Objectives

• Discuss the history of safe handling
• Identify the exposure risks and routes associated with handling of hazardous drugs
• Review the current guidelines on the safe handling of hazardous drugs
• Describe the evidence of exposure risks including genotoxicity of hazardous drugs
• Describe and identify safe handling practices to protect the health care worker from exposure to hazardous drugs
• Review the current clinical evidence on the use of closed system drug transfer devices

What is the Issue?

Many healthcare workers are frequently exposed to hazardous drugs

• Numerous published studies document the presence of hazardous medications in the workplace
• Multiple independent studies have documented hazardous drugs (HDs) in the urine of healthcare workers
• Exposure and uptake present serious hazards to health and safety
Who is Advocating for Protection?

- American Society of Hospital Pharmacists
- American Medical Association
- OSHA Technical Manual
- NIOSH Alert
- USP <797>
- ASHP Technical Advisory Bulletin
- European Society of Hospital Pharmacists
- State and local laws

How are Workers Exposed?

Standard safe handling protocols may not prevent exposure

Healthcare workers can be exposed through:

- CONTAMINATED AIR
  - Aerosols and vapors
- CONTAMINATED SURFACES
  - Direct contact with drugs
- CONTAMINATED PPE
  - Hand to mouth contamination

What’s the Concern?

Exposure to hazardous drugs is a proven danger

- Hazardous drugs have at least one of these characteristics:
  - Carcinogenicity
  - Teratogenicity/developmental toxicity
  - Reproductive toxicity
  - Organ toxicity at low doses
  - Genotoxicity

- Antineoplastic and other hazardous drugs can cause:
  - Cancer
  - Unusual cell development
  - Reproductive issues
  - Organ damage
  - Damage to DNA (chromosomes)
How Serious is the Issue?

The same mechanisms that chemotherapy uses to kill cancer cells also works to damage healthy cells.

Hazardous drugs such as life-saving chemotherapy can be the only option for patients. However, chemo is poison by design. It is a descendant of deadly mustard gas.

A Parallel: Radiation Exposure

Experience proves that no amount of radiation exposure can be considered entirely risk free.

Safety standards are now finally in place.

How Pervasive is the Issue?

Contamination is widespread and prevalent

- More than 2/3 of all areas are contaminated where drugs are prepared and administered.
- Surface and air contamination found despite use of biological safety cabinets.
- Workers and even patients can be exposed.
Joint Statement Stresses the Issue

Recently OSHA, Joint Commission, NIOSH urged facilities to take a leadership role in worker safety and health:

- "Every day in healthcare settings across America, workers are exposed to hundreds of powerful drugs used for cancer chemotherapy, antiviral treatments, hormone regimens and other therapies."
- "While these drugs are used to relieve and heal patients, many of them present serious hazards to the health and safety of your workers."
- "Some of these drugs have been known to cause cancer, reproductive and developmental problems, allergic reactions and other adverse effects that can be irreversible even after low-level exposure."

What are the Risks?

The Personal Reality

"Nurses, pharmacists and others who handle chemo drugs have been getting sick. Despite multiple studies that indicate the drugs actually may cause cancers, the federal government doesn't require safeguards on the job."

"Lifesaving drugs may be killing health workers"
Short-Term Health Risks

Occupational exposure can lead to acute symptoms:

- Headaches
- Hair loss
- Mucosal sores
- Liver damage
- Nausea/vomiting
- Dizziness

Long-Term Health Risks

Prolonged exposure can lead to irreversible adverse effects:

- Cancer
- Genetic
- Organ
- Reproductive
- Developmental

Cancer Risks

Fact: Hazardous drugs can lead to increased rates of cancer:

<table>
<thead>
<tr>
<th>Nurses</th>
<th>Pharmacists</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oncology nurse*</td>
<td>Pharmacy tech*</td>
<td>Affected patients treated with methotrexate**</td>
</tr>
</tbody>
</table>

- Relative risk of leukemia in oncology nurses who handle antineoplastic drugs.
- 2x increase in non-Hodgkin lymphomas.
- 3x increase in non-Hodgkin lymphomas.
- 5x increase in acute myeloid leukemia.
- Increased risk of liver cancer.
- Increased risk of melanoma.
- Increased risk of lung cancer.
Reproductive Risks

Fact: Hazardous drugs can cause reproductive problems

Nurses who handle cancer drugs have:
- 70% more birth defects
- 10% more miscarriages

Incidence of miscarriages among nurses working with antineoplastic drugs is twice the norm. 6

Developmental, Organ and Genetic Risks

Fact: Hazardous drugs can harm developing fetuses
Handling of cytostatic drugs was associated with malformations in the offspring. 13

Fact: Hazardous drugs can damage internal organs
Three consecutive head nurses handling cytostatic agents had liver damage. 14

Fact: Hazardous drugs can damage DNA
Pharmacists and nurses who handle antineoplastic drugs have a 2.5 to 5-fold increase in chromosomal aberrations. 15

Increase in Chromosomal Aberrations

Genetic Risks

Fact: Healthcare workers using standard safety precautions still have DNA damage
Increased aberrations are seen on Chr 5, 7 and 11 – signature markers for many leukemias and myelodysplastic syndromes. 16

Standard Safety Measures Aren’t Enough
What are the Options?

How do We Protect the Providers?

ISOPP recommends following Hierarchic Order of Protection:

**Industrial Hygiene Model**
- Level 1: Elimination, substitution, replacement
- Level 2: Isolation of the hazard/source containment
- Level 3: Engineering controls/ventilation
- Level 3B: Administrative controls/organization methods
- Level 4: Personal Protective equipment

First choice: Stop hazardous drug use.
Second choice: Isolate the drug.

**Administrative Controls**
- Defining Hazardous Drugs in the facility
- Policies and Procedures addressing all aspects of handling hazardous drugs:
  - Safe storage
  - Transport
  - Administration
  - Disposal of HDs
- All employees handling HDs should be required to wear PPE
- Policies should prohibit eating, drinking, smoking, chewing gum or tobacco, applying cosmetics and storing food in areas HDs are used
- Training and documentation of training for all employees that may come in contact with HDs
- Spills should be managed according to HD spill policy and procedure
Work Practice Controls

- Designed to minimize occupational exposure to HDs
- Minimize the generation of HD contamination and maximize the containment of inadvertent contamination
- Similar to administrative controls as they are established procedures
- Consistent and appropriate use of engineering controls and PPE

Examples of work practice controls that can lead to exposure:
- Pricking and cutting BSC without changing gloves
- Puncturing or cutting vs. picking up
- Using gloves in areas where HDs are present
- Using gloves in areas where HDs are present
- Using gloves in areas where HDs are present

Examples of work practice controls that result in decreased contamination:
- Gather all supplies before entering PCC
- Double gloving
- Changing gloves every 30 minutes
- Avoid touching equipment when wearing gloves used to handle HDs
- Use PPE when stocking HDs
- Clean countertops and other surfaces in the work area
- Use a CSTD when working with HDs
Personal Protective Equipment

Gloves:
- Designated Chemotherapy Gloves; thickness, type and time worn are major
determinants of permeability of HDs.
- For drugs to be labeled for use with chemotherapy they must be tested on
the following drugs:
  - Carmustine, Cyclophosphamide, Doxorubicin, Etoposide, 5-FU, Paclitaxel
  and Thiotepa
Gowns:
- No standard exists to test for permeability
- Cloth gowns do not provide adequate protection
- Gowns with polyethylene and vinyl coatings performed the best in a study
  conducted (Harrison and Kloos, 1999)
- Gowns should be changed after each use and not re-used or saved

Personal Protective Equipment

- Eye and Facial Protection

- Respiratory protection
  - Surgical mask is not a respirator and does not protect
  against aerosols or vapors
  - Fit tested NIOSH approved N95 respirator or more protective
  respirator should be worn

Is Technology the Answer?

There are many choices – but also many myths

- Biological Safety Cabinet
- Barrier Isolator
- Compounding Robot
- Filter Devices
- Closed System Transfer Device
What is a CSTD?

Nothing Out: Protects healthcare workers from the dangers of hazardous drug exposure

Nothing In: Prevents microbial ingress, maintaining sterility of the vial contents

Technology Comparison

Closed Systems

Closed System Transfer Device (as defined by NIOSH)

Cytotoxic drug molecule

FILTER

Closed Systems

Closed System Transfer Device

Do CSTDs Really Work?

Elimination of human uptake

Using a CSTD to Reduce Personnel Exposure to Antineoplastic Agents:

<table>
<thead>
<tr>
<th>Agent</th>
<th>Formulation</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytarabine</td>
<td>5%</td>
<td>85%</td>
</tr>
<tr>
<td>Rifamycin</td>
<td>10%</td>
<td>21%</td>
</tr>
<tr>
<td>Doxorubicin</td>
<td>1%</td>
<td>0%</td>
</tr>
</tbody>
</table>

BD PhaSeal 3rd party, peer-reviewed, published clinical studies
- Validate clinical efficacy
- Show elimination of human uptake

Workplace Contamination with Antineoplastic Agents in a Cancer Hospital Using a CSTD:

<table>
<thead>
<tr>
<th>Period of Exposure</th>
<th>Cytarabine</th>
<th>Rifamycin</th>
<th>Doxorubicin</th>
</tr>
</thead>
<tbody>
<tr>
<td>65 weeks</td>
<td>100% (50)</td>
<td>100% (50)</td>
<td>100% (50)</td>
</tr>
<tr>
<td>1 year</td>
<td>50% (100)</td>
<td>50% (100)</td>
<td>50% (100)</td>
</tr>
<tr>
<td>2 years</td>
<td>50% (100)</td>
<td>50% (100)</td>
<td>50% (100)</td>
</tr>
<tr>
<td>3 years</td>
<td>50% (100)</td>
<td>50% (100)</td>
<td>50% (100)</td>
</tr>
<tr>
<td>4 years</td>
<td>50% (100)</td>
<td>50% (100)</td>
<td>50% (100)</td>
</tr>
<tr>
<td>5 years</td>
<td>50% (100)</td>
<td>50% (100)</td>
<td>50% (100)</td>
</tr>
<tr>
<td>6 years</td>
<td>50% (100)</td>
<td>50% (100)</td>
<td>50% (100)</td>
</tr>
<tr>
<td>7 years</td>
<td>50% (100)</td>
<td>50% (100)</td>
<td>50% (100)</td>
</tr>
<tr>
<td>8 years</td>
<td>50% (100)</td>
<td>50% (100)</td>
<td>50% (100)</td>
</tr>
<tr>
<td>9 years</td>
<td>50% (100)</td>
<td>50% (100)</td>
<td>50% (100)</td>
</tr>
<tr>
<td>10 years</td>
<td>50% (100)</td>
<td>50% (100)</td>
<td>50% (100)</td>
</tr>
</tbody>
</table>

* As tested on human samples
Do CSTDs Really Work?

Reduction in surface contamination

<table>
<thead>
<tr>
<th>Drug</th>
<th>Pre-CSTD</th>
<th>Post-CSTD</th>
<th>% Reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>65%</td>
<td>10%</td>
<td>85%</td>
</tr>
<tr>
<td>Ifosfamide</td>
<td>54%</td>
<td>10%</td>
<td>84%</td>
</tr>
<tr>
<td>5-FU</td>
<td>33%</td>
<td>10%</td>
<td>90%</td>
</tr>
</tbody>
</table>

Comparison of Surface Contamination with Cyclophosphamide and Fluorouracil: CSTD vs. Standard Preparation

Surface contamination before the use of CSTD
- Cyclophosphamide: 65%
- Ifosfamide: 54%
- 5-FU: 33%

Clinical Evidence Summary
Extensive clinical evidence from dozens of independent, peer-reviewed, published studies clearly documents the effectiveness of CSTDs.

Results
- Only BD PhaSeal met the NIOSH and ISOPP definition of a CSTD.
- No leakage was observed in any of the manipulations with the BD PhaSeal system.
- Post implementation, no positive urine samples.
- Median values demonstrated reduction for all drugs (cyclophosphamide, ifosfamide, 5-FU) of 95%, 90%, & 65% respectively.

Demonstrated protection outside of a biological safety cabinet.

Summary
- Titanium tetrachloride was selected to simulate the escape of vapor from each product.
- Fluorescein sodium was selected to simulate contamination with dry connections between the vial and syringe and between syringe and access port.
- Liquid with low pH was used as a substitute for active drug.
- Litmus paper was used as a pH indicator. Every component was tested for 10 manipulations.

Surface contamination with and personnel exposure to antineoplastic agents before and after the implementation of a CSTD.
Determined levels of environmental chemotherapy contamination in a new cancer hospital that had exclusively used a CSTD (BD PhaSeal).
114 wipe study samples selected from 22 hospitals.

Determined surface contamination of a CSTD in conjunction with standard preparation outside a BSC.

Who has Endorsed CSTDs?

CSTDs are defined and endorsed by recognized organizations

NIOSH Definition
"A drug transfer device that mechanically prohibits the transfer of environmental contamination into the system and the escape of hazardous drug or vapor concentrations outside the system."

Revised USP <797> Guidelines
"USP <797> states that CSTDs are "vial transfer devices that allow no venting or exposure of hazardous substance to the environment" and that "The use of a CSTD is preferred because of their inherent closed-system process.""

OSHA, The Joint Commission, NIOSH
Recommendations from OSHA, The Joint Commission and NIOSH to follow the 2004 NIOSH Alert for Hazardous Drugs.

ASHP Excerpts:
- CSTDs mechanically prevent the escape of drug or vapor out of the system.
- Studies show reduction in environmental contamination.
- Consider using CSTDs while compounding hazardous drugs.

ONS Excerpt:
- "ONS (2005) "The PhaSeal System is the only documented closed system on the market. This system is designed to prevent leakage of hazardous drug solutions during compounding and administration."

BD PhaSeal also meets USP and APhA guidelines and definitions.
The Future of HD Legislation?

Washington State bill unanimously passed the senate and house.

WASHINGTON STATE LEGISLATURE

- Department of Labor and Industries must establish standards for the handling of antineoplastic and other hazardous drugs by health care personnel in consultation with the Department of Health.
- Must describe drugs to be regulated, exposure control program for handling, engineering controls, safe work practices, use of PPE, notices to employees, emergency response, record keeping and any other requirements to protect the health and safety of health care personnel.
- Rules adopted and go into effect January 1, 2014.

The Time for Safety is Now!

Many healthcare workers are still exposed to harmful effects.

- Handling of hazardous drugs in healthcare requires a systematic approach.
- While use of engineering controls and standard personal protective equipment (PPE) has increased, state regulation is limited; federal legislation is non-existent.
- However, use of CSTDs as a form of PPE is increasing nationwide.
- Comprehensive safe-handling programs should begin with a hazard assessment and include multiple layers of protection including a CSTD.
- CSTDs that meet the NIOSH and ISOPP definitions can reduce human uptake by:
  - Preventing drug exposure.
  - Reducing surface contamination.
References


17. April 4, 2011 Communication from Dr. David Michaels, Asst. Sec. Labor, OSHA; Dr. Paul Schyve, Sr. VP, The Joint Commission, Dr. John Howard, Director NIOSH. Presented at ASHP Midyear Clinical Meeting, December 2007.


5. April 4, 2011 Communication from Dr. David Michaels, Asst. Sec. Labor, OSHA; Dr. Paul Schyve, Sr. VP, The Joint Commission, Dr. John Howard, Director NIOSH. Presented at ASHP Midyear Clinical Meeting, December 2007.


