

Handling Hazardous Drugs

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Extent of Exposure

“Because of the wide use of cancer chemotherapy in recent years, the extent of exposure of individuals engaged in the manufacture, preparation, and administration of chemotherapeutic drugs is of considerable concern.”



Scope of the Problem

- ◆ Cancer is a leading cause of death worldwide
 - In 2007, the disease accounted for 7.9 million deaths (13%)
- ◆ Deaths from cancer worldwide are projected to continue rising:
 - 9 million deaths in 2015
 - 12 million deaths in 2030
- ◆ In the US in 2010:
 - A total of 1,529,560 new cancer cases
 - 569,490 deaths from cancer
 - Totals will double in the US by 2050

World Health Organization. Available at <http://www.who.int/cancer/en/>.

American Cancer Society. *Cancer Facts & Figures 2010*. Atlanta: American Cancer Society; 2010.



Scope of the Problem (cont'd)

- ◆ The number of healthcare workers exposed to hazardous drugs is increasing due to:
 - Increasing numbers of patients
 - Increasing use of hazardous drugs for non-chemotherapy indications
 - Combination chemotherapy
- ◆ The current estimate is that ~5.5 million workers are annually exposed to hazardous drugs



Hazardous Drugs

- ◆ The term was first used by the American Society of Health-Systems Pharmacists (ASHP) in 1990
 - Occupational Safety and Health Administration (OSHA)
 - National Institute for Occupational Safety and Health (NIOSH)
 - Both have adopted the definition
- ◆ Drugs are classified as hazardous if studies in animals or humans indicate that exposures to them have a potential for causing cancer, developmental or reproductive toxicity, or harm to organs



What Are Hazardous Drugs?

- ◆ NIOSH considers a drug hazardous if it exhibits 1 or more of the following 6 characteristics:
 - Carcinogenicity
 - Teratogenicity
 - Reproductive toxicity
 - Organ toxicity at low doses
 - Genotoxicity
 - Structure and toxicity profiles of new drugs that mimic existing drugs determined hazardous by the above criteria



Risk of Handling Hazardous Drugs

- ◆ Late 1970s:
 - First identification that a patient's exposure to chemotherapy can lead to secondary malignancies
 - First evidence with healthcare workers involved positive urine mutagenicity in nurses and pharmacists handling chemotherapy
- ◆ 1980 to 1990 studies:
 - In pharmacists, presence of cyclophosphamide in urine when using horizontal hoods, none with vertical hoods
 - In nursing, presence of hazardous drugs has been detect in multiple studies and remains an issue
 - Contamination inside and outside pharmacy & nursing work areas
 - Vial contamination first identified



Risk of Handling Hazardous Drugs (cont'd)

- ◆ Meta-analysis of 14 studies demonstrated no positive association between hazardous drug exposure and cancer development
- ◆ 9 studies demonstrated a small but positive correlation between hazardous drug exposure and reproductive health
 - The most common effects:
 - Spontaneous abortion
 - Infertility
 - Low birth weight
 - Congenital malformations/abnormalities



Risk for Developing Cancer in Exposed Workers

- ◆ Risk analysis model using cyclophosphamide estimated that the annual increased risk for developing cancer in exposed workers was:

1.4 to 10 cases/million workers



Surface Contamination

- ◆ 6 sites studied in the US and Canada
- ◆ Sampling locations:
 - Biological safety cabinets (BSCs), countertops, floors in and adjacent to preparation areas, tabletops, chairs, and floors in treatment areas
- ◆ Agents sampled
 - Cyclophosphamide, ifosfamide, fluorouracil
- ◆ Measurable amounts of the antineoplastic agents were detected in 75% of the pharmacy samples and 65% of administration samples



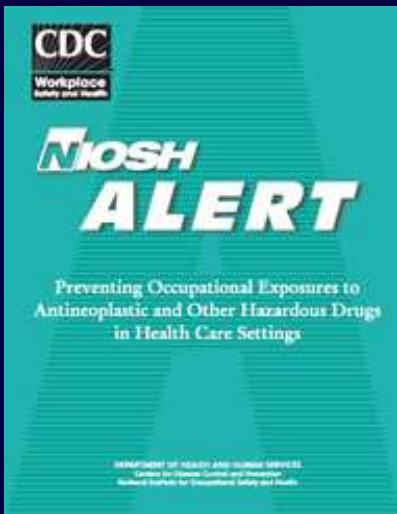
Current Guidelines

- ◆ 1999 – OSHA Technical Manual
- ◆ 2000 – CDC: Guidance on BSC
- ◆ 2001 – EPA: Managing Hazardous Waste
- ◆ 2002 – NIH: Recommendations for Safe Handling
- ◆ 2003 – ONS: Safe Handling Guidelines
- ◆ 2004 – NIOSH Alert
- ◆ 2006 – ASHP: Guidelines on Handling Hazardous Drugs
- ◆ 2008 – USP 797 Pharmaceutical Compounding
- ◆ 2009 – ONS Chemotherapy and Biotherapy Guidelines and Recommendations for Practice (Third Edition)
- ◆ 2009 – ONS/ASCO Guidelines for Safe Administration of Chemotherapy

CDC = Centers for Disease Control and Prevention; EPA = Environmental Protection Agency; NIH = National Institutes of Health; ASHP = American Society of Health-System Pharmacists; USP = United States Pharmacopeia, ONS = Oncology Nursing Society; ASCO = American Society of Clinical Oncology



NIOSH Alert



NIOSH Website: www.cdc.gov/niosh
Tel: 1-800-35-NIOSH
Fax: 513-533-8573
E-mail: pubstaff@cdc.gov

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.



NIOSH Alert (*cont'd*)

- ◆ The purpose of the alert is to increase awareness about the health risks posed by working with hazardous drugs
- ◆ Target audience was health care workers
- ◆ The health risk is influenced by the extent of the exposure and the potency and toxicity of the hazardous drug
- ◆ It provides workers guidelines for protection
- ◆ It provides employers the necessary administrative and engineering controls to maintain a safe workplace
- ◆ Focus is on administrative and personal protection controls; smaller focus on engineering controls



NIOSH Alert (*cont'd*)

- ◆ Provides recommendations for:
 - Assessing hazards in the workplace
 - Handling drugs safely
 - Use and maintenance of equipment
- ◆ Detailed recommendations for:
 - Receiving and storage
 - Preparation and administration
 - Ventilated cabinets
 - Routine cleaning, decontaminating, housekeeping & disposal
 - Medical surveillance



USP Chapter 797

- ◆ Objective is “to prevent harm, including death, to patients that could result from”:
 - Bacterial contamination and excessive endotoxins
 - Variability in intended strengths of ingredients
 - Unintended chemical & physical contamination
 - Ingredients of inappropriate quality
- ◆ Hazardous drugs are a subsection of the chapter
 - Protection for workers discussed in this section
- ◆ Heavy focus on engineering controls



USP Chapter 797 (*cont'd*)

- ◆ Handling hazardous drug recommendations:
 - Stored separately – recommend negative pressure room with sufficient exhaust (12 air changes/hr)
 - PPE described for handling agents at all times
 - All agents prepared in an ISO Class 5 BSC or CACI
 - Preparation areas are to be ISO Class 7
 - Closed-system transfer devices (CSTD) are mentioned
 - CSTD and BSC/CACI can be combined without ISO Class 7 area for low-volume practices
 - Personnel should have adequate training



Summary of Recommendations

- ◆ Assess the hazards in the workplace
 - Working environment, equipment, types of drugs, physical layout, spill response, waste disposal, decontamination
- ◆ Handle drugs safely
 - Program for safe handling, policies and procedures, work practices related to drug manipulation and general hygiene
- ◆ Use and maintain equipment properly
 - Develop workplace procedures for using and maintaining all equipment that functions to reduce exposure



How to Manage Hazardous Drug Exposure

- ◆ Eliminate the source (not an option—no substitutes)
- ◆ PPE
- ◆ Work practice controls
- ◆ Ventilated biological safety cabinet (BSC) or isolator unit (engineering controls)
- ◆ Closed-system drug preparation and delivery
- ◆ Administrative controls



How to Manage Hazardous Drug Exposure

- ◆ Administrative controls
 - Training and education
 - Policies and procedures
- ◆ Exposure Prevention
 - Personal Protective Equipment (PPE)
 - Gloves
 - Gowns
- ◆ Engineering controls
 - Ventilated BSC
 - Compounding aseptic containment isolator unit (CACI) – glovebox
 - Closed-system drug preparation and delivery

Soule RD. Industrial Hygiene Engineering Controls, in Harris, RL (ed). *Patty's Industrial Hygiene*, Vol 2. 5th ed. New York, NY: John Wiley & Sons; 2000:1401-1454.



Administrative Controls

- ◆ Policies and procedures
- ◆ Workflow and access to restricted areas
- ◆ Employee training program with validation
- ◆ Annual competency evaluation
- ◆ Documentation



Exposure Prevention

- ◆ The key to safety is to control (or eliminate) exposure at all potential points
- ◆ Engineering controls and PPE have demonstrated reduced worker exposure
- ◆ Beware of things that can adversely affect the way these agents are handled
 - Increase workloads
 - Budgetary constraints
 - Complex treatment regimens
 - Use of agents in non-oncology areas



Factors That Affect Worker Exposure

- ◆ Work practices & policies
 - Use of ventilated cabinets or isolators
 - PPE
 - Closed-system drug preparation & delivery
 - Training & competency testing
- ◆ Amount of drug prepared
- ◆ Frequency and duration of drug handling
- ◆ Drug handling – Track from receipt to disposal to see if there are areas to improve
 - Shipping and receiving
 - Unpacking and storage
 - Preparation
 - Transportation
 - Administration
 - Disposal of wastes
- ◆ Spill control



Routes of Exposure

- ◆ Inhalation
 - From breathing air contaminated by aerosolized agents
- ◆ Ingestion
 - Hand-to-mouth contact (contaminated food or drink)
- ◆ Accidental injection
 - Contaminated sharps injury
- ◆ Dermal contact
 - Touching contaminated surfaces and vials from industry



Acute Symptoms of Hazardous Drug Exposure

- ◆ Lightheadedness
- ◆ Headache
- ◆ Dizziness
- ◆ Hair loss
- ◆ Abdominal pain
- ◆ Nausea and vomiting
- ◆ Local skin or mucous membrane reactions
- ◆ Allergic reaction
- ◆ Nasal sores
- ◆ Contact dermatitis and eczema



Personal Protective Equipment (PPE)

- ◆ Protects the worker from absorption or inhalation of hazardous drugs
 - Gloves
 - Double gloves, latex-free, powder-free
 - Gowns
 - Chemoprotective, disposable, back closure, cuffs
 - Respirator/mask
 - Aerosols and spill clean-up
 - Eye protection: when splashing is likely



Work-Practice Controls to Reduce Worker Exposure

- ◆ When reconstituting drugs, use of negative pressure technique
- ◆ Luer lock syringes and connections
- ◆ Needleless systems
- ◆ Safety needles and catheters
- ◆ Spiking IV containers before adding hazardous drugs
- ◆ Avoiding unspiking IV containers
- ◆ Closed-system drug preparation and delivery



Engineering Controls

- ◆ Equipment designed to contain a hazardous substance
- ◆ Ventilated biological safety cabinets (BSCs) or isolator glovebox exhausted 100% to the outside
- ◆ Designed to protect workers by containing aerosols generated during the preparation process
- ◆ Negative-pressure clean rooms
- ◆ Closed-system drug preparation and delivery devices



Engineering Controls



\$10,000



\$17,000



Surface Safe®

- ◆ Two-step applicator kit for BSC decontamination
- ◆ **Step 1** – for cleaning contaminated surfaces
 - 5.5" x 10" towelette containing 2% (W/W) specially formulated sodium hypochlorite soap solution
- ◆ **Step 2** – neutralizing solution for Step 1
 - 5.5" x 10" towelette containing 1% (W/W) sodium thiosulfate solution and 0.9% (W/W) benzyl alcohol

Cost: Approximately \$1.89 per application



Closed-System Devices for Drug Preparation and Delivery

- ◆ NIOSH definition
 - Mechanically prevent the transfer of environmental contaminants into the system & the escape of drug or vapor out of the system
- ◆ Eliminate or minimize caregiver & patient exposure to potentially hazardous agents
- ◆ Examples include:
 - PhaSeal®
 - OnGuard™ Contained Medication System
 - Cardinal Health Texium System ™
 - ICU Medical Oncology Clave™ and Spiros™ Products



Closed-System Characteristics

- ◆ Protects integrity of the IV fluid container whether on a syringe for transfer or on the end of an IV set
- ◆ Creates a needle-free closed system
- ◆ Allows safe transport of prepared syringes with hazardous medications
- ◆ Upon disconnect, the system seals and closes the system, reducing or eliminating the risk for drips and spills



Closed-System Considerations

- ◆ Compliance
- ◆ Customization of the application
- ◆ Cost
- ◆ Passive fail-safe design
- ◆ Ease of use
- ◆ Prevents spiking and unspiking of bags by nursing staff



Passive Fail-Safe Systems

- ◆ The device is needless
- ◆ The safety feature is an integral part of the device
- ◆ The device works **passively** (eg, it requires no activation by the user)
- ◆ If user activation is necessary, the safety feature can be engaged with a single-handed technique and allows the worker's hands to remain behind the exposed sharp (if present)



Key Features of Passive Fail-Safe Systems

- ◆ The user can easily tell whether the safety feature is activated
- ◆ The safety feature cannot be deactivated and remains protective through disposal
- ◆ The device performs reliably, is easy to use and practical (eg, compliance)
- ◆ The device is safe and effective for patient care
- ◆ The device is validated with solid and lipid-based drugs



PhaSeal® System Components

Protector
Injector
Connector
Infusion Adapter
Assembly Fixture





PhaSeal® System Components





PhaSeal® System Components





B. Braun OnGuard™ Contained Medication System





Cardinal Health Texium™ and SmartSite® System



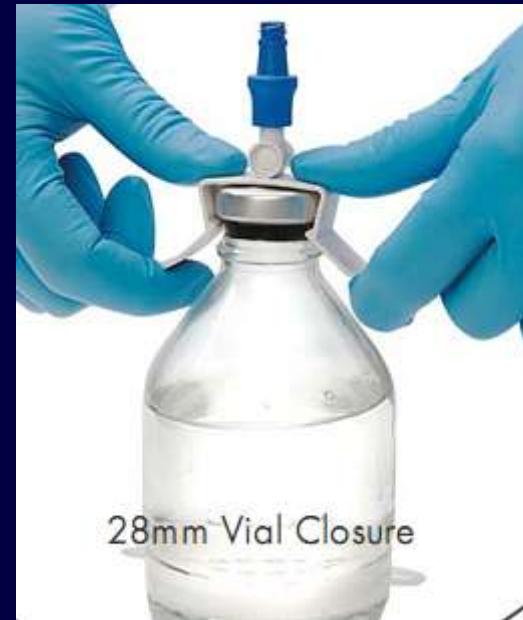


ICU Medicine Genie™





ICU Medicine Clave™ Spike Adaptor





ICU Medicine Spiros™





ICU Medicine CH-12 Adaptor





ICU Medicine Administration Set With Clave® and Spiros™





Monitoring Staff Exposure

- ◆ Environmental monitoring¹
 - Currently a recommendation by USP 797
 - Surface swipe testing
 - BSC
 - Countertops
 - Areas adjacent to BSC
 - Sampling should be at baseline and then every 6 months
 - Common marker agents
 - Cyclophosphamide, ifosfamide, methotrexate, fluorouracil
 - Goal is undetectable levels

1. United States Pharmacopeia (USP) Chapter 797. Pharmaceutical Compounding, Sterile Preparations. 2008.



Monitoring Staff Exposure (cont'd)

- ◆ Medical surveillance programs
 - Recommended by ASHP, ONS,¹ and OSHA²
 - Purpose is to detect changes in health status
 - Signs, symptoms, and physical examination
 - Lab tests:
 - Examples include: Complete blood count (CBC), comprehensive metabolic panel (CMP), liver enzymes, urinalysis
- ◆ Competency testing for aseptic technique

1. ONS Chemotherapy and Biotherapy Guidelines and Recommendations for Practice, Second Edition.

2. OSHA [1999]. OSHA technical manual, TED 1–0.15A, Sec VI, Chapter II: Categorization of drugs as hazardous.



US EPA Resource Conservation and Recovery Act (RCRA)

- ◆ Defines hazardous waste federally in the US
- ◆ Listed on 1 of 2 lists
 - U-list (toxic, ignitable, reactive, corrosive)
 - P-list (acutely hazardous)
- ◆ RCRA list includes:
 - Chlorambucil, cyclophosphamide, daunorubicin, uracil mustard, arsenic trioxide, DES, streptozocin, melphalan, and mitomycin
- ◆ RCRA list has not been updated since 1976
 - >100 new chemotherapeutic entities approved since then



Chemotherapy Waste

- ◆ Disposal protocols for chemotherapy waste
 - Empty vials, syringes, IVs, tubing, gowns, gloves
 - Treated as infectious medical waste
- ◆ Empty for U-listed waste means all contents that can be removed through normal means
- ◆ If container is not empty, it should be placed into a Hazardous Waste Container
- ◆ Different disposal facilities used for Regulated Medical Waste and RCRA designated waste



Common Pharmaceutical Waste

Type of Waste	Box	Contents	Treatment Methods
Sewer		IV solutions, tablets, controlled substances	Wastewater treatment
Trash	White	Packaging, gels, paper	Local landfill
Regulated medical waste Sharps	Red	Biohazardous waste, drugs, vials, non-chemo needles	Autoclave, microwave shredded, landfill
Hazardous waste	Yellow	Bulk & trace chemo items, including needles, tubing, gowns, gloves, etc.	Incineration, microwave, autoclaved, shredded,
RCRA Waste	Black	U-listed and P-listed agents, bulk chemo?	High Temp. incineration with scrubbers, ash capture, special lined landfill



Employer's Responsibility

- ◆ Review guidelines on a regular basis
- ◆ Develop policies and procedures based on the latest guidelines
- ◆ Properly train all staff working with hazardous drugs
- ◆ Monitor staff compliance with established guidelines
- ◆ Provide employees with the necessary controls to minimize exposure to hazardous agents



Summary

- ◆ Exposure to cytotoxic drugs has been recognized as a potential health hazard to workers since the 1970s
- ◆ No long-term adverse effects of occupational exposure have been conclusively demonstrated – but the risk has been deemed serious enough to warrant guidelines
- ◆ OSHA (Occupational Safety and Health Administration), NIOSH (National Institute for Occupational Safety and Health) and USP Chapter 797 have published guidelines for the protection of healthcare workers who work with hazardous agents
- ◆ Compliance with guidelines is a documented issue



Summary

- ◆ Following the current guidelines can reduce employees' exposure to hazardous drugs
- ◆ Passive fail-safe systems should be used
- ◆ Incorporating a closed-system with passive fail-safe characteristics benefits both the caregiver and patient in preventing exposure to hazardous agents
- ◆ Education of clinical and administrative staff is important to develop effective policies and procedures

