A Symposium conducted at the 44th ASHP Midyear Clinical Meeting & Exhibition

Safe Handling of Hazardous Drugs: Risks and Practical Considerations

Faculty

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Research Biologist
Division of Applied Research and Technology
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ProCE

ICU Medical, Inc.

This program is supported by an educational grant from ICU Medical, Inc.

Pharmacy Breakfast CE Program

Safe Handling of Hazardous Drugs: Risks and Practical Considerations

Monday - December 7, 2009

Program Description

Hazardous drugs include potent and toxic agents that may cause immediate and long-term negative health effects in exposed workers. While recommendations for safe work practices have been in effect for decades, new studies show continuing contamination in the workplace and uptake of drugs into workers. This presentation will include the results of new studies on contamination and the use of new biomarkers as evidence of the consequences of exposure to hazardous drugs. An analysis of workplace practices that contribute to contamination and those that are useful in reducing exposure also will be presented.

Location / Agenda

The Venetian Resort Hotel Casino
Casanova Ballroom, Room 505 - 507 (Lower Level)
3355 Las Vegas Blvd. South
Las Vegas, NV

Agenda:
December 7, 2009

6:30 AM - 7:00 AM	Registration & Breakfast
7:00 AM - 8:30 AM	Educational Activity

Learning Objectives

The target audience for this program is pharmacists in health-system settings. At the completion of this program, the participant will be able to:

- 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 healthcare providers to hazardous drugs during handling

Faculty / Funding

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Accreditation

ProCE, Inc. is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. ACPE Universal Activity Number 221-000-09-089-L05-P has been assigned to this live knowledge-based program (initial release date 12-07-09). This program is approved for 1.5 contact hours (0.15 CEUs) in states that recognize ACPE providers. The program is provided at no cost to participants. Statements of credit will be issued online at www.ProCE.com upon successful completion of the program evaluation. Participants must complete a program evaluation to receive pharmacy CE credit. No partial credit will be given.

Faculty Disclosure

It is the policy of ProCE to require the disclosure of the existence of any significant financial interest or any other relationship a faculty member or a sponsor has with the manufacturer of any commercial product(s) discussed in an educational presentation. Mr. Connor and Ms. Power both report having no relevant affiliations or financial relationships to disclose.

Please note: The opinions expressed in this program should not be construed as those of the CE provider or ICU Medical, Inc. The information and views are those of the faculty through clinical practice and knowledge of the professional literature. Portions of this program may include the use of drugs for unlabeled indications. Use of drugs outside of labeling should be considered experimental and participants are advised to consult prescribing information and professional literature.

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Safe Handling of Hazardous Drugs: Risks and Practical Considerations

PROGRAM FACULTY

Thomas H. Connor, PhD

Dr. Connor received his bachelor's and master's degrees from the University of Rhode Island. He earned his doctoral degree in environmental toxicology from the University of Texas Medical Branch. He then joined the faculty of the University of Texas, School of Public Health in Houston, where he taught courses in genetic toxicology, toxicology, and environmental health for 20 years. After completing a fellowship at the National Institute for Occupational Safety and Health, he took a position as a research biologist in the NIOSH Division of Applied Research and Technology. There, he serves as the project officer for a study examining the potential effects of hazardous drugs on healthcare workers. He is also conducting an evaluation of personal protective clothing used in the healthcare industry.

Dr. Connor was a primary contributor to the NIOSH Alert on Hazardous Drugs and is responsible for updating the Alert's list of hazardous drugs. He is involved in writing several NIOSH publications related to the Alert. He was co-chair of a committee that developed the International Society of Oncology Pharmacy Practitioners standard for the safe handling of cytotoxic drugs. He is a member of the ASHP, ISOPP, the Environmental Mutagen Society, and the American Society of Testing and Materials. Dr. Connor was awarded the 2008 ASHP Board of Directors' Award honoring non-pharmacists for their contribution to the practice of pharmacy. Dr. Connor's research area has focused on occupational exposure to hazardous drugs in healthcare settings, and he has lectured extensively on the topic nationally and internationally.

Luci A. Power, BS, MS, RPh

Luci A. Power is an independent lecturer and consultant on pharmacy IV and hazardous drug systems. She was with the Department of Pharmaceutical Services at the University of California Medical Center in San Francisco for more than 25 years, serving in various capacities including Senior Pharmacist and Manager of the Parenteral Support Services. She was also Manager of the IV Additive Services, where she was responsible for the in-patient chemotherapy and other hazardous drug compounding. Luci received her bachelor's and master's degrees in pharmacy from Northeastern University College of Pharmacy in Boston, Massachusetts.

Luci is primary author of both the 1985 and 1990 American Society of Health-System Pharmacists (ASHP) Technical Assistance Bulletins on Handling Cytotoxic and Hazardous Drugs; lead author of the 2006 ASHP Guidelines on Handling Hazardous Drugs; and first author of the ASHP Safe Handling of Hazardous Drugs Video Training Program. Luci is an original member of the National Institute for Occupational Safety and Health (NIOSH) working group on hazardous drugs and an author of the 2004 NIOSH Alert: Preventing Occupational Exposures to Antineoplastics and Other Hazardous Drugs in Health Care Settings. Luci has done numerous presentations and publications on the safe handling of hazardous drugs in oncology practice.

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Learning Objectives

- Define hazardous drugs and negative health effects associated with exposure
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- 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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Thomas H. Connor, PhD

Research Biologist
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Disclaimers

The findings and conclusions in this program have not been formally disseminated by the National Institute for Occupational Safety and Health and should not be construed to represent any agency determination or policy.

Mention of company names or products does not constitute endorsement by NIOSH.

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Outline

- Describe how NIOSH defines “hazardous drugs”
- Identify adverse health effects of hazardous drugs
- Review issues regarding workplace contamination and healthcare worker exposure

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U.S. Guidelines for Safe Handling of Hazardous Drugs

ASHP-1983	Cytotoxic Drugs
ONS-1984	Chemotherapy [several]
ASHP-1985	Cytotoxic Drugs
OSHA-1986	Cytotoxic (Antineoplastic) Drugs
ASHP-1990	Cytotoxic and Hazardous Drugs
NIH-1992	Cytotoxic Drugs
OSHA-1995	Hazardous Drugs
NIH-2002	Cytotoxic Drugs
NIOSH-2004	Antineoplastic and Other Hazardous Drugs
ASHP-2006	Hazardous Drugs
USP <797>	CSP (Hazardous Drugs)

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How Are Hazardous Drugs Identified?

- Some are easier than others; for example:

WARNING

ALKERAN (melphalan) should be administered under the supervision of a qualified physician experienced in the use of cancer chemotherapeutic agents. Severe bone marrow suppression with resulting infection or bleeding may occur. Melphalan is leukemogenic in humans.

Melphalan produces chromosomal aberrations in vitro and in vivo and, therefore, should be considered potentially mutagenic in humans.

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Hazardous Drug Definition

- 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

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NIOSH 2004.

Weight-of-Evidence

"Weight-of-evidence is the process by which multiple measurement endpoints are related to an assessment endpoint to evaluate whether significant risk of harm is posed to the environment" (in this case, the worker).

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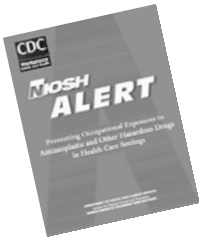
Massachusetts Weight-of-Evidence Workgroup, 1995.

NIOSH Hazardous Drug List

- Antineoplastic Agents-89
- Hormonal Agents-21
- Biological Agents-8
- Antiviral Agents-7
- Immunosuppressant Agents-5
- Antibiotics-1
- Vaccines-1



NIOSH 2004.

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Carcinogenicity of Hazardous Drugs

- Considerable laboratory data from animal studies
- Considerable amount of information from patient populations (continues to expand)
- Little to no information in healthcare workers (has not been studied)

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Carcinogenicity of Antineoplastic Drugs: Patients + Animal Studies

IARC Group	No. Agents	Definition
1	12 + 2 combinations	Known human carcinogen
2A	11	Probable human carcinogen
2B	11	Possible human carcinogen

International Agency for Research on Cancer, 2009.

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Pregnancy Category D or X Drugs in NIOSH Alert

FDA Category	No. Agents	Definition
D	46	Clear evidence of risk to human fetus, but benefits may outweigh risk for pregnant women.
X	5	Clear evidence that medication causes abnormalities in fetus. Risks outweigh any potential benefits for women who are pregnant.

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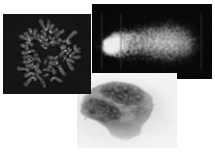
Genotoxicity of Antineoplastic Drugs

- Antineoplastic drugs are genotoxic in:
  - Laboratory studies (*in vitro* and *in vivo*)
  - Treated patients
  - Healthcare workers



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Biomonitoring Studies in Healthcare Workers (1990-2009)

Assay for Genotoxicity	No. Pos.	Total
Urine Mutagenicity	2	3
Chromosomal Aberrations	16	21
Micronucleus	13	19
Sister Chromatid Exchange	8	18
Comet/DNA Damage	8/2	9/4
Miscellaneous	2	3

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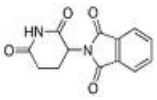
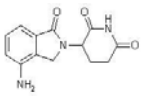
Mimics Structure of Existing Drug

Thalidomide



Lenalidomide



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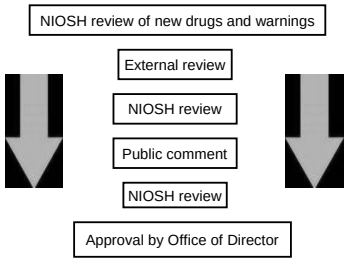
Process to Update NIOSH Hazardous Drug List



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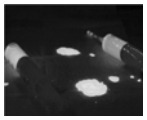
Contamination Issues

- Over 50 published studies on surface contamination
- 100% of published studies measured at least one drug on work surfaces



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Healthcare Worker Exposure

- 22 of 25 published studies measured drug in the urine
- In four studies, the workers were *not* handling the drug that was in their urine
- Since 1990, two-thirds of published studies have shown a significant association between drug handling and a marker of genotoxicity

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Commonly Sampled Antineoplastic Drugs

- Drugs used as "markers" of environmental contamination or exposure
  - Cyclophosphamide
  - Ifosfamide
  - Fluorouracil
  - Methotrexate
  - Doxorubicin
  - Paclitaxel
  - Platinum-containing compounds

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Sources of Surface Contamination

- Drug vial exteriors have been shown to be contaminated with the vial contents

Connor et al. 2005.

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Sources of Surface Contamination

- Surface contamination is found in:
  - Pharmacy areas
  - Nursing and patient areas

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Sources of Surface Contamination

- Working area of BSC

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Sources of Surface Contamination

- Airfoil of BSC

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Sources of Surface Contamination

- IV bags

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Sources of Surface Contamination

- Storage bins

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Sources of Surface Contamination

- Counter tops

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Sources of Surface Contamination

- Waste containers

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Sources of Surface Contamination

- Floors

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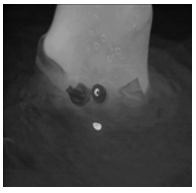
Sources of Surface Contamination



- IV bags have been shown to be contaminated with contents and other drugs

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Surface Contamination in Two U.S. Studies

1999 Study	2009 Study
• 6 Hospitals	• 3 Hospitals
• 3 Drugs	• 5 drugs
• Pharmacy-75% wipe samples positive	• Pharmacy-75% wipe samples positive
• Nursing-65% wipe samples positive	• Nursing-45% wipe samples positive

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Connor et al. 1999; Connor et al. 2009.

Summary/Conclusions

- Healthcare: Occupation with most known or suspected number of human carcinogens
- Healthcare: Occupation with most known or suspected reproductive and teratogenic agents
- Healthcare: Occupation with most known or suspected genotoxic agents

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Summary/Conclusions

- In addition to engineering controls and PPE use, continued vigilance is needed to reduce or eliminate worker exposure
  - Training/retraining
  - Administrative controls
  - Updated work practices
- As long as drug vials are contaminated, environmental contamination will continue to be an issue

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Summary/Conclusions

- Hazardous drugs are not always easy to define
  - Monoclonal antibodies
  - Oral forms of hazardous drugs
  - New drug formulations
    - Nano-drugs
    - Highly potent drugs

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Summary/Conclusions

- NIOSH plans to update hazardous drug list on a regular basis
- External input
  - Federal Register Notices
  - Expert Panel
  - Stakeholders

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Contact Info/Websites

- Thomas H. Connor, PhD
  Tconnor@cdc.gov
- Hazardous Drug Topic Page
  (links to other pages)
  www.cdc.gov/niosh/topics/hazdrug/
- Antineoplastic Drug Topic Page
  (bibliography)
  www.cdc.gov/niosh/topics/antineoplastic/

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Workplace Strategies & Practices

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Crime Scene Investigation

- Evidence-based work practices
- Common-sense work practices
- Best-guess work practices

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Contamination: Where Does It Start? Where Does It Go?

Evidence

- Vial contamination has been shown in over a dozen studies since 1992

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Transfer of Vial Contamination

Evidence

- Drug contamination on vials
- Drug contamination shown in storage areas

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Prevent Transfer of Vial Contamination

Common sense

- Gloves
- Surface protection

Best guess

- Double gloves

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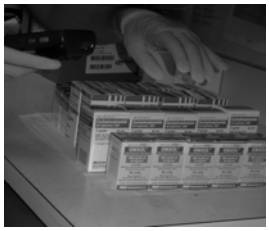
Receiving



Place disposable liner on surfaces.

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Storage: Improve Practice

- Storage of HD shall be separate
- Negative pressure area preferred
- Minimum of 12 ACPH
- **Per USP <797> 2008**

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Where Does It Start? Where Does It Go?

Evidence

- Vial contamination transfers to compounding surface
- HD residue found on gloves & final product

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Photograph courtesy of Seth Eisenberg. Used with permission.

Wiping Down HD Vials

Common sense

- Spray the wiper, not the vial
- Spraying the vial may move HD residue to other items or areas

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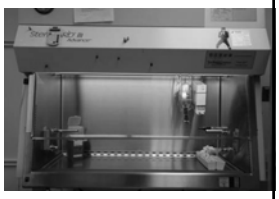
Where Does It Start? Where Does It Go?

Evidence

- Contamination found in BSC

Common sense

- Compounding generates contamination



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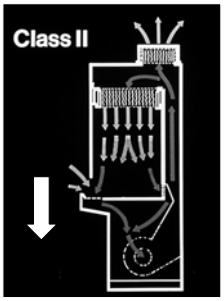
Transfer of Contamination

Evidence

- Studies show contamination on the floor in front of Class II BSC



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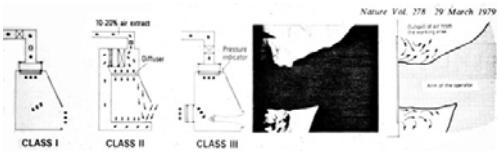
Transfer Through Front Opening?

Evidence



Poor technique!

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Reach Outside BSC to Trash

Common sense

- Reaching out of BSC drops drug residue

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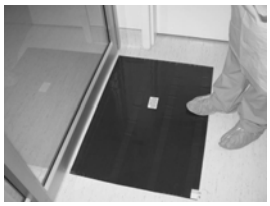
Transfer of Contamination

Common sense

- Contaminated shoes or covers can track drug residue outside compounding area



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Prevent Transfer of Contamination

Evidence

- Studies track HD residue from compounding areas to delivery and other remote areas

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Let's Look at PPE!

- Chemotherapy-resistant gown
- High-quality double gloves
- Sterile gloves for compounding

Evidence or common sense?

Best guess: PPE works ONLY when wearing it!

Is PPE a source of contamination?

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Transfer of Contamination

Evidence

- Gowns have been shown to be contaminated

Common sense

- Saving and reusing gowns may result in drug transfer

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Contaminated Gloves

- Inpatient
  - Preparation: 14/14 pairs
  - Cleaning of hoods: 6/6 pairs
- Outpatient
  - Preparation: 5/7 pairs
  - Cleaning of hoods: 3/4 pairs

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Sessink, et al. *Int Arch Occup Environ Health.* 1992;64:105-112.

Glove Contamination Inpatient Preparation (14 Pairs)

	CP+	CP-	5FU+	5FU-	MTX+	MTX-
Used→	2	12	6	8	9	5
Contam→	0	1	6	8	2	1

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Sessink, et al. *Int Arch Occup Environ Health.* 1992;64:105-112.

Transferred Contamination?

In this same study:

- 8 of 25 pharmacy technicians and nurses were contaminated with CP or IF
- 6 of 8 were not involved in the preparation or administration of either drug

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Sessink, et al. *Int Arch Occup Environ Health.* 1992;64:105-112.

Where Does It Start? Where Does It Go?

- Downstream exposure to HD residue can begin in pharmacy, then spread

Evidence

- HD residue found on remote surfaces and in housekeeping staff as well as nurses and pharmacy techs

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Reduce Contamination

Evidence

- Studies show closed-system transfer devices (CSTDs) are effective
- Studies show work practices have conflicting results and limited effectiveness

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Reduce Contamination

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

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NIOSH 2004 definition.

Closed-System Transfer Devices

- Provide additional protection during drug preparation and administration
- Containment of aerosolized and droplet particles
- Recommended in:
  - 2004 NIOSH Guidelines
  - 2006 ASHP Guidelines
  - USP <797> 2008 update
  - ONS 2009 Guidelines
- Four brands on the market

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Closed Systems: Two Basic Components

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

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Poor HD Technique

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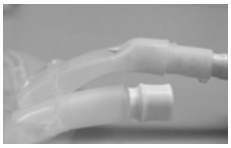
Contamination in Administration

Spiking through the bag



Priming IV tubing

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Photograph courtesy of Seth Eisenberg. Used with permission.

PhaSeal® (Carmel Pharma)

- External chamber to trap vapors
- Published studies demonstrating efficacy
- Uses multiple components
- "Injector" uses internal needle
- Requires adaptor for use with Luer devices

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Genie and Spiros® (ICU Medical)

- Internal balloon traps vapors
- Closed male Luer
- Uses Clave® components
- No additional adaptors required
- Compatible with all standard Luers

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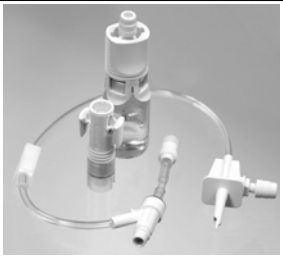
OnGuard™ (B|Braun)

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



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Texium® System (Cardinal Health)

- Closed male Luer using SmartSite® components
- Designed to be compatible with Alaris® tubing
- 0.2 micron vented filter

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Additional Interventions

Common sense

- Transport HD doses in sealed bags
- Inspect IV bags and syringes for leaks
- Always wash hands after removing PPE

Other technology?

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Have the Robot Compound!

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Conclusions

Crime Scene Investigation:

Follow the contamination!

MORE studies = better evidence

Common sense = useful technique

Best guess = better than nothing!

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Questions?

CE Program Evaluation & Statement of Credit Instructions

Safe Handling of Hazardous Drugs: Risks and Practical Considerations

December 7, 2009 - Las Vegas, NV

Below are step-by-step instructions for completing the online program evaluation and receiving your pharmacy CE Statement of Credit.

1. You must complete the program evaluation online **no later than Friday, January 8, 2010** to receive CE credit.
2. Visit http://www.proce.com
3. Click on **Safe Handling of Hazardous Drugs: Risks and Practical Considerations (December 7, 2009 - Las Vegas, NV)** listed below **LIVE MEETING EVALUATION & CE CREDIT**
4. Click on the **Log In** button directly below **If you attended the live event and would like to receive credit please log in.**
5. Click on the **Register Here** button next to **New User?**
   - **Note**: if you have previously created a Username and Password at the ProCE CE Center, enter your Username and Password and click the Log In button, and skip step 6 below and go directly to step 7.
6. Complete the **New User Registration** and finish by clicking on the **Finish Registration** button.
7. Click on the **Enter Live Event Code** button.
8. Enter **127SAFE** in the **Live Event Code** box and then click the **Submit Code** button.
9. Follow the instructions online to complete the program evaluation and to receive and print a pharmacy CE Statement of Credit.
10. If you need assistance with or have questions regarding the evaluation process, please contact ProCE at 630-540-2848 or via email at info@proce.com.

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