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Practical Strategies for Compliance with USP <800>: Performing an Assessment of Risk

Patricia C. Kienle, RPh, MPA, FASHP
Director, Accreditation and Medication Safety
Cardinal Health Innovative Delivery Solutions
Laflin, Pennsylvania

Disclaimer

- Patricia Kienle is a member of the USP Compounding Expert Committee, but this presentation is not endorsed by or affiliated with USP

Objectives

- Cite the document that defines hazardous drugs
- Identify the drugs and dosage forms eligible for an Assessment of Risk
- Design an Assessment of Risk to be used at your organization
- List the facility and monitoring elements for compliance with USP <800>
- Prioritize gaps in compliance that need to be addressed within your organization

Preparation

- Read Assessment of Risk section from USP <800>
- Review NIOSH 2016 Hazardous Drug list for the drugs and dosage forms you handle at your system

Why <800>?

- <800> Hazardous Drugs – Handling in Healthcare settings protects
  - Patients
  - Personnel
  - Environment
- It adds to – does not replace - <795> and <797> on Nonsterile and Sterile Compounding
- First enforceable standard that protects healthcare personnel from risk of hazardous drugs

Enforceability of <800>

- <800> will become federally enforceable on July 1, 2018
- States may place <800> into state regulations
  - State Board of Pharmacy
  - Other state agencies

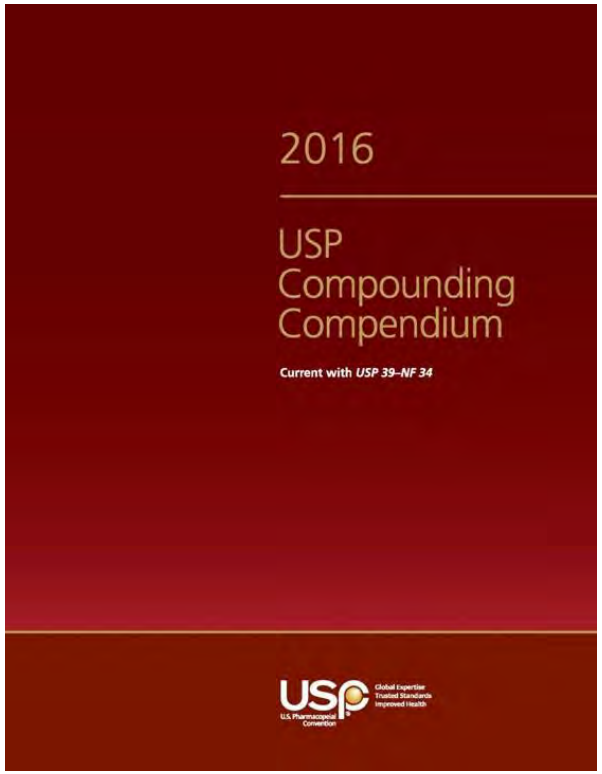

Photo courtesy of USP

www.usp.org → Compounding Compendium

Genesis of USP <800>

Drug Distribution and Control: Preparation and Handling—*Guidelines* 101

ASHP Guidelines on Handling Hazardous Drugs

In 1990, the American Society of Health-System Pharmacists (ASHP) published its revised technical assistance bulletin (TAB) on handling cytotoxic and hazardous drugs.[1] The information and recommendations contained in that document were current to June 1988. Continuing reports of workplace contamination and concerns for health care worker safety prompted the Occupational Safety and Health Administration (OSHA) to issue new guidelines on controlling occupational exposure to hazardous drugs in 1995.[2] In 2004, the National Institute for Occupational Safety and Health (NIOSH) issued the "NIOSH Alert: Preventing Occupational Exposure to Antineoplastic and Other Hazardous Drugs in Health Care Settings."[3] The following ASHP Guidelines on Handling Hazardous Drugs include information from these recommendations and are current to 2006.

Purpose

The purpose of these guidelines is to (1) update the reader on new and continuing concerns for health care workers handling hazardous drugs and (2) provide information on recommendations, including those regarding equipment, that have been developed since the publication of the previous TAB. Because studies have shown that contamination occurs in many settings, these guidelines should be implemented wherever hazardous drugs are received, stored, prepared, administered, or disposed.[1,2]

Comprehensive reviews of the literature covering anecdotal and case reports of surface contamination, worker contamination, and risk assessment are available from OSHA,[2] NIOSH,[3] and individual authors.[4-7] The primary goal of this document is to provide recommendations for the safe handling of hazardous drugs.

These guidelines represent the recommendations of many groups and individuals who have worked tirelessly over decades to reduce the potential harmful effects of hazardous drugs on health care workers. The research available to date, as well as the opinions of thought leaders in this area, is reflected in the guidelines. Where possible, recommendations are evidence based. In the absence of published data, professional judgment, experience, and common sense have been used.

Background

Workers may be exposed to a hazardous drug at many points during its manufacture, transport, distribution, receipt, storage, preparation, and administration, as well as during waste handling and equipment maintenance and repair. All workers involved in these activities have the potential for contact with uncontained drug.

Early concerns regarding the safety of workers handling potentially hazardous drugs focused on antineoplastic drugs when reports of second cancers in patients treated with these agents were coupled with the discovery of mutagenic substances in nurses who handled these drugs and cared for treated patients.[8,9] Exposure to these drugs in the workplace has been associated with acute and short-term reactions, as well as long-term effects. Anecdotal and case reports in the literature range from skin-related and ocular effects to flu-like symptoms and headache.[4,5,10-17] Two controlled surveys have reported significant increases in a number of symptoms, including sore throat, chronic cough, infections, dizziness, eye irritation, and headaches, among nurses, pharmacists, and pharmacy technicians routinely exposed to hazardous drugs in the workplace.[18,19] Reproductive studies on health care workers have shown an increase in fetal abnormalities, fetal loss, and fertility impairment resulting from occupational exposure to these potent drugs.[20-23] Antineoplastic drugs and immunosuppressants are some of the types of drugs included on lists of known or suspected human carcinogens by the National Toxicology Program[24] and the International Agency for Research on Cancer.[25] Although the increased incidence of cancers for occupationally exposed groups has been investigated with varying results,[26,27] a formal risk assessment of occupationally exposed pharmacy workers by Sessink et al.[28] estimated that cyclophosphamide causes an additional 1.4–10 cases of cancer per million workers each year. This estimate, which considered workplace contamination and worker contamination and excretion in combination with animal and patient studies, was based on a conservative exposure level. Connor et al.[29] found greater surface contamination in a study of U.S. and Canadian clinical settings than had been reported in European studies conducted by Sessink and colleagues.[30-32] Emslie et al.[33] reported an almost fivefold greater daily average excretion of cyclophosphamide in their study than that reported by Sessink. These later findings could add 7–90 additional cancer cases per year per million workers to Sessink's estimate. From these and other studies that show variations in work practices and engineering controls,[34,35] it may be assumed that such variations contribute to differences in surface and worker contamination.

Routes of Exposure. Numerous studies showed the presence of hazardous drugs in the urine of health care workers.[36-38,39-43] Hazardous drugs enter the body through inhalation, accidental injection, ingestion of contaminated foods/coffee or mouth contact with contaminated hands, and dermal absorption. While inhalation might be suspected as the primary route of exposure, air sampling studies of pharmacy and clinic environments have often demonstrated low levels of or no airborne contaminants.[36-41,43] Recent concerns about the efficacy of the sampling methods[37] and the possibility that at least one of the marker drugs may be volatile[38,44] and thus not captured on the standard sampling filter leave the matter of inhalational exposure unresolved. Surface contamination studies do, however, suggest that dermal contact and absorption may be a primary route of exposure.[36,40] While some hazardous drugs are dermally absorbed, a 1992 report showed no detectable skin absorption of doxorubicin, daunorubicin, vincristine, vinblastine, or melphalan.[45] An alternative to dermal absorption is that surface contamination transferred to hands may be ingested via the hand-to-mouth route.[36,38] One or more of these routes might be responsible for workers' exposure.

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

http://www.ashp.org/DocLibrary/BestPractices/PrepGdlHazDrugs.aspx

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NIOSH Occupational Exposure Information

http://www.cdc.gov/niosh/topics/antineoplastic/

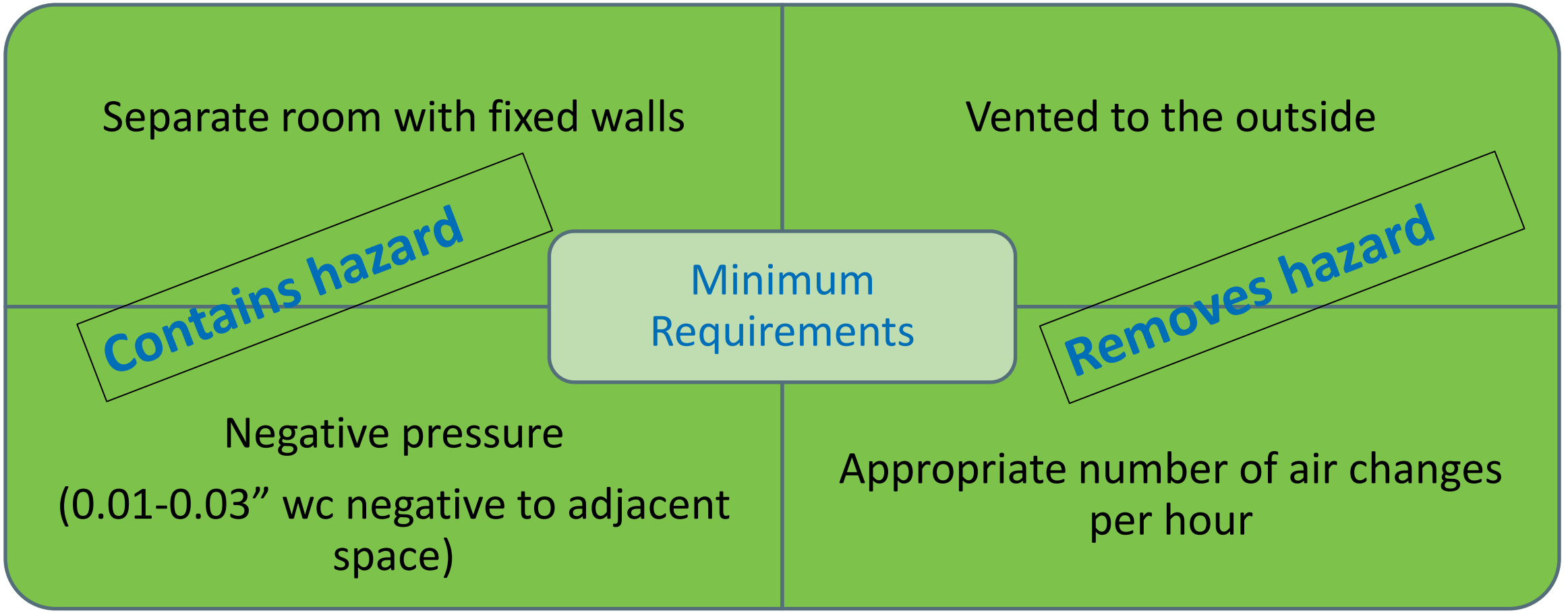
NIOSH Hazardous Drug Information

http://www.cdc.gov/niosh/topics/hazdrug/default.html

Major Components of <800>

- Facilities
- Hazardous Drug list
- Work practices
  - Containment of HDs
  - Technique to limit exposure
  - Decontamination of areas exposed to HDs
- Assessment of Risk
- Monitoring
  - Personnel
  - Facilities

<800> Storage and Compounding Requirements



Two Design Options for Sterile Compounding

- Cleanroom suite
  - Positive pressure ISO 7 anteroom opening into negative pressure ISO 7 buffer room with biological safety cabinet (BSC) or compounding aseptic containment isolator (CACI)
- Containment Segregated Compounding Area
  - Separate space with BSC or CACI
  - Limited to 12 hour beyond-use date (BUD)
  - NOTE: Not currently allowed by <797>
- NOTE: Low Volume Exemption is no longer allowed

Design for Nonsterile Compounding

- Primary Engineering Control
  - Containment Ventilated Enclosure (“powder hood”)
- Secondary Engineering Control
  - Room that is separate from non-hazardous drugs, and is under negative pressure, vented to the outside, and has the appropriate number of air changes per hour (ACPH)
- Occasional nonsterile compounding can be done in the sterile compounding area; details are in <800>

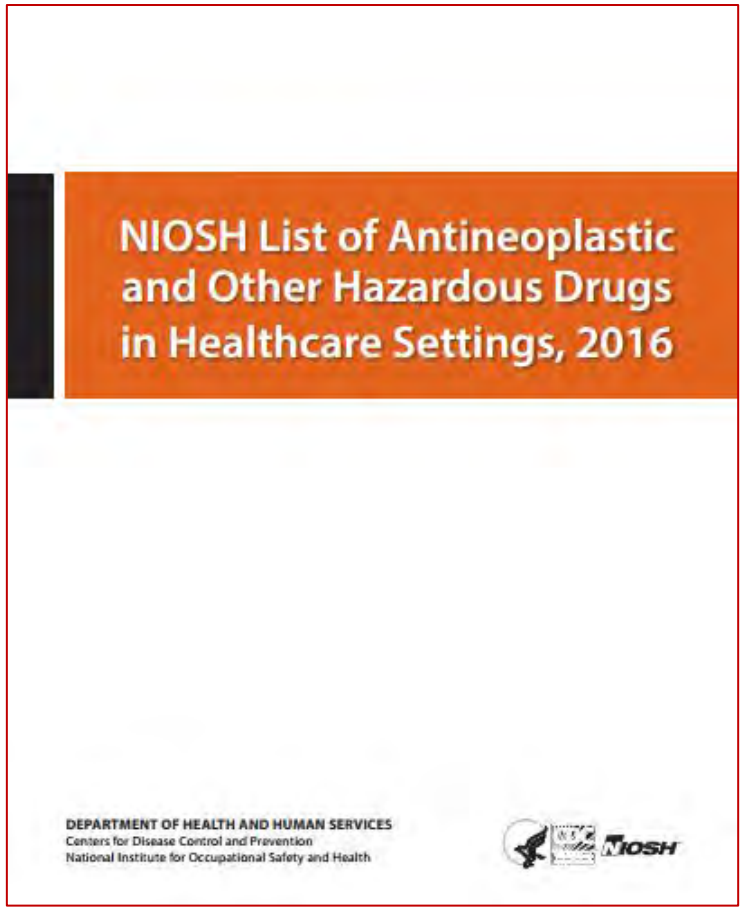
Hazardous Drugs

- Carcinogen
- Genotoxin
- Teratogen
- Reproductive toxin
- Organ toxicity at low dose in humans or animals
- New drugs that mimic existing HDs in structure or toxicity

Original reference: ASHP Guidelines on Handling Hazardous Drugs, 1990

NIOSH List of Hazardous Drugs

- Antineoplastics
- Non-antineoplastics
- Reproductive only hazards



www.cdc.gov/niosh/docs/2016-161/pdfs/2016-161.pdf

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What's the Assessment of Risk All About?

- USP <800> establishes the containment strategies and work practices best known to control hazardous drug contamination
  - Engineering controls
  - Protective equipment
  - Work practices

https://www.cdc.gov/niosh/topics/hierarchy/

Ideal Situation

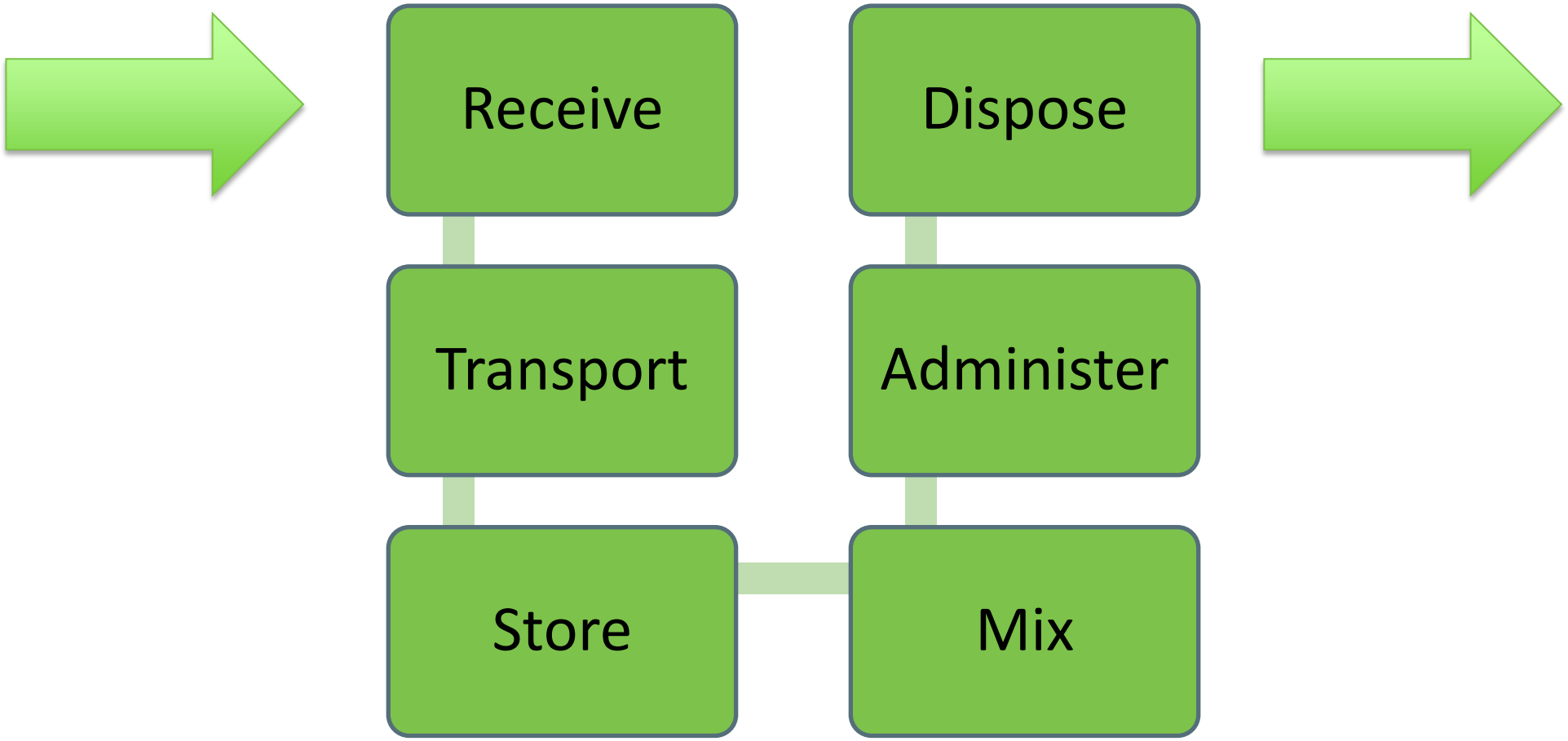
- Handle every drugs in every dosage form on the NIOSH list with all the containment strategies and work practices identified in <800>
- Is that possible in every case?
- Is that practical in every case?

Your Options

Handle every drug and dosage form on the NIOSH list with all the precautions and work practices listed in <800>

Perform an Assessment of Risk for some dosage forms of some drugs on the list

HD Life Cycle in Your Organization



Personnel to Consider

- Receiving
- Transport
- Pharmacy technicians
- Pharmacists
- Nursing
- Procedural personnel
  - Surgical Services
  - Emergency Department
  - Obstetrics

Your Hazardous Drug List

1. Review the NIOSH list of hazardous drugs
2. Identify the drugs and dosage forms you handle
3. Perform an Assessment of Risk
4. Document review of the list annually

Required Assessment of Risk Elements

- Drug
- Dosage form
- Risk of exposure
- Packaging
- Manipulation
- Documentation of alternative containment strategies and/or work practices
- Review annually and document

Your HD List

Require ALL containment strategies detailed in <800>	Alternative containment strategies can be considered and implemented
• Active Pharmaceutical Ingredient (API) of any HD on the list	• Antineoplastics you only need to count or package
• Antineoplastics that require manipulation	• Non-antineoplastics
• Dosage forms that don't fit your Assessment of Risk	• Reproductive only hazards

Consider

- Drug, dosage form, and packaging
- Where manipulation occurs and by whom
- Life cycle of the HD throughout your organization

What drug and dosage forms present the biggest questions related to including them in an Assessment of Risk?

-
-
-
-
-
-
-

So What Happens With …

- API
- Antineoplastics that must be compounded
- Antineoplastics that must be repackaged
- Antineoplastic dosage form dispensed intact
- Antineoplastic oral dosage form that must be crushed
- Non-antineoplastics or reproductive hazards that your committee feels should not be entity exempt
- Oral agents on Tables 2 and 3
- Injectable agents on Tables 2 and 3 that are dispensed intact
- Injectable agents on Tables 2 and 3 that must be compounded

Assessment of Risk Worksheet

Assessment of Risk Worksheet

DRUG	DOSAGE FORM/ PACKAGING	RISK OF EXPOSURE	RECEIVING	TRANSPORT TO STORAGE	MANIUPLATION NEEDED	FINISHED DOSAGE FORM	ADMINIS-TRATION	DECONTA-MINATION	DISPOSAL
			Integrity Decontamination	Containment	C-PEC/C-SEC/CSTD/PPE	To PCU To Pt	CSTD	Oxidizer	Regs

API of Any HD on the NIOSH List

- Active Pharmaceutical Ingredient of any antineoplastic, non-antineoplastic, or reproductive hazard

- No option → must treat with all the containment strategies and work practices in <800>

Antineoplastic Agents

- If any manipulation is required

  Examples

  - Drawing methotrexate from a vial
  - Crushing tablets or opening capsules to make a suspension
  - Splitting tablets

- No option → must treat with all the containment strategies and work practices in <800>

Antineoplastic Agents

- For antineoplastic agents that only require counting or packaging
  - Methotrexate tablets
  - Conventionally-manufactured fluorouracil cream

Examples

- You can consider these dosage forms in your Assessment of Risk
- But …
  - This was intended for outpatient pharmacies

Oral Antineoplastics

- Transport into negative buffer room for storage of intact bottle
- Once a table is needed, package the entire bottle at once, using the same facilities and precautions you do with parenterals
- Pack each UD into individual sealed bag
- No sterile compounding can occur during this
- Once it is packaged, it is a finished dosage form, so can be transported to the regular storage area and stored in a yellow lidded bin

Examples

Packaging Oral HDs = Nonsterile Compounding

- Best: use a powder hood
- Acceptable: <800> allows use of BSC/CACI for occasional nonsterile compounding
  - No concurrent sterile compounding
  - Total clean of C-PEC before resuming sterile compounding

Photo courtesy of Labconco

HDs Other Than Antineoplastic Agents

- Non-antineoplastics
- Reproductive only hazards

- All can be considered for your Assessment of Risk
  - But some are concerning

Can I establish a policy stating that all meds/dosage forms in Tables 2 and 3 are entity exempt?

A. Yes
B. No

Approach to Assessment of Risk

- The NIOSH list has links and information concerning why the drug is on the list
- Look at that information, and evaluate it based on your circumstances
- Some are situational hazards
  - Hazards in third trimester

Example

Consider for Non-Injectables

- Purchase unit dose from manufacturer
  - Wipe off to remove potential HD residue
- Purchase bulk and package into unit dose or unit-of-use
  - Use BSC and garb if you have that available
    - Antineoplastics
    - Others
  - Decontaminate counting tray and spatula

Examples

Consider for Injectables

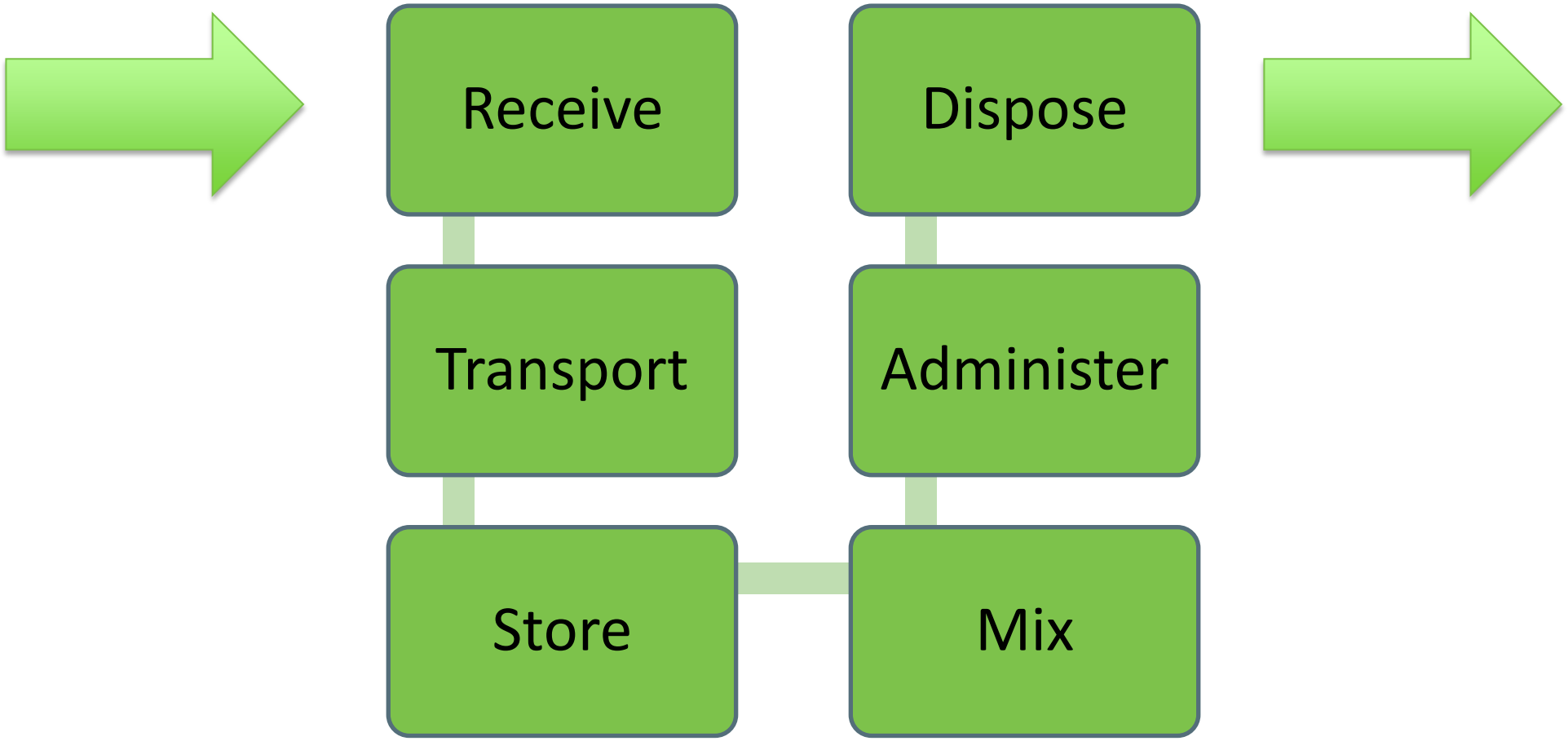
- Separate BSC for Table 2 and 3 meds
  - Could also be used for occasional use for non-sterile compounding
- Closed System Drug-Transfer Devices (CSTDs) must be used for parenteral antineoplastics when the dosage form allows
  - Should be used for compounding

Photo courtesy of BD

Do you use CSTDs for drugs in Tables 2 and 3?

A. Yes
B. No
C. We don't use CSTDs yet

HD Life Cycle in Your Organization



Assessment of Risk Requirements

- If you exempt specific drugs and dosage forms in your entity, you must identify the alternative containment strategies and/or work practices
- Determine how you will document this
  - Spreadsheet?
  - Separate form for each dosage form?

Receiving

- What HDs will be handled with all precautions and which will be exempted for some or all elements based on your Assessment of Risk?
  - Antineoplastics – injectables
  - Antineoplastics – non-injectables
  - Table 2 and 3 meds
- Need to identify – specific to drug and dosage form – those agents that will be handled differently and identify strategies in Assessment of Risk

Receiving

- Antineoplastics → to negative pressure
- Others (as you determine) → to negative pressure
- Ones that will have alternative strategies→ identify and document the strategy
  - Identify as HD
  - Wipe off

Examples

Drug Storage

- Identify as HDs
- Store in yellow, lidded bins
- Clearly note what must be done if manipulation of the dose is required

Examples

If Oral HDs are Stored in Buffer Room

- Maintain a list of those agents stored there
- Develop policy and procedure concerning who can package them
  - Where they will be packaged
  - Detailed procedure noting containment strategies
- Use only manual packaging system

Photo courtesy of Medi-Dose

Unit dose methotrexate is on backorder. Pharmacy must buy bulk and unit dose package it. Are personnel risks similar or different between the pharmacy tech and nurse?

A. Similar
B. Pharmacy tech is at higher risk since handling bulk drug
C. Nurse is at higher risk because the nurse must touch the drug

Packaging Strategies

- Risk will be different for pharmacy personnel (who have to package) vs. nursing personnel (who will handle a finished dosage form)
- Consider this in your Assessment of Risk

Final and Finished Dosage Forms

- Determine where they will be stored
  - UD packaged items
  - Finished dosage forms
    - Parenteral
    - Non-parenteral
  - Waiting for transport to a patient care or procedural unit
  - Waiting for patient pick-up

Example Containment Strategies

- Buy in unit dose
- Buy in bulk, then unit dose package in a powder hood using a manual system
- Place each UD into individual bag
- Store in <800> compliant Containment Secondary Engineering Control (C-SEC) until finished dosage form
- Wear chemo gloves
- Dedicate specific equipment which is decontaminated after use

Example Containment Strategies

- Mark lidded ADC bins with PPE precautions
  - Antineoplastics: Hazardous drug precautions
  - Others: Wear chemo gloves
- Use CSTDs for IV non-antineoplastics and reproductive only hazards
- Remove oxytocin vials from unit stock
- Package all partial tablets in pharmacy using manual system
- Prepare all liquid doses in patient-specific oral syringes
- Package topical creams/ointments into unit-of-use

Assessment of Risk Worksheet

Assessment of Risk Worksheet

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			Integrity Decontamination	Containment	C-PEC/C-SEC/CSTD/PPE	To PCU To Pt	CSTD	Oxidizer	Regs

Examples – Table 1 Antineoplastics

- Methotrexate IM for ectopic pregnancies
- Mitomycin ophthalmic
- BCG for bladder installation

Examples

- Table 2: Non-antineoplastics
  - Azathioprine
  - Carbamazepine
  - Risperdone
  - Spironolactone
- Table 3: Reproductive only hazards
  - Clonazepam
  - Fluconazole
  - Oxytocin
  - Warfarin

Resources

- Upcoming ASHP Publication *The 800 Answer Book*

- JCR Toolkit

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Key Takeaways

- Review the 2016 NIOSH List of Hazardous Drugs to identify the drugs and dosage forms handled at your organization
- Establish a multidisciplinary committee to review how the HDs are handled throughout your organization
- Perform an Assessment of Risk to determine alternative containment strategies and/or work practices for all dosage forms of HDs that you determine don't need to be handled with all the precautions detailed in <800>
- Review and document your Assessment of Risk at least every 12 months