Road to Compliance to USP Chapter 800: Handling Hazardous Drugs in Healthcare Systems

April 6, 2017

Fred Massoomi, Pharm.D., FASHP
Senior Director
Visante, Inc.

© Copyright Visante, Inc. All rights reserved | www.visanteinc.com

Disclosures

- Recommendation to the audience to review nationally accepted guidelines, FDA approvals, and peer reviewed studies for clarification of information presented.

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Predictive Safety Needs

"…Recommendations support ..maintaining product sterility while providing for the safety of the personnel involved in preparing and administering chemotherapy"

Am J Hosp Pharm. **1981** ;38(11):1686-1693.

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Hazardous Drug Compounding USP <800>

First Release	March 2014
Comment Due Date	July 31, 2014
Second Release	December 2014
Comment Due Date	May 31, 2015
Approved	February 1, 2016
Official Compliance Date	July 1, 2018

http://www.usp.org/usp-nf/notices/general-chapter-hazardous-drugs-handling-healthcare-settings

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Polling Question

How compliant is your site with USP <800>?

A. Meets or exceeds USP <800>
B. Meets most of USP <800>
C. Meets some of USP <800>
D. Planning to formally address USP <800>
E. No plans for compliance

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Failing Grade on Handling HDs

USP <800> compliance as **low as 47%**

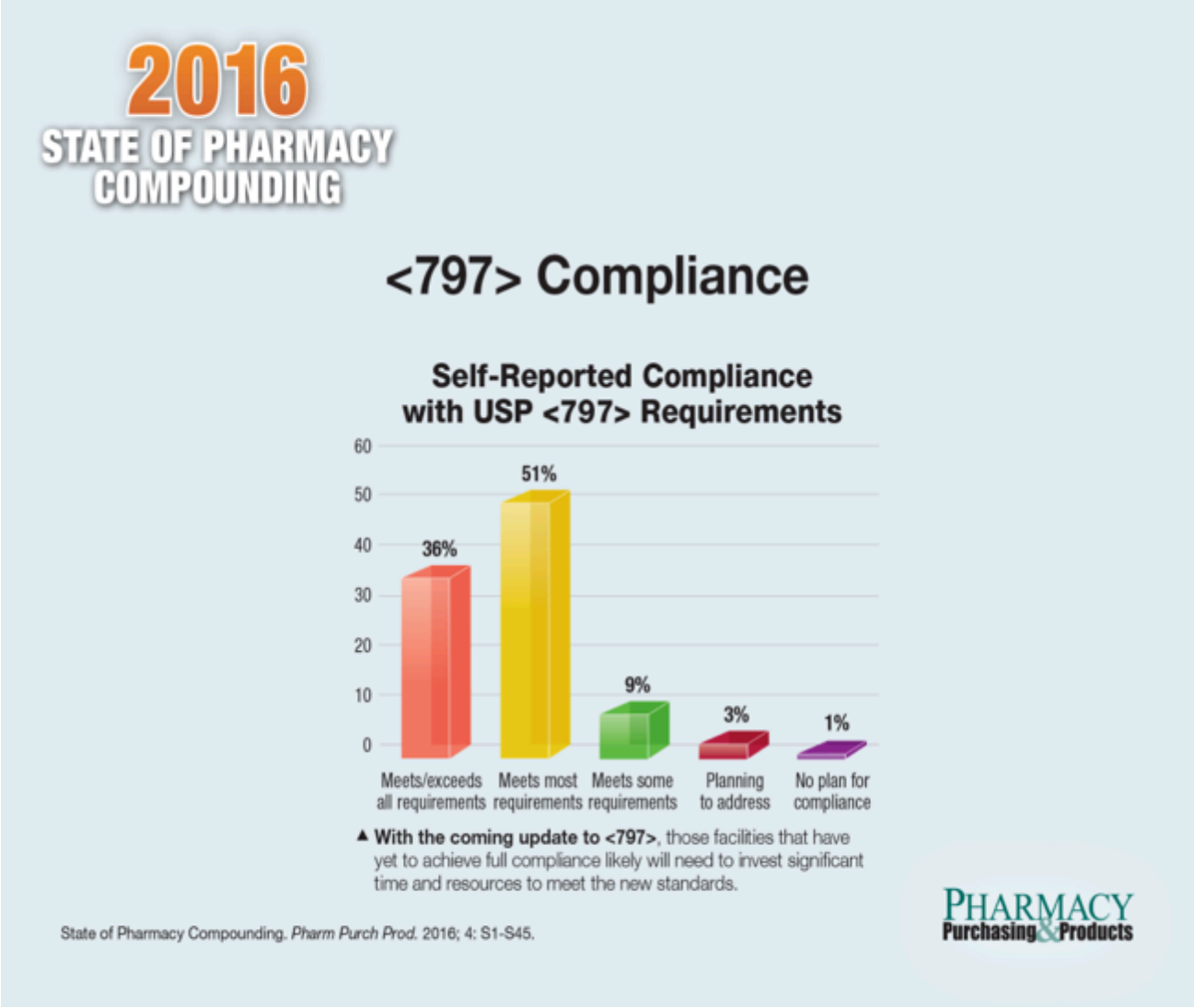
Las Vegas – Some health systems pharmacies do not effectively protect their staff from exposure to cytotoxic agents, according to survey findings presented at the ASHP 2016 Midyear Clinical Meeting.

The survey of almost 900 facilities found that roughly two-thirds of workers handling hazardous drugs complied with U.S. Pharmacopeial (USP) Chapter <800> requirements.

Source: Pharmacy Practice News: February 7, 2017

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Hospital Compliance …36%



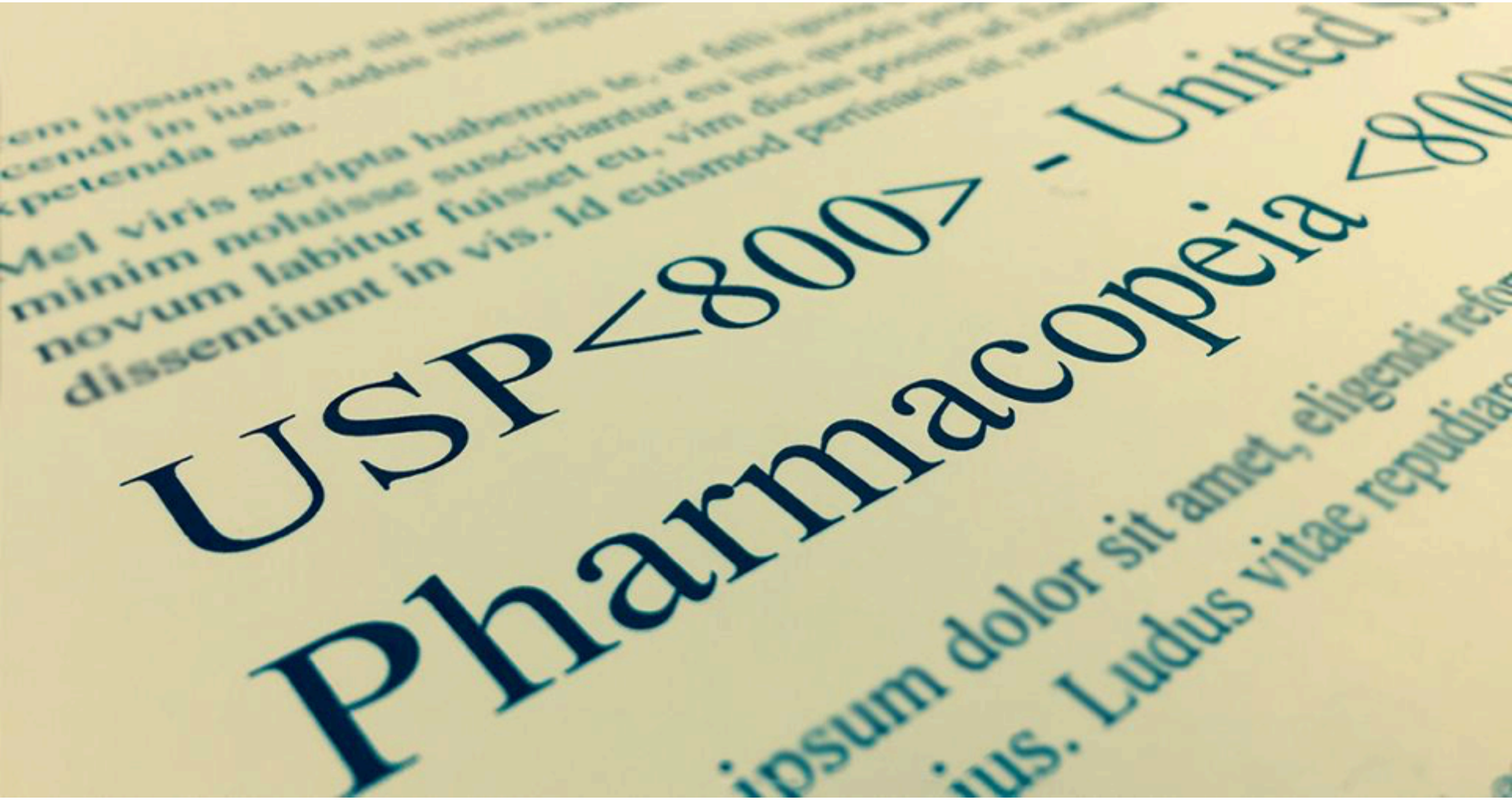
© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Educating Administration

1. USP <797> Pharmaceutical Compounding – Sterile Compounds
2. USP <800> Hazardous Drug - Handling in Healthcare Settings
3. MM.09.01.01 Antibiotic Stewardship Standard
4. 503A & 503B Compounding
5. 340B Mega-Guidance Withdrawn

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

What's Inside the Final Chapter?



© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Road Map to Safety

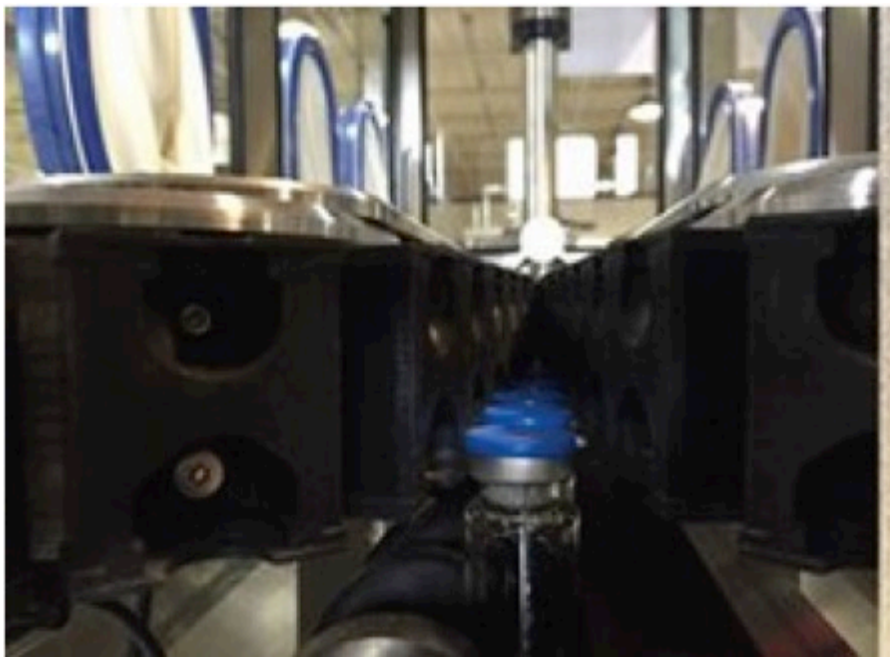
- Introduction and scope
- List of Hazardous Drugs
- Types of exposure
- Responsibilities of handling HDs
- Facilities and engineering controls
- Environmental quality and control

- Personal protective equipment
- Hazard communication program
- Personnel training
- Receiving
- Labeling, packaging, transport & disposal
- Dispensing final dosage forms

- Compounding
- Administering
- Deactivating, decontaminating, cleaning, & disinfecting
- Spill Control
- Documentation and standard operating procedures (SOPs)
- Medical surveillance

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

The Source

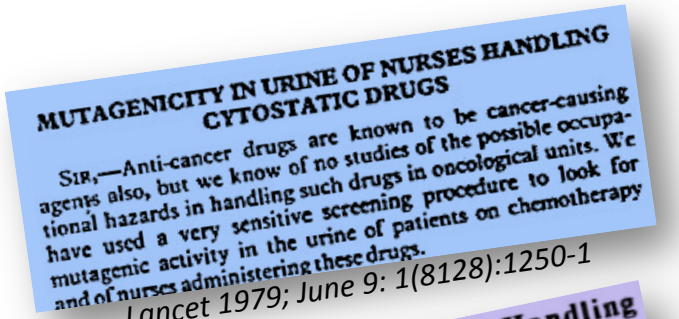


Source: Massoomi, Firouzan

Source: http://www.pharmaceuticalonline.com/doc/reducingtherisksofparticlesontheoutsideofvials0001?sectionCode=Editorial&templateCode=Single&user=31…

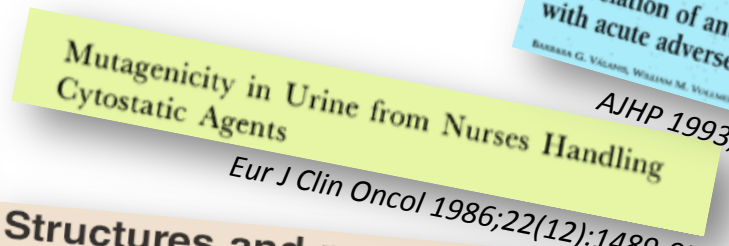
© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

What is Missing?

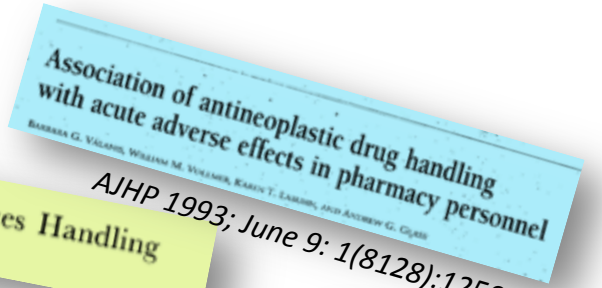

MUTAGENICITY IN URINE OF NURSES HANDLING CYTOSTATIC DRUGS

SIR,—Anti-cancer drugs are known to be cancer-causing agents also, but we know of no studies of the possible occupational hazards in handling such drugs in oncological units. We have used a very sensitive screening procedure to look for mutagenic activity in the urine of patients on chemotherapy and of nurses administering these drugs.

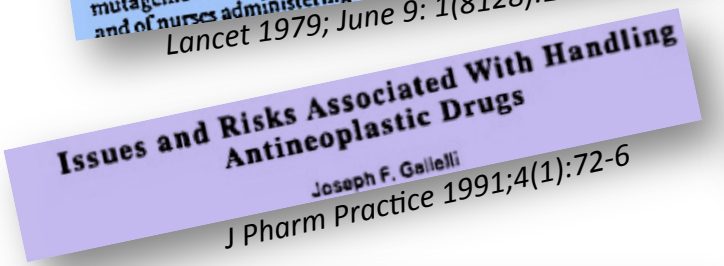
Lancet 1979; June 9: 1(8128):1250-1


Mutagenicity in Urine from Nurses Handling Cytostatic Agents

Eur J Clin Oncol 1986;22(12):1489-95

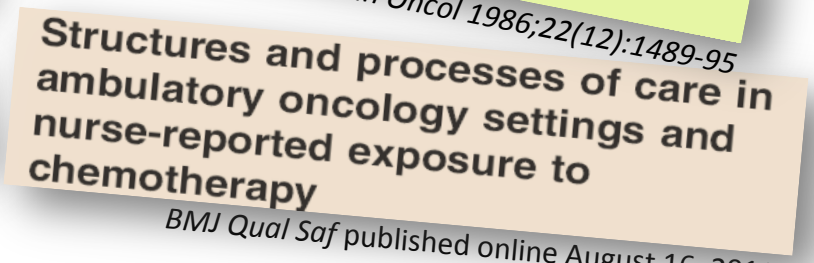

Association of antineoplastic drug handling with acute adverse effects in pharmacy personnel

AJHP 1993; June 9: 1(8128):1250-1

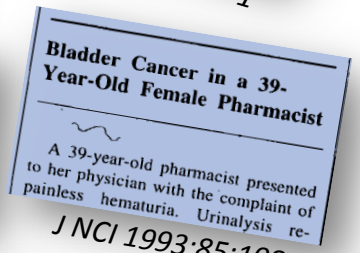

Issues and Risks Associated With Handling Antineoplastic Drugs

Joseph F. Gallelli

J Pharm Practice 1991;4(1):72-6

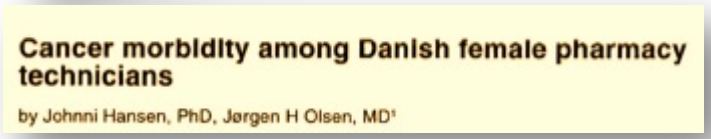

Structures and processes of care in ambulatory oncology settings and nurse-reported exposure to chemotherapy

BMJ Qual Saf published online August 16, 2011


Bladder Cancer in a 39-Year-Old Female Pharmacist

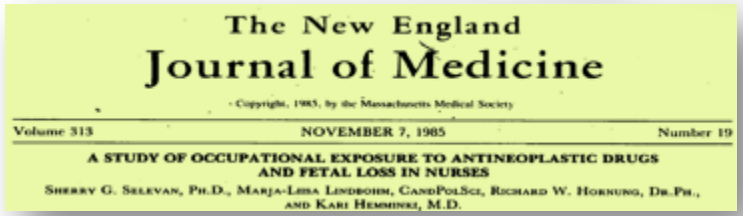
A 39-year-old pharmacist presented to her physician with the complaint of painless hematuria. Urinalysis re-

J NCI 1993;85:1089-90


Cancer morbidity among Danish female pharmacy technicians

by Johnni Hansen, PhD, Jørgen H Olsen, MD[1]

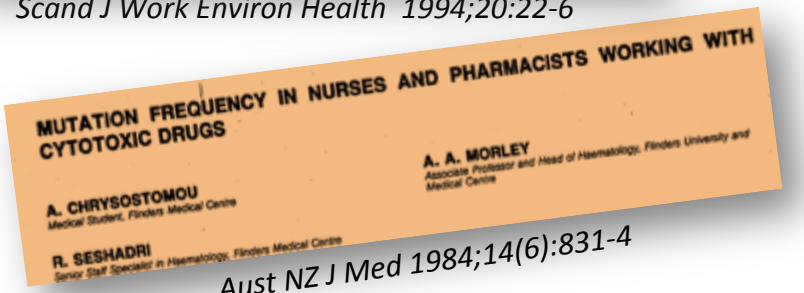
Scand J Work Environ Health 1994;20:22-6


The New England Journal of Medicine

Volume 313 NOVEMBER 7, 1985 Number 19

A STUDY OF OCCUPATIONAL EXPOSURE TO ANTINEOPLASTIC DRUGS AND FETAL LOSS IN NURSES

NEJM 1985;313(19):1173-8

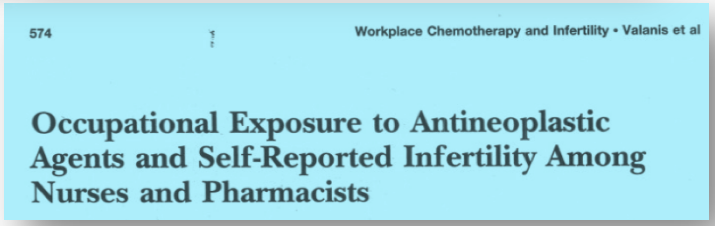

MUTATION FREQUENCY IN NURSES AND PHARMACISTS WORKING WITH CYTOTOXIC DRUGS

A. CHRYSOSTOMOU

A. A. MORLEY

R. SESHADRI

Aust NZ J Med 1984;14(6):831-4


574 Workplace Chemotherapy and Infertility • Valanis et al

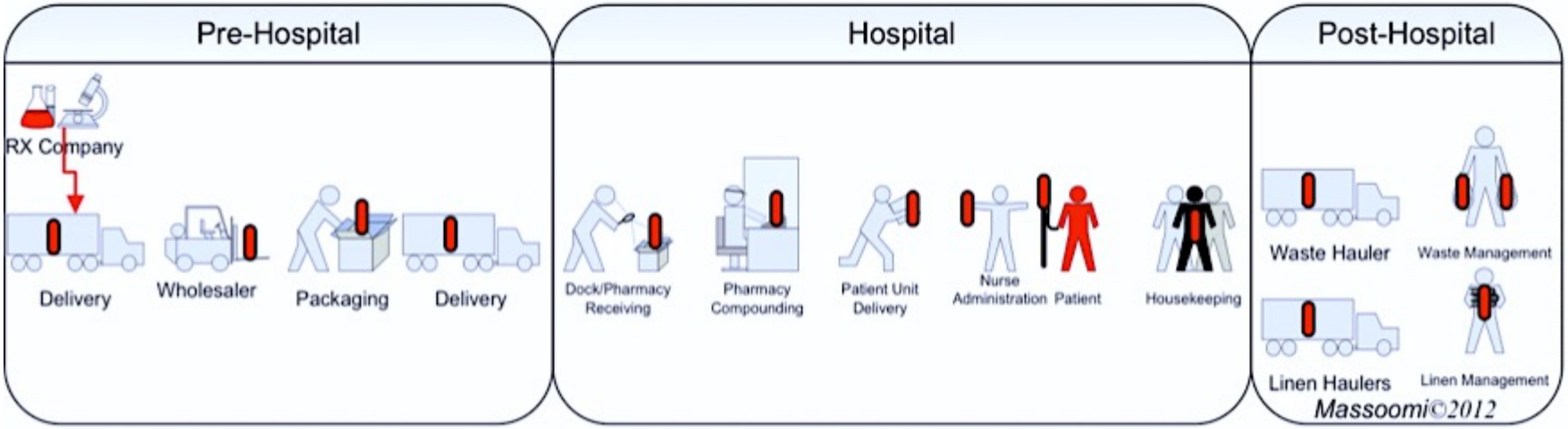
Occupational Exposure to Antineoplastic Agents and Self-Reported Infertility Among Nurses and Pharmacists

J Occup Environ Med 1997;39(6):574-80

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Introduction & Scope

"This chapter describes practice and quality standards for handling hazardous drugs (HDs) to promote patient safety, worker safety, and environmental protection. "



- Pharmacists, pharmacy technicians, nurses, physicians, physician assistants, home healthcare workers, vets, and vet technicians
- Not listed: Manufacturers; Wholesale personnel; Researchers; Family
- **Must** incorporate into Occupational Safety Plan

http://www.usp.org/usp-nf/notices/general-chapter-hazardous-drugs-handling-healthcare-settings

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

List of Hazardous Drugs

Must have a list (USP, TJC, NIOSH)

Type of HD:	Antineoplastic	Non-antineoplastic	Reproductive Risk

Risk of Exposure

NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings, 2016		
Drug	**Route**	**Class**
Adotrastizumab	IV	Antineoplastic
Arsenic trioxide	IV	Antineoplastic
Azacitidine	IV/SQ	Antineoplastic
Bacillus Calmette-Guerin(BCG)	Intravesical/Intradermal	Vaccine
Belinostat	IV	Antineoplastic
Bendamustine	IV	Antineoplastic
Bleomycin	IV	Antineoplastic
Bortezomib	IV/SQ	Antineoplastic
Brentuximab	IV	Antineoplastic
Busulfan	IV	Antineoplastic

National Institute for Occupational Safety and Health. NIOSH List of antineoplastic and other hazardous drugs in healthcare settings 2016 http://www.cdc.gov/niosh/docs/2014-138/pdfs/2014-138.pdf. Accessed March 18, 2016.

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Facilities & Engineering Controls

Designated areas **must** be available for HDs:

- Receipt & unpacking
- Storage
- Non-sterile compounding
- Sterile compounding

Photos: Firouzan Massoomi, Pharm.D, FASHP

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

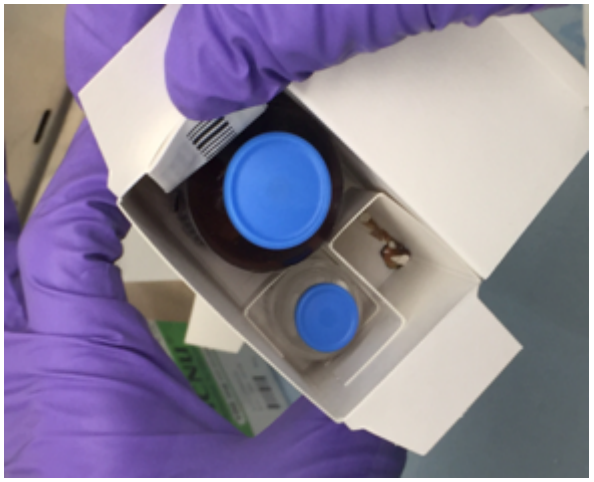
Receipt & Storage

Receipt

- HDs **must** be unpacked in a designated area
  - Neutral/Negative pressure

Storage

- **Must** be stored in manner to prevent spillage/breakage
- HDs requiring manipulation stored separately
  - Externally vented, Negative pressure,
  - 12 air changes per hour (ACPH)

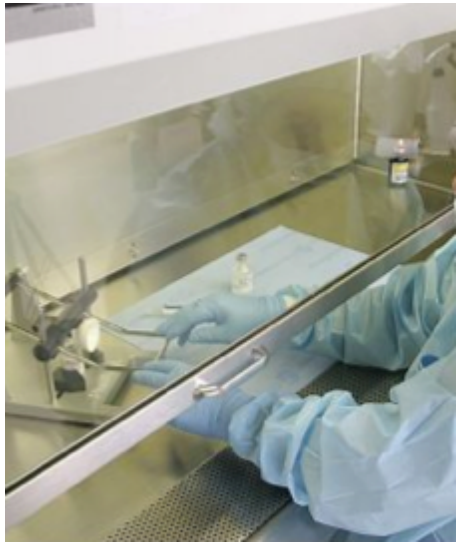


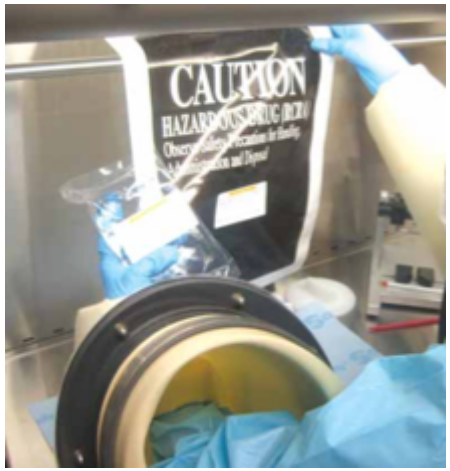
© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Compounding

Containment Primary Engineering Controls (C-PEC)

- **Low volume exemption is no longer acceptable**
- **Biological Safety Cabinet**
  - Class II BSC types A2, B1, or **B2**
- **Containment Aseptic Compounding Isolator (CACI)**
  - USP <797> = **RABS** (Restricted Access barrier system
  - MUST be in a negative pressure room
- **Must** follow UPS <795> for non-sterile compounding and USP <797> for sterile compounding





© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Compounding

Containment Secondary Engineering Controls (C-SEC)

- C-SEC= The Room
- Externally vented
- Physically separated
- Negative Pressure
  - 0.01 and - 0.03 Inches Water Column

- Eyewash Station Available
  - Bottles **NOT** Acceptable

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Containment Segregated Compounding Area (C-SCA)

- C-PEC is placed in an unclassified C-SCA with fixed walls
  - No ISO 7 or HEPA system for room
- Negative pressure 0.01 and 0.03 inches of water
- Minimum of 12 ACPH
- C-SCA (room) must be externally vented
- Sink must be placed at least 1 meter from C-PEC (hood)
  - may be either inside the C-SCA
- Only low- and medium-risk HD CSPs
  - Dating segregated compounding area is 12 hours max

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Compounding

Supplemental Engineering Controls

Closed System Transfer Devices CSTDs

Pharmacy Compounding: **Should**

Nursing Administration: **Must**

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

FDA Cleared Closed System Transfer Devices

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

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

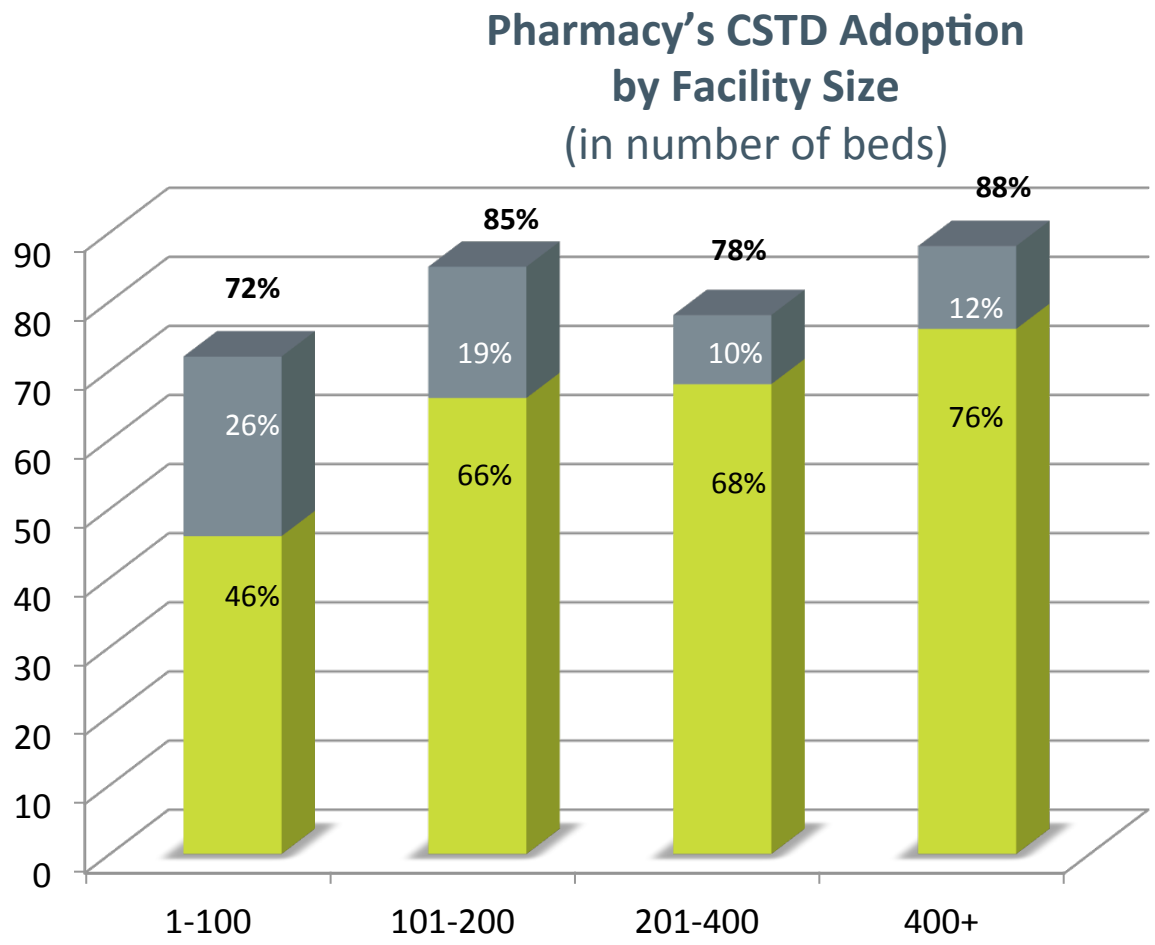
Polling Question

Has your site implemented a CSTD?

A. Yes, on the pharmacy side only
B. Yes, on the nursing side only
C. Yes, both pharmacy and nursing sides
D. Planning to implement prior to July 1, 2018
E. No plans for compliance

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

CSTDs for Drug Preparation



< **CSTD implementation will continue apace** as adoption rates are Projected to break 80% of health Systems in the next few years.

Projected adoptions

CSTDs in Use

State of Pharmacy Compounding. Pharm Purch Prod.2016; 4: S1-45
USMP/MG1/16-0084 10/16

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Who Regulates the CSTDs?

- FDA for clearance and 510K process
- FDA for ONB designation as a CSTD
- NIOSH recommending body for best practices
  - CDC and OSHA
- NO Regulatory Oversight
- CSTD defined as part of 2004 NIOSH Alert

"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"

Nothing in and Nothing Out!

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

CSTD Timeline

- **1998 First FDA approved CSTD**
- **2004** NIOSH Defines CSTSD
- **2015** NIOSH publishes or comment NIOSH Alcohol Vapor protocol
- **2016** NIOSH creates new Vapor test with new substrates based on feedback
  - Substrates mimic hazardous drugs
  - Comment period through **June 2017**
- **2016** NIOSH Town Hall Meeting CSTD Testing Protocol
- **Present: NO standardized tests for CSTDs**

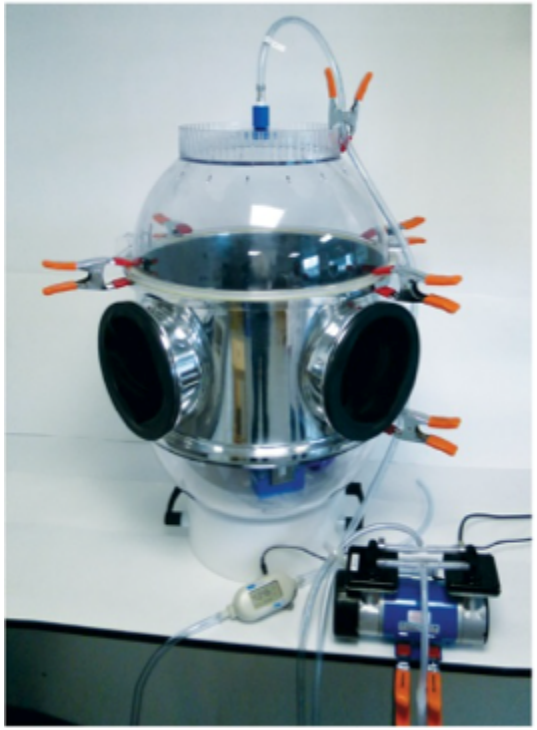
Source: https://www.federalregister.gov/articles/2015/09/08/2015-22525/a-vapor-containment-performance-protocol-for-closed-system-transfer-devices-used-during-pharmacy

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Proposed Surrogates for NIOSH Test

This information is distributed solely for the purpose of pre-dissemination peer review under applicable information quality guidelines. It has not been formally disseminated by the NIOSH. It does not represent and should not be construed to represent any agency determination or policy.

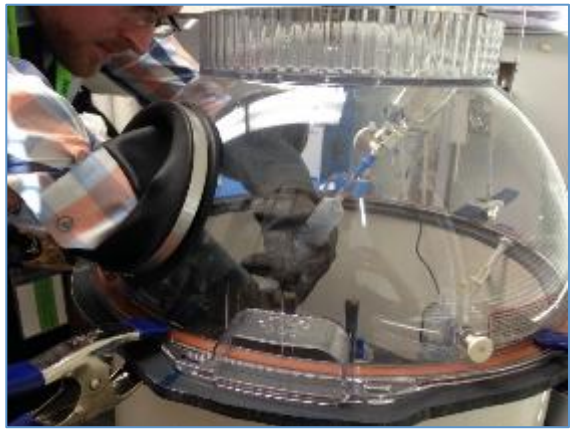
Compound
Dimethyl sulfoxide
Trimethyl phosphate
Tetramethylurea
Triacetin
Propylene glycol
Tetraethylurea
Triethyl phosphate
2-Phenoxyethanol
Tripropyl phosphate



Source: https://www.cdc.gov/niosh/docket/review/docket288a/pdfs/aperformancetestprotocolforclosedsystemtransferdevices.pdf

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Updated NIOSH Protocol



- Two positive control samples, each where one droplet of propylene glycol was placed in the chamber, produced measureable results.
- Pilot test runs were completed in accordance with the proposed protocol. Results shown below.

Positive Control ng/sample	CSTD w/air filtration during draw	CSTD w/air filtration during draw	CSTD w/air cleanser during push into vial	CSTD w/air cleanser during push into vial
3000 ng/ sample	BDL	BDL	BDL	BDL
2300 ng/ sample	BDL	BDL	BDL	BDL

BDL 'Below Detectable Limit'

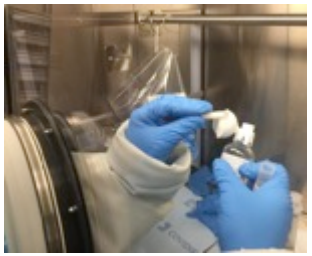
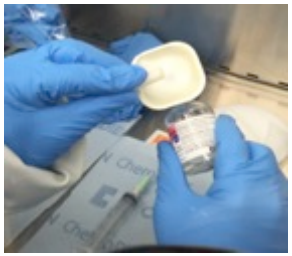
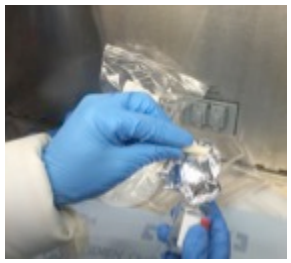
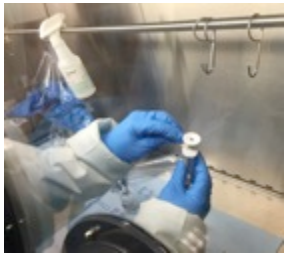
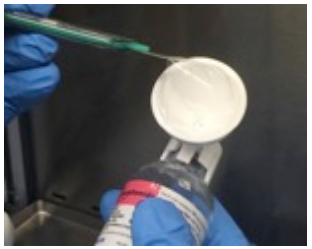
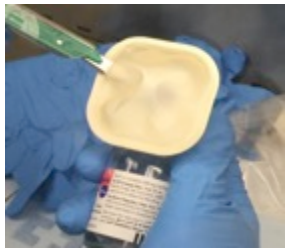
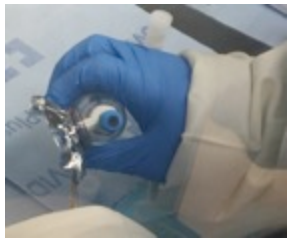
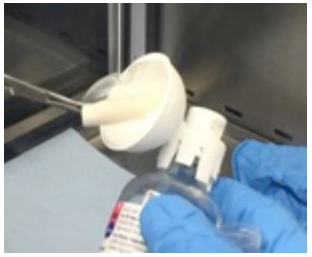
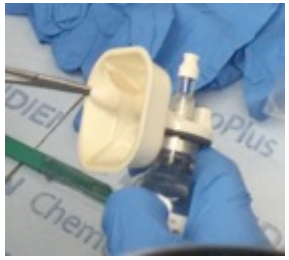
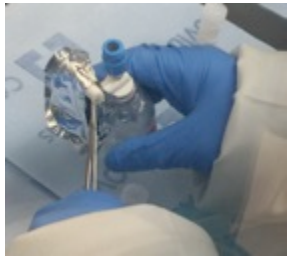
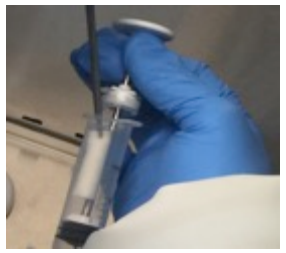
- Results show a universal protocol can used to test vented and barrier technologies

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Opening the CSTD

Do they really contain vapors?

Marker: Cyclophosphamide

Phaseal	Vialshield	Chemolock	Equashield
			
			
			

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Containment Confirmed

Cyclophosphamide Concentration ng/ft^2

CSTD	Control	Outside	Inside
Phaseal	ND/ND	ND/ND	652.04/720.99
Vialshield	ND/ND	ND/ND	ND/ND
ICU	ND/ND	ND/ND	>2000/>2000
Equishield	ND/ND	ND/ND	105.61/89.72

Negative Control	ND/ND
Positive Control	>2000/>2000

Source: Fred Massoomi, Pharm.D.; Presented at the ASHP MCM New Orleans, LA 2015

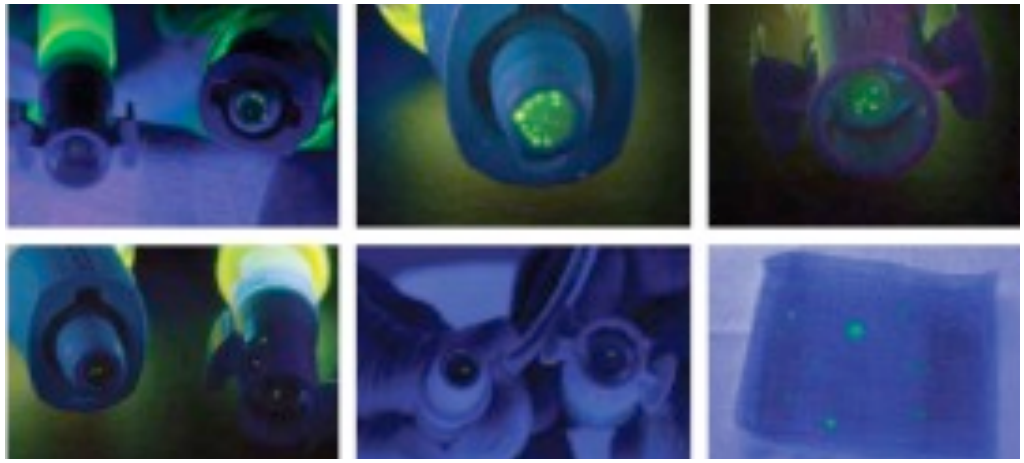
Submitted to NIOSH by: Fred Massoomi, Pharm.D., FASHP

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

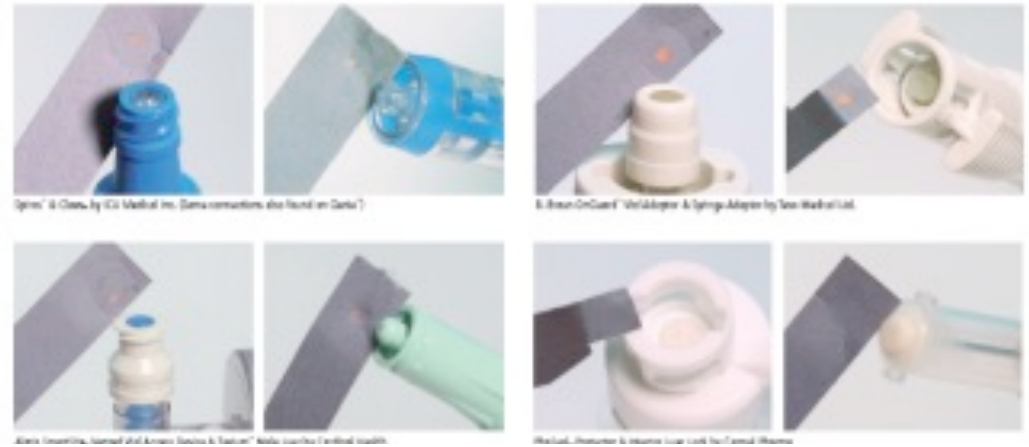
The way it was. Maybe still is.

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Visualizing Dry Connections



Fluorescein 0.05%



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.

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Thoughts On The NIOSH Tests

- Can we just agree that CSTDs are better than a needle and syringe?
- Once a test is decided upon where is FDA?
- How does the consumer interpret results?
  - Especially conflicting results
- Most tests published are outdated
- Strive for no human manipulation with HDs

Submitted to NIOSH by: Fred Massoomi, Pharm.D., FASHP

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Considerations in CSTD Selection

Key CSTD Features
1. Containment ??
2. User interface
3. Device interface
4. Integration
5. Workflow
6. Repetitive strain reduction
7. Pre-bonded components

=

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

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Non-Sterile Compounding

- **Must** follow USP <795>
- C-PEC not required for final dosage
  - Counting
  - Repackaging

- C-PEC required for some manipulations
  - Cutting, crushing
  - Containment Ventilated Enclosure

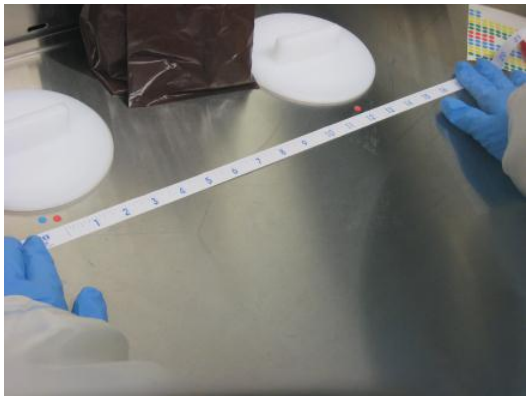
Photo Courtesy of Firouzan Massoomi, Pharm.D, FASHP

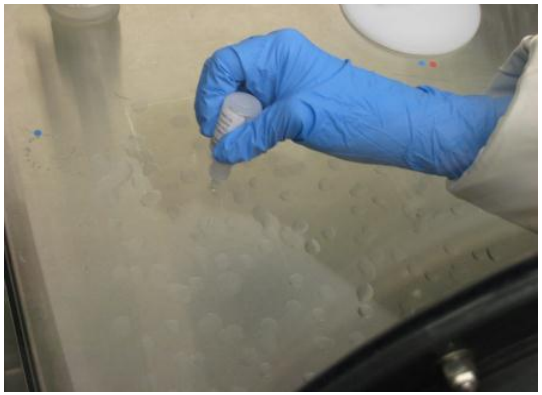
© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

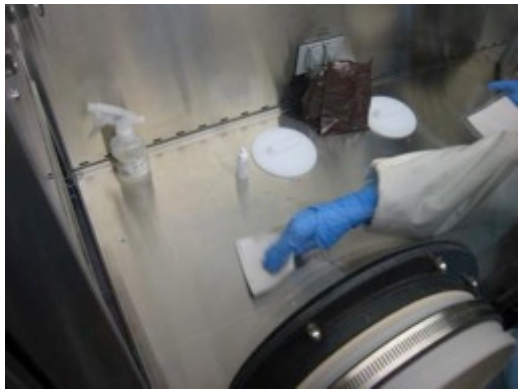
Environmental Quality & Control

Recommended ‘Routinely’ = initially then **every 6 months**

Verify cost for testing supplies







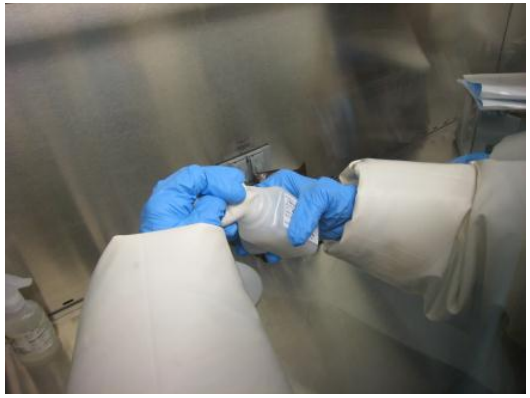


Photo Courtesy of Firouzan Massoomi, Pharm.D, FASHP

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Personal Protective Equipment

Head covers
Beard covers

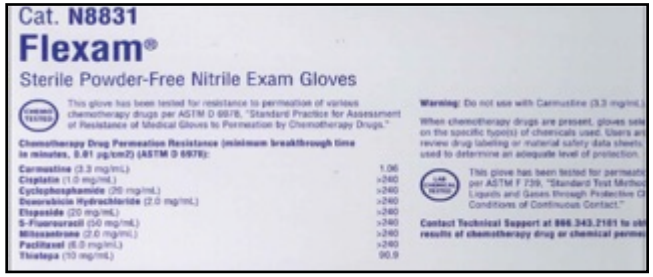
Eye protection for
-spill protection

Face mask
–limited safety

Powered air-purifying respirator
-for spills

Disposable Gowns
Polyethylene or laminate
Close in the back

2 pairs



2 pairs

Don 2 pairs prior to entry
Remove outer when leaving
Anti-skid

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Compliance with the Basics

241 nurses and 183 pharmacy practitioners who compounded hazardous drugs in the seven days prior to the survey

Compounding Practice Assessment	Nursing	Pharmacy
Lack of safe handling procedures	**20%**	**11%**
Not wearing 1 pair of gloves	8%	10%
Not wearing 2 pairs of gloves	85%	47%
Not always using a CSTD	75%	53%
Not always using a BSC/CACI	9%	15%
Lack of medical surveillance	61%	45%
Reported skin contact with HD	11%	4%

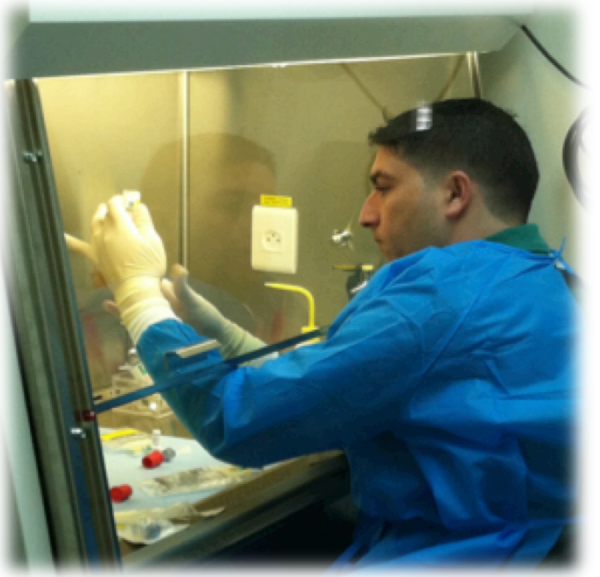
Source: Boiano JM, Steege AL, Sweeney MH. ***Journal of Occupational and Environmental Hygiene*** *Volume 12, Issue 9, 2015*

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Defect Visualizing the Concerns

Source; E.Kastango

Source; S.Eisenberg



Source; F. Massoomi

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

38

Personnel & Training

- **Must** have a designated specialist
- All personnel who handle HDs **must** be trained based on their job functions
- **Must** be assessed every 12 months
- **Must** be trained on new HDs and equipment
- **Must** document competencies

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

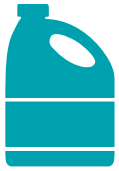
Labeling, Packaging, Transport & Disposal

- Labeling
  - Precaution clearly labeled
- Packaging
  - Protect against damage, leakage, contamination, and degradation
- Transport
  - Transport containers
  - **Must Not** transport via pneumatic tubes any liquid HDs

Photos: Firouzan Massoomi, Pharm.D, FASHP

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Deactivation, Decontaminating, Cleaning & Disinfecting



Deactivation

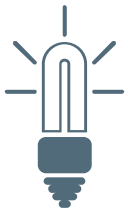
2% Sodium Hypochlorite solution

Cleaning

Tri or Quadra-valent detergent

Decontamination

- Physical wiping of surface
- Peroxide RTU (ready-to-use)



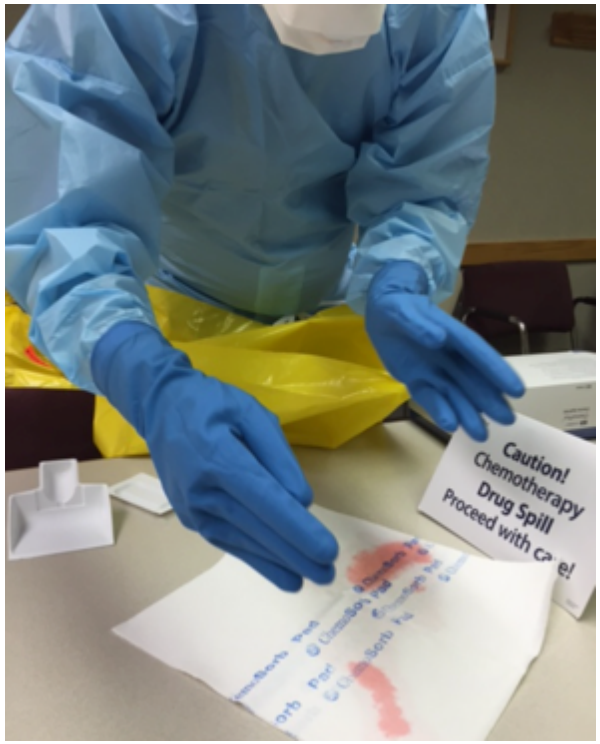
Disinfecting

- Sterile Isopropyl Alcohol 70%
- UV-C light

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Spill Control

- **Must** have proper training for spill management
- **Must** have spill kits readily available
- Spill materials disposed of as hazardous wastes
- SOPs **must** address size of spills



Photos: Firouzan Massoomi, Pharm.D, FASHP

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Segregated HD Linen

Source: Uline S-12986Y

Source; F.Massoomi

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Medical Surveillance

Plan should be **consistent with Human Resource's Plan**

Identify folks at risk of HD exposure

Quantify handling risk

Medical Assessment on hire and routinely

Develop **exit interview** assessment strategy

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

USP <800>'s Implications to Nursing Practices

- Section 1: Identified as at risk healthcare provider
- Section 2: Knowledge of institution's hazardous drug list
- Section 3: Competent Personnel
- Section 5.3.1 Non-sterile Compounding
- Section 7: Personal Protective Equipment (PPE)
- Section 14: Hazardous Drug Administration
- Section 16: Spill Control
- Section 17: Documentation and Standard Operating Procedures
- Section 18: Medical Surveillance

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

USP <800> Section 14 Administering

- Administered safely using protective devices & techniques
  - Needless systems
  - Closed System Transfer Devices
  - Spiking or priming IV tubing with non-HD solution
  - Crushing tablets in a plastic pouch
- Appropriate PPE must be donned and doffed
  - Disposed as hazardous waste
- Proper waste disposal of equipment used to administer Hazardous Drugs
- CSTD MUST be used for Hazardous Drug administration
  - CAUTION on when systems need to open for administration
- ANY manipulation or sterile and non-sterile formulation require PPE
  - Includes crushing

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Hazardous Drug Considerations What Happens After Treatment?

Exposure of family members to **antineoplastic drugs via excreta of treated cancer patients**

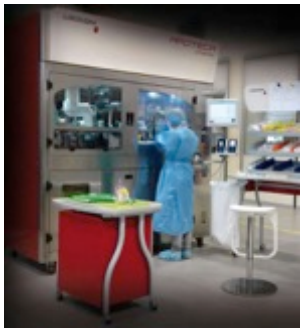
Journal of Oncology Pharmacy Practice

- 42 Urine samples were collected from the three patients and their family members; ALL samples were positive for cyclophosphamide and 5-FU
- Cyclophosphamide detected levels of **0.03–7.34 ng/cm2** in 8 of the 12 wipe samples from the homes
- Measured contamination of the home setting and exposure of family members

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Hazardous Drug Consideration

Monster Robots on the US market



Micro-Robot on the US market

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Surveying Bodies for Hazardous Drug Handling

- State Boards of Pharmacy
- FDA: Food and Drug Administration
- CMS: Centers for Medicare/Medicaid Services
- OSHA: Occupational Safety & Health Administration

- TJC: The Joint Commission
- DNV Healthcare
- HFAP: AOA's Healthcare Facilities Accreditation Program
- ACHC: Accreditation Commission for Healthcare
- AAASC/FASA: Ambulatory Surgical Centers

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

The Joint Commission

Log In | Request Guest Access

Forgot password? | Log In Help

Contact Us |

Search

Accreditation | Certification | Standards | Measurement | Topics | Abo

Home > Certification > Medication Compounding > Medication Compouding Providers

Twitter Facebook

Medication Compounding Providers

Tuesday 5:23 CST, February 21, 2017

USP U.S. Pharmacopeial Convention

Global Expertise
Trusted Standards
Improved Health

First customer certified in February 2017.

© Copyright Visante, Inc. All rights reserved. | www.visanteinc.com

Questions/Discussion

Visante

© Copyright Visante, Inc. All rights reserved | www.visanteinc.com