Unforeseen Dangers:
Drugs That Are Hazardous to Us

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Disclosure

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

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What's All the Fuss?

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Preventing Occupational Exposure

Warning!
Working with or near hazardous drugs in health care settings may cause skin rashes, infertility, miscarriage, birth defects, and possibly leukemia or other cancers

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Purpose of USP <800>

- Approximately 8 million workers are potentially exposed to hazardous drugs (HDs) each year
- <800> was developed to promote patient safety, worker safety, and environmental protection
- Defines practice and quality standards for handling HDs
- Builds on existing science, guidelines, and expertise

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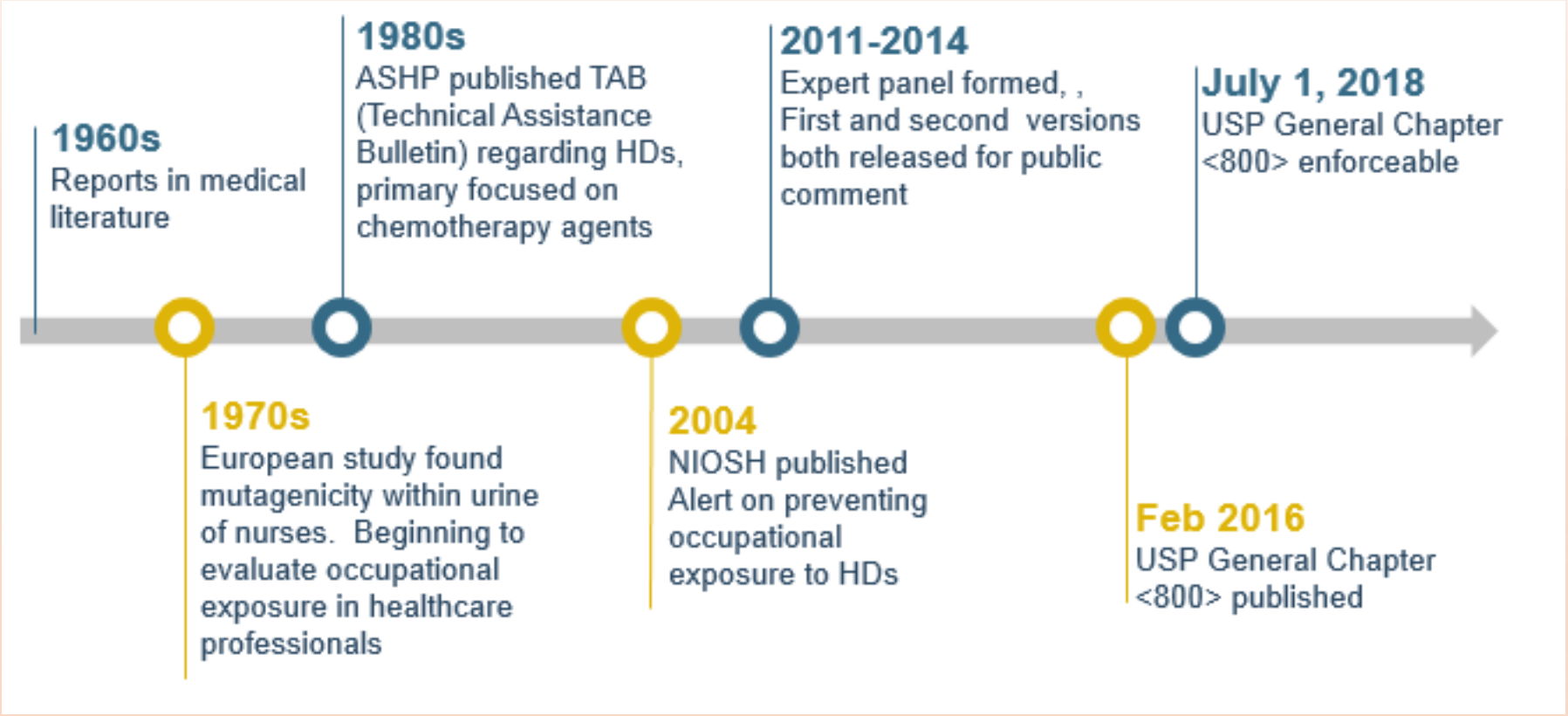
Hazardous Drug Guidance



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Who Enforces USP Standards?

- FDA and other federal agencies
- States – such as boards of health
- Accreditation organizations – medication preparation standards apply throughout an organization, not just to pharmacy

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But Nurses Don’t Compound

- USP compounding chapters are broad in scope, and cover any mixing of medications
- USP <797> contains information on mixing sterile preparations for immediate use
- USP <800> includes that and more

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Scope of <800>

- Life Cycle of HDs
- All Healthcare Entities
- All Healthcare Personnel

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What Drugs are Hazardous?

- Any drug identified by at least one of the following criteria
  - Carcinogenicity
  - Teratogenicity or other developmental toxicity
  - Reproductive toxicity
  - Organ toxicity at low doses
  - Genotoxicity
  - Structure and toxicity profile of new drug that mimics existing HD

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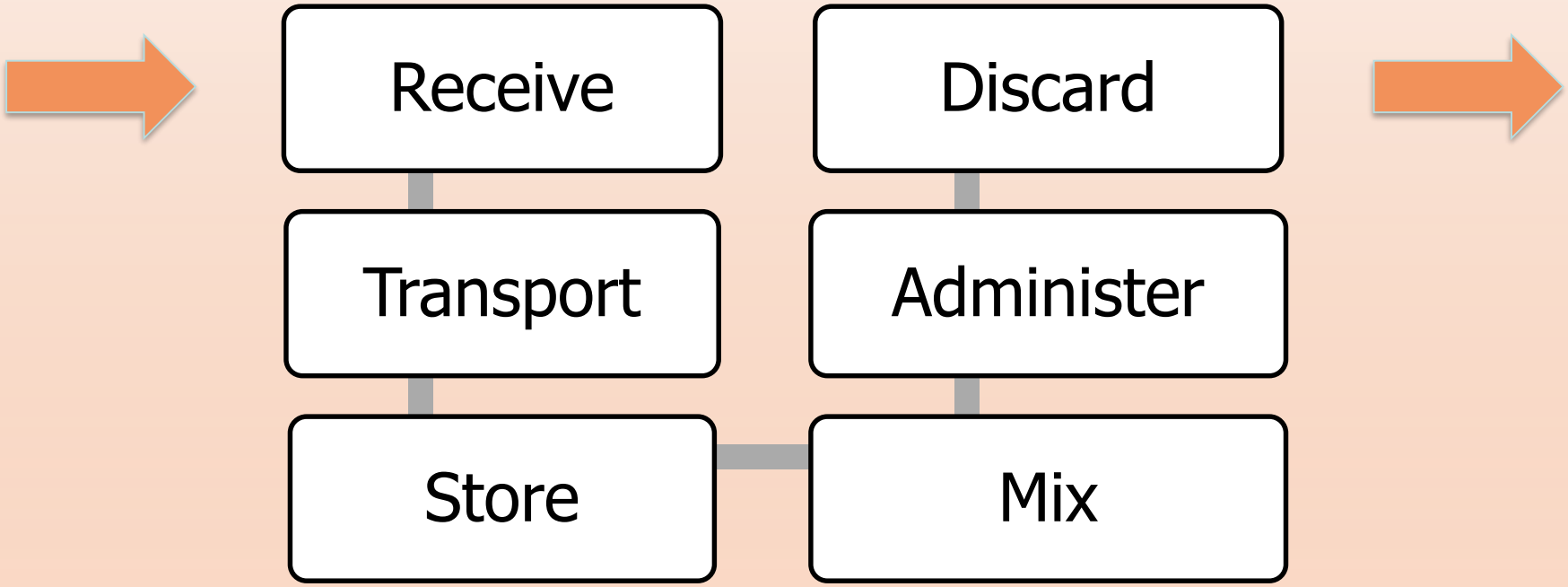
Scope of <800>



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Official Date of USP <800>

- Official on December 1, 2019
  - This is a recent change
- Enforceable
  - Federal agencies
  - State agencies
  - Accreditation organizations

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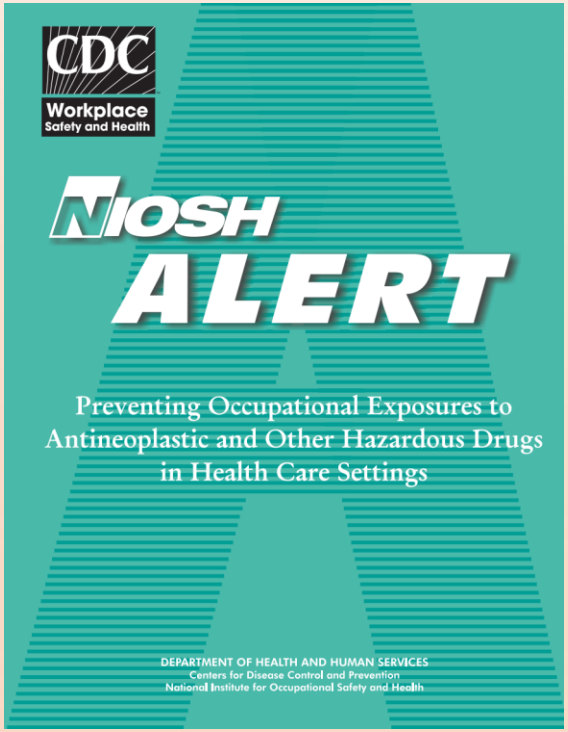
Genesis of <800>



Drug Distribution and Control: Preparation and Handling–*Guidelines* 95

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.[2,3] 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."[4] The following ASHP Guidelines on Handling Hazardous Drugs include information from these recommendations and are current to 2004.

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.[2,3]

Comprehensive reviews of the literature covering anecdotal and case reports of surface contamination, worker contamination, and risk assessment are available from OSHA,[2,3] NIOSH,[4] and individual authors.[5–7] 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] Ensslin 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 7–50 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.[10–14,36–41] Hazardous drugs enter the body through inhalation, accidental injection, ingestion of contaminated foodstuffs 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.[30–32,40] Recent concerns about the efficacy of the sampling methods[42] and the possibility that at least one of the marker drugs may be volatile[42–45] 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.[31,46] While some hazardous drugs are dermally absorbed, a 1992 report showed no detectable skin absorption of doxorubicin, daunorubicin, vincristine, vinblastine, or melphalan.[47] An alternative to dermal absorption is that surface contamination transferred to hands may be ingested via the hand-to-mouth route.[41,48] One or more of these routes might be responsible for workers' exposure.

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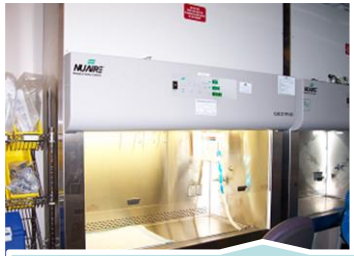
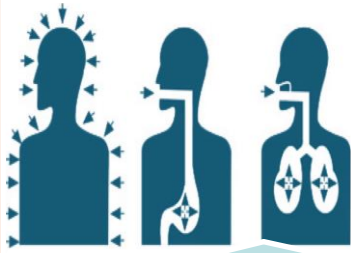
Elements of <800>



Facilities

PPE



Hazard Communication

Transport & Disposal

Dispensing & Administration

Compounding

Cleaning

Medical Surveillance

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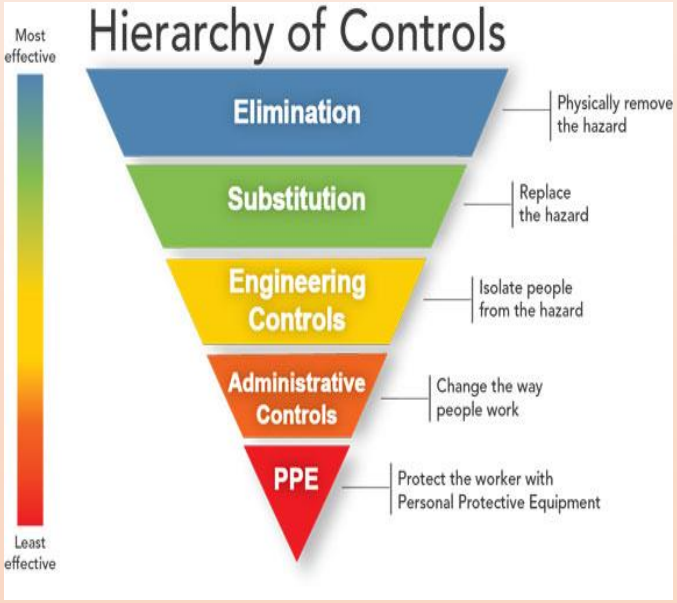
NIOSH Approach

- 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

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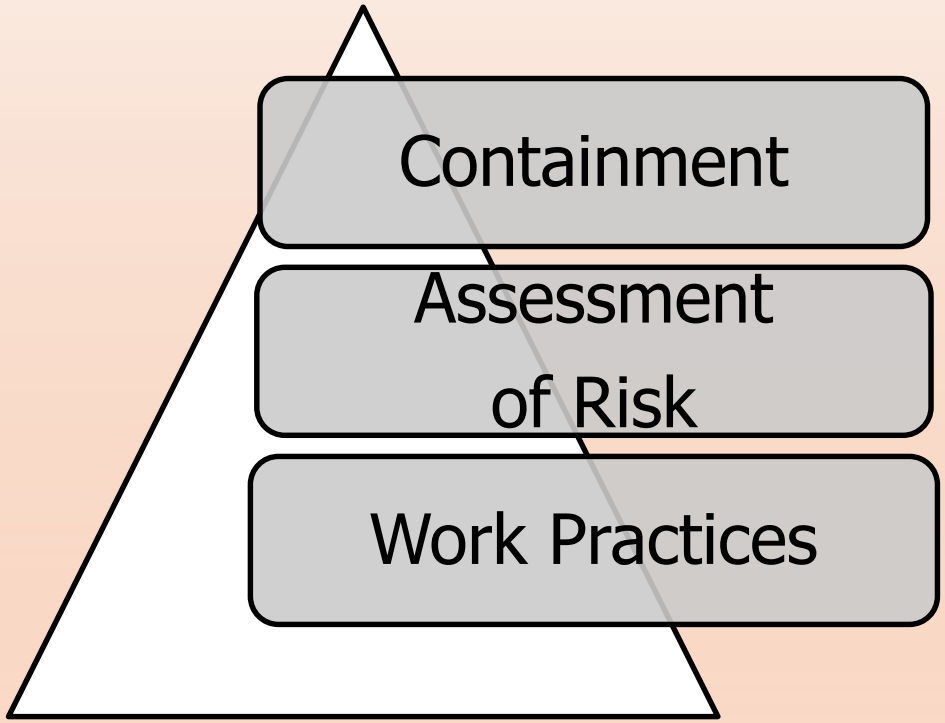
Key Elements of <800>



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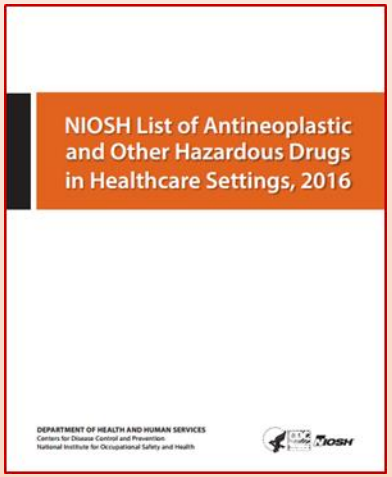
NIOSH List of Hazardous Drugs

- Hazardous to healthcare personnel
  - Different from EPA hazardous materials which are hazardous to the environment
- Use of the list is required
  - Tables 1, 2, and 3
- Use of Table 5 Personal Protective Equipment (PPE) is not required, but provides a comprehensive list for policy development



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

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Your HD List

- Must contain all the HDs on the NIOSH list that you handle
- Must be specific to the dosage form level

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NIOSH List of Hazardous Drugs

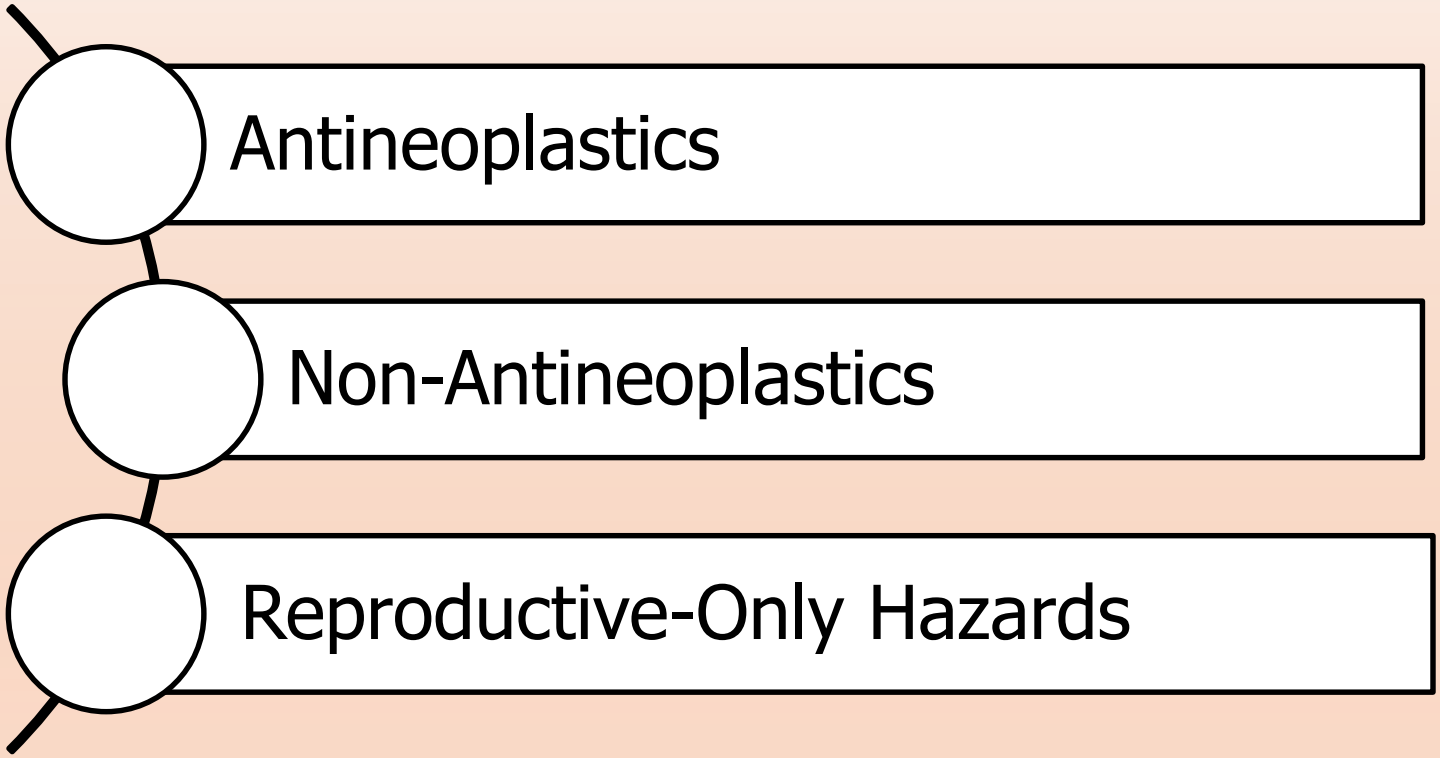

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Table 2 Examples

- Azathioprine
- Cyclosporine
- Fosphenytoin
- Risperidone
- Spironolactone
- Zidovudine

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Table 3 Examples

- Clonazepam
- Colchicine
- Fluconazole
- Oxytocin
- Pamidronate
- Warfarin

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Options

Handle all drugs and dosage forms with all containment and work practices listed in <800>

Perform an Assessment of Risk to determine alternative containment strategies and work practices

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What Drugs Can Be Handled Differently?

All <800> Precautions Apply	Can Be Included in Assessment of Risk
Raw chemical of any HD on the list	Antineoplastics that only need to be counted or packaged
Antineoplastics that need to be manipulated	Table 2 drugs
Items that don't fit the Assessment of Risk	Table 3 drugs

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Compliance with All <800> Elements

- Facilities
  - Hood: Primary Engineering Control (PEC)
  - Room: Secondary Engineering Control (SEC)
- Personal Protective Equipment
- Work Practices
  - Policies and procedures
  - Containment from receiving to administering
  - Decontamination of work surfaces

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OK to Consider for Assessment of Risk

- Antineoplastics that only need to be counted or packaged
- Non-antineoplastic meds (Table 2)
- Reproductive-only hazards (Table 3)

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Alternative Strategy Examples For Assessment of Risk

- Purchase unit-dose or unit-of-use
- Store in lidded bins
- Use closed system drug-transfer devices (CSTDs)
- Handle with chemo gloves
- Designate tackle boxes for transport

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“Must” vs “Should”

- Must or shall = requirement
  - PPE
  - CSTDs for administration when the dosage form allows
  - Work practices that promote containment
- Should = recommendation
  - Use of CSTDs for compounding
  - Wipe samples for environmental sampling
  - Medical surveillance

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Receiving and Storage

- HDs can be received in the same area as other drugs
  - Should have a designated area
  - Can be neutral/normal or negative pressure
  - Cannot be positive pressure
- HDs (unless entity-exempt through the Assessment of Risk)
  - Must be stored with proper containment

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Closed System Drug-Transfer Device

- CSTDs mechanically prohibit the transfer of environmental contaminants into the system and the escape of hazardous drug or vapor
- Required for administration when the dosage form allows
- Recommended for use when compounding

Photo courtesy of BD

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Personal Protective Equipment (PPE)

- Gloves tested to ASTM D6978
- Gowns that are impervious, close in back, knit or elastic sleeves
- In certain cases
  - Respirator
  - Eye protection

Disposable PPE cannot be re-used

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Work Practices

- Policies and procedures
- Containment
  - Outside of container once compound completed
  - Waiting for administration
- PPE
- Decontamination procedures

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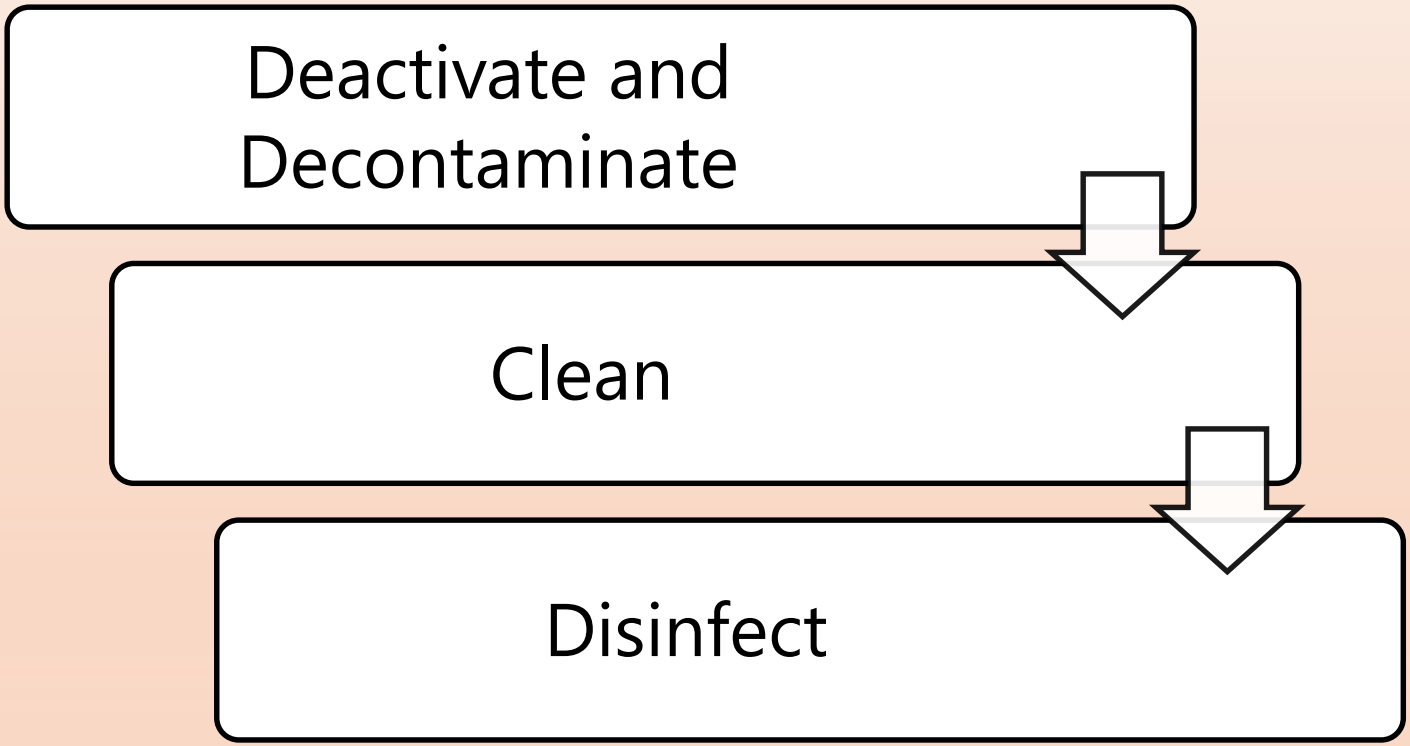
Cleaning Process for HDs



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Cleaning Steps

Function	Agent
Deactivate and decontaminate	Properly-diluted EPA-approved oxidizer intended for use with HDs
Clean	Germicidal detergent
Disinfect	70% isopropyl alcohol (sterile for sterile compounding)

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Resources

- USP <800> FAQs
  - http://www.usp.org/frequently-asked-questions/hazardous-drugs-handling-healthcare-settings
- www.readyfor800.com
  - One hour panel discussion (physician, nurse, pharmacist
  - Short (~5 minute) videos targeted to specific audiences
  - Ready for 800 checklist
- *Perform an Assessment of Risk to Comply with USP <800>*
  - Pharmacy Purchasing and Products (www.pppmag.com), March 2017

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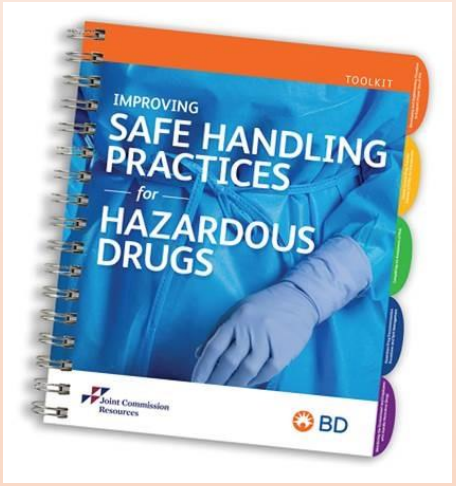
References

www.ons.org



www.hazmedsafety.com

www.ashp.org

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