New Guidelines for Handling Hazardous and Cytotoxic Agents

Implementation of USP 800

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Disclosures

- None

Objectives

- Review USP 800 and USP 797 guidelines.
- Discuss changes in practice for nursing, pharmacy, radiation, environmental services, and other healthcare workers in the handling of hazardous and cytotoxic agents.
- Describe implementation of specific practices at Aspirus Regional Cancer Center to limit exposure including the installation of a robot for hazardous medication admixture

You really want to know…

What's taking so long?

Why do I have to wear this?

What's that smell?

Alphabet Soup

- USP: United States Pharmacopeia
- NIOSH: National Institute for Occupational Safety and Health
- OSHA: Occupational Safety and Health Administration
- EPA: Environmental Protection Agency

Alphabet Soup

- HD: Hazardous Drug
- PPE: Personal Protective Equipment
- HEPA: High-Efficiency Particulate Air
- CSTD: Closed-System Transfer Device
- BSC: Biological Safety Cabinet
- PAPR: Powered Air-Purified Respirator
- SDS: Safety Data Sheet

USP 800: General Chapter on Hazardous Drugs- Handling in Healthcare Settings

USP 800: why

- “Provides standards for safe handling of hazardous drugs to minimize the risk of exposure to healthcare personnel, patients and the environment”

USP 800
Risks

- 8 million healthcare workers potentially exposed to chemotherapy agents in US annually
- Data from 1970s and 80s with minimal or no controls
  - Odds ratio for miscarriage 2.3 for nurses exposed to chemo
  - No significant association with congenital malformations or stillbirths
  - Acute symptoms of skin exposure
  - High levels of exposure over long-term associated with liver damage
- No studies looking at data after improved controls

USP 800: what

- Federally enforceable standard (NOT a guideline)
  - FDA
  - State law
  - Other regulatory agencies
- Joint Commission
  - May use as a standard of practice for accreditation

USP 800: what

- Describes **requirements** for:
  - personnel handling hazardous drugs
  - facility and engineering controls
  - procedures for deactivating, decontaminating and cleaning
  - spill control
  - documentation of the above

USP 800: who

Applies to **all healthcare personnel** who receive, prepare, administer, transport or otherwise come in contact with hazardous drugs

- Pharmacists/pharmacy technicians
- Nurses
- Providers
- Home health workers
- Veterinarians/vet technicians

USP 800: where

Applies to **all entities** in which they are handled

- Pharmacies
- Hospital or other healthcare institutions
- Clinics
- Physician practices
- Veterinary offices

USP 800: when

- Soon!
- Enforceable by December 1, 2019

NIOSH Guidelines

NIOSH List

- NIOSH Alert published in 2004
  - Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Healthcare Settings
  - HD list compiled from 4 institutions as well as lists from PhRMA
  - Updated in 2010, 2012, 2014, and 2016

Hazardous Drug (HD)
NIOSH Definition

- Carcinogenicity
- Teratogenicity
- Reproductive toxicity
- Organ toxicity at low doses
- Genotoxicity
- Structure and toxicity profiles of new drugs that mimic existing drugs determined hazardous by the above criteria
- In addition, drugs with safe-handling guidelines from manufacturers automatically on the list

NIOSH 2016

Hazardous Drug (HD)

NIOSH List

- Group 1: Antineoplastic Drugs
- Group 2: Non-antineoplastic drugs that meet one or more of the NIOSH criteria for a hazardous drug
- Group 3: Drugs that primarily pose a reproductive risk to men and women who are actively trying to conceive and women who are pregnant or breastfeeding

Hazardous Drug (HD)

Group 1: Antineoplastic Drugs (examples)

- Capecitabine
- Cisplatin
- Doxorubicin
- Etoposide
- Methotrexate
- Temozolomide
- Vincristine
- Fulvestrant
- Letrozole
- Leuprolide
- Megestrol
- Pertuzumab
- Tamoxifen

NIOSH 2016

Hazardous Drug (HD)

Group 2: Non-antineoplastic HD (examples)

- Azathioprine
- Cyclosporine
- Ganciclovir
- Mycophenolate
- Tacrolimus
- Thalidomide
- Valganciclovir
- Zidovudine
- Carbamazepine
- Divalproex
- Estrogens
- Medroxyprogesterone
- Phenytoin
- Risperidone
- Spironolactone

NIOSH 2016

Hazardous Drug (HD)

Group 3: Reproductive Risk (examples)

- Clomiphene
- Finasteride
- Misoprostol
- Ribavirin
- Testosterone
- Warfarin
- Clonazepam
- Colchicine
- Fluconazole
- Oxytocin
- Pamidronate
- Paroxetine
- Zoledronic acid

NIOSH 2016

Personal Protective Equipment (PPE)

NIOSH Guidance

- Double chemotherapy gloves
- Protective gown
- Eye/face protection
- Respiratory protection
- Ventilated engineering control
- Applies to all drugs in tables 1-3

USP 800 Standard

USP 800

Must → Requirement

Should → Recommendation

Institution HD list

USP requirement

- USP 800 requires that each institution create an HD list which includes all drugs on the NIOSH list that they utilize
- An assessment of risk (AoR) must be done for each drug that doesn't follow all safe handling guidelines
- Process for assessing drugs new to market

Containment
USP 800 Requirement

- Must be followed for:
  - any HD active pharmaceutical ingredient
  - Antineoplastic requiring manipulation
- All requirements do not need to be followed for (assessment of risk needed):
  - Final dosage forms of HDs
  - Conventionally manufactured HDs
  - Antineoplastics that do not require further manipulation other than counting or repackaging

Assessment of Risk (AoR)

USP 800 Requirement

- Type of HD
- Dosage form
- Risk of exposure
- Packaging
- Manipulation
- Document alternative containment strategies or work practices to minimize exposure
- Review and document every 12 months

Types of Exposure
USP 800

- Receipt
- Dispensing
- Compounding or manipulation
- Administration
- Patient-care activities (body fluids, etc.)
- Spills
- Transport
- Waste

Personnel Responsibilities

USP Requirements

- Designated person
- Training

Facilities and Engineering Controls

USP 800 Requirements

- Designated areas for
  - Receipt and unpacking
  - Storage
    - Negative pressure room for anti-neoplastics requiring manipulation

Facilities and Engineering Controls

USP 800 Requirements

- Compounding
  - Hood externally vented
  - Located in a clean room, anteroom, or segregated compounding area
  - Negative pressure

Facilities and Engineering Controls

- USP 800 is silent regarding compounding robots

Closed-System Transfer Devices

USP 800

- **Should** be used for compounding HDs when the dosage form allows
- **Must** be used for administering antineoplastic HDs (NIOSH group 1) when dosage form allows

Environmental Quality Control
USP 800

- Wipe sampling should be performed routinely
  - Chemo hood
  - Chemo room surfaces
  - Patient administration areas
- No standard for acceptable limits

PPE
USP 800 **Requirements**

- Compounding
  - Gowns, head, hair, shoe covers, and two pairs of chemo gloves for all antineoplastic HDs

PPE
USP 800 **Requirements**

- Administration
  - Two pairs of chemo gloves and gowns for injectable antineoplastic HDs (NIOSH group 1)
  - Gowns, eye and face protection when risk of splashing

PPE

USP 800 **Recommendations**

- Assessment of risk for each HD that does not require further manipulation
- Chemotherapy gloves **should** be worn for handling all HDs (NIOSH groups 1, 2, 3). This includes receiving, unpacking, and placing in storage
- This may be addressed in the assessment of risk

PPE
USP 800 **Recommendations**

- Respiratory protection when needed
  - Fit-tested N95 respirator for airborne particles
  - Full-face-piece chemical cartridge respirator or powered air-purifying respirator (PAPR) for spills larger than spill kit can contain, cleaning under C-PEC work surface, known vapors or powders

Hazard Communication Program
USP 800

- Establish policies and procedures for all aspects of HD handling
  - Implementation plan
  - Identifying HDs
  - SDS readily accessible
  - Personnel training on HD
  - Personnel of reproductive capability must confirm in writing that they understand the risk of handling HDs
  - Alternative duty

Personnel Training
USP 800

- Overview of HD list
- Review of policies and SOPs
- PPE
- Engineering controls
- Response to HD exposure
- Spill management
- Disposal

Compounding
USP 800

- Must additionally follow all other compounding standards for sterile and non-sterile drugs
  - USP 797
  - Includes the recording of lot and expiration date for each ingredient

Administering
USP 800

- Protective devices
  - CSTD
  - Needleless systems
- Protective practices
  - Spiking or priming IV tubing in C-PEC
  - Crushing tablets in a plastic pouch
  - PPE for opening capsules or crushing tablets

Deactivating, Decontaminating, Cleaning, and Disinfecting

USP 800

- Deactivation – inactivates compound
- Decontamination – removes residue
- Cleaning – removes organic and inorganic material
- Disinfection – destroys microorganisms (for sterile environment)

Deactivating, Decontaminating, Cleaning, and Disinfecting

USP 800

- Bleach → sodium thiosufate → germicidal → sterile alcohol

  Peroxide → peroxide →sterile alcohol
- C-PEC decontaminated at least daily
- Under trays in C-PEC at least monthly
- Must wear PPE
- Respiratory protection may be required to clean under trays

Spill Control
USP 800

- PPE
- Spill kit
- Document spill
- Qualified personnel trained to clean HD spill
  - Must be available any time an HD is handled
- Respiratory protection available if spill larger than contained in spill kit or risk of vapors

Medical Surveillance

USP 800 Recommendation

- Identify personnel potentially exposed to HDs
- Baseline health status and medical history
- HD exposure history or estimate
- Physical or laboratory assessment, if needed
- Periodic evaluation
- Follow-up plan for personnel with health changes for potential acute exposure

HD Handling

- ASHP
- ONS
- OSHA
- NIOSH
- USP

ASCO HD Handling Standards

- 2019 review of current standards and literature by expert panel
- 4 areas where additional evidence needed
  - Medical surveillance
  - CSTDs
  - External ventilation
  - Alternative duty

J Clin Oncol 2019;37:598-609

USP 800 Implementation

- Gather experts
- Determine which entities handle HDs
- Review current policies and procedures
- Explore standards, guidelines, and recommendations
- Develop HD list
- Perform assessments of risk
- Training
- Communication

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Questions?