1-11-2020

Precautions & Handling of Hazardous Chemotherapeutic Agents

Paula Sayegh
Miami Cancer Institute, PaulaMS@baptisthealth.net

Precautions & Handling of Hazardous Chemotherapeutic Agents

Paula Sayegh, Pharm.D., BCPS
PGY-2 Oncology Pharmacy Resident
Miami Cancer Institute | Baptist Hospital of Miami
January 11, 2020

Objectives

- Review NIOSH listed hazardous drugs (HDs) requiring handling precautions in hospital and community settings
- Discuss the importance and highlight proper handling and disposal of hazardous chemotherapy as outlined in USP <800>
- Review counseling points for precautions and handling of oral chemotherapy agents at home

Pre-Assessment Questions

- True or False
  - Patients on oral chemotherapy do not need to wear gloves during administration
- True or False
  - Oral chemotherapy is safe to dispose in the everyday trash, as long as it is in its original container
- True or False
  - Precautions during every day handling are to protect the hazardous drug, not the user

What is a Hazardous Drug (HD)?

- Term first used by ASHP in 1990
- National Institute for Occupational Safety and Health (NIOSH) definition:
  - Any drug (or active pharmaceutical ingredient) that is identified as having ≥ 1 of the following:
    - Carcinogenicity
    - Teratogenicity (or developmental toxicity)
    - Reproductive toxicity *in humans*
    - Organ toxicity (at low doses *in humans or animals*)
    - Genotoxicity
    - Drug that mimics an existing hazardous drug in structure or toxicity

NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings 2016

Why do we care about HDs?

- ~8 million US healthcare workers are potentially exposed to HDs
  - Contamination can occur during transport, compounding, cleaning and administration
  - May lead to absorption by healthcare workers

- Consider HD use at home causing contamination
  - Oral chemotherapy

NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings 2016

Types of Exposure

- Dermal contact and absorption
- Inhalation
- Injection
- Ingestion

Patient Care Areas

- Contamination also extends beyond the pharmacy and into patient care areas
  - Not only patients in these areas

- Avoiding surface contamination
  - Surface contamination has been definitively linked to hand contamination

NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings 2016

What are the potential risks?

- Acute effects
  - Hair loss
  - Cardiac toxicity
  - Kidney damage
  - Hearing loss
  - Nausea
  - Rashes
- Long term effects
  - Cancer
  - Reproductive outcomes
  - Infertility

NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings 2016

Who is at risk?

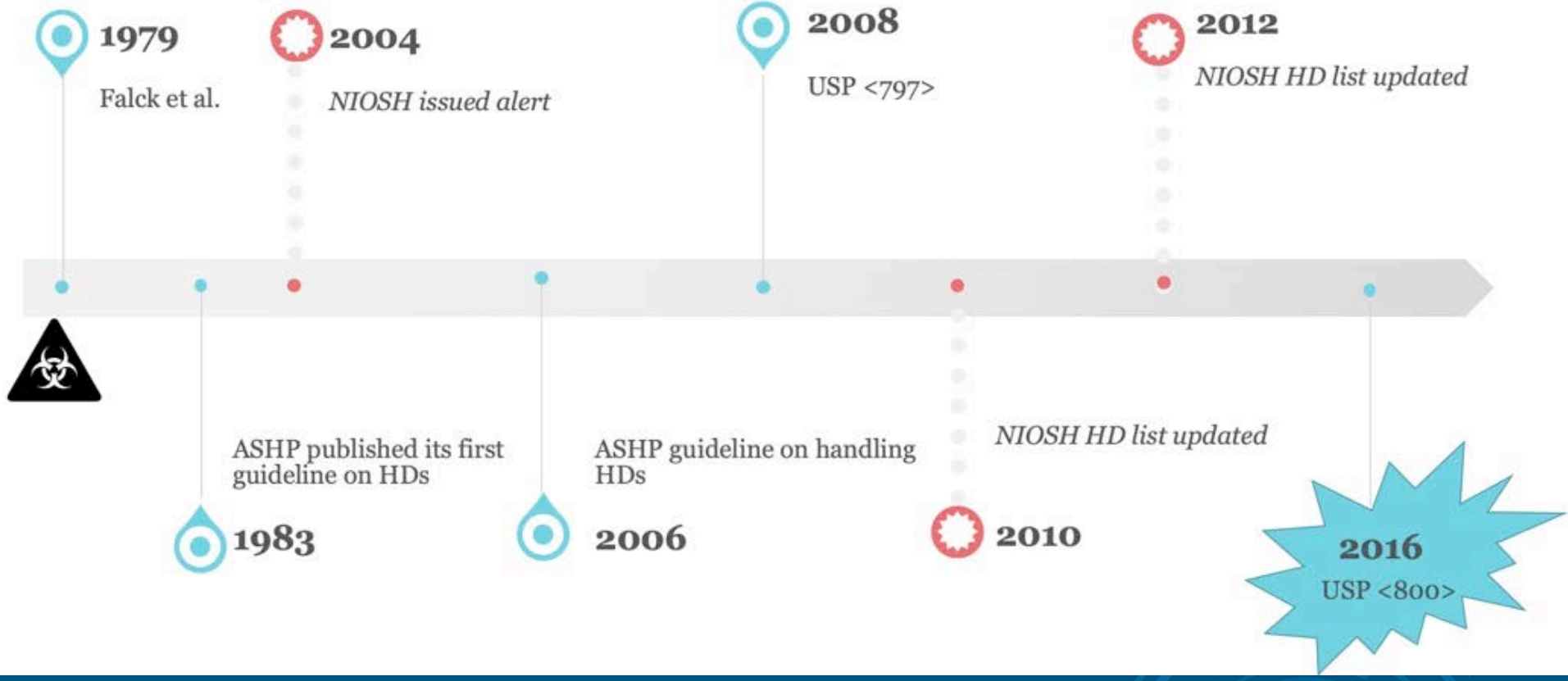
Anyone handling hazardous drugs is at risk of exposure[1]

- Pharmacists
- Pharmacy Technicians
- Nurses
- Physicians
- Surgeons
- Physician Assistants
- Respiratory Therapists
- Home Health Aides
- Nurses' Aides
- Housekeeping
- Janitorial Services
- Environmental Services
- Veterinarians
- Veterinarian Technicians
- Veterinarian Assistants

USP <800> Inforgraphic

NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings 2016

The Evolution of Safe Handling



The Oncology Nurse. 9 September 2019

Clin J Oncol Nurse. 2015; 20(4):377-384

NIOSH HD List

CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

All A-Z Topics

Search | All CDC

The National Institute for Occupational Safety and Health (NIOSH)

NIOSH Publications & Products > NIOSH-Issued Publications

NIOSH Publications & Products

NIOSH-Issued Publications

NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings, 2016

Publication Types

Order Publications

Promoting productive workplaces through safety and health research NIOSH

NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings, 2016

DHHS (NIOSH) Publication Number 2016-161 (Supersedes 2014-138) Sept 2016

The National Institute for Occupational Safety and Health (NIOSH) Alert: Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings was published in September

https://www.cdc.gov/niosh/docs/2016-161/default.html

NIOSH HD List

- HDs are categorized into three groups:
  - Group 1: Antineoplastic drugs
  - Group 2: Non-antineoplastic drugs
  - Group 3: Reproductive risk
- NIOSH notes that many drugs in group 1 and 2 also carry reproductive risk
- Document provides guidance for personal protective equipment (PPE) and ventilated engineering controls

NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings 2016

NIOSH HD List

- Drugs with safe-handling guidelines from the manufacturer are automatically put on the list
- NIOSH internal committee performs an initial review of all new FDA drug approvals and new warnings on existing drugs for a 2-year period
- This is followed by an expert panel that reviews the proposals (additions or deletions)

NIOSH HD List

Notice

September 25th, 2019

The manufacturers of trabectedin (Yondelis®), inotuzumab ozogamicin (Besponsa™), and polatuzumab vedotin (Polivy™) recommend that they be handled as hazardous drugs. Therefore, NIOSH considers these drugs to be included in Table 1 of the NIOSH listof hazardous drugs. For additional information, see the package inserts for these drugs.

Drug	AHFS Classification	Links	Date Approved
trabectedin (Yondelis®)	10:00 Antineoplastic Agents	DailyMed	October 23, 2015
inotuzumab ozogamicin (Besponsa™)	10:00 Antineoplastic Agents	DailyMed	August 17, 2017
polatuzumab vedotin (Polivy™)	10:00 Antineoplastic Agents	DailyMed	June 10, 2019

https://www.cdc.gov/niosh/docs/2016-161/default.html

NIOSH Recommendations

- Each organization should create its own list of drugs considered to be hazardous, based on drugs in its formulary

- Primarily because reliance on lists of HDs provided by NIOSH quickly becomes outdated
  - If you use a drug that is not included in the list, check the available literature to see whether the unlisted drug should be treated as a HD

NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings 2016

Handling and Disposal in Healthcare settings

United States Pharmacopeia (USP)

- USP is the only independent, not-for-profit, nongovernmental pharmacopeia in the world
  - Develop and revise standards
    - Standards are enforceable by the FDA and state boards of pharmacy
    - Identity, strength, quality and purity
      - Medicines
      - Food ingredients
      - Dietary supplements

https://www.usp.org/compounding/general-chapter-hazardous-drugs-handling-healthcare

United States Pharmacopeia (USP)

- Important chapters to know about
  - USP <795>
    - Non-sterile compounding
  - USP <797>
    - Sterile compounding
  - USP <800>
    - HD handling in healthcare settings
  - USP <825>
    - Compounding radiopharmaceutical drugs

- Revisions for <795> and <797> have been released

USP <800>

- Describes the practice & quality standards for handling HDs
  - Philosophy: no acceptable level of exposure to HDs
  - Purpose is to promote the protection of:
    - Patients
    - Healthcare worker safety
    - Environment
- Applies to **all healthcare personnel** who handle HDs and all entities that store, prepare, transport, or administer them
- Introduces element of containment

USP Compounding Expert Committee. USP General Chapter <800>

USP <800>

- Management of HDs must include:
  - A list of HDs
  - Facility and engineering controls
  - Competent personnel
  - Safe work practices
  - Proper use of personal protective equipment (PPE)
  - Policies for HD waste segregation and disposal

USP Compounding Expert Committee. USP General Chapter <800>

Maintain a HD List

- Must use NIOSH list as a basis
- Agents on the NIOSH list that must follow USP <800>
  - HD active pharmaceutical ingredients
  - All antineoplastics that require manipulation
- Other agents on the NIOSH list
  - Perform risk assessment
  - If no risk assessment performed, must handle as hazardous and according to USP <800> requirements
- Entity must review their list at least every 12 months

USP Compounding Expert Committee. USP General Chapter <800>

Assessment of Risk

- Consider the following:
  - Category of HD based on NIOSH
  - Dosage form
  - Risk of exposure
  - Packaging
  - Any manipulation that might be required

- Examples of assessments of risk can be found online
  - National Community Pharmacy Association

USP Compounding Expert Committee. USP General Chapter <800>
P Kienle and K Douglas. Perform an assessment of risk to comply with USP <800>

Facilities

- Restrict access to areas where HDs are handled
  - Protects persons not involved in HD handling
- Designated areas must be available for:
  - Receipt and unpacking
  - Storage of HDs
  - Nonsterile HD compounding (if performed by the entity)
  - Sterile HD compounding (if performed by the entity)
- Also use dedicated equipment
  - Ex: designated counting tray for HDs

USP Compounding Expert Committee. USP General Chapter <800>

Receipt & Storage

- Antineoplastic HDs and all HD APIs must be unpacked in an area that is neutral/normal or negative pressure
  - Do not unpack in sterile compounding areas or in positive pressure areas

- HDs and APIs requiring manipulation **must be stored separately** from non hazardous medications in an externally ventilated, negative-pressure room with at least 12 air changes per hour (ACPH)

USP Compounding Expert Committee. USP General Chapter <800>

Engineering Controls

- Required to protect the preparation from cross-contamination and microbial contamination (if sterile compounding)

- Engineering controls for containment
  - Primary
  - Secondary
  - Supplemental

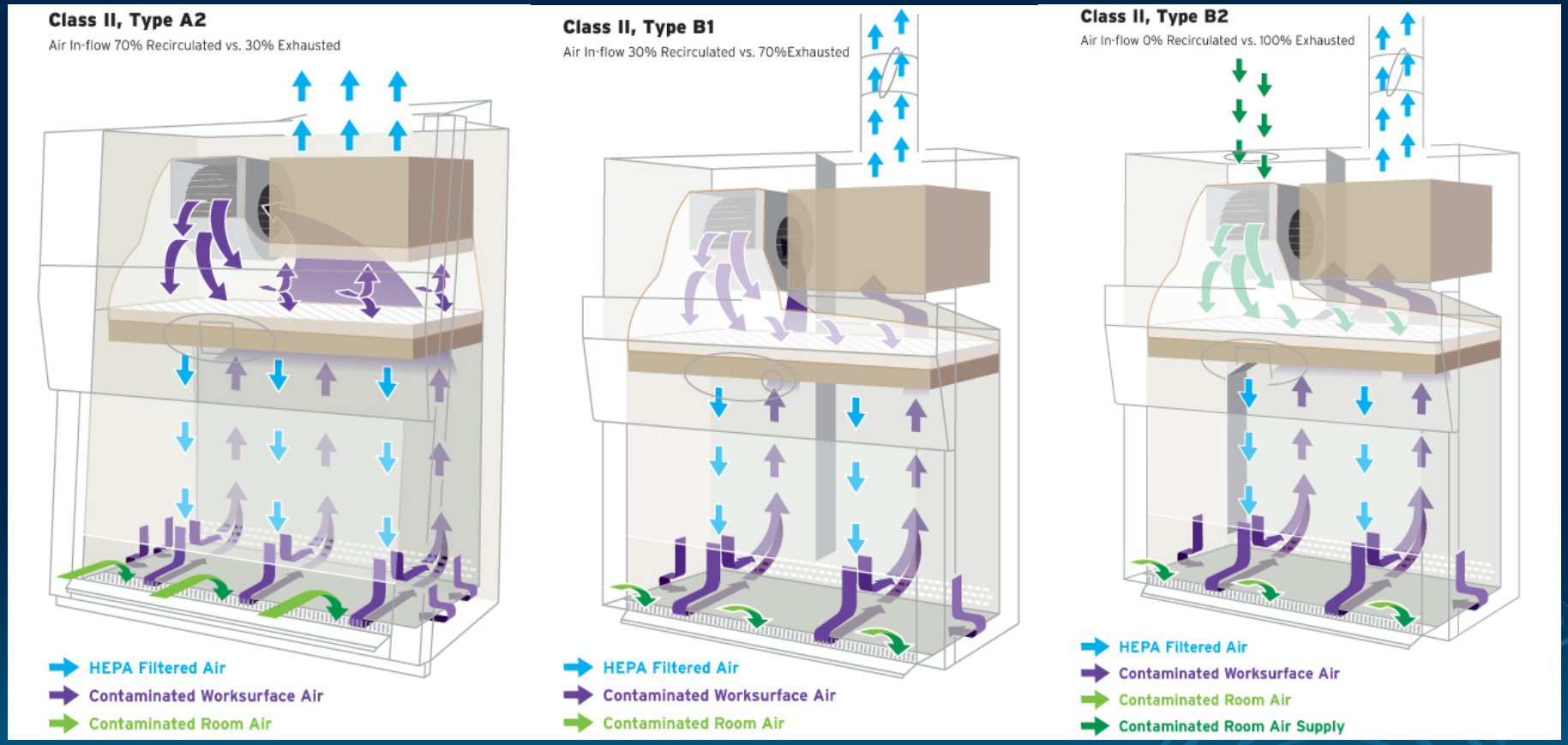
USP Compounding Expert Committee. USP General Chapter <800>

Engineering Controls

- Containment primary engineering control (C-PEC)
  - Ventilated device designed to minimize worker and environmental HD exposure
  - Required:
    - Class II Biological Safety Cabinets (BSC)
      - *OR*
    - Compounding Aseptic Containment Isolator (CACI)

USP Compounding Expert Committee. USP General Chapter <800>

Class II BSCs



https://www.nuaire.com/how-class-two-bsc-work

CACI

- Compounding aseptic containment isolator (CACI)

https://www.nuaire.com/how-class-two-bsc-work

Engineering Controls

- Containment secondary engineering control (C-SEC)
  - The room in which the C-PEC is placed, which must:
    - Be externally vented
    - Be physically separated (i.e., a different room from other preparation areas)
    - Have an appropriate air exchange (e.g., ACPH)
    - Have a negative pressure

USP Compounding Expert Committee. USP General Chapter <800>

Engineering Controls

- Supplemental engineering controls
  - Closed system transfer devices (CSTD)
    - MUST be used when administering antineoplastic HDs when the dosage form allows
      - Not mandated for use in compounding
    - CSTDs known to be physically or chemically incompatible with a specific HD must not be used for that HD

USP Compounding Expert Committee. USP General Chapter <800>

Personal Protective Equipment (PPE)

- Provides worker protection to reduce exposure to hazardous drug (HD) aerosols and residues
- Appropriate PPE must be worn when handling HDs, including during:
  - Receipt
  - Storage
  - Transport
  - Compounding (sterile & nonsterile)
  - Administration
  - Deactivation/decontamination, cleaning and disinfecting
  - Spill control
  - Waste disposal

USP Compounding Expert Committee. USP General Chapter <800>

Chemotherapy Gloves

- Must meet American Society for Testing and Materials (ASTM) standard D6978
- Should be worn when handling all HDs
  - Including non-antineoplastics & for reproductive risk HDs
- Must be powder free
- Inspect prior to use
- When used for sterile compounding, **outer gloves must be sterile**
- Should be changed every 30 minutes unless otherwise recommended by the manufacturer

USP Compounding Expert Committee. USP General Chapter <800>

Chemotherapy Gloves

Chemotherapy Gowns

- Must be disposable and shown to resist permeability
- Must close in the back, be long sleeved, and have closed cuffs that are elastic or knit
- Lab coats, scrubs or other absorbent materials are not appropriate
- Potentially contaminated clothing must not be taken home under any circumstance

USP Compounding Expert Committee. USP General Chapter <800>

Head, Hair, Shoe and Sleeve Covers

- Provide protection from contact with HD residue
- When compounding HDs, a 2nd pair of show covers must be donned before entering the cleanroom and doffed when exiting
- Shoe covers worn in HD handling areas must not be worn to other areas

USP Compounding Expert Committee. USP General Chapter <800>

Eye and Face Protection

- Appropriate eye and face protection must be worn when there is a risk for spills or splashes of HD
  - Administration in the surgical suite or cleaning a spill

- Goggles & face shields

USP Compounding Expert Committee. USP General Chapter <800>

Personal Protective Equipment (PPE)

Coverall or "Bunny Suit"

Consider adopting bunny suits to ensure overall protection for staff, while minimizing cross-contamination to adjacent locations and colleagues.

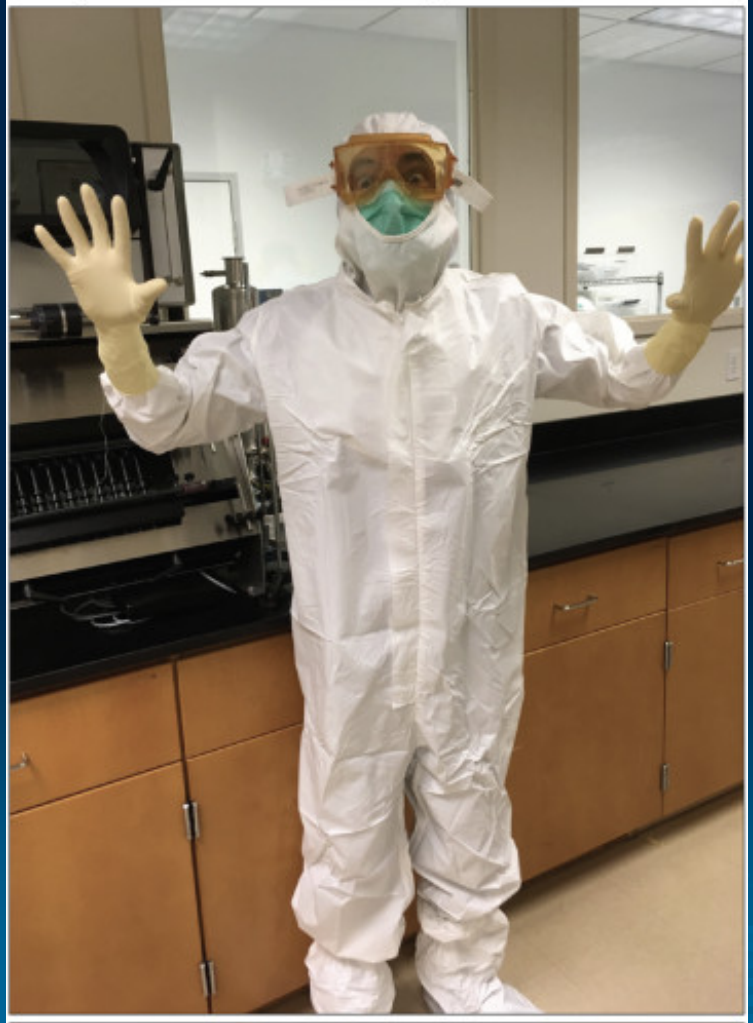


Image courtesy of Fred Massoomi

Disposal of Used PPE

- Consider all PPE worn when handling HDs contaminated

- Place them in appropriate waste container per local, state, and federal regulations

USP Compounding Expert Committee. USP General Chapter <800>

Personal Protective Equipment

PPE	Sterile Compounding	Non-Sterile Compounding	Cleaning	Unpacking Orders	Administering	Cleaning up Spills
Gowns	✓	✓	✓	*Per institutional SOPs*		
Head / Hair Covers	✓	✓	*Per institutional SOPs*			
Shoe Covers	2 pairs	2 pairs	*Per institutional SOPs*			
Chemotherapy gloves	2 pairs (outer must be sterile)	2 pairs	2 pairs	✓	2 pairs	*Per institutional SOPs*
Eye / Face Protection	*Per institutional SOPs*		If splashing likely	*Per institutional SOPs*		✓
Respiratory Protection	*Per institutional SOPs*		Yes when cleaning under surface of C-PEC	Yes if HDs not contained in plastic	*Per institutional SOPs*	Yes when spills to large for a spill kit

Smith A. USP <800> What you need to know. Illinois Pharmacy Association
USP Compounding Expert Committee. USP General Chapter <800>

Disposal

- All personnel who perform routine custodial waste removal/cleaning activities in HD handling areas
  - Must be trained in appropriate procedures!
    - To protect themselves and the environment

- Disposal of all HD waste (including unused HDs and trace-contaminated PPE) must comply with all applicable federal, state, and local regulations

USP Compounding Expert Committee. USP General Chapter <800>

Disposal of HDs

CHEMO

Yellow Chemo Bin

For TRACE (Empty) Chemotherapy Waste with biohazardous/ infectious waste symbol

- Trace PPE
- Empty Chemo IV Bags
- Empty Chemo Vials

Anything that is not considered EMPTY is disposed in BLACK Container

What about cleaning?

- Must establish written procedures for decontamination, deactivation and cleaning
  - For sterile compounding, also disinfection
- Must wear appropriate PPE
  - 2 pairs of gloves and impermeable disposable gowns
- Wet wipe approach

USP Compounding Expert Committee. USP General Chapter <800>

4 Step Cleaning Process

- All areas and reusable equipment where HDs are handled must be deactivated/decontaminated & cleaned

Cleaning Step	Purpose	Example Agents
Deactivation	Render compound inert or inactive	• Sodium hypochlorite *or* EPA registered oxidizer • Peroxide formulations
Decontamination	Remove HD residue	• Sterile alcohol • Sterile water • Peroxide • Sodium hypochlorite
Cleaning	Remove organic and inorganic material	• Germicidal detergent
Disinfection	Destroy microorganisms	• Sterile alcohol and/or EPA-registered disinfectant

USP Compounding Expert Committee. USP General Chapter <800>

Deactivation & Decontamination

- Carefully selected agent
  - Hazardous byproducts
  - Respiratory effects
    - Some solutions may require the addition of respiratory protection
  - Caustic damage to surfaces
    - Sodium hypochlorite causes corrosion
      - MUST be neutralized with sodium thiosulfate or by following with another agent (ex: sterile alcohol) to remove it

Deactivator

Decontaminator

USP Compounding Expert Committee. USP General Chapter <800>

Cleaning & Disinfecting

- Cleaning
  - Removal of contaminants and HD residue
  - Detergents or solvents

- Disinfection
  - Kills microorganisms
  - Used after cleaning
  - Sterile compounding areas

Cleaner & Disinfectant

USP Compounding Expert Committee. USP General Chapter <800>

Spills

- MUST be contained and cleaned immediately
  - By qualified personnel with appropriate PPE
- Facility dependent processes
  - Must have a clear policy and checklist
    - Document competence of personnel, circumstances and management of spills
      - Spill kits
      - Respirators (if too large for a spill kit)

USP Compounding Expert Committee. USP General Chapter <800>

Spill Kit Example

Oral Chemotherapy Handling and Disposal

Oral Chemotherapy

- Traditional oral chemotherapy agents available since 1950s
- Prescriptions of oral chemotherapy are becoming more common
- Make up around 25% of the oncology market
- Convenient but not just any pill
  - Still requires extra caution

Association of Community Cancer Centers. Oral chemotherapy: what your patients need to know

Oral Chemotherapy

Oral chemotherapy: Handling Safely at Home | Dana-Farber Cancer Institute

https://www.dana-farber.org/chemotherapy/oral-chemotherapy/

Safe Handling at Home

- Principles of safe handling
  - Keep in original container
  - Storage
    - Store in a cool, dry place and away from sunlight
    - Safe space away from children and pets
  - Wash hands before and after handling
  - Do not crush, break or chew
  - Stay consistent with administration
  - Do not dispose in the toilet or in the garbage

- Incorporate these key items in your counseling

https://www.dana-farber.org/chemotherapy/oral-chemotherapy/

Wearing Gloves at Home

- Gloves help protect caregivers from absorbing chemotherapy through the skin
  - Some package inserts recommend gloves to be used
  - Should be worn any time chemotherapy is handled by someone other than the patient

- Patients do not need to wear gloves when taking their medication
  - Washing hands thoroughly before and after handling will help minimize exposure to other household members

https://www.dana-farber.org/chemotherapy/oral-chemotherapy/

Don’t Forget!

- Topical Chemotherapy
  - Applied to the skin
  - Cream, gel, or ointment
  - Example: 5-fluorouracil
  - Consider recommending the use of gloves when applying topical agents

Oral/Topical Chemotherapy Disposal

- Improper disposal pollutes the water and ground and is toxic to plants, animals and humans

- Only a few drug manufacturers provide instructions on oral chemotherapy disposal
  - Celgene, the maker of lenalidomide, thalidomide, and pomalidomide provides patients with packaging material to return unused medications

Association of Community Cancer Centers. Oral chemotherapy: what your patients need to know

Oral/Topical Chemotherapy Disposal

- Most cities have a hazardous waste disposal policy that patients can follow
  - Most fire/police stations and retail pharmacies will not dispose of oral chemotherapy
- Different options for patients
  - Contact dispensing pharmacy for disposal
  - Hazardous waste pick up through state of Florida
  - Drug take back site or program

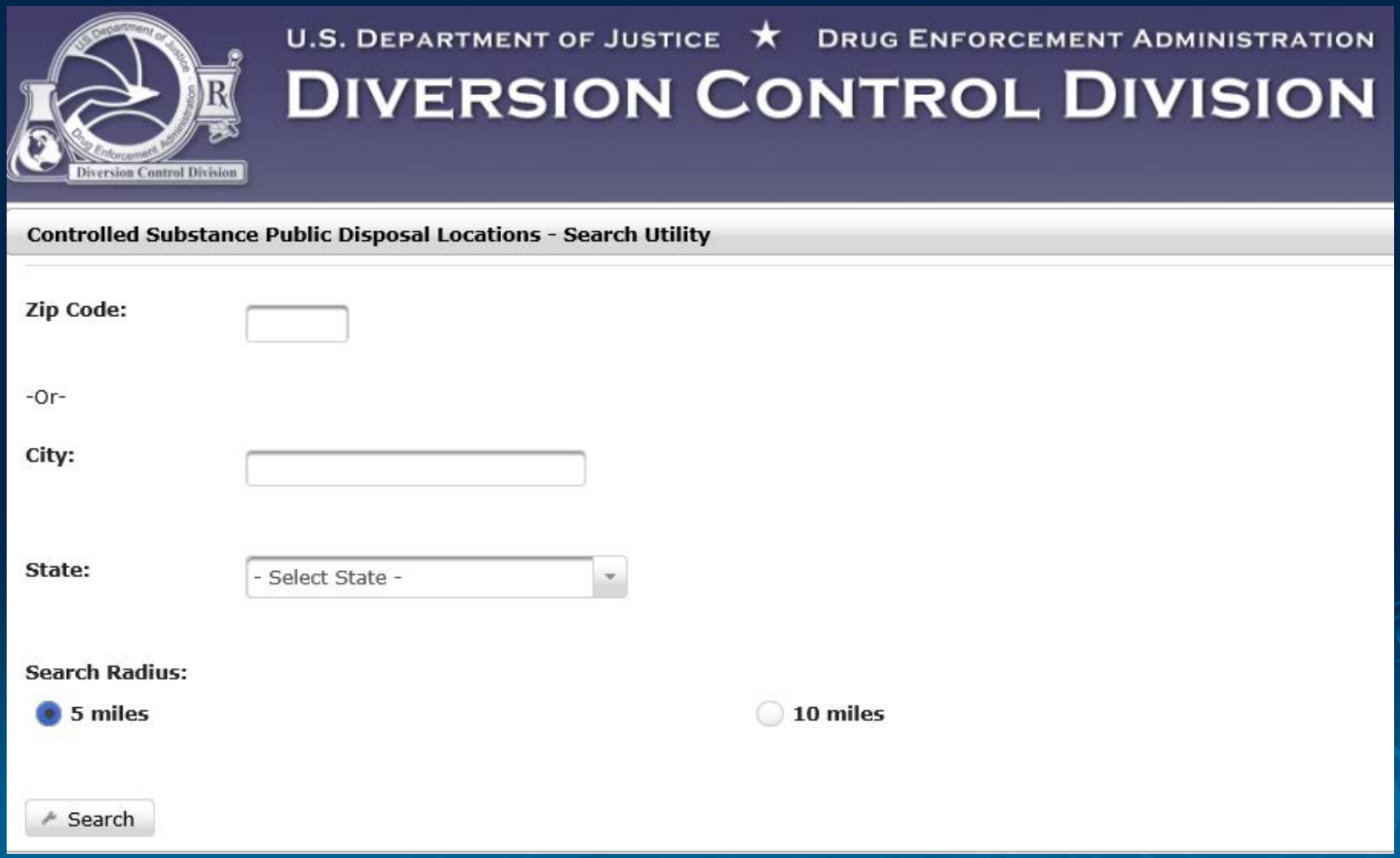
Association of Community Cancer Centers. Oral chemotherapy: what your patients need to know

Oral/Topical Chemotherapy Disposal

- Drug take back site or program
- Patients can locate an authorized collection location in their area online
  - https://apps2.deadiversion.usdoj.gov/pubdispsearch/spring/main?execution=e1s1

Association of Community Cancer Centers. Oral chemotherapy: what your patients need to know

Oral/Topical Chemotherapy Disposal



https://apps2.deadiversion.usdoj.gov/pubdispsearch/spring/main?execution=e1s1

DEA National Drug Take-Back Day

- **April 25, 2020**
- Liquid medications and IV medications are not accepted
- Results of October 2019
  - Total Law Enforcement Participation: **4,896**
  - Total Collection Sites: **6,174**
  - Total Weight Collected: **882,919 lbs. (441.5 Tons)**

https://www.oncolink.org/blogs/2019/10/tomorrow-is-national-prescription-drug-take-back%E2%80%8B-day/

Assessment Questions

- True or False
  - Patients on oral chemotherapy do not need to wear gloves during administration
- True or False
  - Oral chemotherapy is safe to dispose in the everyday trash, as long as it is in its original container
- True or False
  - Precautions during every day handling are to protect the hazardous drug, not the user

Assessment Questions

- True or False
  - Patients on oral chemotherapy do not need to wear gloves during administration
- True or False
  - Oral chemotherapy is safe to dispose in the everyday trash, as long as it is in its original container
- True or False
  - Precautions during every day handling are to protect the hazardous drug, not the user

Assessment Questions

- True or False
  - Patients on oral chemotherapy do not need to wear gloves during administration
- True or False
  - Oral chemotherapy is safe to dispose in the everyday trash, as long as it is in its original container
- True or False
  - Precautions during every day handling are to protect the hazardous drug, not the user

Assessment Questions

- True or False
  - Patients on oral chemotherapy do not need to wear gloves during administration
- True or False
  - Oral chemotherapy is safe to dispose in the everyday trash, as long as it is in its original container
- True or False
  - Precautions during every day handling are to protect the hazardous drug, not the user

Thank You!

We all have that one guy that takes USP 800 way too seriously

Questions?

Email: paulams@baptisthealth.net

References

1. The Evolution of the Safe Handling of Hazardous Chemotherapy Drugs. The Oncology Nurse. 9 September 2019. Available at http://www.theoncologynurse.com/ton-supplements/ton-supplements/16784-the-evolution-of-the-safe-handling-of-hazardous-chemotherapy-drugs. Accessed January 5, 2020.
2. National Institute for Occupational Safety and Health. NIOSH List of Antineoplastic and Other Hazardous Drugs in Healthcare Settings 2016. https://www.cdc.gov/niosh/docs/2016-161/default.html. Accessed January 5, 2020.
3. USP Compounding Expert Committee. USP General Chapter <800> Hazardous Drugs–Handling in Healthcare Settings. 2019. The United States Pharmacopeial Convention.
4. M. Polovich, ed., Safe Handling of Hazardous Drugs (Pittsburgh: Oncology Nursing Society, 2011). Based on information from McDiarmid and Curbow 1992.
5. Association of Community Cancer Centers. Oral chemotherapy: what your patients need to know. www.accc-cancer.org. November-December 2014. Accessed January 6, 2020.
6. S Eisenberg. A Call to Action for Hazardous Drug Safety: Where We Have Been and Where We Are Now. Clin J Oncol Nurse. 2015; 20(4):377-384.
7. USP infographic. Know your exposure to hazardous drugs. https://www.usp.org/sites/default/files/usp/document/our-work/healthcare-quality-safety/800-know-your-exposure-to-hazardous-drugs.pdf. Accessed January 6, 2020.
8. P Kienle and K Douglas. Perform an assessment of risk to comply with USP <800>. Pharmacy Purchasing Magazine. 2017. www.pppmag.com. Accessed January 6, 2020.

Florida State Board of Pharmacy Laws

- Effective: 08/19/2019
- 64B16-27.797 The Standards of Practice for Compounding Sterile Products
  - Beginning on October 1, 2014, all sterile compounding shall be performed in accordance with the minimum practice and quality standards of the following chapters of the United States Pharmacopeia (USP):
  - (a) Chapter 797, Pharmaceutical Compounding-Sterile Preparations;
  - (b) Chapter 71, Sterility Tests;
  - (c) Chapter 85, Bacterial Endotoxins Test;
  - (d) Chapter 731, Loss on Drying.