# Hazardous Drug Management

## Healthcare's Dirty Little Secret


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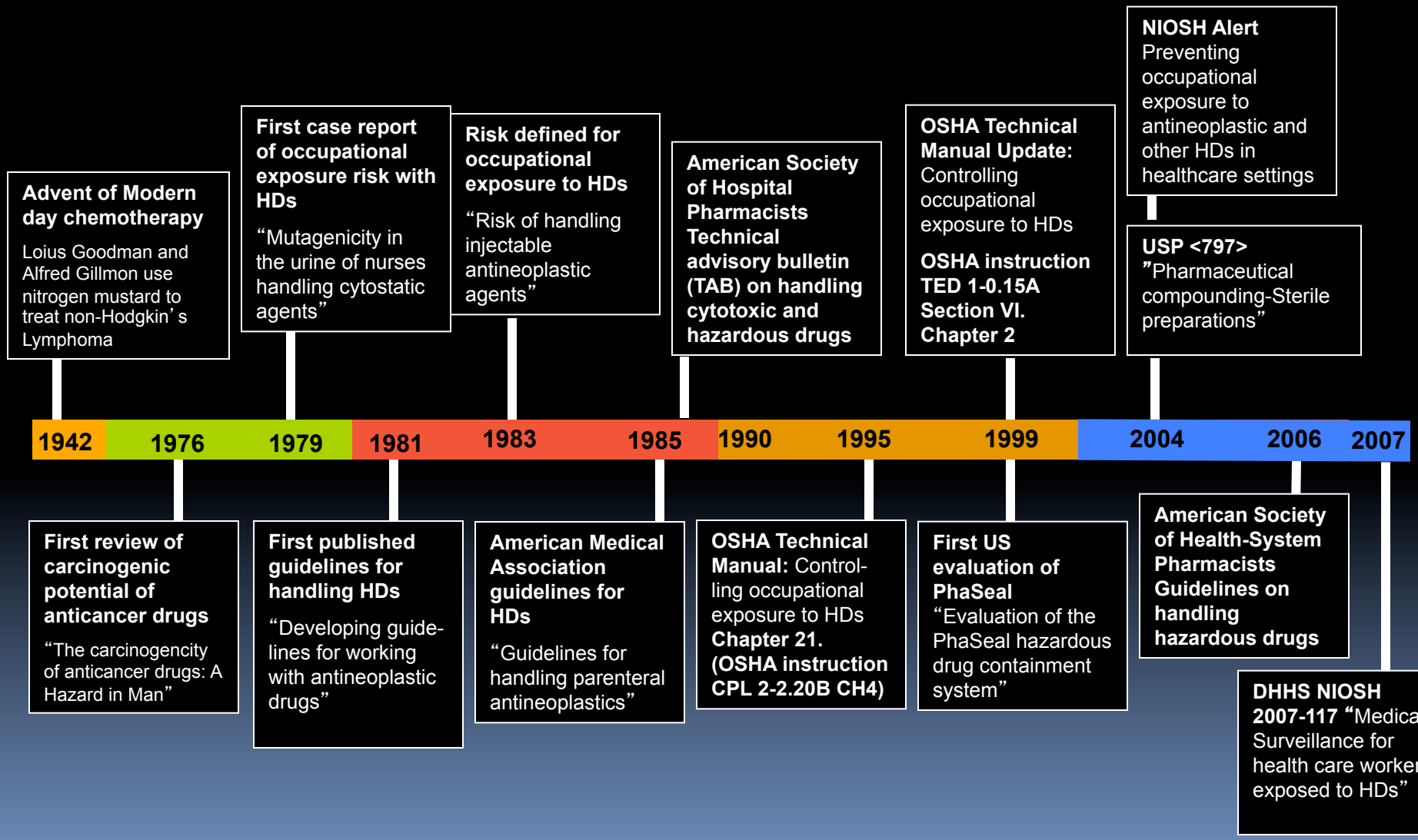
# Significance

- 5.5 million healthcare workers potentially exposed to hazardous drugs (HDs)
  - Pharmacy and nursing staff involved in mixing and administering at highest risk

- Exposure is associated with adverse health outcomes:
  - Acute symptoms
  - Organ toxicity
  - Reproductive risks
  - Cancer

# Timeline of Significant Studies and Guidelines for Hazardous Drugs



# Guidelines for Hazardous Drugs

| Source | Year |
| --- | --- |
| ASHP | 1982, 1984, 1990, 2006 |
| AMA Council on Scientific Affairs | 1985 |
| OSHA | 1986, 1995, 1999 |
| Oncology Nursing Society | 1988, 2003, 2009 |
| NIOSH Alert | 2004, 2006*, 2008*, 2010 |
| USP <797> | 2004, 2008 |
| HOPPA | 2009 |
| UHC's Guidelines | 2010 |

# Hazardous Drug Team

- Primary
  - Pharmacist
  - Pharmacy technicians/Interns
  - Pharmacy purchasing
  - Nursing
  - Risk Management
  - Employee health
  - Environmental services
- Secondary
  - Hospital administration
  - Safety Officer
  - Physician office managers

**Primary Goal Establish a hazardous drug safety program**

# Legal Requirements for Hazards

- The Occupational Safety and Health (OSH) Act
  - Employers subject to the OSH Act have a general duty to provide work and a workplace free from recognized, serious hazards
- OSHA has no standard for exposure to HD but has generated three guidelines
- Controlling occupational exposure to hazardous drugs.
  - In: *OSHA Technical Manual*,
  - TED 1–0.15A, Sec VI, Chap II: 1995, 1999
- Hazard Communication Standard (29 CFR part 1910 – 1200)
  - "Right to know"
- Hazardous Waste Operations and Emergency Response
  - (HAZWOPER) Standard (29 CFR 1910.120)
    - Liability falls on source of hazardous waste
      - Contracted services employees

# Hazardous Drug Effects

## Patient or Employee

### Acute Effects

- Nausea
- Vomiting
- Headache
- Dizziness
- Hair Loss
- Mucosal Sores
- Liver Damage
- Abdominal Pain
- Contact Dermatitis
- Skin Injury
- Eye Injury

### Long-Term Effects

- Reproductive
- Developmental
- Genetic
- End Organ Damage
- Cancer

# Hazardous Drug Exposure Points

- Broken shipping containers
- External contamination of drug **vials**
  - Production and packaging
- Drug **preparation**
  - Preparation techniques
  - Vapors, Spray and Spills
- Drug delivery
  - External contamination of final product
- Drug **administration**
  - Administration techniques
- Spills
- **Patients**
- Clothing & laundry
- Room Turnover process
- Waste
- Building maintenance/contractors

# Training on Handling of Hazardous Wastes

**Education Plan**

- Orientation to hazardous chemicals
  - Key contacts within the organization
  - Location of policies
- Encourage employees to notify their physician of their possible occupational exposure to hazardous drugs
- Educate employees of signs and symptoms
  - Based on the agents
    - Acute vs. chronic
  - Annual review of critical process and hazardous chemicals
  - Plan in place to educate on new chemicals

# Each Hospital Has Different Formulary Hazards

- Collaborative formulary assessment
  - NIOSH Appendix A & IARC

| Hazardous Drug Required Personal Protective Equipment (PPE) & Precautions According to Class and Dosage Form | | | | | |
|---|---|---|---|---|---|
| **Class 1** (Cont.) | Handle with required PPE and dispose of properly. **Do not tube or load in pyxis** Any alteration to occur in BSC. | | | | |
| **Commonly includes drugs that are antineoplastic, cytotoxic, immunosuppressive and antiviral** | **Pharmacy Precautions** | **Nursing Administration Precautions (Who can Administer)** | **Nursing Body fluid Precautions** | **Housekeeping/Ancillary Precautions** | **Trying to conceive, Pregnant or Breastfeeding** |
| **IM/Subcut/Intradermal** | **BSC, Sterile Double Chemo Gloves, Chemo Gown, Face Shield** | Double Chemo Gloves, Chemo Gown, Face Shield (Onc RN with required PPE) | Chemo Gloves & Chemo Gown. Add Face Shield if splashing possible. | Chemo Gloves & Chemo Gown. Add Face Shield if splashing possible. | Recommended to refrain from preparing, handling, administering, or being in contact with body fluids or excreta for 48 hours post last dose of medication. However, if so desired may prepare, handle, administer, be in contact with body fluids or excreta and/or clean room 48 hours post last dose on medication after receiving HD training, signing consent and with required PPE and precautions in place. |
| **IV Push, IVPB, IV Continuous Infusion** | **BSC, Sterile Double Chemo Gloves, Chemo Gown, Face Shield** | Double Chemo Gloves, Chemo Gown, Face Shield (Onc RN with required PPE) | Chemo Gloves & Chemo Gown. Add Face Shield if splashing possible. | Chemo Gloves & Chemo Gown. Add Face Shield if splashing possible. | |

- Material Safety Data Sheets (mandated by OSHA)
- Electronically tagging orders in documentation system(s)

# Technique Validation

- Technique
  - ChemoChek ®
    - Fluorescence testing
      - Requires black light
    - Traditional methodology
  - Nursing validation/certification program
    - Covidien and Kendall

- Technique & Aseptic skills
  - ChemoTEQ®
    - Red dye + growth media broth
    - Validates methodology with surface wipes
      - no black light required
    - $90 per assessment
    - Videos and training materials on line
    - www.valiteq.com

# Garbing Requirements
## -Per USP <797>

| Garb requirement | Immediate-use | Low Risk (12 hr) | Med Risk | High Risk |
|---|---|---|---|---|
| Makeup/Jewelry restrictions | N | Y | Y | Y |
| Hand washing | Y | Y | Y | Y |
| Hair/facial cover | N | Y | Y | Y |
| Shoe covers | N | Y | Y | Y |
| Low-shed gown | N | Y | Y | Y |
| Sterile Gloves | N | Y | Y | Y |
| Masks | N | Y | Y | Y |

# Personal Protective Equipment (PPE)

## Training Documentation

Hands & elbows scrubbed CDC
Hand hygiene document

www.cdc.gov/handhygiene

**Proper demonstrative use**

**Goal**

Minimize Contamination

*From product to employee

& visa versa

No Make-up or Jewels

No Fake fingernails

No iPods

No exemptions from garbing requirements

# Selection of the Right Glove

## Cytotoxic Permeation Performance

NITRITEX

| | |
|---|---|
| **Product Name:** | **BioClean Ultimate™** |
| **Product Code:** | BUPS |

**Cytotoxic Drugs Tested**

| [4] | ASTM 6978-05 [1] | ASTM F 739 [2] | EN 374 [3] |
|---|---|---|---|
| **Specified limit** | **0.01 µg/cm²/Min** | **0.1 µg/cm²/Min** | **1.00 µg/cm²/Min** |
| **Cisplatinum** | > 480 Min (Class 6) | > 480 Min (Class 6) | > 480 Min (Class 6) |
| **Carmustine** | 2 Min (Class 1) | 38 Min (Class 2) | > 480 Min (Class 6) |
| **Cyclophosphamide** | > 480 Min (Class 6) | > 480 Min (Class 6) | > 480 Min (Class 6) |
| **Doxorubicin Hydrochloride** | > 480 Min (Class 6) | > 480 Min (Class 6) | > 480 Min (Class 6) |
| **Fluorouracil** | > 480 Min (Class 6) | > 480 Min (Class 6) | > 480 Min (Class 6) |
| **Methotrexate** | > 480 Min (Class 6) | > 480 Min (Class 6) | > 480 Min (Class 6) |
| **Etoposide** | > 480 Min (Class 6) | > 480 Min (Class 6) | > 480 Min (Class 6) |
| **Paclitaxel** | > 480 Min (Class 6) | > 480 Min (Class 6) | > 480 Min (Class 6) |
| **Thio Tepa** | 47.7 Min (Class 2) | 55.6 Min (Class 2) | > 480 Min (Class 6) |

[1] **ASTM 6978-05** – Standard practice for assessment of resistance of medical gloves to permeation by chemotherapy drugs

[2] **ASTM F 739 – 99a** – Standard test method for resistance of protective clothing materials to permeation by liquids or gases under conditions of continuous contact. Methodology is similar to EN374-3:2003 but permeation is measured at more stringent level of 0.1 µg/cm²/Min

[3] **EN 374-3:2003** – Protective gloves against chemicals and micro organisms. Determination of resistance to permeation by chemicals

[4] Table shows the time in minutes, after exposure to the chemical, at which the permeation rate reaches the defined limit.

**"Gloves used for hazardous drugs must be tested to ASTM standard: D 6978-05 - Standard Practice for Assessment of Resistance of Medical Gloves to Permeation by Chemotherapy Drugs (2005)"**

Tom Connor, PhD (NIOSH)

DOUBLE GLOVING!!!!!!

Sterile gloves must be used when compounding

Sterile Gloves over chemo gloves

Clean gloves must be used when handling final product

# Gowns

- Gowns
  - NO cloth gowns
  - Polyethylene vs. Polypropylene
  - Chemical impermeable
  - Disposable
- Design
  - Low Lint
  - Tight Cuffs
  - Back closure
- Suits
  - Major spill clean up?
    - Not required but ….

# Mask, Respirators, Shields

- **Paper surgical mask**
- Do NOT prevent occupational exposure to drug vapors
  - Designed to protect product from worker
- Respirator/masks
  - Aerosols, liquids
  - Spill clean-up
- N95 rated (N, R, P)
  - Fitted! Annually or…….

- Face shields
  - Primary function
    - Physical barrier
    - Dermal absorption
  - NO engineering controls
  - Spill Clean up

Kimberly-Clark: Fluidshield

# Garb-on Sequence

Hands & elbows scrubbed
CDC Hand hygiene document
www.cdc.gov/handhygiene

Dirtiest to cleanest

No Make-up or Jewels

No iPods

**Goal**

Minimize Contamination

*From employee to product

Step 1 Shoe Covers 1,2

Step 2 Hair Cover

Step 3 Mask

Step 4 Glove Pair #1 HD

Step 5 Gowns

Step 6 Glove Pair #2 HD

Step 7

Gloved hands scrubbed according to CDC Hand hygiene document

# Garb-Off Sequence

**Goals**

Minimize Contamination

*To employee

*To environment

Step 1 Shoe Cover #1
*Once away from area

Step 2 Outer Gloves

Step 3 Hair Cover

Step 4 Gown

Step 5 Shoe cover #2

Step 6 Mask

Step 7 Inner Gloves

Step 8 Hands scrubbed according to CDC Hand hygiene document

# Good Primary Engineering Controls

Traditional Biological Cabinet
Class II Type B2 BSC

Chemo Valet

Isolator Glove Box
Compounding Aseptic Containment Isolator (CACI)

Room where Hazardous Drugs are stored &Compounded
-should be separate from other drugs
-should be negative pressure

# Closed System Transfer Devices

"A drug transfer device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of hazardous drug or vapor outside the system"

**NIOSH Alert**

Preventing Occupational Antineoplastic and Other Hazardous Drugs in Health Care Settings

CDC 2004

# Closed System Transfer Devices

## Only 1 part of a safety program

- Continuous device assessment
  - Currently 5 US products
    - PhaSeal
    - Smartsite/Texium
    - On-Guard or Tevadaptor
    - Genie/Spiros
    - Equashield
  - 3 US pending devices in development

- Budget impact
  - What is the set-up cost to get started!!!!
    - PhaSeal 8 Pieces
    - On-Guard 5 Pieces
    - Smartsite/Texium 5 Pieces
    - ICUMedical 6 Pieces
    - EquaShield 12 Pieces
  - What is the minimum order quantity? Look at case quantities?
  - Monthly compounding volumes??
    - Think of doses requiring multiple vials: ICE methotrexate

# Vapor Pressure Antineoplastic Drugs

*Kiffmeyer et al., Pharm J 2002; 268:331-7*

| Antineoplastic Drug | Mol. Weight | Vapor pressure (Pa) at 20°C | Max. concentration ($mg/m^3$) |
|---|---|---|---|
| Carmustin | 214 | 0.019 | 1.7 |
| Cisplatin | 300 | 0.0018 | 0.22 |
| Cyclophosphamide | 261 | 0.0033 | 0.36 |
| Etoposide | 289 | 0.0026 | 0.63 |
| 5-Fluorouracil | 130 | 0.0014 | 0.08 |

Some antineoplastic drugs possess a low vapor pressure

Maximum concentrations possible by insufficient ventilation

Protective clothes not designed to protect workers from vaporized

# PhaSeal®

## First to market

Membrane, needle hub, luer system with closed expansion chamber

*Marketed by Carmel Pharma*

# On-Guard®

Charcoal filtration methodology

with needle, membrane system

No luer lock, push lock

*Marketed by B.Braun*

# Alaris Smartsite®

Paper filter and
luer lock, needle,
membrane system

*Marketed by Cardinal*

# Spiros/Genie®

Utilizes luer Clave IV system
in combination with internal vial
Balloon (on certain vial sizes)

*Marketed by ICU Medical*

# Equashield®

Utilizes a syringe, needle, membrane system with closed chamber In the syringe device

*Marketed by Equashield*

# Containing the Drug in the System
## Complex Test

Spivey S, Jorgenson J. Contamination Comparison of Transfer Devices Intended for Handling Hazardous Drugs. Study presented at ONS Congress, April, 2007, Las Vegas, NV.

# Containing the Drug in the System
## Simple Test

Lemon juice with Litmus paper

Jorgenson J. Contamination Comparison of Transfer Devices Intended for Handling Hazardous Drugs. Study presented at ONS Congress, April, 2007, Las Vegas, NV.

# Containing Vapors: Complex Test

Titanium tetrachloride gas

Jorgenson J, Spivey S, Cam A, et al. Hosp Pharmacy 2008

# Containing Vapors: Simple Test

# Points of Exposure Risk Strategies

- Drug Administration
  - Most ready to use form for administration IV Line Priming
  - Education & skills assessed for administration
    - All personnel including MD's and surgery staff
  - Examine drug administrators devices for compliance
  - Policy on tubing sets not removed from original bags
- Housekeeping
  - Education & Personal Protective Equipment
  - All wastes placed appropriate waste containers & labeled
  - Cleaning rooms with hypochlorite solutions
  - Proper management of linen
- Contractors
  - Waste haulers
  - Building maintenance & Construction
- Environmental sampling
  - Not mandated and no standards given
  - Paul J.M. Sessink PhD
    - Exposure Control B.V., The Netherlands
    - www.exposurecontrol.nl

# Proper Decontamination

- "Decontamination" of cabinets & areas
  - Surface Safe® (15/case) $1.50/ea
    - step 1: 2% sodium hypochlorite detergent
    - step 2: 1% sodium thiosulfate & 0.9% benzyl alcohol
      - azathioprine, bleomycin, daunorubicin, etoposide, fluorouracil, etoposide, mitomycin, vinblastine, vincristine
      - cyclophosphamide, melphalan, ifosfamide, methotrexate
  - TexChlor AL® (20/case) $15/ea
    - Point of use 'Bleach wiper' 9 wipes/pack
    - Uses sodium dichloroisocyanurate (pH 5-6)

- "Sanitization" of cabinets
  - Caution sterile isopropyl alcohol use in Type II-A & II-B3
  - Must be in contact for 30 seconds

# Cleaning of Cyclophosmamide-spiked Vials
## (wiped with 1 mL 0.03 M NaOH)

| Treatment | % Remaining | S.D. (N=6) |
|---|---|---|
| 0.03 M NaOH | 0.0 | 0.0 |
| Soap | 0.4 | 1.0 |
| Water | 0.8 | 1.3 |
| K persulfate | 1.5 | 0.2 |
| Bleach | 1.8 | 2.9 |
| Ethanol | 20.9 | 29.4 |
| Isopropanol | 28.9 | 21.1 |
| Rey et al. 2008 | (2.5 mg/mL 10 µgL/vial) | |

# Hazardous Drug Spill Policy

- Develop a collaborative policy
  - Risk management, Employee health input
  - Pharmacy and Nursing
  - Environmental services and Safety
- Define volume limits
  - Who is responsible for what volume
- Define detailed steps
  - From alerting to disposal to recordkeeping
- Develop or purchase ‘spill kits’
  - Location of kits
  - Training on kits
- Drill Spills
- Educate on policy – on hire and annually

# What a formal spill management Program Should Look Like

Formal Spill Kit
-Homegrown vs. commercial
-Location of storage
-Training

Spill Notification
-Restricted area vs. Public
-Isolation of area (vapors)

# What a formal spill management Program Should Look Like

All PPE Characteristics
-rated supplies

-What if:
  -Vapors
  -Glass debris
  -Powder dust

# What a formal spill management Program Should Look Like

Cover the spill
-adsorbent
-cloths
-paper

Scoop the spill
-NOT with hands
-Disposable scoops

Decontamination
-Site residue

# What a formal spill management Program Should Look Like

Bag soft & Bin sharps

De-gown carefully

Dispose as EPA Waste not Yellow

Document spill
-Who, What, Where, When
-Witnesses
-Steps taken to clean
-follow-up

# Regulated Pharmaceutical Waste

- Resource Conservation and Recovery Act
  - RCRA
  - Regulated by the EPA since 1976
- Listed chemicals
  - P-list (acutely hazardous )
  - U-list (toxic, ignitable, corrosive, reactive)
- Characteristic chemicals
  - AKA D-list
    - Ignitability (D001)
    - Corrosivity (D002)
    - Reactivity (D003)
    - Toxicity (D number specific to chemical)
    - **NOTE: primary drug may not be what is listed!

# EPA Defined Hazardous Drugs

## P-listed

| | |
|---|---|
| P012 | Arsenic Trioxide |
| P042 | Epinephrine |
| P075 | Nicotine |
| P081 | Nitroglycerin |
| P204 | Physostigmine |
| P188 | Physostigmine salisylate |
| P001 | Warfarin >0.3% |

## U-listed

| | |
|---|---|
| U034 | Chloral Hydrate |
| U035 | Chlorambucil |
| U044 | Cloroform |
| U058 | Cyclophosphamide |
| U059 | Daunomycin |
| U075 | Dichlorodifluromethane |
| U089 | Diethylstilbestrol |
| U122 | Formaldehyde |
| U129 | Lindane |
| U150 | Melphalan |
| U151 | Mercury |
| U010 | Mitomycin C |
| U182 | Paraldehyde |
| U188 | Phenol |
| U200 | Reserpine |
| U201 | Resorcinol |
| U202 | Saccharine |
| U205 | Selenium |
| U206 | Streptozocin |
| U237 | Uracil Mustard |
| U248 | Warfarin <0.3% |

http://www.access.gpo.gov/nara/cfr/waisidx_05/40cfr261_05.html

# Exemptions are State Specific

- EPA guidance on exemptions
  - Nitroglycerin Federal Register: May 16, 2001 (Volume 66, Number 95)
  - Epinephrine Salts USEPA Memo Dated 10/07/2007

- States who do NOT allow exemptions

## Nitroglycerin

Connecticut
Hawaii
Maine
Michigan

## Epinephrine salts

Connecticut
Hawaii
New York – exempted 7/15/09
Washington

*Florida, Michigan, Minnesota, Washington

# EPA Defined Hazardous Drugs

## D-Listed Characteristic

| | | | |
|---|---|---|---|
| D004 | Arsenic | 5 | mg/L |
| D005 | Barium | 100 | mg/L |
| D022 | Chloroform | 6 | mg/L |
| D007 | Chromium | 5 | mg/L |
| D024 | M-Cresol | 200 | mg/L |
| D013 | Lindane | 0.4 | mg/L |
| D009 | Mercury | 0.2 | mg/L |
| D101 | Selenium | 1 | mg/L |
| D011 | Silver | 5 | mg/L |

www.access.gpo.gov/nara/cfr/cfrhtml_00/Title_40/40cfr261_00.html

# Waste Segregation Cost

**Biohazard Infectious (Regulated Medical)**

Blood products, sharps, items contaminated with liquid blood, etc.

$0.01/pound

**Hazardous & Non-Hazardous**

Empty chemotherapy vials, syringes, IVs, tubing, gowns, packaging, gloves, etc.

$0.10/pound

**RCRA Hazardous**

Bulk chemo in vials, unused IV's, P, U, toxic & ignitable
Overtly contaminated gowns, glove, chemo spill clean up materials

$1.00/pound

**RCRA Biohazardous**

$1.20/pound

# Electronic Sorting of Waste

- Electronically logging managed waste
- All United States NDC#s
- Barcode segregation
- Cart and wall configuration
- Alerts staff when full
- Completes required USEPA and DOT manifests

*“Scan  Dispose  Close”*

www.vestara.com

# When the EPA Comes to Visit

- Methodist Hospital: September 02, 2004
  - What Cyclophosaphamide waste manifest
  - Violation NO RCRA RX Hazardous Waste stream
  - Result Day 50 of 90 met compliance, no fine

- Eastern Kansas Health Care System August 18, 2009
  - What $51,501 civil penalty & $482,069 supplemental project
  - Violations
    - No hazardous waste determinations
    - No proper hazardous waste containers
    - No documentation of inspection of hazardous waste storage
    - No documentation of personnel training
    - Unpermitted on-site incineration of hazardous waste
    - Unlawful shipping of hazardous waste

# “HAZARDOUS DRUG ROUNDS”

Preparation

Administration

Disposal

# Medical Surveillance

- OSHA & NIOSH recommends, NOT mandated
  - Formal approach to surveillance
    - **Tier-One** Self Surveillance
      - Education by employer of hazards
      - Notification of employee to primary care physician
    - **Tier-Two** Employer/Supervisor Surveillance
      - Annual basic physical exam with reproductive questionnaire
      - Trending of sick calls
    - **Tier-Three** Comprehensive Medical Surveillance
      - Complete Blood Count with differential at hire and annually
      - Urinalysis with dipstick at hire and annually
      - Liver function & transaminase test at hire and annually
    - **Tier-Four** Post-Exposure Surveillance
      - Comprehensive physical directed towards hazardous exposure
      - Notation in employee's medical record with date and drug
      - Continuous self-monitoring and employer-monitoring

Massoomi F, PPP 2008

# Cost of Protecting Pharmacy Staff

Cap $0.09

Mask $0.13

Gown $0.72

Gloves $2.00

Shoe Cover $0.23

Total Gowning per Person

$3.17

Surface Safe $2.86

ChemoMat $0.87

CSTD* $15.00

Annual Lab Test* $9.00

Total Gowning per Person

$3.17

Ancillary cost per Person

$18.73*

Total Cost

$21.90

ChemoSpill Kit $30.00

# Hazardous Drug Management

## Healthcare's Dirty Little Secret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