Closed systems transfer devices "Reconciling recommendations and real life practice"

Pre-congress workshop: Good Compounding Practice in Oncology

2018 Asia Pacific Oncology Pharmacy Congress

7th September 2018

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Thank you, Singapore and PSP!

Disclosure Information

Eric S. Kastango, BS Pharm, MBA, FASHP

- I have the following financial relationships to disclose:
  - Grant/Research support from: Equashield, Contec, BD Medical, and Braun (past client)
  - Principal of: Clinical IQ, and CriticalPoint, LLC

- I will not discuss off label use and/or investigational use in my presentation.

- List References here

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Acknowledgements

Thanks to Fred Massoomi, Luci Power, Kate Douglass, and Patti Kienle for the use of slides/information presented in this slide deck!

What's all the fuss?

Preventing Occupational Exposure

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

Source: NIOSH Alert: Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings, 2004

Evidence: Health Effects

1970s Secondary malignancies identified in patients following treatment[1]

1980s Association between exposure to antineoplastics and adverse reproductive effects: miscarriages, congenital malformations, low birth weight and infertility

1990s Link of cancer occurrence to healthcare workers exposure to antineoplastics

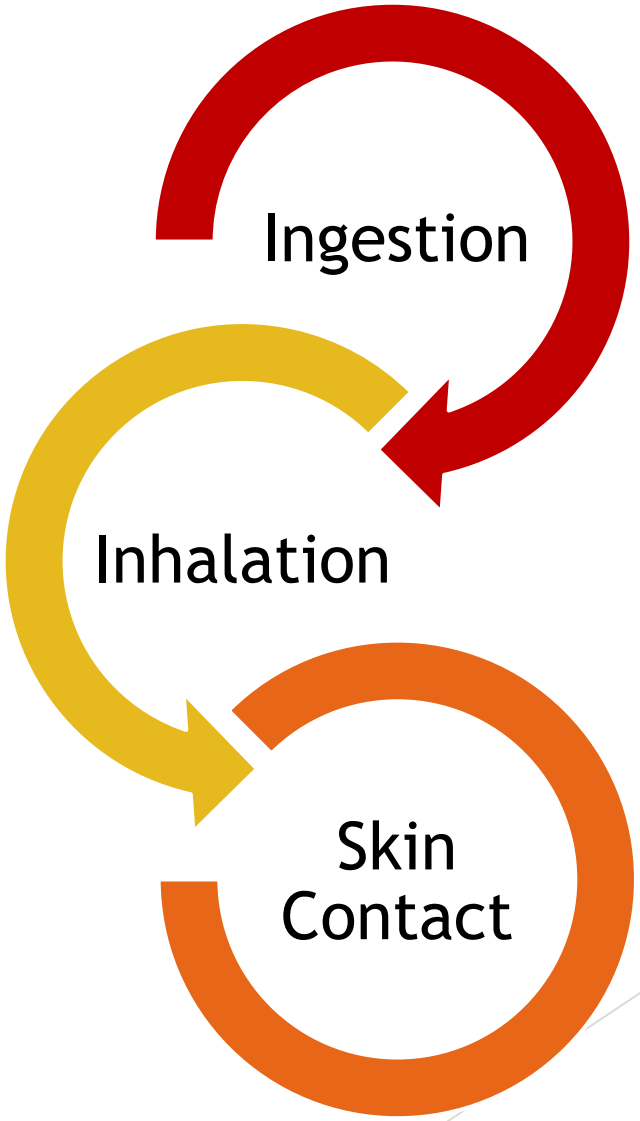
[1]Roussel C. et al. Meta-analysis of chromosomal aberrations as a biomarker of exposure in healthcare workers occupationally exposed to antineoplastic drugs. Mutation Research/Reviews in Mutation Research. (2017). Retrieved -2/22/2018.

Evidence: Exposure

- Biological Markers
- Studies demonstrate antineoplastics in urine
- Present in workers who did not handle HDs

Hazardous Drug Dangers

- Toxicity of the drug
- Exposure of workers



Organizational Interest

Safe Handling of HDs

Early 1970s	Europe
1981	Australia
1983	USA

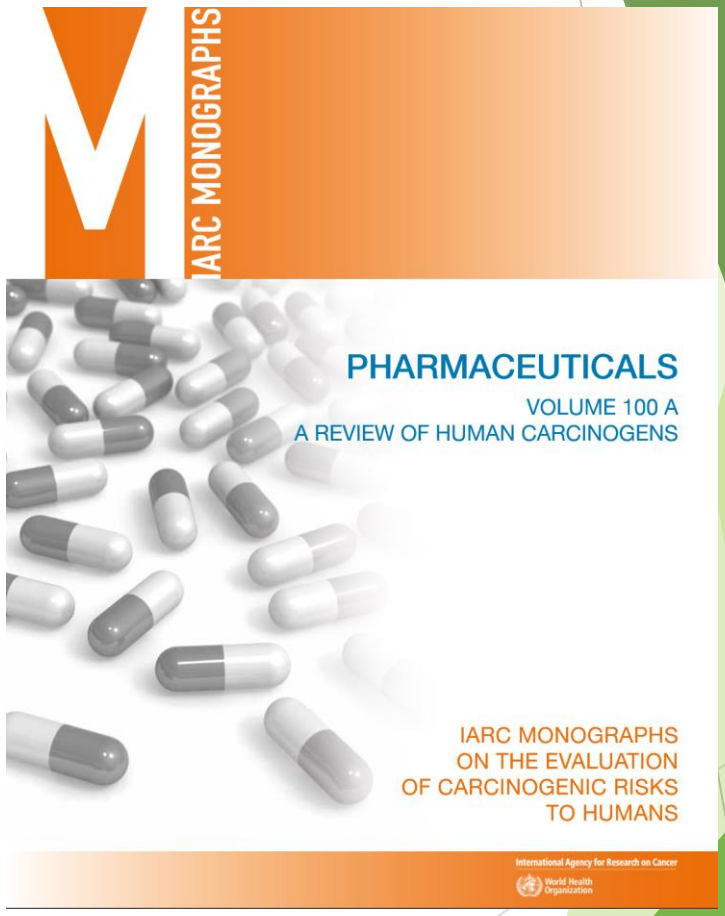
30+ years of pharmacy awareness in US alone

IARC

- International Agency for Research on Cancer
  - Division of the World Health Organization
  - Interdisciplinary organization
  - Mission to develop international collaboration in cancer research

IARC (continued)

- A Review of Human Carcinogens – Pharmaceuticals
  - Group 1 Human carcinogens
  - Group 2A Probably carcinogenic in humans
  - Group 2B Possibly carcinogenic in humans
  - Group 3 Not classifiable as to carcinogenicity in humans
  - Group 4 Probably not carcinogenic humans

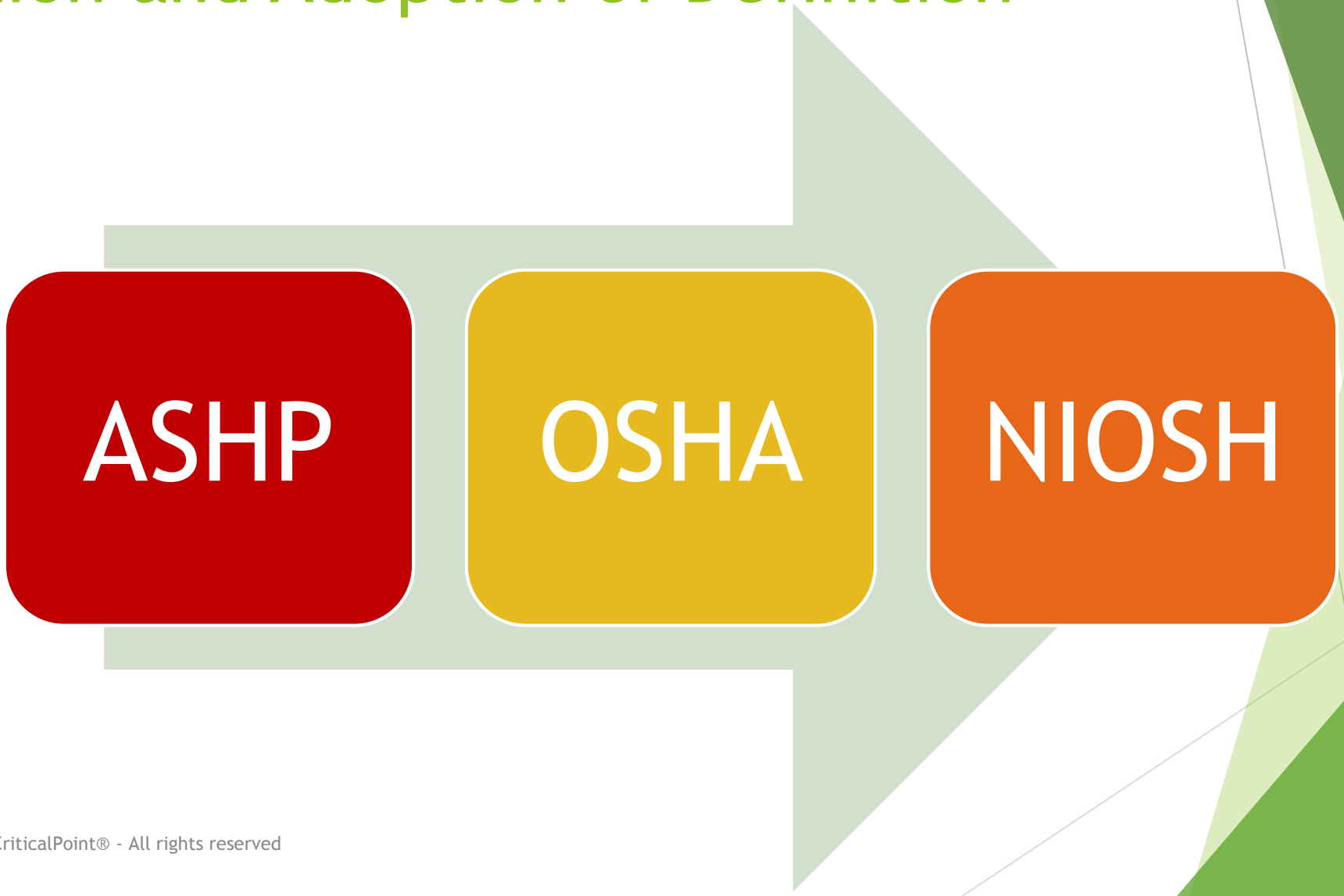


Occupational Hazard Characteristics of HDs

- Genotoxicity (mutagenicity)
- Carcinogenicity in animal models
- Teratogenicity or fertility impairment
- Evidence of serious organ or other toxicity at low doses

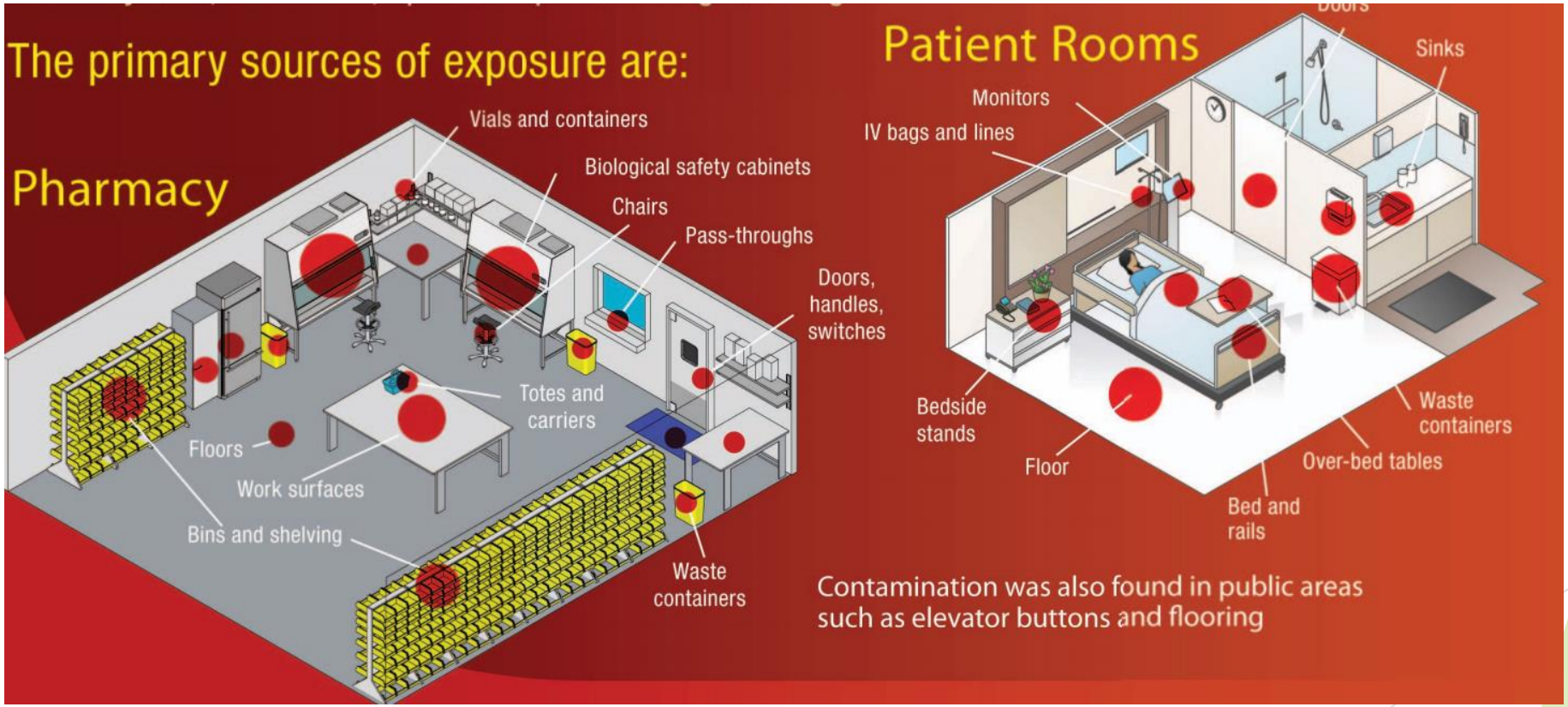
Source: ASHP TAB on Handling Cytotoxic and Hazardous Drugs, 1990

Evolution and Adoption of Definition



The Contaminated Environment

- More than 70 published studies
  Most surfaces that come in direct contact with hazards
  Some with in-direct contact with hazards



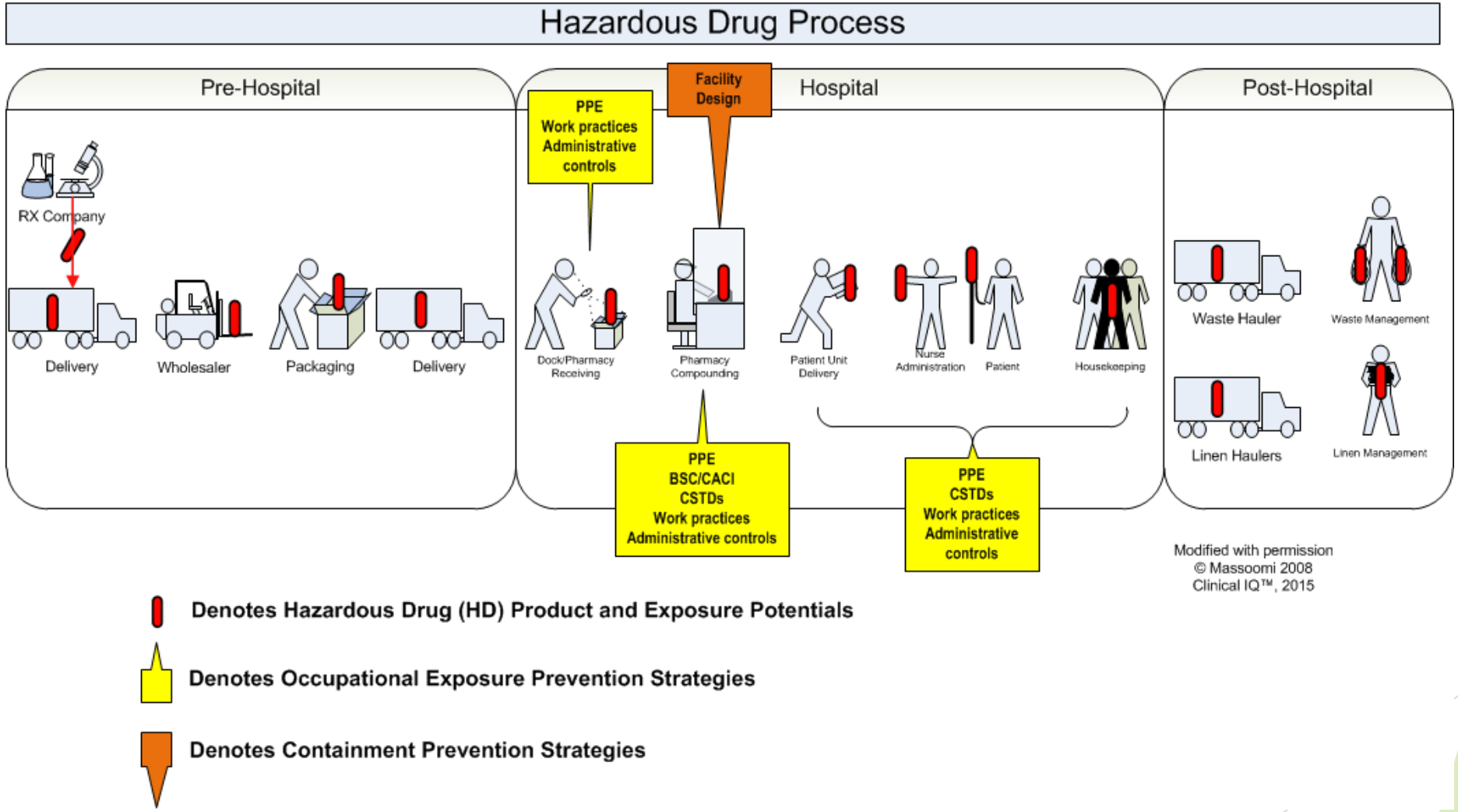
Source: B. Braun

Skin contact

- Workers from 6 Canadian hospitals sampled
- Wiped front and back of hands
- Analyzed for cyclophosphamide
- 44/225 (20%) had levels above the limit of detection
- A number of workers from various job categories had contaminated hands
  - Volunteer, oncologist, aide and dietician
  - Pharmacist, pharmacy technician, pharmacy receiver, nurse, transporter

Hon CY, Teschke K, Demers PA and Venners S. Antineoplastic drug contamination on the hands of employees working throughout the hospital medication system. Ann Occup Hyg. 2014; 58:761-770.

Occupational Exposure Strategies-CSTDs



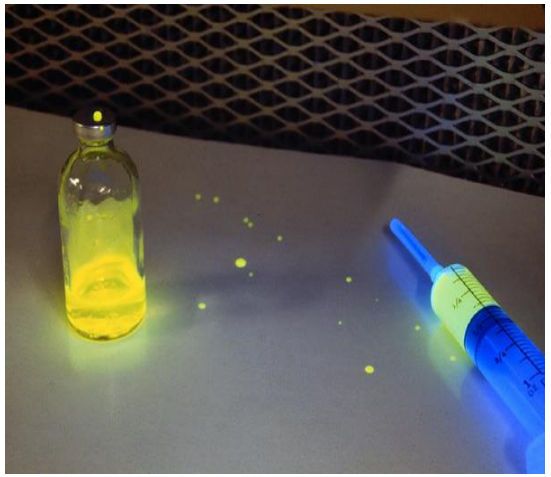
Contamination of drug vials

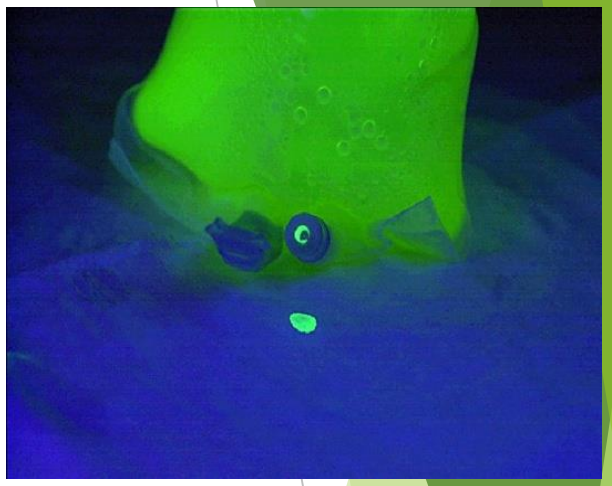
- The exterior of many drug vials are contaminated with their contents
- The contamination is not the result of breakage during transportation
- Some facilities pre-clean the exterior of the vials before use

Connor TH, Sessink PJM, Harrison BR et al. Surface contamination of chemotherapy drug vials and evaluation of new vial-cleaning techniques: Results of three studies. Am J Health-Syst Pharm. 2005; 62:475-484.

What can we conclude from surface contamination with hazardous drugs?

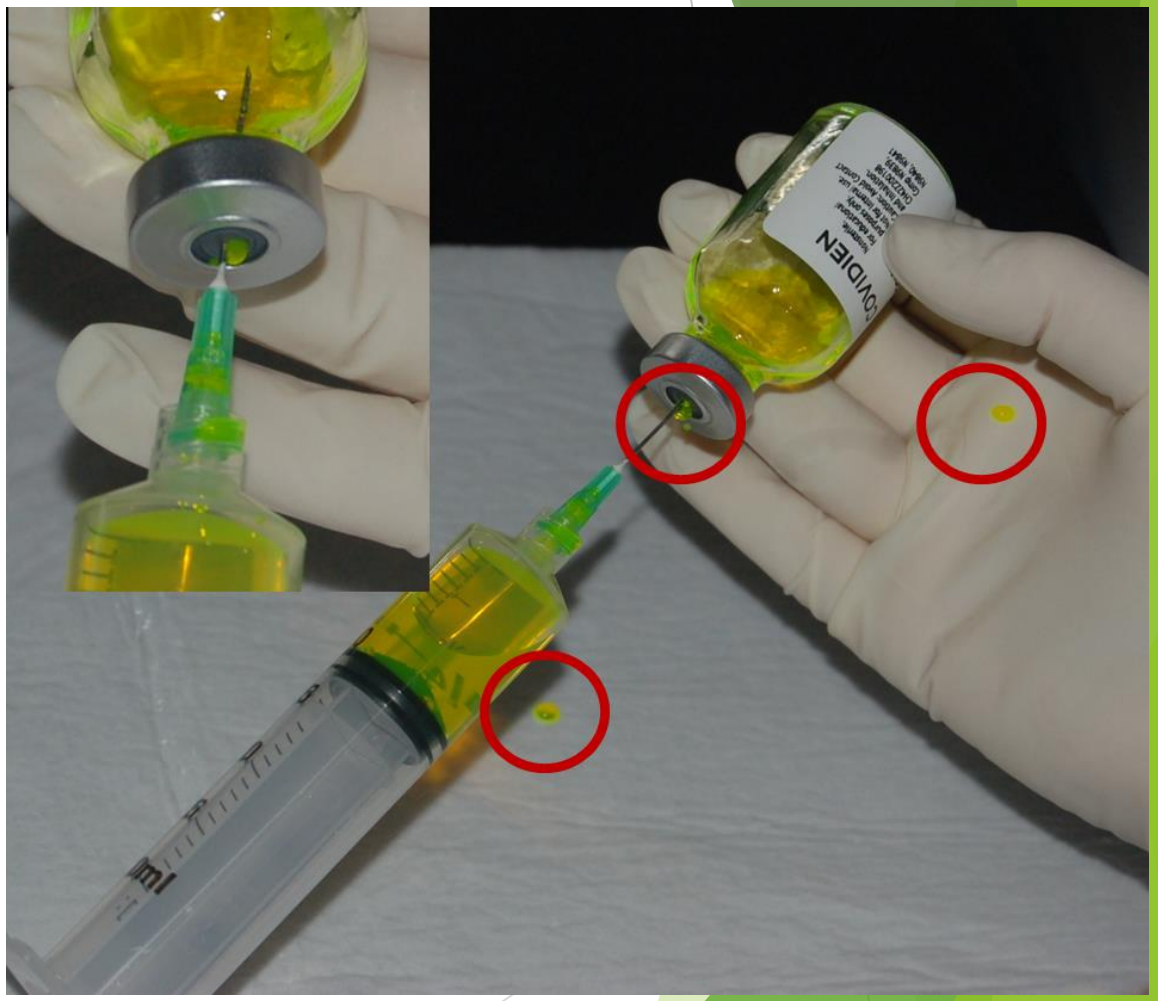
- Surface contamination is common in pharmacy and nursing areas and where drugs are handled
- It has been well documented with ~5% of drugs in use
- Status of other 95% is unknown
- Uptake of several drugs has been documented in healthcare workers





HD Compounding Strategies: Negative Pressure

- Negative pressure compounding techniques ensure that the pressure within the drug container is always maintained at a slight negative pressure
- Too much negative pressure can cause fluid to leak from the needle when withdrawn
- Positive pressure can cause the HD to spray out around the needle or through the needle hole
- Always use a syringe that is 25% larger in volume than the total volume to be withdrawn



Engineering Controls for Containment: Definitions

Containment Primary Engineering Control (C-PEC)

- Ventilated device to minimize worker and environmental exposure
- For sterile compounding, also provides product protection

Containment Secondary Engineering Control (C-SEC)

- The room in which the C-PEC is placed

Containment Supplemental Engineering Controls

- Adjunct controls to offer additional levels of protection
- Closed System Drug-Transfer Devices (CSTDs)

HD Compounding Strategies: Use of CSTDs

- USP 800 uses the term supplemental engineering controls
  - Must be used in containment primary engineering control (BSC or CACI)
- These devices are adjunct controls that may be used with C-PECs and C-SECs to offer additional levels of protection (containment)
- Facilitate enhanced occupational protection especially during drug administration
- Closed System Drug-Transfer Devices are the only kind of Containment Supplemental Engineering Control available at this time
- Two types of CSTDs
  - Capture vapors
  - Filters

Supplemental Environmental Controls

Closed System Transfer Devices (CSTDs)

- Compounding : Recommended
- Administration : Required

- Currently 8 US products
  - PhaSeal®: BD
  - Smartsite with Texium: Carefusion:BD
  - VialShield® with Texium®: Carefusion:BD
  - On-Guard®: B.Braun
  - Chemoclave® /Spiros®: ICU Medical
  - ChemoLock®: ICU Medical
  - Equashield®
  - Halo®: Corvida Medical

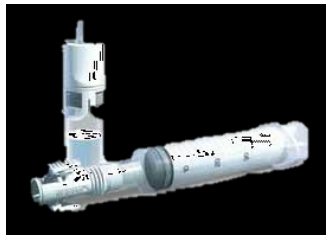
PhaSeal

Vialshield/Texium

Equashield

ChemoClave

ChemoLock



On-Guard

Halo

Definition – Closed System Transfer Device (CSTD)

- According to the National Institute for Occupational Safety and Health (2004 NIOSH), a closed-system transfer device (CSTD) is “a drug transfer device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of hazardous drug or vapor concentrations outside the system.”
  - Intent: Nothing in and Nothing Out!
  - No testing procedures are described to prove this point

Definition

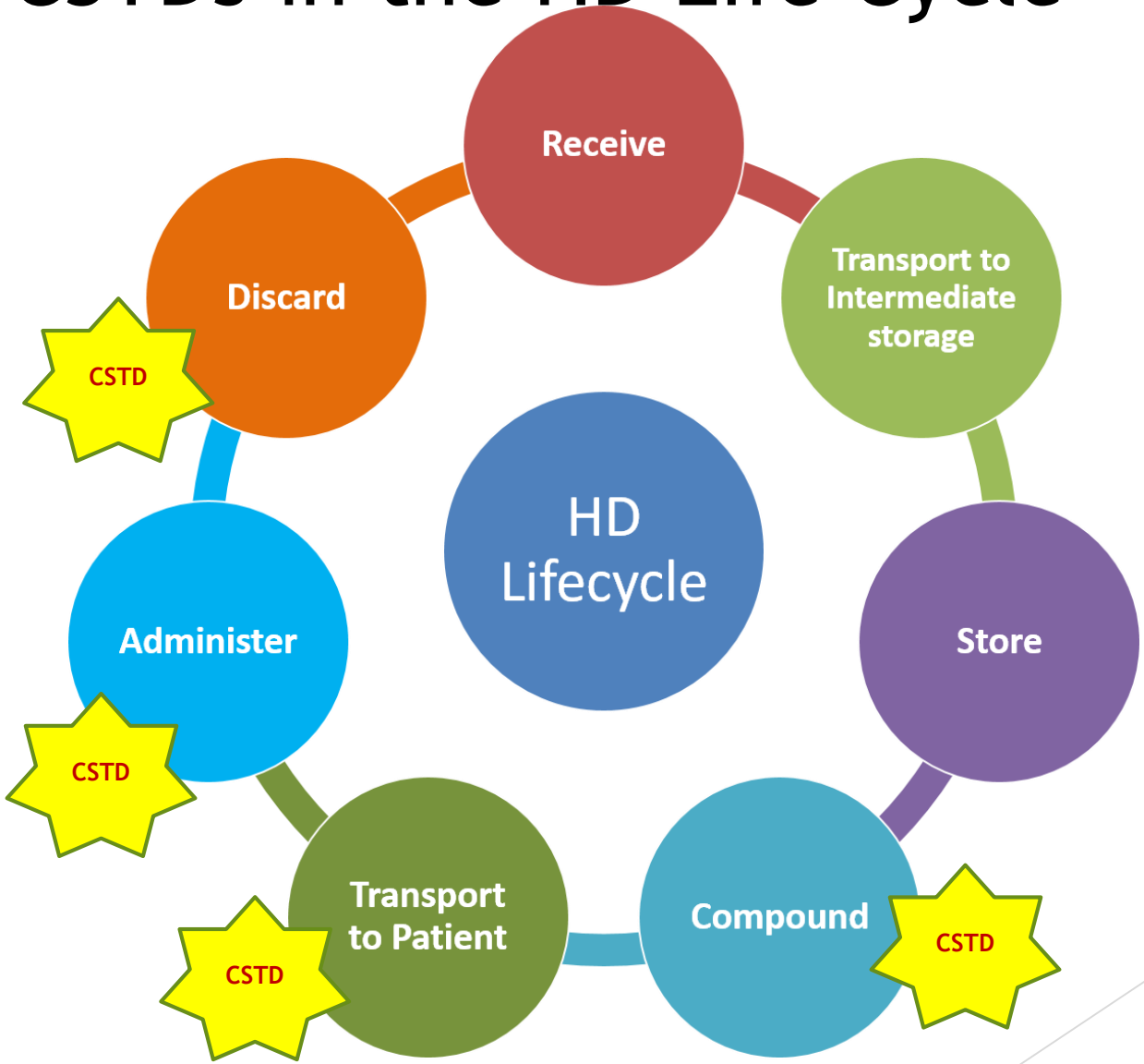
- In addition to preventing transfer of environmental contaminants (e.g., bacteria) into vials in which parenteral medications are prepared, CSTDs serve the important function of protecting health care professionals compounding and administering hazardous drugs (HD) from the occupational hazard of chronic, low-level exposure to carcinogenic and/or teratogenic medications.
- Microbial Ingress Testing
  - Expected Testing – Not clearly defined by FDA
  - Many CSTD manufacturers have tested their product

Summary of CSTDs

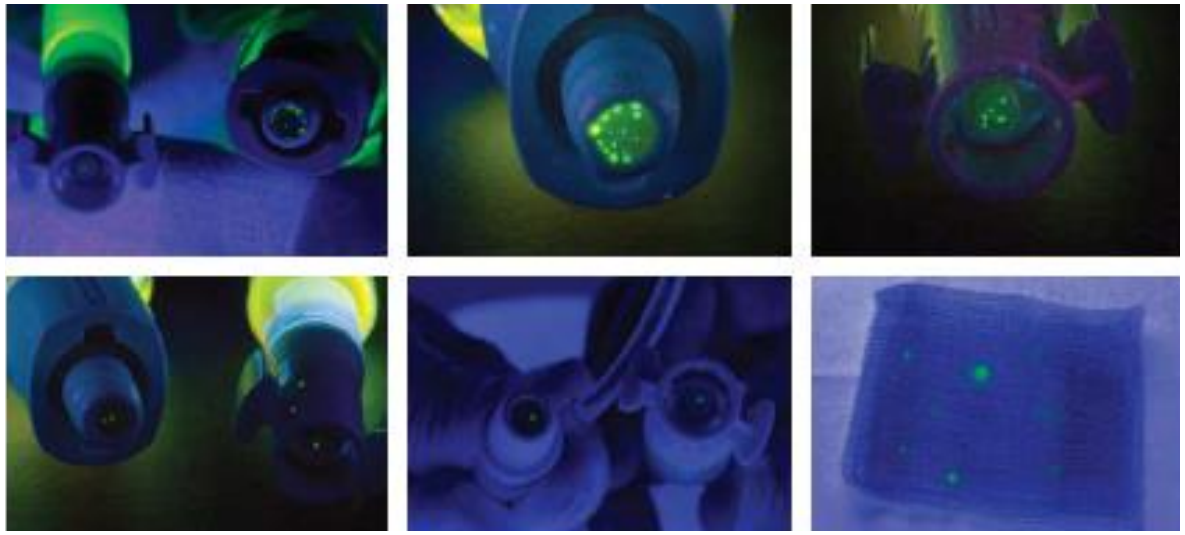
Device	Manufacturer	FDA Cleared
BD Phaseal™ System	Becton Dickenson and Company; Carmel Pharma, Inc. (original)	1998
Spiros®	ICU Medical, Inc.	2005
Texium™ with SmartSite™	Becton Dickinson and Company; CareFusion, Inc. (original)	2006
OnGuard® with Tevadaptor®	B. Braun Medical Inc. (U.S. distributor) TEVA Medical, Ltd. (manufacturer)	2006
ChemoClave®	ICU Medical, Inc.	2006
Equashield®	Equashield, LLC; Plastmed, Ltd. (original)	2008
ChemoLock®	ICU Medical, Inc.	2013
ChemoSafety	Becton, Dickinson and Company; CareFusion, Inc. (original)	2013
EquaShield II®	Equashield, LLC	2014
Halo®	Corvida Medical	2015
Arisure®	Baxter	2017

Source: BD & the Joint Commission Resources; Improving safe handling Practices for Hazardous Drugs. Toolkit 2016

The use of CSTDs in the HD Life Cycle



Visualizing Dry Connections



Fluorescein

Litmus with Lemon Juice

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

Visualizing Vapors

Figure 1. *PhaSeal* with no release of titanium smoke.

Figure 2. *OnGuard Tevadaptor* with release of titanium smoke.

Figure 3. *Alaris Smart Site* with release of titanium smoke.

Figure 4. Codan *Chemoprotect Spike* with release of titanium smoke.

Figure 5. *Chemo Mini-Spike Plus* with release of titanium smoke.

- 5 Devices tested
  - PhaSeal; Onguard; Texium; Chemo Protectspike; Chemo Minispike plus
- Titanium tetrachloride, generates visible smoke with moisture in the air
  - Forms hydrochloric gas and titanium dioxide
  - Vapor particle is less than 0.2 micron
- 1 of the 5 demonstrated to contain vapor

Source: Jorgenson J, et al. Hosp Pharm—2008;43:723–727

HD Compounding Strategies: Use of CSTDs

- Key CSTD Features
  - Containment
    - Performance Testing Criteria – VAPOR
    - Performance Testing Criteria – Microbial Ingress Testing (Container Closure Integrity Testing)
  - User & Design interface
  - Integration
  - Workflow
  - Repetitive strain reduction
  - Pre-bonded components

Source: Massoomi. Pharmacy Purchasing Products 2015; February S1-S12

HD Compounding Strategies: Use of CSTDs

- Provides additional safeguards to prevent occupational exposure to nursing and other staff who administer these drugs
- Provides additional safeguards to patients, families and organizational environments by reducing risk of exposure to HDs
- Increased operational cost associated with CSTD use
  - Reimbursement isn't routinely available

Remember, CSTDs still can't prevent damage or spills from poor handling or transport!

Performance of CSTDs – Caveat Emptor

- CSTDs have shown ability to limit (not prevent) the potential of generating aerosols and reduce (not eliminate) HD contamination in the workplace.
- Not all marketed CSTDs have been studied
- Capture technology appears to perform better than other technologies

Key Points

- Reduces HD contamination inside the C-PEC thereby reducing the amount of HD contamination available for migration out of the C-PEC into the C-SEC and C-SCA
- Improves compounding efficiency since negative pressure compounding techniques significantly increase the length of sterile compounding
- An efficiency study[1] that actually has shown that using a CSTD actually decreases the amount of time from preparation to administration

1. Knolla K, Greisen D, Massoomi F. Time and motion study of 5 closed system transfer devices for IV chemotherapy drug compounding and administration. Poster presented at: American Society of Health-System Pharmacists Clinical Midyear Meeting; December 2011; New Orleans, Louisiana.

Resources

- Centers for Disease Control and Prevention - National Institute for Occupational Safety and Health. Preventing occupational exposure to antineoplastic and other hazardous drugs in health care settings 2004 [Internet]. Publication number 2004-165, Cincinnati (OH). 2004 [cited 2011 Nov 30]. Available from: http://www.cdc.gov/niosh/docs/2004-165/
- Centers for Disease Control and Prevention. Occupational exposure to antineoplastic agents and other hazardous drugs. CDC website. www.cdc.gov/niosh/topics/antineoplastic/pubs.html
- Forshay CM, Streeter SO, Salch SA, and Eckel SF. Application of the 2015 proposed NIOSH vapor containment performance protocol for closed system transfer devices used during pharmacy compounding and administration of hazardous drugs. J Oncol Pharm Practice 2018; 0(0) 1–7.
- Knolla K, Greisen D, Massoomi F. Time and motion study of 5 closed system transfer devices for IV chemotherapy drug compounding and administration. Poster presented at: American Society of Health-System Pharmacists Clinical Midyear Meeting; December 2011; New Orleans, Louisiana.

Questions?