PREMIER
Alternate Site Programs

Virtual Meeting
& Expo

OCTOBER 12 – 13, 2020

USP Compounding Chapters Update:
Focus on Your Assessment of Risk

Patricia C. Kienle, RPh, MPA, BCSCP, FASHP

Disclosures

- Patricia Kienle is an employee of Cardinal Health. Ms. Kienle is an instructor for CriticalPointLLC. She is also a member of the USP Compounding Expert Committee, but this talk is not affiliated with or endorsed by USP.
- This continuing education activity is managed by Innovatix* and AffinityCE. Innovatix* is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.
- Innovatix* and AffinityCE as well as planners and reviewers have no relevant financial interest or relationships to disclose. Neither Innovatix* nor Affinity CE support or endorse any product or service mentioned in this activity. Disclosure will be made when a product is discussed for an unapproved use.
- The material presented for this session has been reviewed by the Innovatix* Institute CE Committee and AffinityCE and has been found to be free of any content influence or commercial bias.
- Commercial Support was not received for this activity.

*Innovatix now operates under ***Premier Alternate Site Programs***

Objectives

- 1.Define the status of the four USP compounding-related chapters: USP <795>, <797>, <800>, and <825> and where they apply
- 2.Name the reasons a hazardous drug could be listed on NIOSH Table 1 requiring all components of USP <800> to be followed
- 3.List three strategies that could be used as alternative approaches for hazardous drugs and dosage forms that qualify for an Assessment of Risk

Agencies and Organizations

- CDC – Centers for Disease Control and Prevention
- EPA – Environmental Protection Agency
- IARC – International Agency for Research on Cancer
- NIOSH – National Institute for Occupational Safety and Health
- NTP – National Toxicology Program
- OSHA – Occupational Safety and Health Administration
- USP – United States Pharmacopeia

Acronyms

- AECA – Allergen Extracts Compounding Area
- API – Active Pharmaceutical Ingredient
- BSC – Biological Safety Cabinet
- BUD – Beyond-Use Date
- C-SCA – Containment Segregated Compounding Area
- CACI – Compounding Aseptic Containment Isolator
- CAI – Compounding Aseptic Isolator
- CSP – Compounded Sterile Preparation
- CSTD – Closed system drug-transfer device
- HD – Hazardous drug
- MSHI – Manufacturer's Special Handling Information
- PPE – Personal Protective Equipment
- SCA – Segregated Compounding Area

Do you compound …

A. Nonsterile mixtures
B. Sterile compounds
C. Allergenic extracts
D. Hazardous drugs

USP Compounding Chapters

Chapter	Current Version	Impending Revision?
<795> Nonsterile compounding	2014	Yes – watch for update
<797> Sterile compounding	2008	Yes – watch for update
<800> Hazardous drugs	2016 with recent edit concerning Table 1 antineoplastic agents	No
<825> Radiopharmaceuticals	2019 with official date of December 1, 2020	No

Applies to all healthcare professionals performing activities listed in the Chapters

<795> and <797> Appeals

- <795> and <797> were published on June 1, 2019 and expected to be official on December 1, 2019. It was appealed and is now being evaluated by the new USP Compounding Expert Committee.
- The appeal concerns extending beyond-use dates longer than what was published in 2019

<795> Differences (2014 v. 2019)

- Categories of compounding (simple, moderate, complex) eliminated
- Administration and preparation per manufacturer's labeled out of scope
- Requirement for Designated Person
- Requirement for gloves
- Need to evaluate containment when weighing, measuring, or otherwise manipulating components that could generate airborne particles

<797> Differences (2008 v. 2019)

- Categories changed from risk-based (low, medium, high) to Category 1 (mixed in segregated compounding area) and Category 2 (mixed in a cleanroom suite)
  - CSPs mixed in a CACI must be in a cleanroom suite to have full BUDs assigned
  - BUDs in a SCA can go up to 24 hours if refrigerated
- Administration and preparation per manufacturer's labeling out of scope
- Requirement for Designated Person
- Personnel monitoring required every 6 months
- Surface sampling must be done monthly
- Specific documentation
  - Master Formulation Record
  - Compounding Records

Expiry Terms

- Expiration Date – assigned by a manufacturer based on scientific studies of the dosage form, packaging, and storage temperature
- Beyond-Use Date – assigned by the compounder based on <797>
- In-Use Time – time a dosage form can be used
  - Multiple-dose vial – 28 days or as noted in package insert
  - Single-dose vial – in some cases, may be used for 6 hours when maintained in ISO 5 (inside the hood)
  - Ampule and single-dose vial opened outside ISO 5 – use and discard
- Infusion Time – time a product or preparation may be infused, based on organizational policy

Allergenic Extracts Preparation Options

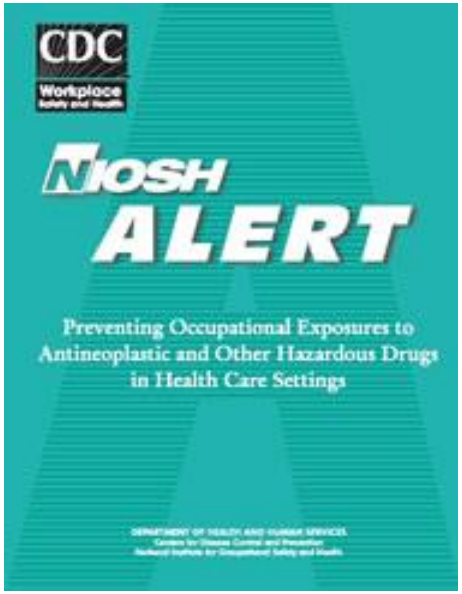
- Cleanroom suite dedicated to preparation of allergen extracts
- Segregated Compounding Area (SCA) dedicated to preparation of allergen extracts
- Primary Engineering Control (hood)
- Allergenic Extracts Compounding Area (AECA)
  - Separate room recommended
  - Visible perimeter
  - Accessible sink but not within 1 meter of work surfaces
  - Other requirements similar to an SCA

<800> Differences from 2008 <797>

- <800> is official but its federal enforcement depends on the revised <795> and <797> chapters
- Differences
  - All HD compounding (unless entity-exempt by an Assessment of Risk) must be done in negative pressure
  - Closed system drug-transfer devices (CSTDs) must be used for administration of Table 1 antineoplastics when the dosage form allows

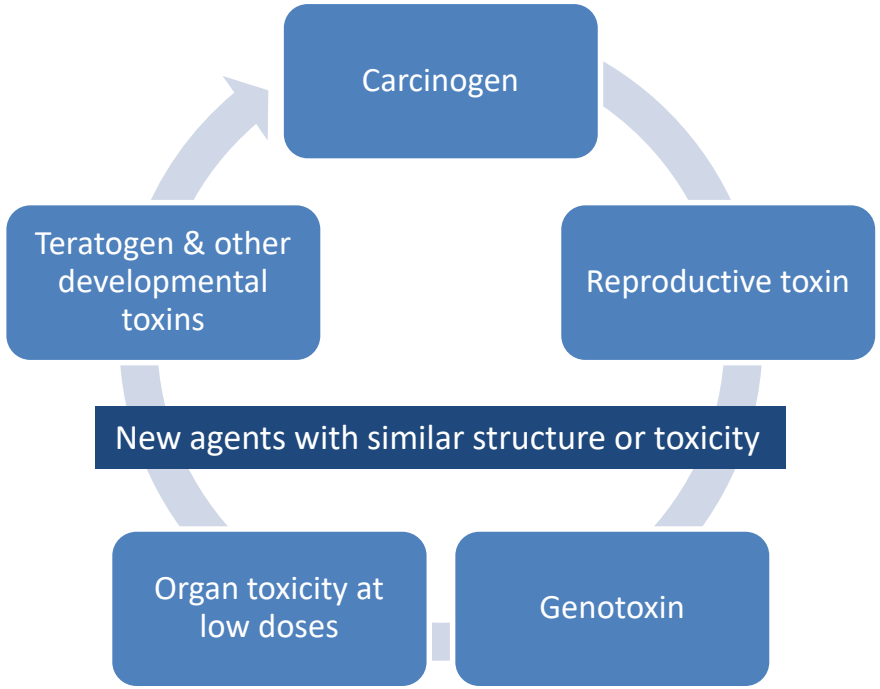
HD Standards Timeline

- OSHA Hazard Communication Standard
- USP <795> Nonsterile Preparations
- USP <797> Sterile Compounding
- NIOSH Alert

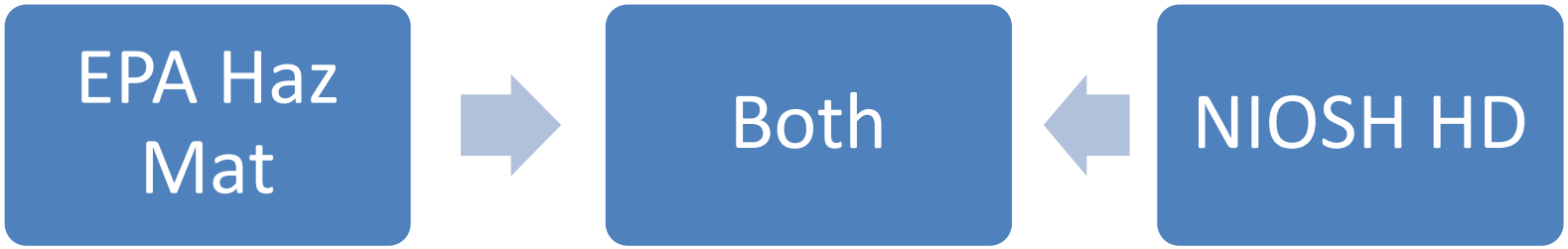


https://www.cdc.gov/niosh/docs/2004-165/pdfs/2004-165.pdf

What Drugs Are Hazardous to Us?



Hazardous Materials



Hazardous to the environment

Hazardous to health professionals

List of Hazardous Drugs

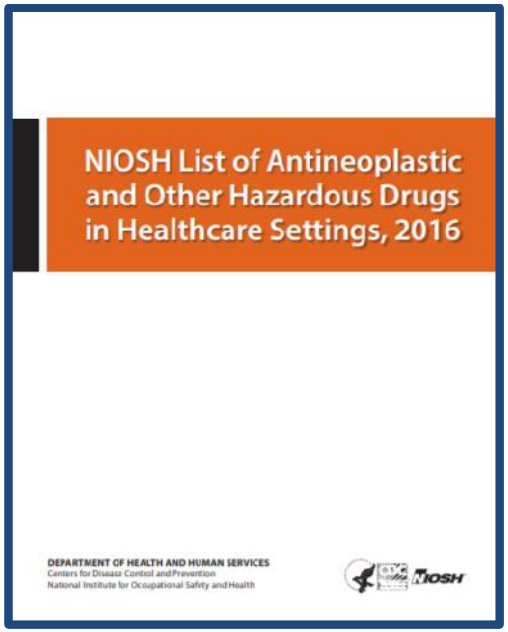
- <800> requires use of the NIOSH list of HDs
- Not all HDs need to be handled the same way
  - Any NIOSH Table 1 HD that has to be manipulated or Active Pharmaceutical Ingredients (API) of any HD must follow all requirements of <800>
  - Other HDs can be entity-exempt if an Assessment of Risk is done and alternative containment and/or work strategies are identified and implemented

What is the purpose of the NIOSH list?

A. Risk assessment
B. Hazard identification
C. Regulatory requirement
D. Liability prevention

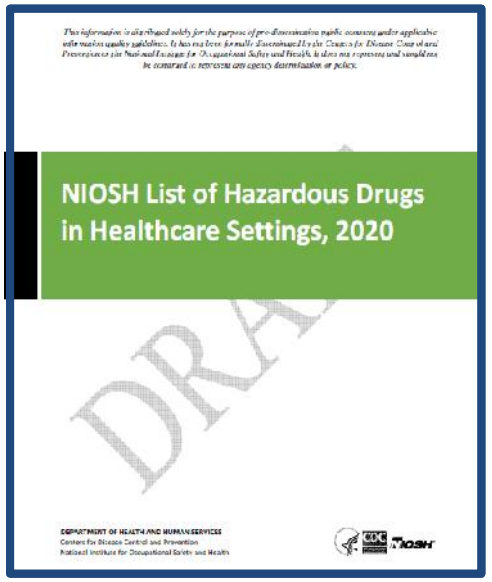
2016 List of Hazardous Drugs

- Three Tables
  - Table 1: Antineoplastics
  - Table 2: Non-antineoplastics
  - Table 3: Reproductive hazards



2020 Draft List of Hazardous Drugs

- Table 1
  - HD with Manufacturer's Special Handling Instructions (MSHI)
  - "Known to be a human carcinogen" listing on National Toxicology Program (NTP)
  - Group 1 (known human carcinogen) or Group 2A (probable human carcinogen) listing by International Agency for Research on Cancer (IARC)
- Table 2
  - All other HDs on the NIOSH list



Significant Changes …

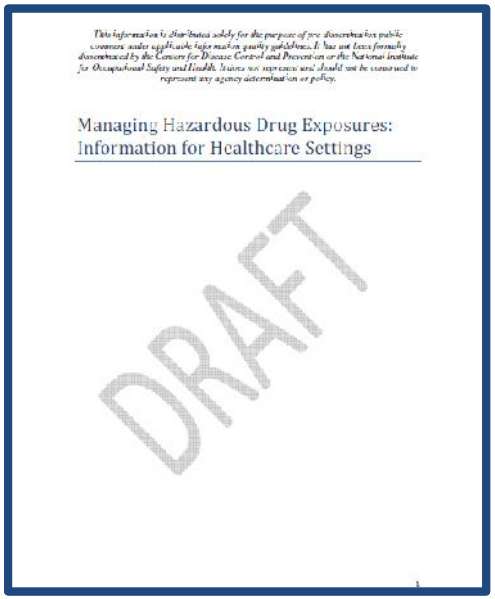
- Antineoplastics appear on both Tables
- Immunosuppressants move to Table 1
- Estrogens move to Table 1
- Hormones move to Table 2
- BCG is no longer on the list

Why?

ASHP podcast: https://podcasts.apple.com/us/podcast/hazardous-drugs-discussion-on-draft-niosh-list-hazardous/id1483670125?i=1000487282127

… Significant Changes

- 2004 Alert (revised information) and 2016 Table 5 (PPE) moved to a new document
- This guidance is recommended to be included into your policies and procedures



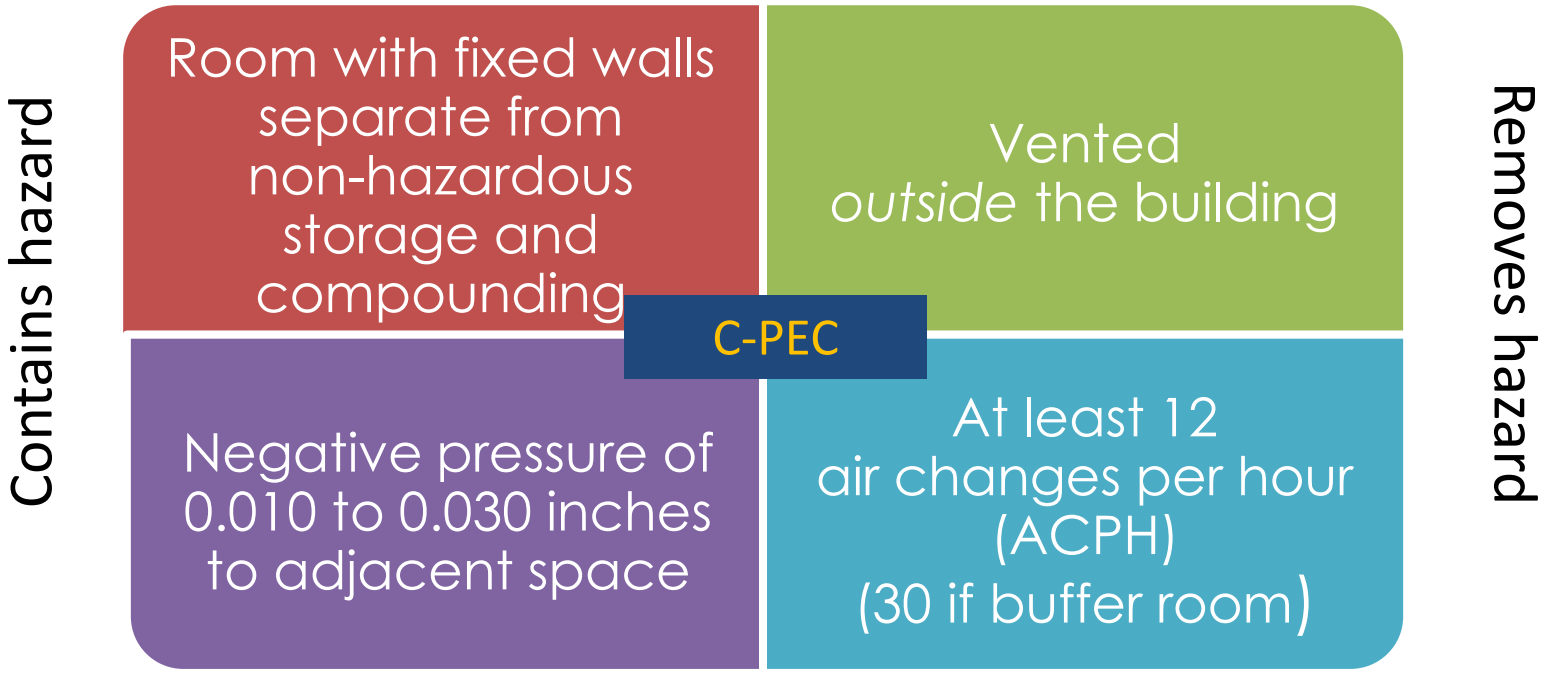
How often must your Assessment of Risk be reviewed?

A. Every 6 months
B. Every 12 months
C. Every 2 years
D. Every 3 years

Your Assessment of Risk

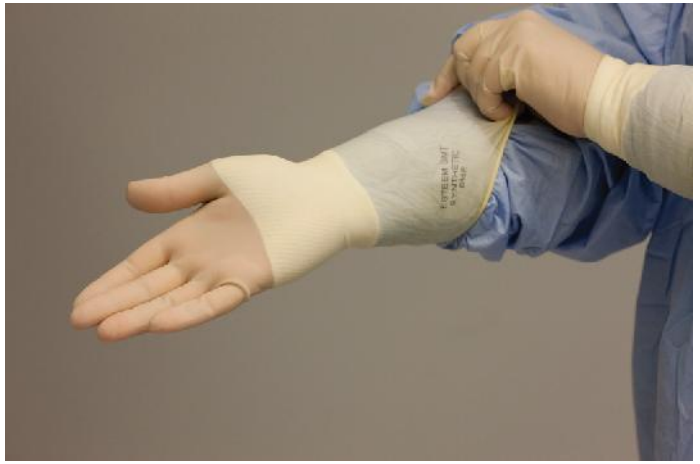
- Must list all HDs you handle
  - Assess all?
  - Assess just the ones you use?
- List must include the drug and dosage form
- Note: this is a list of marketed hazardous drugs, not necessarily investigational agents or hazardous biologics

Facilities – Storing and Compounding



Personal Protective Equipment (PPE)

- Gloves that meet ASTM Standard D6978
- Gowns
  - Laminate material
  - Long sleeves with closed cuff
  - No opening in the front
  - ASTM standard in draft
- Head, hair, and shoe covers
- Masks (to protect the preparation)



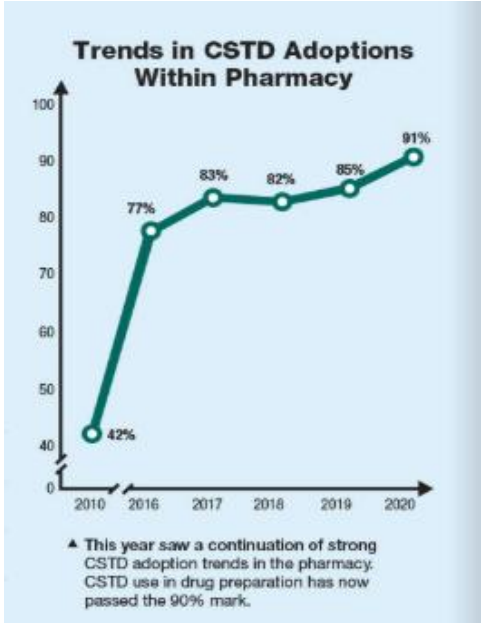
Additional PPE as Necessary

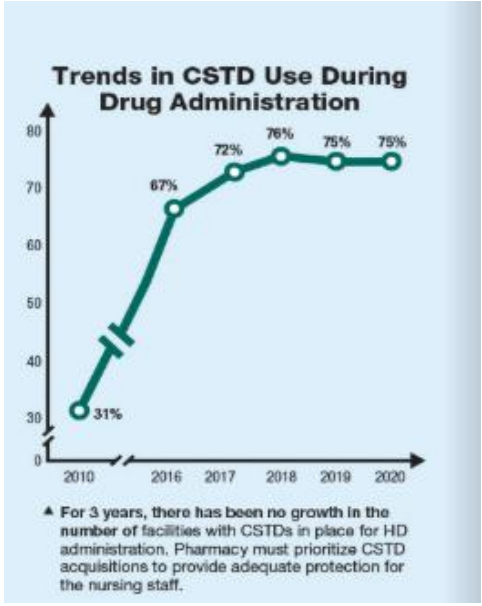
- Respirators
- Goggles
- Sleeve covers

Are closed system drug-transfer devices used at your practice site?

A. Yes, for compounding
B. Yes, for administration
C. Yes, for both compounding and administration
D. No

CSTD Use





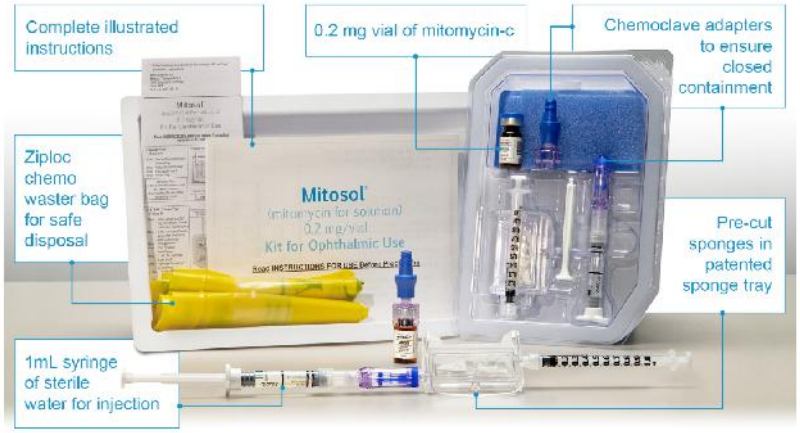
State of Pharmacy Compounding 2020, Pharmacy Purchasing and Products, www.pppmag.com

Closed System Drug-Transfer Devices

- CSTDs required in 2008 <797> if using “low use” exemption
- CSTDs required in <800> when administering parenteral Table 1 antineoplastics when the dosage form allows
- CSTDs recommended in <800> when compounding HDs

Other Closed Systems

EXAMPLES



Mitosol Kit, Mobius Therapeutics: https://mitosol.com/the-mitosol-kit/

Methotrexate Kit, EDGEPharma: https://edgepharma.com/assets/Uploads/EmGYN-kit-logo-b3.jpg

Elements to Consider

Follow all requirements in <800>	Consider alternative practices
Active Pharmaceutical Ingredient (API)	NIOSH Table 1 antineoplastic HDs you only count or package
NIOSH Table 1 antineoplastic HDs that will be manipulated	NIOSH non-antineoplastic Table 1 HDs
NIOSH Table 1 non-antineoplastics and NIOSH Table 2 antineoplastics	
Items you decide to NOT exempt based on risk	NIOSH Table 2 dosage forms that present lower risk to you and your employees

Work Practices

- Receipt
- Unpacking
- Transporting
- Storing
- Compounding
- Delivery to patient, caregiver, nurse
- Discarding infusion containers and PPE

Receipt and Unpacking …

- These are different processes
- Receiving
  - NIOSH Table 1 antineoplastic HDs should come from suppliers in marked packages with HDs bagged in impervious plastic
  - Some suppliers also mark/bag other HDs

… Receipt and Unpacking …

- Designated area for HD unpacking
  - Can be as simple as a designated counter space or use of chemo prep pad
- Person unpacking Table 1 antineoplastic HDs should wear one pair of chemo gloves
  - Access to other PPE
  - Aware of action to take for damaged package
  - Access to spill kit

… Receipt and Unpacking …

- NIOSH Table 1 antineoplastics that will be manipulated
  - Keep those meds in the plastic bag
  - Check in
  - Transport bag to HD storage
  - Unpack in the HD storage area
- Other HDs
  - Handle in your Assessment of Risk

Photo courtesy of Phononic

… Receipt and Unpacking

- For HDs that will be co-mingled with other stock, consider
  - Separate shelf
  - Distinctive color bin
  - Shelf sticker
  - Tactile clue

Consider …

Prepare	Compound and Dispense	Administer
• Receive • Unpack • Transport • Store	• Compound • Dispense	• Administer • Discard

… Consider …

Function	Containment	Work Practice
• Receive • Unpack • Transport • Store • Compound • Dispense • Administer • Discard	• Hood • Negative environment • Separate area • Separate equipment • PPE • Closed system drug transfer device • Other closed system	• Distinctive bins or labels • Enclose in chemo bag • Decontaminate surfaces • Limit access

… Consider

- NIOSH Table 1 antineoplastics that you manipulate prior to administering
- NIOSH Table 1 HDs you only need to count or package
- Other HDs with increased risk based on your handling practices
- Other HDs you handle
- Other hazards not on NIOSH list

NIOSH: Control Approaches for Safe Handling of HDs by Activity and Formulation

		Control Approaches					
Activity	**Formulation**	**Ventilated engineering control (BSC or CACI)**	**Closed system transfer device**	**Double chemo-therapy gloves**	**Protective gown**	**Eye, face hair, sleeve, and shoe protection**	**Respiratory protection[1]**
Receiving, unpacking, and placing in storage	All types of hazardous drugs	No, unless a leak is suspected	N/A[2]	Yes	No, unless a leak is suspected	Protective sleeves. Add additional protection if a leak is suspected.	No, unless a leak is suspected
Transportation within facility	Intact pills or capsules, manufacturers' prefilled syringes	No	N/A	Single glove	No	No	No
	Cut or crushed tablets or capsules (in containers), powders,	No	N/A	Yes	No	No	No

Example: 5 FU, Vincristine, Gancyclovir

Required Practices
Primary Engineering Control (PEC)
Secondary Engineering Control (SEC)
Supplemental Engineering Control (CSTD)
PPE
All listed work practices

Example: Leuprolide

Required Practices
Evaluate how it is manipulated prior to administration

Consider
Using manufacturer-supplied closed system, prepare by RN for bedside administration

Example: Other HDs

Activity	Practices to Consider
PPE	
Compounding	
Delivery to Patient or Caregiver	
Administration	

Hazardous Biologics Not on NIOSH List

Activity	Practices to Consider
PPE	
Compounding	
Delivery to Patient or Caregiver	
Administration	

Example: Hazards Not on NIOSH List

Activity	Practices to Consider
PPE	
Compounding	
Delivery to Patient or Caregiver	
Administration	

Recommendation: Do not include in your NIOSH HD list or policy; develop a separate policy

Disposal

- <800> refers you to applicable laws and regulations
- Your waste hauler can provide state-specific information
- Partial doses may have state-specific requirements

Spills

- Place spill kits in receiving, storage, compounding, and administration areas
- Be sure contents meet your needs

Resources: Assessment of Risk

- ASHP Assessment of Risk Toolkit, https://www.ashp.org/Pharmacy-Practice/Resource-Centers/Sterile-Compounding/USP-Chapter-800-Assessment-of-Risk-Toolkit
- Joint Commission Resources, www.hazmedsafety.com
- Kienle PC and Douglass K, Perform an Assessment of Risk to Comply with USP <800>,https://www.pppmag.com/article/2012/?search=assessment%20of%20risk
- NCPA, Assessment of Risk Template, https://www.ncpanet.org/innovation-center/diversified-revenue-opportunities/compounding

Resources …

- *USP Compounding Compendium*, www.usp.org
- USP <800> FAQs, www.usp.org
- ASHP Guidelines on Handling Hazardous Drugs (2018), https://www.ashp.org/-/media/assets/policy-guidelines/docs/guidelines/handling-hazardous-drugs.ashx
- ONS Toolkit for Safe Handling of Hazardous Drugs for Nurses in Oncology, https://www.ons.org/sites/default/files/2018-06/ONS_Safe_Handling_Toolkit_0.pdf

… Resources

- Smith CA, Skibinski K, Livingston M, Waste Handling: Doing Right by Employees, Patients, https://www.pharmacypracticenews.com/Operations-Management/Article/12-19/Waste-Handling-Doing-Right-by-Employees-Patients/56461
- Kienle PC, *The Chapter <800> Answer Book*, www.ashp.org
- McLeod EN, Fillis CJ, Blind JE, Practical Approach to Assess the Hazardous Exposure Potential of Investigational Drugs, AJHP, 1 May 2020