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Expiration Date: December 21, 2012.

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Objectives

- Define hazardous drugs and negative health effects associated with exposure.
- Identify work practices that present a risk of exposure to hazardous drugs.
- Outline workplace strategies and practices to reduce exposure and prevent contamination from hazardous drugs.
- Describe technological advances that may reduce the exposure of health care providers to hazardous drugs during compounding and administration.

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Program Faculty



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Faculty disclosure:

Seth Eisenberg and **Luci Power** both report having no relevant affiliations or financial relationships to disclose. A portion of grant funds received by ProCE from ICU Medical will be used to compensate the faculty for this presentation.

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Hazardous Drugs Defined

- Carcinogenicity
- Teratogenicity / developmental toxicity
- 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

ASHP, 1990; NIOSH, 2004.

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Background

- Concern for occupational exposure to chemotherapy and other hazardous drugs dates to the early 1970s
- 1980: First English language guidelines
- Continued evidence of contamination and uptake by workers has required more stringent environments, equipment, and work practices

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Potential Routes of Exposure

- Dermal absorption:
 - Direct drug contact
 - Contact with contaminated surfaces
- Injection:
 - Sharps
 - Breakage
- Ingestion via contaminated:
 - Food, gum
 - Hand-to-mouth transfer
- Inhalation:
 - Aerosols
 - Vapors

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Adverse Health Outcomes of HD Exposure

- Acute symptoms:
 - Gastrointestinal
 - Skin
 - Allergic
 - Infectious
 - General systemic
- Chronic health changes

Harrison, 2001; Valanis et al, 1993a, 1993b.

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Reproductive Outcomes of HD Exposure

- Menstrual dysfunction
- Infertility, longer time to conception
- Spontaneous abortions, miscarriages
- Fetal abnormalities
- Premature labor, low-birthweight infants
- Learning disabilities in offspring

Fransman, 2007; Hemminki et al, 1985; Martin, 2005; Stucker, 1990;
Valanis et al, 1999; Valanis et al, 1997.

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Cancer Outcomes of HD Exposure

- Leukemia in nurses & physicians
- Lymphoma & skin cancer in pharmacists
- Overall increased cancer occurrence
- Cyclophosphamide calculated risk assessment is 1.4-10.0 cancers per year per million workers

Hansen & Olsen, 1994; Martin, 2005; Sessink et al, 1993, 1995; Skov et al, 1990, 1992. ¹³

Evidence of HD Exposure

- Contamination on external vial surfaces
 - 11 studies since 1992
- Surface contamination
 - 16 studies since 1994
- Fluorescent scans
- Urinary excretion of drugs and drug metabolites
 - >20 studies since 1992



For example: Valanis, 1998; Connor et al, 1999; Connor et al, 2005; Turci, 2003; Ensslin, 1994.

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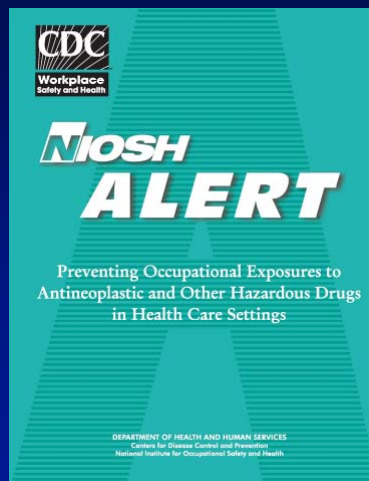


Current Guidelines

- OSHA:
 - *Controlling Occupational Exposure to Hazardous Drugs*
- ASHP:
 - *Technical Assistance Bulletin/Guidelines on Handling Cytotoxic & Hazardous Drugs*
- ONS:
 - *Chemotherapy & Biotherapy Guidelines and Recommendations for Practice*
- NIOSH:
 - *Preventing Occupational Exposures to Antineoplastic & Other Hazardous Drugs in Healthcare Settings*

OSHA, 1986, 1995, 1999; ASHP, 1985, 1990, 2006; ONS, 1988, 1996, 1999, 2001, 2005, 2009; NIOSH, 2004. 15

NIOSH Alert 2004



Tear-out sheets and list of hazardous drugs available in Spanish (website and print versions)

<http://www.cdc.gov/niosh/docs/2004-165/>

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NIOSH Alert on Hazardous Drugs

- Updating list of hazardous drugs in 2008
 - Being reviewed as highly influential information by Office of Management and Budget guidelines
 - Reviewed all new FDA-approved drugs and drug warnings since 2004 (MedWatch)
 - 62 out of ~150 recommended for further review
 - 24 on proposed update to list

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NIOSH

- Additional studies document continuing contamination:

NIOSH Safety and Health Topic:
Occupational Exposure to
Antineoplastic Agents

<http://www.cdc.gov/niosh/topics/antineoplastic/>

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Regulatory Standard – HCS

HCS – Hazard Communication Standard

- The “Right to Know”
- Requires Material Safety Data Sheets (MSDS)
- Requires training programs and worker protection
- Defines hazardous chemicals

www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS&p_id=10099

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Hazard Communication Standard. 29 C.F.R. part 1910–1200.

HCS Definition of Hazardous Chemical

Any chemical which is a physical hazard or a health hazard for which there is statistically significant evidence based on at least one study conducted in accordance with established scientific principles that acute or chronic health effects may occur in exposed employees.

It includes carcinogens, toxic or highly toxic agents, reproductive toxins, irritants, corrosives, sensitizers, and agents that produce target organ effects.

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Hazard Communication Standard. 29 C.F.R. part 1910–1200.



Regulatory Standard – USP <797>

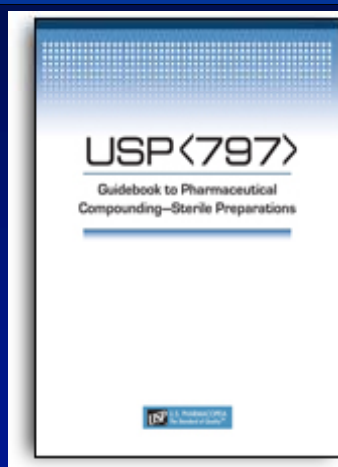
- USP <797> Pharmaceutical Compounding of Sterile Preparations
- Regulates all sterile compounding in all settings
- Regulates sterile hazardous drugs as *Compounded sterile preparations (CSPs) 2008*
- Addresses compounding: *Environment, equipment, training & evaluation*
- Applies to all persons who prepare CSPs
- **Enforceable standards:**
Intended to improve patient safety

United States Pharmacopeia, 2004, 2008.

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USP <797> 2008

- Revised General Chapter <797> became official on June 1, 2008
- Enforceability and Recognition of General Chapter <797>



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HD Preparation: Environment

- Protect sterile products from microbial contamination
- Control the number of particles per meter³
- Reduce the potential for particulate-borne colony forming units (CFUs)
 - HEPA filters
 - Air changes per hour

ISO 14644-1.

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HD Preparation: Environment

- **Direct compounding area:**
Primary engineering control - PEC for containment
- **Buffer area:**
Except with negative pressure CACI
- **Negative pressure:**
Except with CSTDs and low compounding volume
- **Ante room:**
Physical separation of mixing environment

United States Pharmacopeia, 2004, 2008.

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HD Preparation: Equipment

- Biological Safety Cabinet (BSC) or Compounding Aseptic Containment Isolator (CACI)
 - Externally vented (preferred)
 - Cleaned and decontaminated routinely
 - Inspected and maintained every 6 months
- Protect the operator from aerosols
- Protect the product from contamination

NIOSH, 2004; USP, 2008.

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Primary Engineering Controls



Class II BSC



CACI

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HD Preparation: Supplemental Equipment

- +/- Closed-system transfer device (CSTD)
 - A device that mechanically prevents the transfer of environmental contaminants into the system and the escape of hazardous drug or vapor outside the system*

*NIOSH, 2004; USP, 2008.

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Personal Protective Equipment (PPE)

- Personal Protective Equipment (PPE) provides physical barriers to the contamination
- Bugs – CFUs that may contaminate the compounded sterile preparation (CSP)
- Drugs – HD residue that may contaminate the workplace, environment, and worker

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PPE – Bugs Vs Drugs



Courtesy of Eric Kastango

- A person in a cleanroom is considered a broad-spectrum particle generator enclosed by inefficient mechanical filters, which may also be sources of particulates
- The human body harbors an average of 150 - 200 different classes of bacteria
- Hands have an average of 100,000 organisms/mm²
- The body sheds 5 grams of skin fragments each day along with shedding 1 layer of skin every 5 days (size range 10 to 300 microns)

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HD Preparation: Personal Protective Equipment (PPE)

- To protect the worker:
 - Chemotherapy gown
 - Double chemo-tested gloves
 - Respirator
 - Face shield
- To protect the sterile product:
 - Face mask
 - Hair & shoe covers



} As needed

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ASHP, 1990; NIOSH, 2004; ONS, 2009; OSHA, 1999; USP, 2008.



PPE

- Chemotherapy-resistant gown
- High-quality double gloves
- Sterile gloves for compounding
- Eye protection
(if risk of splashing)



Polovich M, et al, eds. *Chemotherapy and Biotherapy Guidelines and Recommendations for Practice*. 2009; USP <797> 2008 edition.

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Gowns for HD handling

- Low-permeability fabric such as polyethylene or vinyl
- Solid front with long sleeves and tight cuffs
- Single-use: not reapplied after removal

Polovich M, et al, eds. *Chemotherapy and Biotherapy Guidelines and Recommendations for Practice*. 2009.

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Gloves

- Effectiveness influenced by material, thickness, and wear-time
 - Nitrile (latex-free rubber)
 - Latex
 - Polyurethane
 - Neoprene
- Long cuffs and powder-free
- 30-minute wear time

Polovich M, et al, eds. *Chemotherapy and Biotherapy Guidelines and Recommendations for Practice*. 2009; Connor, 1999; Klein, 2003; Wallemacq, 2006.

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Gloves

- Gloves marketed for chemotherapy have been tested
- General purpose exam gloves may or may not maintain integrity after contact with chemotherapy
- Always assess glove integrity before administering chemotherapy
- Double gloving recommended
- Wash hands thoroughly after removal



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Eye Protection

- Goggles or face shields should be readily available
- Used in situations where splashing could occur (e.g., bladder instillation)

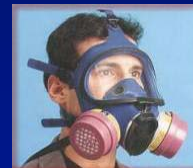


Polovich M, et al, eds. *Chemotherapy and Biotherapy Guidelines and Recommendations for Practice*. 2009; Connor, 1999; Klein, 2003; Wallemacq, 2006.

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Masks

- **Paper masks are ineffective**
- Use if risk of aerosol exposure
- N95 or N100 and canister-type respirators are recommended but require fit-testing for each wearer



Polovich M, et al, eds. *Chemotherapy and Biotherapy Guidelines and Recommendations for Practice*. 2009; Connor, 1999; Klein, 2003; Wallemacq, 2006.

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HD Preparation: Training & Evaluation

- Pre-handling and annually:
 - Risks of HDs
 - Safe handling precautions
 - Safe aseptic manipulation practices
 - Correct use of CSTDs
 - Containment, cleanup, disposal
 - Treatment of personnel exposure

OSHA, 1994; NIOSH; 2004; USP, 2008.

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Where Does It Start, and Where Does It Go?

- Seth Eisenberg RN OCN®

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Where Does It Start, and Where Does It Go?

- Nursing exposure to chemotherapy can begin in the pharmacy
- Contamination can then spread by to nurses and the surrounding environment



Hedmer M, et al. *Ann Occup Hyg.* 2005;49:629-637.

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Contamination

Direct contamination from
improper or damaged PPE



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Administration

While priming IV tubing or purging air from a syringe



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Administration

Leaking connections or failure to connect tubing to patient



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Administration

Spiking through the bag



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Inadequate Cleaning After a Spill

Chemotherapy is not
inactivated by alcohol
or germicidal cloths



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During Disposal of Excreta

- Unchanged drug and metabolites can be excreted in:
 - Urine
 - Feces
 - Emesis

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Excretion Trivia

- Excreted **unchanged** in urine within first 24 hours:

Etoposide	55%
Cyclophosphamide	25%
Fludarabine	40%
Dacarbazine	40%



Source: Micromedex.

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Dermal Pathways

- Most contamination is thought to occur from skin contact during
 - Preparation
 - Administration
 - Handling of urine or soiled linens
- Inhalation can occur under specific circumstances

Kromhout, et al. 2000; Fransman, et al. 2005.

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Protection

- To avoid exposure, PPE should be worn when:
 - Preparing, handling, or administering chemotherapy
 - Disposing or cleaning spills
 - Handling excreta

Polovich M, et al, eds. *Chemotherapy and Biotherapy Guidelines and Recommendations for Practice*. 2009.

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Poor Compliance with PPE

- Perceived immunity to risk
 - “I’m not worried”
 - “My practice is safe”
- Knowledge deficit
 - Ben Ami surveyed 61 oncology nurses in 2 hospitals
 - 67% did not believe chemotherapy could be absorbed through skin

Ben Ami, et al. 2001.

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Knowledge Deficit

94% of the RNs consumed food or beverage in the drug preparation area



Nutrition Facts

Serving Size 1 potato (148g/5.3oz)

Amount Per Serving
Calories 100 Calories from Fat 0

% Daily Value*

Total Fat	0g	0%
Saturated Fat	0g	0%
Cholesterol	0mg	0%
Sodium	0mg	0%
Cytosax	720mg	21%
Total Carbohydrate	26g	9%
Dietary Fiber	3g	12%
Sugars	3g	
Protein	4g	

Vitamin A 0% • Vitamin C 45%

Calcium 2% • Iron 6%

Thiamin 8% • Riboflavin 2%

Niacin 8% • Vitamin B₆ 10%

Folate 6% • Phosphorous 6%

Zinc 2% • Magnesium 6%

*Percent Daily Values are based on a 2,000 calorie diet.

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Poor Compliance

- Low potential for immediate injury
 - Most effects from exposure are long-term
- Poorly designed or cumbersome PPE
 - Gloves or gowns don't fit
 - Gowns too hot and heavy
- Inconveniently located PPE
- Cost of PPE

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Martin & Larson Survey

- 500 outpatient and office nurses
- 263 responses

	Preparation	Administration	Disposal
Gloves	99%	94%	94%
Gowns	53%	31%	26%

Martin and Larson, 2003

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2008 Chemo SIG Survey

- 4,000 chemotherapy SIG Nurses
- 668 responses

<i>2008 SIG Survey</i>	Administration	Disposal
Gloves	94%	93%
Gowns	51%	45%

<i>2003 Martin & Larson</i>	Administration	Disposal
Gloves	94%	94%
Gowns	31%	26%

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Additional Safeguards

An automotive analogy

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Evolution of US Automotive Safety

- 1967: Seatbelts become mandatory in all cars sold in US
- 1968: 3-point shoulder belts are advocated
- 1974: First airbags are sold in cars
- 1994: Airbags become mandatory
- 2003: Side-impact airbags available

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Evolution of Chemotherapy Safety

- 1983: Vertical flow biologic safety cabinets
- 1985: Personal protection equipment
- 2004: Double gloving
- 2007: Closed-system transfer devices

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Closed-System Transfer Devices

- Provide additional protection during drug preparation and administration
- Containment of aerosolized and droplet particles
- Recommended in 2006 ASHP Guidelines, USP <797> 2008 update, and ONS 2009 Guidelines
- Four brands on the market

Polovich M, et al, eds. *Chemotherapy and Biotherapy Guidelines and Recommendations for Practice*. 2009; Connor, 1999; Klein, 2003; Wallemacq, 2006.

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Closed Systems

Two basic components:

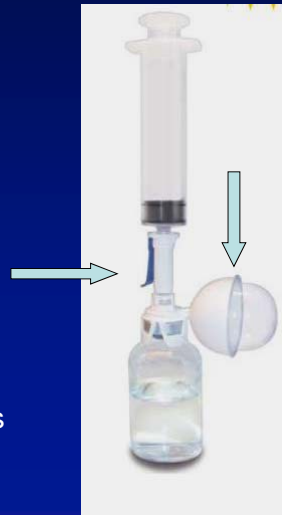
1. A vial adaptor used during drug preparation to prevent leakage and vapor release
2. A closed valve used on tubing and syringes to prevent leakage before, during and after administration

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PhaSeal® (Carmel Pharma)

- First system on the market (1999)
- Used by a number of institutions
- External chamber to trap vapors
- Several published studies demonstrating efficacy
- Uses multiple components
- “Injector” uses internal needle
- Requires adaptor for use with Luer devices



Genie and Spiros® (ICU Medical)

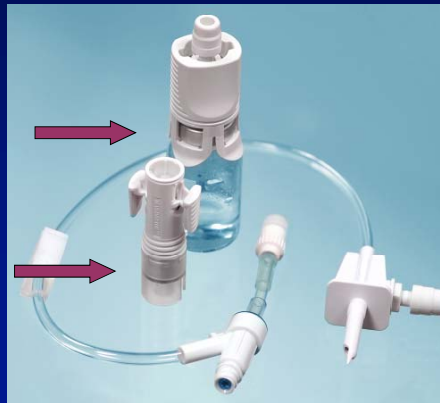
- Genie has internal balloon traps vapors
- Spiros® closed male Luer using Clave® components
- Permanently locks on syringe or tubing
- Creates vacuum at disconnect
- No additional adaptors required
- Compatible with all standard Luer connections



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OnGuard™ (B|Braun)

- Uses Teva components
- Uses special dual-layer microfilter to trap particles and vapors
- Valve has internal needle
- Requires adaptor for use with Luer devices



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Texium® System (Cardinal Health)

- Uses a 0.2-micron vented filter on vial adaptor
- Closed male Luer using SmartSite® components
- Designed to be compatible with Alaris® tubing



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Closed Systems: Other Considerations

- Difficulty comparing products
- Lack of published, unbiased comparisons
- Additional cost

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Additional Interventions

- Transport chemotherapy in sealed bags
- Inspect IV bags and syringes for leaks
- Always wash hands after removing PPE
- Place soiled linen in leak-proof bag

Polovich M, et al, eds. *Chemotherapy and Biotherapy Guidelines and Recommendations for Practice*. 2009; Connor, 1999; Klein, 2003; Wallemacq, 2006.

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Bodily Fluids

- Double gloves, gown when handling excreta, emesis or blood within 48 hours of chemotherapy administration
- Flush toilet with lid closed (if possible)
 - Consider covering with pad (e.g., Chux™) if no lid
- There is no evidence to support double-flushing in hospitals
 - May be of some use in settings with low volume/flush toilets
- Caregivers at home should wear gloves when emptying emesis basin

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Chemotherapy Disposal

- Waste should be placed in sealable bags or hard-sided containers



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Spill Management

- Kit contents:
 - Two pair of gloves
 - Gown and booties
 - Absorbent pads
 - Face shield
 - Respirator
 - Two or more sealable chemotherapy bags
 - Scoop and hard container for glass

Polovich M, et al, eds. *Chemotherapy and Biotherapy Guidelines and Recommendations for Practice*. 2009; Connor, 1999; Klein, 2003; Wallemacq, 2006.

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Neutralizing

- Bleach (5.25%) shown to be effective in laboratory tests for most drugs
- Difficult to use in clinical settings due to toxic vapors and corrosive properties
- Needs to be “neutralized”
- ONS guidelines recommend detergent



Dorr R, Alberts D. 1992; Benvenuto, et al. 1993; Castegnaro M, et al. 1997; Hansel S, et al. 1997.

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Neutralizing

- Surface Safe®
- Two-chemical packet
 - Sodium hypochlorite (bleach)
 - Sodium thiosulfate (neutralizer)
 - Not completely effective with mitoxantrone or carmustine



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General Spill Procedure

- Assess the size of the spill
- Put on PPE (use double-gloves)
- Use NIOSH-approved respirator
- Use pads to soak up spill
- Put cleanup supplies into chemotherapy disposal bag and double-bag when done
- Use detergent (or Surface Safe®)
- Document per policy

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Body Contamination

- Wash skin exposure immediately with soap and water
- Change clothing and put into chemotherapy bag
- Launder separately in detergent
- Complete appropriate documentation



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