Ie. > 24% alcohol, Heavy metals, silver, strong acids / bases

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
| 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
Which one of these medications are hazardous drugs?

- a. Finasteride
- b. Estradiol
- c. Tamoxifen
- d. Phenytin
- e. Tacrolimus
- f. All of the above

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

TRUE

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.

What are the sources of exposure and risk related to the 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
- Newly published Document in 2016, harmonized with USP 800
- Bulletin on Medical Surveillance - 2012
- Hazardous Drug Handling - 2004

NIOSH National Institute for Occupational Safety and Health
- Maintain Hazardous Drug List, updated Q 2 Years, use 2018 Drug List!
- 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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