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Managing Hazardous Drug Exposures: Information for Healthcare Settings

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

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Foreword

Many pharmaceutical drugs intended for individual use can be hazardous to healthcare workers with potential occupational exposure to those who handle, prepare, dispense, administer, or dispose of these drugs. Workplace exposure to hazardous drugs can result in negative acute and chronic health effects in healthcare workers including adverse reproductive outcomes.

In Chapter 8 of this document, there is a *Table of Control Approaches for Safer Handling of Hazardous Drugs*, which was derived from the table *Personal Protective Equipment and Engineering Controls for Working with Hazardous Drugs in Healthcare Settings* (often referred to as Table 5), published in previous iterations of the *The NIOSH List of Antineoplastic and Other Hazardous Drugs*. That table, referred to here as the Table of Control Approaches, provides information for some of the possible scenarios that workers may encounter in healthcare settings when handling hazardous drugs. Find the latest information, including current publications, at [NIOSH Hazardous Drug Exposures in Healthcare](#).

Executive Summary

To increase awareness of potential adverse health effects of occupational exposure to hazardous drugs, NIOSH has updated the *NIOSH List of Hazardous Drugs in Healthcare Settings (List)* approximately every two years since 2010 [NIOSH 2016]. NIOSH uses a sequential approach for assessing and interpreting scientific information to determine whether a Food and Drug Administration (FDA)-approved drug meets the NIOSH definition of a hazardous drug. The NIOSH definition of a hazardous drug is a drug that is

A. Approved for use in humans¹ by FDA’s Center for Drug Evaluation and Research (CDER),²

B. Not otherwise regulated by the U.S. Nuclear Regulatory Commission,³ and

C. Either

1. Is accompanied by prescribing information in the “package insert”⁴ that includes a manufacturer’s special handling information (MSHI),⁵ or
2. Is determined to be a carcinogenic hazard, developmental hazard, reproductive hazard, genotoxic hazard, or other health hazard by exhibiting one or more of the following toxicity criteria in humans, animal models, or in vitro systems:
 - Carcinogenicity,
 - Developmental toxicity (including teratogenicity),
 - Reproductive toxicity,
 - Genotoxicity,

¹Although only drugs approved by FDA for use in humans are included in the definition of hazardous drug, some of those drugs may be used in veterinary settings for treatment of animals and may be a hazard for veterinary care workers.

²Although biological products, such as vaccines, blood and blood components, allergenics, somatic cells, gene therapy, tissues, and recombinant therapeutic proteins, are included in the FDA definition of a drug, they are not included in the drugs that NIOSH evaluates for potential inclusion on the *List* because they are approved for use by FDA’s Center for Biologics Evaluation and Research (CBER), not by FDA’s CDER. This provision makes clear NIOSH’s long-standing practice of only considering drugs approved by FDA CDER.

³10 CFR Parts 19, 20, and 35. See <https://www.nrc.gov/materials/miau/med-use.html>. Drugs regulated by the Nuclear Regulatory Commission are not included on the *List*.

⁴See Drug Advertising: A Glossary of Terms at <https://www.fda.gov/drugs/resourcesforyou/consumers/prescriptiondrugadvertising/ucm072025.htm>. “Prescribing information is also called product information, product labeling, or the package insert (“the PI”). It is generally drafted by the drug company and approved by FDA. This information travels with a drug as it moves from the company to the pharmacist. It includes the details and directions healthcare providers need to prescribe the drug properly. It is also the basis for how the drug company can advertise its drug. The prescribing information includes such details about the drug as: its chemical description; how it works; how it interacts with other drugs, supplements, foods, and beverages; what condition(s) or disease(s) it treats; who should not use the drug; serious side effects, even if they occur rarely; commonly occurring side effects, even if they are not serious; effects on specific groups of patients, such as children, pregnant women, or older adults and how to use it in these populations.”

⁵MSHI includes language that informs those handling the drug of the need to follow heightened handling and disposal procedures. For example, language such as “follow special handling and disposal procedures,” or “procedures for proper handling and disposal of anticancer drugs should be considered” is frequently used in package inserts. However, NIOSH does not consider language pertaining to packaging and temperature controls as MSHI.

- Organ toxicity at low doses,⁶ or a
- Structure and toxicity profile that mimics existing drugs determined hazardous by exhibiting any one of the previous five toxicity types.⁷

However, if a drug also exhibits a molecular property⁸ that may limit the potential for adverse health effects from exposure to the drug in healthcare workers, it may be determined it is not a hazard.

This document builds upon previous work by NIOSH including the *NIOSH Alert: Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs* and the table *Personal Protective Equipment and Engineering Controls for Working with Hazardous Drugs in Healthcare Settings* (often referred to as “Table 5”), published in previous iterations of the *List*.

Exposure to hazardous drugs has been associated with many adverse health effects, such as an increase in the risk of leukemia and other cancers, a risk of damage to organs or organ systems, and a risk to the ability to successfully conceive and have healthy babies [Connor et al. 2014; NIOSH 2004a; NTP 2019; ONS 2018]. Some hazardous drug(s), (subsequently identified as drug(s) in this document), can damage DNA, leading to an increased risk of many types of cancer. Some drugs can damage organs or organ systems, such as the liver or nervous system. Some drugs can harm those who may become pregnant, or put the health of the fetus at risk. Some drugs handled or used in the healthcare workplace by those who are breastfeeding can also harm their children by entering breast milk. Some drugs can affect fertility and make it harder to conceive.

Occupational risks include the potential for and severity of adverse effects in workers from their exposure to workplace hazards. Risk results from the combination of the hazard (harm from a substance) and the likelihood and consequences of exposure [AIHA 1997]. Employers can reduce these risks by developing and implementing a risk

⁶All drugs have toxic side effects, but some exhibit toxicity at low doses. The level of toxicity reflects a continuum from relatively nontoxic to production of toxic effects in patients at low doses (for example, a few milligrams or less). For example, a daily therapeutic dose of 10 milligrams per day (mg/day) or a dose of 1 milligram per kilogram (mg/kg) per day in laboratory animals that produces serious organ toxicity, developmental toxicity, or reproductive toxicity has been used by the pharmaceutical industry to develop occupational exposure limits (OELs) of less than 10 micrograms per cubic meter ($\mu\text{g}/\text{m}^3$) after applying appropriate uncertainty factors [Naumann and Sargent 1997; Sargent and Klirk 1988; Sargent et al. 2002]. OELs in this range are typically established for potent or toxic drugs in the pharmaceutical industry.

⁷NIOSH [2004]. *NIOSH Alert: preventing occupational exposures to antineoplastic and other hazardous drugs in health care settings*. By Burroughs GE, Connor TH, McDiarmid MA, Mead KR, Power LA, Reed LD, Coyle BJ, Hammond DR, Leone MM, Polovich M, Sharpnack DD. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2004-165.

⁸Properties of a drug molecule that may limit adverse effects in healthcare workers are typically chemical, physical, and structural properties that affect its absorption (ability to enter the cells of the body), e.g., chemical structure, molecular weight, or mass. See Clementi F, Fumagalli G [2015]. *Molecular pharmacology*. Hoboken, NJ: Wiley & Sons; Di L, Kerns EH [2016]. *Drug-like properties: concepts, structure, design, and methods*. Oxford, UK: Elsevier; Mattson P, Kihlberg J [2017]. How big is too big for cell permeability? *J Med Chem* 60(5):1662–1664, <https://doi.org/10.1021/acs.jmedchem.7b00237>.

management plan. Effective risk management requires four elements described herein: hazard identification (Chapter 3), exposure assessment (Chapter 4), risk assessment (Chapter 5), and risk management (Chapter 6).

A risk management plan identifies the engineering controls, administrative controls, and personal protective equipment (PPE) that will be implemented to reduce the risks identified in the risk assessment. Risk management also includes periodic exposure assessments and medical surveillance that should be conducted to determine the degree of control obtained. The written risk management plan should be part of an overall Safety Management System.

Several organizations developed approaches to protect workers from occupational exposure to hazardous drugs [ASHP 2006; NIOSH 2004a; ONS 2018; OSHA 1999, 2016; Power and Coyne 2018; USP 2016]. In general, these approaches adhere to the hierarchy of controls for standard industrial hygiene practice. These controls can include hazard elimination or substitution (when feasible), followed by the use of engineering controls, administrative controls and PPE [NIOSH 2015; ONS 2018].

Engineering controls prevent or reduce exposures by extracting the drug from the workplace or placing a barrier between the worker and the drug, which isolates and contains the process or equipment. Well-designed engineering controls are typically independent of worker interactions or are integrated easily into tasks and can provide a high level of protection.

Administrative controls, such as work practices, are most effective when they are made part of a greater safety and health culture within an organization. They can reduce the surface and airborne concentrations of workplace contaminants or remove workers from sources of workplace contaminants and thus can reduce a worker's potential exposure.

PPE provides worker protection to reduce exposure to hazardous drugs. PPE is the least-effective measure for protecting workers but may be necessary when other controls haven't been implemented, are not fully protective, or are infeasible. Selection of PPE should be based on an assessment of workplace hazards per the Department of Labor's Occupational Safety and Health Administration (OSHA) PPE Standard in 29 CFR § 1910.132. It is important to understand the proper use and limitations of any selected PPE to ensure that it fits correctly and is constructed of materials that offer protection from exposure to the hazardous drugs in use [NIOSH 2004a,b].

Medical surveillance has been successful as secondary prevention in other occupational settings for early detection of adverse health effects. Medical surveillance can help identify sentinel adverse health effects among workers, thereby suggesting where improvements in primary prevention are needed.

The potential for exposure of workers when handling a hazardous drug depends on several factors unique to each work setting. Such factors include the following: (1) the dosage form of the drug, (2) the routes of exposure, (3) the frequency and duration of the task, (4) work practices, and (5) the presence or absence of any exposure controls such as engineering controls, administrative controls, or PPE. The Table of Control Approaches in Chapter 8 provides information for some of the possible scenarios that workers may encounter in healthcare settings when handling hazardous drugs.

Efforts should be made to reduce all worker exposures to hazardous drugs. Occupational exposure to hazardous drugs merits serious consideration, as workers may be exposed daily to multiple hazardous drugs over many years. NIOSH suggests careful precautions and safeguards to protect workers, fetuses, and breastfed infants.

Periodic exposure assessments are needed to evaluate whether the risk management plan is effectively preventing healthcare worker exposures.

Healthcare facility or healthcare system worker safety and health management should consult with senior medical leadership to communicate the risks to workers from hazardous drugs and explore ways to reduce that risk while maintaining desired levels of patient care.

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Acronyms

AIHA	American Industrial Hygiene Association
ALARA	as low as reasonably achievable
ANA	American Nurses Association
ANSI	American National Standards Institute
ASHP	American Society of Health-System Pharmacists (formerly known as American Society of Hospital Pharmacists)
ASL	acceptable surface limit
BSC	biological safety cabinet
CACI	compounding aseptic containment isolator
CBER	Center for Biologics Evaluation and Research
CDER	Center for Drug Evaluation and Research
CFR	Code of Federal Regulations
C-PEC	containment-primary engineering control
C-SCA	containment-segregated compounding area
C-SEC	containment-secondary engineering control
CSTD	closed system drug-transfer device
CVE	containment ventilated enclosure (powder containment hood)
DNA	deoxyribonucleic acid
EPA	Environmental Protection Agency
FDA	Food and Drug Administration
HEPA	high efficiency particulate air
HIPEC	hyperthermic intraperitoneal chemotherapy
HVAC	heating, ventilation, and air conditioning
IARC	International Agency for Research on Cancer
IV	intravenous
MSHI	manufacturer's special handling information
NG	nasogastric
NIOSH	National Institute for Occupational Safety and Health
NSF	National Science Foundation
NTP	National Toxicology Program
OEL	occupational exposure limit
ONS	Oncology Nursing Society
OSHA	Occupational Safety and Health Administration

PAPR	powered air-purifying respirator
PO	administering of drug by mouth (from Latin “per os”)
PPE	personal protective equipment
RCRA	Resource Conservation and Recovery Act
SOP	standard operating procedure
SDS	safety data sheet (formerly material safety data sheet)
USP	United States Pharmacopeia

Glossary

Except as referenced, NIOSH is defining the following terms for purposes of this document:

Administering: The giving or application of a pharmacologic or other therapeutic agent.

Administrative controls: Controls that alter the way the work is done, including work practices and procedures (including timing of work, housekeeping, and personal hygiene practices).

Antineoplastic drug: A chemical agent that inhibits or prevents the growth and spread of tumors or malignant cells.

Biological safety cabinet (BSC): An enclosed, ventilated laboratory workspace for safely working with biologically active materials. There are three classes of BSCs, distinguished by the level of personnel and environmental protection provided and the level of product protection provided.

Carcinogenicity: The ability to produce cancer.

Chemotherapy drug: A chemical agent used to treat diseases. The term usually refers to a drug used to treat cancer.

Closed system drug-transfer device (CSTD): A drug-transfer device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of hazardous drug or vapor concentrations outside the system.

Compounding: Process of combining, mixing, or altering ingredients by or under the direct supervision of a licensed pharmacist or physician to create a prescribed medication tailored to the needs of an individual patient.

Compounding aseptic containment isolator (CACI): Primary engineering control compounding isolator that is designed to protect the sterile compounding process while also using air pressurization and isolation techniques to protect the operator.

Containment Ventilated Enclosure (CVE): A full or partial enclosure that uses ventilation principles to capture, contain, and remove airborne contaminants through HEPA filtration and prevent their release into the work environment. This is sometimes referred to as a “powder containment hood.”

Containment-primary engineering control (C-PEC): A ventilated device designed and operated to minimize worker and environmental exposures to hazardous drugs by controlling emissions of airborne contaminants.

Containment-segregated compounding area (C-SCA): A type of C-SEC limited for use with a BSC or CACI when preparing low- or medium-risk-level sterile preparations.

Containment-secondary engineering control (C-SEC): The room in which the C-PEC is placed. It incorporates specific design and operational parameters required to contain the potential hazard within the compounding room (e.g., restricted access, barriers, special construction technique, ventilation, and room pressurization may be components of the secondary control strategy).

Cytotoxicity: A detrimental action on or destruction of cells within the body.

Deactivation: Renders a hazardous drug compound inert or inactive.

Decontamination: Removes hazardous drug residue.

Developmental hazard: A hazard that alters the structure or function of a developing embryo or fetus, apparent either before or after birth.

Disinfection: A process of inhibiting or destroying microorganisms.

Engineering controls: Devices or systems designed to eliminate or reduce worker exposures to chemical, biological, or physical hazards. Examples of those used in healthcare include laboratory fume hoods, glove bags, needleless systems, closed system drug-transfer devices, biological safety cabinets, containment isolators, and robotic systems.

Exposure assessment: The multi-disciplinary process of estimating or measuring the magnitude, frequency, and duration of exposure to an agent. It includes the sources, pathways, routes, and uncertainties in the assessment. It is often used to compare exposures to established exposure limits; develop exposure-response relationships; inform risk assessment studies; and evaluate the effectiveness of risk management plans.

Genotoxicity: The ability to damage or mutate DNA. Genotoxic substances are not necessarily carcinogenic.

Glove bag: A flexible, sometimes inflatable, plastic chamber with built-in gloves that allows isolation of a small work volume.

Hazardous drug: A drug that is, according to the NIOSH definition,

- A. Approved for use in humans¹ by FDA's Center for Drug Evaluation and Research (CDER),²
- B. Not otherwise regulated by the U.S. Nuclear Regulatory Commission,³ and
- C. Either

- 1. Is accompanied by prescribing information in the "package insert"⁴ that includes manufacturer's special handling information (MSHI)⁵ or

2. Is determined to be a carcinogenic hazard, developmental hazard, reproductive hazard, genotoxic hazard, or other health hazard by exhibiting one or more of the following toxicity criteria in humans, animal models, or in vitro systems: carcinogenicity; developmental toxicity (including teratogenicity); reproductive toxicity; genotoxicity; organ toxicity at low doses;⁶ or a structure and toxicity profile that mimics existing drugs determined hazardous by exhibiting any one of the previous five toxicity types,⁷ unless the drug also exhibits a molecular property⁸ that may limit the potential for adverse health effects in healthcare workers from exposure to the drug.

Healthcare settings: Settings include but are not limited to acute-care hospitals; long-term care facilities, such as nursing homes and skilled nursing facilities; physicians' offices; urgent-care centers; outpatient clinics; home healthcare (i.e., care provided at home by professional healthcare providers), and emergency medical services.

Hierarchy of controls: The preferred order of approaches used to reduce or eliminate exposures to hazards. For chemicals, this specifies that when elimination or substitution with a less toxic substance is not feasible, exposure controls should be preferentially implemented in the following decreasing order of efficacy: engineering controls, administrative controls, and personal protective equipment.

Package insert: A manufacturer's printed guideline for the use and dosing of a drug; includes the pharmacokinetics, dosage forms, and other relevant information about a drug.

Personal protective equipment (PPE): Items such as gloves, gowns, respirators, goggles, and face shields that protect the individual worker from injury, infection, or hazardous physical, chemical, or biological agents by providing a barrier between the worker and the hazardous agent.

Reproductive hazard: An agent that interferes with the ability to achieve a pregnancy ending in a healthy, live birth. Reproductive hazards may affect fertility, conception, pregnancy, or delivery.

Restricted Access Barrier System (RABS): An advanced aseptic processing unit for pharmaceutical compounding.

Risk Assessment (RA): The overall process of hazard identification, risk analysis, and risk evaluation.

Sharps injury: A puncture or cut from a needle, scalpel, or another sharp object that may result in exposure to blood, other body fluids, or hazardous drugs.

Teratogenicity: The ability to produce physical or functional defects in the human embryo or fetus after the pregnant woman is exposed to a substance.

Ventilated cabinet: A type of engineering control designed to protect workers. Examples include BSCs and isolators designed to prevent hazardous drugs inside the cabinet from escaping into the work environment.

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1 Purpose and Scope

This document contains risk management information and a Table of Control Approaches describing some of the possible scenarios that workers may encounter in healthcare settings when handling hazardous drugs. The potential exposure of workers from handling a hazardous drug depends on several factors unique to each work setting. Such factors include (1 the dosage form of the drug, (2 the routes of exposure, (3 the frequency, duration, and magnitude of exposure, (4 work practices, and (5 the presence or absence of any exposure controls such as engineering controls, administrative controls, or personal protective equipment (PPE). The National Institute for Occupational Safety and Health (NIOSH encourages healthcare settings to conduct a facility-specific assessment to determine the most effective exposure control strategies for controlling the risks identified in the assessment. Healthcare facilities should repeat these assessments when operating procedures are modified, new controls are put in place, the volume of patients or drug-handling activities increase compared to the baseline, new drugs enter the workplace, hazardous-drug-related injuries occur, illnesses or near-miss incidents are reported, or when deviations from assigned control practices are identified.

2 Background

2.1 History of the NIOSH Hazardous Drug List

To increase awareness of the potential adverse health effects from occupational exposure to hazardous drugs, in 2004 NIOSH published an *Alert* titled, *Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Healthcare Settings*. It contained information for reducing exposures to hazardous drugs for all healthcare workers, as well as a list of drugs determined to be hazardous to workers' health [NIOSH 2004a]. NIOSH has updated the list of hazardous drugs from the *Alert* about every 2 years since 2010 [NIOSH 2016].

In response to stakeholders' need to better understand how to manage risks when handling hazardous drugs in the workplace, the 2014 and 2016 NIOSH *List of Hazardous Drugs in Healthcare Settings* also provided a table titled *Personal Protective Equipment and Engineering Controls for Working with Hazardous Drugs in Healthcare Settings* (referred to as Table 5). The table contained information on the safe handling of hazardous drugs and ways to reduce exposure through the use of engineering controls and PPE. This informational table, now titled *Control Approaches for Safer Handling of Hazardous Drugs by Activity and Formulation* (Table of Control Approaches, has been revised, removed from the *List*, and is presented in Chapter 8 of this document. The new table, along with this current document, the *NIOSH List of Hazardous Drugs in Healthcare Settings* (the *List*), and *Procedures for Developing the NIOSH List of Hazardous Drugs*

in *Healthcare Settings (Procedures)*, are all available on the [NIOSH Hazardous Drug Exposures in Healthcare](#) website.

This document is relevant to places of employment where workers handle hazardous drugs. Workers potentially exposed to hazardous drugs in these settings may include pharmacists and pharmacy technicians, nurses, nursing assistants, physicians, dentists, physician assistants, operating room personnel, shipping and receiving personnel, waste handlers, maintenance workers, laundry workers, environmental services workers, laboratory personnel, veterinarians, veterinary technologists, and other veterinary care workers. The current number of healthcare workers in the United States potentially exposed to hazardous drugs exceeds 8.5 million [BLS 2020].

2.2 Addressing the Risks of Hazardous Drugs

Occupational risks include the potential for and severity of adverse effects in workers from their exposure to workplace hazards. Risk is from the hazard (or potential harm from an agent) and the exposure (whether a worker interacts with an agent) [AIHA 1997]. Employers can mitigate these risks by safeguards derived from a combination of scientific assessment and best management practices. Effective risk management requires four elements: hazard identification, exposure assessment, risk assessment, and the risk management plan [NRC 2011]. After the healthcare facility identifies hazardous drugs and assesses exposures, the next step is to conduct a risk assessment. This involves analysis and evaluation of the risks associated with the use of hazardous drugs in the workplace. The components and products of risk assessment provide the focus for the risk management program (Figure 1).

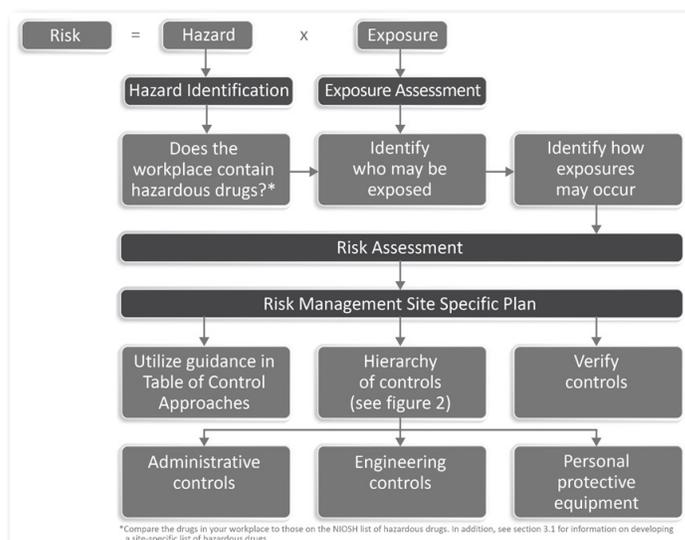


Figure 1. Elements of risk assessment provide the focus for a risk management program.

A risk management program should identify the potential safety and health hazards, characterize the opportunities for human or environmental exposures (including exposure by both intended use and accidental release), and include a plan to control the potential exposures [NRC 2011]. Because there are known hazards associated with all of the drugs on the hazardous drugs list, managing the potential for exposure during receiving, storage, use, and disposal of hazardous drugs should be part of a documented risk management program. Chapter 6, Risk Management Plan, addresses the steps to control potential exposures to minimize the risks.

The risks from exposure to hazardous drugs vary

The chance that hazardous drugs will harm healthcare workers and the severity of the harm depend on the drugs toxicity, formulation, routes of exposure and work practices.

- **A drug's toxicity** refers to the harm it can cause to a person's health. Cytotoxic drugs are administered to have a detrimental action on or destroy cells, such as cancer cells, but they may also kill healthy cells in healthcare workers who work with or handle them, leading to adverse health effects. Some drugs may harm a person's ability to reproduce, and some drugs have been associated with leukemia and other cancers.
- **Drug formulation** refers to the form the drug takes—such as capsules, tablets, powders, liquids, creams, transdermal patches, or prefilled syringes.
- **Route of exposure** applies to how workers may be exposed to the drug, such as through inhalation, absorption through skin or mucous membranes, ingestion, or accidental injection.
- **Workplace activity** involves how healthcare workers use and handle the drug in the workplace—such as opening shipments, compounding, administering, or cleaning up after use or spills.

Possible health risks from occupational exposure

Exposure to hazardous drugs has been associated with many adverse health effects, including an increase in the risk of leukemia and other cancers, a risk of damage to organs or organ systems, and a risk to the ability to reproduce (successfully conceive and have healthy babies) [ASHP 2006; Connor and McDiarmid 2006; Connor et al. 2014; Lawson et al. 2012; NIOSH 2004a; NTP 2019; ONS 2011; Power and Coyne 2018]. Some drugs handled or used in the healthcare workplace can also be a concern for those who breastfeed because their exposure to hazardous drugs in the workplace may enter their breast milk. In addition, many drugs that are known carcinogens have no known safe levels of exposure.

The following chapters contain information on the four elements of managing risk: hazard identification, exposure assessment, risk assessment, and risk management.

3 Hazard Identification

NIOSH uses a procedural approach for assessing and interpreting scientific information to determine whether a drug approved by the Food and Drug Administration Center for Drug Evaluation and Research (FDA CDER) meets the NIOSH definition of a hazardous drug [NIOSH 2023]. Drugs considered hazardous include those accompanied by prescribing information in the package insert that includes the manufacturer's special handling information (MSHI) or those determined to meet one or more of the following toxicity criteria: carcinogenicity; developmental toxicity (including teratogenicity); reproductive toxicity; genotoxicity; organ toxicity at low doses; or a structure and toxicity profile that mimics existing drugs determined hazardous by exhibiting any one of the previous five toxicity types, unless the drug also exhibits a molecular property that may limit the potential for adverse health effects in healthcare workers from exposure to the drug.

Workers in healthcare and related settings are at risk for adverse health effects if they handle, compound, administer, or dispose of hazardous drugs; handle drug waste; handle drug-contaminated body fluids; or clean equipment used with hazardous drugs. The possible adverse health effects include ocular irritation, headache, cough, dizziness, nausea and vomiting, skin rashes, adverse reproductive outcomes, and possibly leukemia and other cancers [ASHP 2006; Connor and McDiarmid 2006; Connor et al. 2014; NIOSH 2004a; NTP 2019; ONS 2009; ONS 2018; Power and Coyne 2018].

3.1 Developing a Facility-specific Hazardous Drug List

Hazardous drug evaluation must be a continuous process completed on a routine basis. Employers can develop a facility-specific list of hazardous drugs by comparing the drugs in their workplace to those on the *List*. In addition, they should assess the hazards of new drugs as they are added to the workplace's formulary or as new information on the potential hazards of drugs become available. They should then reassess whether the drugs should be included on the facility-specific list.

The *Procedures for Developing the NIOSH List of Hazardous Drugs in Healthcare Settings* [NIOSH 2023] provides information on how NIOSH creates a list of hazardous drugs and how other organizations developed various approaches to identifying and classifying hazardous drugs [Badry et al. 2014; Chaffee et al. 2010; Kaestli et al. 2013]. Employers can obtain information about the toxicity, carcinogenicity, and other hazards associated with a particular drug from the drug package insert or from authoritative sources, such as the National Toxicology Program (NTP) or the International Agency for Research on Cancer (IARC). Facilities may need to consider factors that affect them specifically, such as product formulation, chemical characteristics, handling procedures, dosing needs, and workplace-specific practices.

Toxicological data may be incomplete or unavailable for some drugs, specifically investigational drugs. Until adequate information becomes available, it is prudent to handle investigational drugs as hazardous if the mechanism of action suggests that there may be a concern.

4 Occupational Exposure Assessment

All of the drugs on the *List* are considered hazardous, but the risk to the worker depends on exposure. Exposure can occur through inhalation, skin or mucous membrane contact, ingestion, accidental injection, or combinations thereof. Healthcare workers can be exposed to hazardous drugs when these drugs are present in or on work surfaces, drug vials, containers, clothing, medical equipment, and patient excreta and secretions such as urine, feces, vomit, and sweat.

Some activities related to handling hazardous drugs are more likely than others to result in worker exposure, such as bladder instillation [Polovich and Giesecker 2011], administration of the drugs in the operating room [Mellinger et al. 2010; Muehlbauer et al. 2006; Villa et al. 2015], aerosolization [Darwiche et al. 2013], or administration by inadequately trained healthcare professionals [Menonna-Quinn 2013; ONS 2011]. These activities can create aerosols or generate dust, thereby increasing exposure [ASHP 2006; NIOSH 2004a; ONS 2009; OSHA 1999, 2016; Power and Coyne 2018]. Skin absorption and inhalation are the most common ways a healthcare worker may be exposed to hazardous drugs, although ingestion (from hand-to-mouth transfer) or accidental injection through a needle stick or other sharps injury also is possible [NIOSH 2004a, 2016]. In addition, spills and other situations such as disconnected intravenous (IV) lines, leaking IV bags, broken vials, or handling patient waste and soiled linen (e.g., urine, feces, vomit) can lead to substantial worker exposure. These events are also common in the treatment of animals in veterinary settings [Couch et al. 2013; Meijster et al. 2006; NIOSH 2010].

NIOSH recommends that after the initial exposure assessment in facilities where hazardous drugs are handled, periodic follow-up assessments should be conducted, such as when operating procedures are modified, new controls are put in place, the volume of patients or drug-handling activities increases compared to the baseline, new drugs enter the workplace, hazardous drug-related injuries occur, illnesses or near-miss incidents are reported, or when deviations from assigned control practices are identified. The exposure assessment should include an inventory of the known hazardous drugs and determine who may come in contact with the drugs or potentially contaminated work areas [Connor et al. 2016]. An assessment of the potential for exposure should consider chemical properties (such as vapor pressure), each type of dosage formulation,

any potential manipulations of the dosage formulation that may be performed, and the work practices used when handling those drugs.

Some drugs defined as hazardous may not pose a substantial health risk from direct occupational exposure because of their dosage formulation (e.g., coated tablets or capsules—solid, intact medications that are administered to patients without modification of the formulation) [NIOSH 2004a]. However, they may pose a risk if the formulations are altered, such as by crushing tablets, making solutions from bulk powders, or emptying capsules outside of a ventilated cabinet [Goodin et al. 2011; Simmons 2010]. Uncoated tablets may present a potential exposure from dust by skin contact or inhalation when the tablets are handled [Ahmad et al. 2015; Shahsavarani et al. 1993].

Exposure factors that should be assessed include the following:

- Hazardous drugs used during work
- Workers who may be exposed and how those exposures may occur
- Volume, frequency, and form of drugs handled (tablets, coated versus uncoated, powder versus liquid)
- Existing controls such as ventilated cabinets, closed system drug-transfer devices (CSTDs), glove bags, needleless systems, and PPE
- Effectiveness of controls
- Physical layout of work areas
- Procedures for equipment maintenance, decontamination and cleaning, waste-handling and spill-response

5 Risk Assessment

NIOSH recommends that after identifying the hazards and assessing the exposure factors, employers must analyze and evaluate the risks associated with the use of hazardous drugs in the workplace. This activity is often referred to as facility-specific risk assessment. In general, the risks to workers are assessed by considering these factors:

- The hazards,
- The probability of occurrence of adverse health outcomes, and
- The severity of the health effects.

For this document, the hazards are those associated with the hazardous drugs identified in the occupational exposure assessment step described previously. The risk assessment should include evaluating the dosage form and identifying the probability of exposure.

5.1 Probability of Occurrence

For each of the exposure scenarios identified in the exposure assessment, the probability or likelihood that the particular exposure would result in harm to workers is evaluated. This evaluation may include consideration of the dosage form and packaging of the material in the workplace, activities undertaken, frequency of exposure, and engineering controls in place. Exposures may be quantified through exposure monitoring (which provides the most reliable information) or by evaluation of the probability of exposure by a categorical approach, such as sorting scenarios into likely acceptable, uncertain, and unacceptable exposures. This analysis should help to determine potential risk mitigation interventions.

5.2 Severity of Health Effects

NIOSH recommends that employers estimate how serious the potential health effects to workers may be from potential exposures. This step may include consideration of worst-case scenarios, such as identifying a maximum concentration that a worker may be exposed to and the potential resulting health effects. This step helps to identify which scenarios require risk mitigation, given the hazards and likelihood of exposures [AIHA 2015; NIOSH 2003].

Employers should use this risk assessment to identify areas, processes, and scenarios of concern, and to create and implement a facility-specific risk management plan for the safe handling of hazardous drugs. The risk management plan should establish work policies and procedures specific to the handling of hazardous drugs according to the hierarchy of controls (including engineering controls; administrative controls and PPE; verification of controls; and planning for spill response, see Chapters 6 and 7), and it should consider the information presented in the Table of Control Approaches (Chapter 8).

6 Risk Management Plan

The risk management plan is informed by the hazard identification, exposure assessment, and risk assessment, and it identifies points of intervention to mitigate exposures and reduce risks to workers. A risk management plan typically comprises means of implementing engineering controls, administrative controls, PPE, periodic exposure assessments, and medical surveillance based on the sources of exposure and the risks determined in the risk assessment. This chapter describes in general the elements of a risk management plan and the factors employers should consider in addressing those elements.

Occupational exposure to individual drugs merits serious consideration and employers should implement careful precautions and safeguards to prevent exposures to protect

workers. However, workers may be exposed to multiple hazardous drugs, sometimes daily over many years, and the combined effects of hazardous drugs are rarely studied. Therefore, efforts should be made to reduce worker exposures to all hazardous drugs to protect workers, fetuses, and breastfed infants.

Several organizations developed recommendations on how to protect workers from occupational exposure to hazardous drugs, including the American Society of Health-System Pharmacists (ASHP), Oncology Nursing Society (ONS), Occupational Safety and Health Administration (OSHA), and United States Pharmacopeia (USP) General Chapter <800>, Handling of Hazardous Drugs in Healthcare Workers [USP 2016] (see Resources section). In general, the recommendations adhere to the hierarchy of controls (Figure 2) for standard industrial hygiene practices that include elimination or substitution, when feasible, and the use of engineering controls, administrative controls, and PPE [NIOSH 2015].

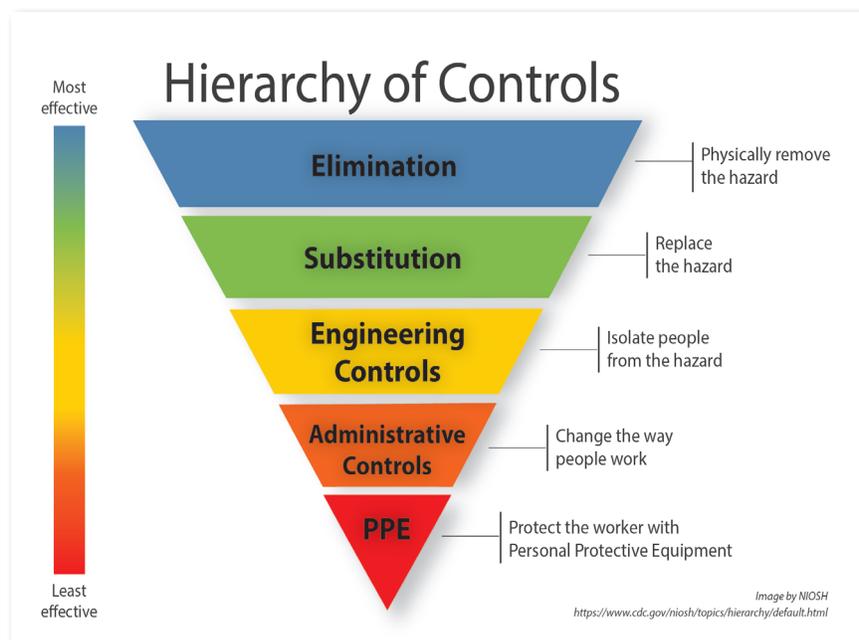


Figure 2. Hierarchy of controls, NIOSH [2015], <https://www.cdc.gov/niosh/topics/hierarchy/>.

The controls at the top of the hierarchy are the most effective and provide the best business value. These improvements in business value are related not only to lower worker compensation rates and healthcare costs to care for injured workers but also to improved operational efficiency, improved employee morale, and decreased employee absenteeism and turnover [AIHA 2008]. Physicians and other prescribers should be made aware of adverse occupational exposure issues with hazardous drugs and should consider substituting nonhazardous drugs when prescribing treatments. Because the use of drugs that are hazardous to healthcare workers who handle them is often unavoidable, the most effective means of decreasing employee exposure to hazardous drugs are engineering controls, administrative controls, and PPE [ONS 2018]. A written plan that details how the institution will implement the hierarchy of controls helps workers, supervisors, and supporting departments understand their respective roles and responsibilities for handling hazardous drugs safely.

6.1 Written Plan

The risk management plan should be written and communicated to and readily available and accessible to all employees, including temporary employees, contractors, and trainees. The comprehensive plan should address all aspects of safe handling of hazardous drugs throughout the facility (receiving, storage, compounding, administration, waste handling, and spill control). It should be developed in a collaborative effort involving all affected departments and specify measures that the employer is taking to ensure employee protection (such as the use of engineering controls, administrative controls, and PPE) [OSHA 2016]. Because hazardous drugs are hazards identified in the Hazard Communication standard, the requirements of the Hazard Communication standard must also be met for drugs posing a health hazard (with the exception of those in solid, final form for direct administration [i.e., tablets]) [29 CFR § 1910.1200]. The written risk management plan should be part of an overall Safety Management System designed to manage all safety risks (including hazardous drugs) in the workplace.

6.2 Engineering Controls

Engineering controls are used when hazardous drug elimination is not possible and less hazardous substitutes are not available or not practical to implement. Engineering controls are implemented to reduce exposures by extracting a hazardous drug from the work environment, such as by ventilation, or by placing a barrier between the worker and the hazard. Barriers typically isolate the process or equipment to contain the hazard and thus prevent it from entering the work environment.

Well-designed engineering controls are typically independent of routine worker interactions or are integrated easily into tasks and provide a high level of protection.

Engineering controls include biological safety cabinets (BSCs) and compounding aseptic containment isolators (CACIs) (Figure 3). Closed system drug-transfer devices (CSTDs) (Figure 4), robotic systems (Figure 5), and needleless systems are considered supplemental controls that should be used only in combination with primary engineering controls (i.e., BSCs and CACIs) to further protect against worker exposures to hazardous drugs. Engineering controls require proper installation, inspection, preventive maintenance, and repair.



Figure 3. Compounding aseptic containment isolator (CACI) cabinet.



Photo by NIOSH



Photo by NIOSH

Figure 4. CSTD devices include a bag or infusion adapter attached to an IV bag and a vial with syringe. Learn more about CSTDs at <https://www.cdc.gov/niosh/topics/hazdrug/CSTD.html>.



Figure 5. A robotic drug preparation system is considered a supplemental control.

The introduction of Class II BSCs for the preparation of hazardous drugs in the 1980s substantially reduced the potential for worker exposure, although surfaces immediately adjacent to the BSCs were typically found contaminated with levels of the antineoplastic agents [Anderson et al. 1982; Connor et al. 1999]. The use of CACIs have been introduced more recently, but adoption has not been widespread. Additionally, CACIs have not been demonstrated to provide more protection for workers than BSCs [Kopp et al. 2013; Mason et al. 2005; Seger et al. 2012]. Use of robotic systems to prepare hazardous drugs may reduce environmental contamination and worker exposure to these drugs. However, their relatively high cost is prohibitive for most facilities [Seger et al. 2012]. The use of CSTDs for the preparation and administration of hazardous drugs has been shown to reduce surface contamination and possibly worker exposure but may not completely eliminate potential exposure [Bartel et al. 2018; Connor et al. 2002; Harrison et al. 2006; Sessink et al. 2011, 2013; Wick et al. 2003]. Workers may experience CSTD failures, resulting in inadequate protection [Friese et al. 2020]. Putting needles on CSTDs makes the systems open and leakage can occur; therefore, workers should use plastic-backed pads.

Devices such as CSTDs, glove bags, and needleless systems should be considered when transferring hazardous drugs from primary packaging (such as vials) to dosing equipment (such as infusion bags, bottles, or pumps). CSTDs limit the potential for

generating aerosols and exposing personnel who are handling hazardous drugs. The literature demonstrates a decrease in internal Class II BSC contamination when a CSTD is used [Connor et al. 2002; Miyake et al. 2013; Nygren et al. 2002; Sessink et al. 1999; Siderov et al. 2010a; Spivey and Connor 2003; Vandenbroucke and Robays 2001; Wick et al. 2003]. However, a CSTD is not an acceptable substitute for a filtered and externally ventilated cabinet, and hazardous drugs should be prepared within a ventilated cabinet.

Formulations of hazardous drugs—including tablets, capsules, powders, transdermal, and liquid, sterile or nonsterile—should be compounded inside a BSC or CACI designed to prevent releases into the work environment. Compounding personnel should prime the IV tubing and syringes inside the ventilated cabinet or prime them in-line with nondrug solutions or by use of a CSTD to prevent the escape of hazardous drugs.

Ventilated cabinets should be selected based on the need for aseptic processing. Aseptic technique is important for protecting hazardous drugs from possible contamination. However, it is also important to consider worker protection and to ensure that worker safety and health are not sacrificed. Therefore, when asepsis is required or recommended, use ventilated cabinets designed for both hazardous drug containment and aseptic processing. Aseptic requirements are generally regulated by each State Board of Pharmacy [Pickard et al. 2016].

When aseptic technique is required, use one of the following types of ventilated cabinets:

- Class II BSCs. BSCs that exhaust filtered cabinet air to the outdoors are recommended. BSCs that exhaust cabinet air back into the segregated engineering control (SEC) are discouraged. When the work activity requires handling volatiles, a risk analysis should be conducted to identify the appropriate Class II BSC selection to ensure that any air recirculation internal to the BSC does not result in vapor accumulation.
- Class III BSCs.
- Isolators intended for asepsis and containment (aseptic containment isolators) [NSF/ANSI 2002; PDA 2001].

When asepsis is not required, a Class I BSC, a containment ventilated enclosure (CVE), or an isolator intended for containment applications (a “containment isolator”) may be sufficient.

Certain areas may be well served to be maintained at negative pressure relative to surrounding areas to contain hazardous drugs and minimize the potential of exposure. Consideration should be given to providing uninterrupted power sources for the ventilation systems to maintain negative pressure in the event of power loss.

The engineering control methods described above are considered as containment-primary engineering controls (C-PECs). A containment-secondary engineering control (C-SEC) is the room in which the C-PEC is placed. The C-SEC should be externally vented to the outside (preferred). Alternatively, if conducting nonsterile compounding with non-volatiles, route the exhaust through redundant HEPA filters in series and recirculate back into the C-SEC. The C-SEC should have fixed walls and doors that separate it from other areas, and maintain a negative pressure relative to adjacent spaces [ASHP 2006; Power and Coyne 2018].

A separate doffing area should be established inside all C-SECs and containment-segregated compounding areas (C-SCAs) for removal of PPE, as one way to minimize tracking of hazardous drug residue to outside the compounding area.

Installation, Air Flow, and Exhaust of Ventilated Cabinets

To properly use ventilated cabinets, follow these recommendations:

- Install, maintain, deactivate, decontaminate, clean, and disinfect the BSC.
- Field-certify BSC performance (1) after installation, relocation, maintenance repairs to internal components, and high efficiency particulate air (HEPA) filter replacement and (2) every 6 months thereafter [NSF/ANSI 2002; OSHA 1999].
- Have readily available or display a current field-certification label prominently on the ventilated cabinet [NSF/ANSI 2002].
- Equip each ventilated cabinet with a continuous monitoring device to confirm adequate air flow before each use.
- Use a HEPA filter for the exhaust, and exhaust 100% of the filtered air to the outside (preferred). Alternatively, if conducting nonsterile compounding with non-volatiles, route the exhaust through redundant HEPA filters in series and recirculate back into the C-SEC.
- Ensure that the air exhausted outside is not pulled back into the building by the heating, ventilation, and air conditioning (HVAC) systems or by the windows, doors, or other points of entry.
- Place fans downstream of the HEPA filter so that contaminated ducts are maintained under negative pressure.
- Use ventilated cabinets that do not exhaust air back into the room environment unless the hazardous drug(s) in use will not volatilize (evaporate) during handling or after being captured by the HEPA filter. Information about volatilization should be supplied by the drug manufacturer and may be available in the safety data sheet (SDS); in some cases, the potential to volatilize can be determined by air or surface sampling data.
- Seek additional information about placement of the cabinet, exhaust system, and stack design from NSF/ANSI 49-2002 [NSF/ANSI 2002]. Incorporate those recommendations regardless of the type of ventilated cabinet selected.

- Establish negative pressure relative to surrounding areas to contain hazardous drugs and minimize the potential of exposure.
- Provide uninterrupted power sources for the ventilation systems to maintain negative pressure in the event of power loss. If power is lost during hazardous drug preparation, follow proper procedures per the manufacturer's guidelines before restarting the compounding.
- Follow the equipment guidelines outlined in these three USP Chapters: General Chapter <795> (Nonsterile compounding), General Chapter <797> (Sterile Compounding), and General Chapter <800> (Handling of Hazardous Drugs) [USP 2022a, 2022b, 2016]; see <https://www.usp.org/compounding-standards-overview>.

Maintenance of Engineering Controls

Develop and implement standard operating procedures (SOPs) for maintaining engineering control systems. The SOPs should be specific to the type of equipment and hazardous drugs used. Workers performing maintenance should be qualified persons and trained to implement the SOPs. The workers should also be included in a hazard communication program and be trained on the PPE needed to reduce exposure during maintenance activities. PPE and work practices should address hazards associated with the cleaning/disinfection agents to be used and any substances used as part of the maintenance activity.

- Give advance notice that maintenance will occur and notify occupants in the affected areas immediately before the maintenance activity begins. Place warning signs on all equipment that may be affected.
- Remove all hazardous drugs and chemicals and decontaminate the ventilated cabinet before beginning maintenance activities.
- Decontaminate and bag equipment parts removed for replacement or repair before they are taken outside the facility.
- DO NOT break, crush, tear, or otherwise distort used filtration media removed from a ventilated cabinet. Seal used filtration media in plastic immediately upon removal and tag it for disposal as Resource Conservation and Recovery Act (RCRA) hazardous waste. Alternatively, dispose of it as otherwise directed by the environmental safety and health office or applicable regulation.

As the potential for exposure increases, it becomes more important to ensure that the engineering controls are working as designed and effectively protecting workers.

6.3 Administrative Controls

Administrative controls, including work practices, are most effective when they are part of and supported by a safety and health culture within an organization. Administrative

controls can reduce the airborne and surface concentration of workplace contaminants or remove workers from sources of workplace contaminants and thus can reduce workers' potential exposure.

Administrative controls include the following:

- Educate and train workers frequently, specifically when the facility brings in new hazardous drugs. Workers should undergo training and demonstrate competency before they work with hazardous drugs.
- Limit the time workers handle hazardous drugs.
- Limit access to the areas where workers use hazardous drugs.
- Implement good cleaning practices (such as using dedicated cleaning tools for areas where workers use hazardous drugs, wet wipes for cleanup, and HEPA-filtered vacuums).
- Close toilet lid or use a plastic-backed absorbent pad placed over the toilet without a lid during flushing in areas where workers administer hazardous drugs and in patient rooms [ONS 2018].
- Prohibit the use of automated counting machines for hazardous drugs unless an evaluation of the machines confirms they do not release powders.
- Implement labeling of containers of hazardous drugs and posting signage where workers use and store hazardous drugs.
- Mandate handwashing with soap and water before eating, drinking, smoking, using the bathroom, removing or applying cosmetics, or leaving the workplace.
- Prohibit consumption of food and drink, chewing gum, using tobacco, or applying cosmetics in the areas where workers handle hazardous drugs.
- Provide training on spill response and use of spill kits in areas where workers use hazardous drugs. Consider having spill-response exercises or drills.
- Continuously monitor compliance to policies and procedures, and resolve causal factors for non-compliance.

The facility should identify designated areas for receipt and unpacking, storage, and compounding. Protocols should be established that prohibit the use of unventilated areas, such as storage closets, for drug storage or for any tasks involving hazardous drugs. Work surfaces should be deactivated, decontaminated, and cleaned before and after each activity and at the beginning and end of the work shift. Disposal of cleaning materials should follow the facility SOPs.

Counting and pouring hazardous drugs should be done carefully to avoid spillage, and dedicated equipment should be used with these drugs. Crushing tablets or opening capsules should be avoided, and liquid formulations should be used whenever possible.

Healthcare personnel should avoid crushing or manipulating tablets outside a controlled environment, that is, in areas not designed for handling hazardous drugs (such as intensive care units or rehabilitation settings). Tablet and capsule forms of hazardous drugs should not be placed in an automated counting machine unless a facility risk assessment validates that the specific machine does not produce dust and contamination; most counting machines can stress tablets and capsules and thereby introduce powdered contaminants into the work area [Fent and Durgam 2012; Fent et al. 2014].

Initial training should be conducted before any workers handle a hazardous drug, clean an area where hazardous drugs are used, or perform work tasks that will potentially expose them to the body fluids of a patient who is taking hazardous drugs. Training should also be completed when new equipment or procedures are introduced. The ability of workers to translate training into work practices that reduce risks and that promote safe working conditions should be evaluated regularly by supervisors. In addition, these supervisors must work in partnership with health and safety professionals to ensure workers' competency. Refresher training should generally be completed annually, but measures of worker understanding, actions, and feedback can be used to determine the needed frequency of training, the need for retraining, and the need to revise training methods.

6.4 Personal Protective Equipment

OSHA requires selection of PPE based on an assessment of workplace hazards [29 CFR § 1910.132]. Wearing assigned PPE is recommended for workers performing any task involving hazardous drugs to reduce exposure and provide a barrier of protection. Workers should use PPE in the context of a documented PPE program that provides for initial training, retraining, and periodic testing of workers' knowledge of the proper use of PPE.

It is important to understand the attributes and limitations of any selected PPE and ensure that it is designed to protect the wearer from hazardous drug exposure and is used properly by workers handling hazardous drugs [NIOSH 2004b]. Incorrectly used PPE may increase a worker's exposure. Donning and doffing of PPE should follow the organization's procedures and the manufacturer's instructions. Workers should use care in donning and doffing all items to prevent damage to the PPE and to reduce the spread of contamination. Prior to use, workers should inspect all PPE for defects or damage.

The Table of Control Approaches in Chapter 8 provides information on the recommended PPE for each activity and formulation type of hazardous drugs.

Gloves

In areas where hazardous drugs are present, the surfaces and external parts (e.g., syringes, tubes, bottles, or vials) that are handled may be contaminated with these drugs;

thus, gloves should be used to prevent dermal exposures [NIOSH 2004a]. Different glove types offer different protection from dermal exposure to hazardous drugs. Some gloves may permit rapid permeation of hazardous drugs. For example, polyvinyl chloride exam gloves offered little protection when evaluated against 13 different cytotoxic drug exposures [Wallemacq et al. 2006]. Although thicker gloves may offer better protection, glove thickness does not always indicate the level of protection. In addition, thicker gloves may decrease dexterity and make work activities more difficult. If possible, gloves should be selected based on test information provided by the glove manufacturer that demonstrates permeation resistance to specific hazardous drugs, including any solvents or diluents present. Currently, guidelines are available for testing only “chemotherapy gloves” [ASTM 2019], and information may not be available for other types of hazardous drugs.

Here are suggested work practices for using gloves (see also Table of Control Approaches):

- Review the gloving advice in the hazardous drug manufacturer’s SDS.
- Inspect gloves for defects before use and change gloves on a regular basis. The manufacturer’s documentation frequently provides glove-changing recommendations, and a facility risk assessment may provide other guidelines, but generally accepted practice is that gloves should not be used for more than 30 minutes [ASHP 2006; NIOSH 2004a; Power and Coyne 2018]. Whenever gloves are damaged or contact with a drug is known or suspected, carefully remove and dispose of them by following the facility SOPs.
- Use powder-free gloves because the powder can contaminate the work area and might adsorb and retain hazardous drugs.
- Do not wear latex gloves because latex allergies can develop [NIOSH 2008].
- Wearing a single pair of chemotherapy gloves may be adequate when administering intact tablets or capsules or the manufacturers’ prefilled syringes.
- Wear double chemotherapy gloves (two pair of gloves, one worn over the other) when compounding, administering, and disposing of hazardous drugs with a high potential for exposure (e.g., when cutting or crushing tablets or capsules; withdrawing injections from a vial; administering topical drugs, irrigation solutions, or aerosol treatments; handling drug-contaminated excreta; or cleaning up spills) [NIOSH 2008].
- Use double gloves for administering syringes that were filled in-house because the external syringe may be contaminated.
- When using two pairs of gloves and a gown, place the inner glove under the gown cuff and the outer glove over the cuff. Place gloves with long cuffs over the cuff

of the gown to protect the wrist and forearm [ASHP 2006; ONS 2011; Power and Coyne 2018].

- When compounding sterile preparations, apply sterile 70% alcohol to gloves and allow them to dry; ensure that the selected gloves are not degraded by the alcohol [NIOSH 2008].
- When removing gloves, turn them inside out so that contaminated surfaces do not touch uncontaminated surfaces.
- Wash hands thoroughly with soap and water after removing and disposing of gloves. Avoid alcohol-based hand gel and similar agents.

Gowns

Gowns protect workers from spills and splashes of hazardous drugs and waste materials. Gowns must be designated for single use, be disposable, and be shown to resist permeation by the types of hazardous drugs used [NIOSH 2008]. Gowns should not have seams or closures that could allow drugs to pass through, and they should close in the back. They should also have long sleeves with tight-fitting cuffs. Disposable gowns made of polyethylene-coated polypropylene or other laminate materials offer better protection than those made of noncoated materials [ASHP 2006; NIOSH 2004a, 2009; Power and Coyne 2018]. Cloth laboratory coats, surgical scrubs, and other absorbent materials permit the penetration of hazardous drugs and can hold spilled drugs against the skin and increase exposure.

Here are suggested work practices for wearing gowns (see also Table of Control Approaches):

- Wear gowns whenever there is a possibility of a splash or spill, such as in compounding, administering, or disposing of hazardous drugs.
- Avoid spreading drug contamination by not wearing gowns outside the compounding or administration area.
- Dispose of gowns after one use (or at a frequency determined by the employer) and immediately after a spill or splash in an appropriate disposal container that is labeled “Waste” and then covered and sealed. Reusing gowns increases the likelihood of exposure to hazardous drugs.

Respiratory Protection

The healthcare environment contains hazards such as bacteria, viruses, and chemicals (including hazardous drugs) that workers may inhale and cause injury or illness. To protect their workers and the patients they serve, hospitals and other healthcare organizations have established respiratory protection programs.

Respirators are designed and regulated to provide a known minimum level of protection when used within the context of a comprehensive and effective respiratory protection program. Selection of respirators for specific tasks and drugs should be based on the NIOSH Respirator Selection Logic [NIOSH 2004b]. All respirators must be NIOSH-approved and have the NIOSH approval number on the respirator itself or on a separate NIOSH approval label, which is found on or within the packaging or respirator box.

For most activities requiring respiratory protection, a NIOSH-approved N95 or more protective respirator is sufficient to protect against airborne particles [NIOSH 2004b]. However, N95 respirators offer no protection against gases and vapors and little protection against direct liquid splashes. A surgical N95 respirator is a NIOSH-approved N95 respirator that has also been cleared by FDA for use as a surgical mask. A surgical N95 respirator provides the respiratory protection of an N95 respirator and the splash protection of a surgical mask. Typical loose-fitting surgical masks are not N95 respirators and are not NIOSH approved for use as respirators. Loose-fitting surgical masks do not provide respiratory protection and should not be used to compound or administer hazardous drugs when respiratory protection is required due to potential penetration through the surgical mask [NIOSH 2004a; Rengasamy et al. 2009].

The type of filter that effectively removes a drug from the worker's breathing zone may vary with the type of drug (Figure 6). Therefore, it may be necessary to work with the respirator manufacturer to identify the types of filtration needed in a facility.

Here are suggested work practices for using respiratory protection (see also Table of Control Approaches):

- Use a fit-tested N95 respirator for routine handling of hazardous drugs if there is potential for inhalation of fine powders [NIOSH 2008].
- Use a surgical N95 respirator for handling of hazardous drugs if there is potential for splashes of bodily fluids or liquid drugs [NIOSH 2008]. Also consider use of a face shield or goggles in addition to the surgical N95 in this situation.
- Use a full-facepiece combination particulate/chemical cartridge-type respirator [42 CFR Part 84; NIOSH 2004b] if your facility determines it is necessary for certain spill events, such as when an IV bag breaks or a line disconnects and leaks, or where airborne exposure to volatile drugs, vapors, or gases is known or suspected.
- Use a full-facepiece combination particulate/chemical cartridge-type respirator or a powered air-purifying respirator (PAPR) whenever handling volatile hazardous drugs or aerosolizing hazardous drugs for inhalation or nebulized therapy [ONS 2018].
- Provide medical evaluations, fit testing, and training to workers who use respiratory protection. Follow all requirements in the OSHA Respiratory Protection Standard [29 CFR § 1910.134] (www.osha.gov/SLTC/etools/respiratory/index.html).



Figure 6. Examples of (from left) an N95 disposable respirator, a full-facepiece combination particulate/chemical cartridge-type respirator, and a loose-fitting powered air-purifying respirator (PAPR).

Eye and Face Protection

Eye and face protection are needed whenever hazardous drugs may splash (such as during compounding, administration, or disposal of contaminated human excreta) because many hazardous drugs are irritating to eyes and may be absorbed through the eyes or mucous membranes.

Here are suggested work practices for using eye and face protection:

- Use eye and face protection when compounding a drug outside the BSC or isolator (e.g., in the operating room); working at or above eye level; cleaning a BSC, containment ventilated enclosure (CVE), or containment isolator; or cleaning a spill [NIOSH 2008].
- Use face shields in combination with goggles to provide a full range of protection against splashes to the face and eyes. Face shields alone do not provide full eye and face protection because splashes to the eyes could still occur. A full-facepiece respirator and PAPR will also provide both eye and face protection [NIOSH 2008].
- Use a face shield in combination with eyeglasses or safety glasses with side shields; glasses with side shields alone do not adequately protect the eyes from splashes [NIOSH 2008].

Head, Hair, Shoe, and Sleeve Covers

Head and hair covers (covering beard and mustache, if applicable) and shoe and sleeve covers should be worn when there is potential for contact with hazardous drug residues during compounding (see also Table of Control Approaches).

Here are suggested work practices for use of head, hair, shoe, and sleeve covers:

- Use hair and shoe covers made of coated materials to reduce the possibility of particulate or microbial contamination in compounding areas, clean rooms, and other sensitive areas.

- Consider using sleeve covers if there is a gap between the gown and the glove; these are made of coated materials to provide additional protection for the areas of the arms that may come in contact with the drug.
- Remove hair, shoe, and sleeve covers before exiting drug compounding areas to avoid spreading drug contamination to other areas and possibly exposing nonprotected workers.
- Don a second pair of shoe covers before entering the C-SEC when compounding hazardous drugs and remove this extra pair when exiting the C-SEC [Power and Coyne 2018].
- Remove PPE in the following order: hair and shoe covers, sleeve covers, outer gloves, face shield, gown, respirator/mask, inner gloves [ONS 2018].

PPE Disposal

Consider all PPE worn when handling hazardous drugs as being contaminated with at least trace quantities of hazardous drugs.

Here are suggested work practices for disposing of PPE after handling hazardous drugs:

- Remove PPE at the entrance to the compounding areas and immediately after handling potentially contaminated materials to prevent contamination of clean areas of the facility (e.g., offices, breakrooms, and common areas).
- Contain and dispose of such PPE either as trace or bulk contaminated waste [NIOSH 2004a; ONS 2018]. Most PPE will be trace waste, but PPE visibly contaminated with hazardous drugs should be disposed of in a RCRA hazardous waste container.
- Consider using hands-free or foot-pedal waste containers to decrease hand contact.
- Do not reach into waste containers when discarding PPE.
- Seal waste containers when they are three-fourths full.
- Wash hands thoroughly with soap and water after removing and disposing of PPE. Avoid using alcohol-based hand gels or other, similar agents.

6.5 Surface Contamination

Measurement of surface contamination is currently the best indication of the environmental contamination level in areas where hazardous drugs are prepared, administered to patients, or otherwise handled (such as receiving areas, transit routes throughout the facility, and waste storage areas) [Hon et al. 2011]. Environmental wipe sampling for hazardous drug residue should be performed routinely (e.g., initially as a benchmark and at least every 6 months or more often as needed, to verify containment)

[USP 2016]. Workplace contamination with hazardous drugs continues to be an issue in the United States [Connor et al. 1999, 2010; Davis et al. 2011; Harrison et al. 2006; Kiffmeyer et al. 2013; Salch et al. 2019; Sessink et al. 2011, 2013; Walton et al. 2020; Wick et al. 2003].

Hon et al. [2014a] reported that 20% of workers sampled in a recent study of hospital workers had detectable amounts of one antineoplastic drug, cyclophosphamide, on their hands, which could result in systemic exposure. These workers covered a wide range of job descriptions, from pharmacists and nurses to transportation personnel, volunteers, and dieticians. Several studies have shown an association between surface contamination and worker exposure, and surface contamination is the most commonly used metric for evaluating the workplace for hazardous drugs [Connor et al. 2010; Pethran et al. 2003; Villarini 2011]. A U.S. study reported nurses had exposure to the skin or eyes 17% of the time when handling chemotherapy drugs [Friese et al. 2011]. Other recent research has shown that even when recommended controls are used in healthcare settings, the potential for exposure to antineoplastic drugs is not eliminated [Berruyer et al. 2015; Chu et al. 2012; Connor et al. 2010; Friese et al. 2020; Hon et al. 2013, 2014b, 2015; Kopp et al. 2013a,b; Merger et al. 2013; Odraska et al. 2014; Salch et al. 2019; Schierl et al. 2009; Sessink et al. 2011, 2013, 2015; Siderov et al. 2010b; Sottani et al. 2012; Turci et al. 2011; USP 2016; Viegas et al. 2014; Walton et al. 2020; Yoshida et al. 2010].

Acceptable surface limits (ASLs) are used to establish a quantitative measure for the potential risk from exposure by dermal contact from active pharmaceutical ingredients that are known to cause pharmacological or toxicological effects. An ASL can be used, together with appropriate analytical methods and industrial hygiene monitoring, to assess workplaces for potential dermal exposure, and to protect the health and safety of individuals who might come in direct contact with contaminated surfaces in the workplace. ASLs are also used to evaluate the adequacy of cleaning measures and the effectiveness of engineering containment approaches, or to determine whether a chemical is present on surfaces where it is not intended to be (e.g., in lunchrooms or offices or on the outside surfaces of packaging materials) [Kimmel et al. 2011; Walton et al. 2020]. Commercial test kits are available to assess hazardous drug surface contamination, and some industrial hygiene analytical laboratories are capable of analyzing hazardous drug contamination by using specified types of surface wipe media [Connor and Smith 2016; Hon et al. 2013; Smith et al. 2019].

There are few occupational exposure limits (OELs) to help guide control of exposure to hazardous drugs in healthcare settings [Connor et al. 2016; NIOSH 2004a]. Until OELs are available that are based on health effects, some authors suggest following an ALARA (as low as reasonably achievable) approach, similar to that used for radiation exposure [10 CFR § 20.1003; Baker and Connor 1996; ONS 2011; Zeedijk et al. 2005].

6.6 Medical Surveillance

NIOSH, ONS, OSHA, and USP all recommend the use of a medical surveillance program as an additional part of a comprehensive exposure control program to protect the health of workers [NIOSH 2012; ONS 2018; OSHA 2016; USP 2016]. Medical surveillance has been successful in other occupational settings. It can identify sentinel adverse health effects among workers suggesting failures in controlling exposures and thus identify the need for improvements in workplace controls, such as engineering or administrative controls or personal protective equipment. Also, individual workers may benefit from detection of disease in early stages when it may be more treatable with better clinical outcomes.

Several issues should be considered in designing a medical surveillance program for workers who handle hazardous drugs. The first is to develop a systematic approach to identifying workers who are potentially exposed to hazardous drugs on the basis of their job duties. This should be part of the risk assessment process. The second is to provide medical surveillance that focuses on detecting anticipated potential adverse health effect caused by exposure to the classes of hazardous drugs in use or on detecting drugs or drug metabolites that would provide a direct indication of exposure. Healthcare workers typically handle and may be exposed to a variety of hazardous drugs [Boiano et al. 2014, 2015; NIOSH 2004a, 2012]. No single biomarker is suitable for all hazardous drugs. Organizations should use information obtained through medical surveillance to address identified health issues among affected workers and to identify and correct system failures that may have resulted in harmful exposures.

Elements of a medical surveillance program for workers exposed to hazardous drugs should include the following:

- **Consideration of a baseline clinical evaluation to allow for an individualized point of comparison should adverse health effects of exposure to hazardous drugs be suspected in the future.** Whether a worker should undergo baseline clinical evaluation should be based on the availability of clinical examinations and tests that can be targeted toward specific hazardous drugs and health endpoints, as well as their corresponding performance characteristics, such as sensitivity, specificity, and predictive value. If a baseline clinical evaluation is performed, it can include a targeted (1) medical history, including current medications and relevant past medications of a similar class or that have similar toxicities as the hazardous drugs to be handled, (2) physical examination, and (3) laboratory testing. Selection of baseline evaluation components should be informed by the toxicities of the hazardous drugs to be handled.
- **Health questionnaires administered by a healthcare professional at the time of hire and periodically thereafter** (see ONS 2011 and 2018 for a sample

questionnaire). The questionnaires should include information about relevant symptoms and medical events. Reproductive outcomes such as miscarriage should be included whenever anticipated as an adverse outcome of hazardous drug exposure because their occurrence may go unreported.

- **History of drug handling as an estimate of prior and current exposure**, including dates of duty assignment related to hazardous drugs and similar types of information.
- **A follow-up plan, as needed, for workers who have had health changes suggesting toxicity or have experienced acute exposure** (for example, from substantial skin contact or inhalation or from cleaning a large spill, such as a broken IV bag, leaking IV line, etc.) [NIOSH 2012].

7 Waste and Spill Control

7.1 Hazardous Drug Waste

Healthcare facilities typically have several waste streams, including medical waste and hazardous drug waste, which can be further classified in three groups:

1. Resource Conservation and Recovery Act (RCRA) hazardous waste: Drug waste that meets the definition of a U.S. EPA RCRA hazardous waste (P-listed, U-listed, or D-coded) commonly contained in a black Packing Group II container that is managed by incineration at a permitted hazardous waste facility. This can also include any PPE that is visually contaminated with hazardous drugs.
2. Trace chemotherapy waste: Ampules, empty vials, syringes, trace-contaminated PPE (including gloves), swabs, pads, etc., contained in a yellow hard-plastic container or a yellow hamper for soft items labeled as chemotherapy and biohazardous waste and managed by incineration at a regulated medical waste incinerator.
3. Nonhazardous pharmaceutical waste: Drug waste that does not meet the criteria noted above and is commonly contained in a white or blue container and managed by incineration at any incinerator permitted for nonhazardous pharmaceutical waste.

Trace chemotherapy waste should be closed and sealed according to established practice for regulated medical waste and stored in the regulated medical waste area of the facility. Any RCRA hazardous waste containers should be kept closed at all times when not in active use, labeled appropriately according to both state and federal regulations, and moved to a central accumulation area when full.

Facilities should assess risks and work with their waste management company to develop facility-specific SOPs. Check and comply with all local, state, and federal regulations.

7.2 Spill Control

Facilities should prepare for spill control of hazardous drugs, create SOPs that address responsibilities of employees (such as those who observe the spill or are responsible for the cleanup), have spill kits readily available, train workers, and consider holding periodic spill-control drills.

Suitable facilities for quick drenching or flushing of the eyes and body (eyewash and emergency showers) with tempered potable water should be provided within the work area for immediate emergency use whenever corrosive drugs are handled.

A plan for the disposal of items used in the management of spills of hazardous drugs should be prepared in conjunction with the waste management company. Facilities should have a plan to assist with determining the waste stream for all of the spill-response items (such as PPE and drug-contaminated wipes) and to assist with identifying whether the items are either trace waste or overtly contaminated and should be disposed as RCRA hazardous waste.

8 Control Approaches for Safer Handling of Hazardous Drugs by Activity and Formulation

8.1 Introduction to Table of Control Approaches

The Table of Control Approaches for Safer Handling of Hazardous Drugs by Activity and Formulation (Table of Control Approaches) provides information for some of the possible scenarios that workers may encounter in healthcare settings when handling hazardous drugs, but it cannot address all possible situations. Given the variety of drugs, additions of new drug formulations, and the variety of ways to administer drugs, no single approach can cover the diverse potential occupational exposures to hazardous drugs.

Although all hazardous drugs represent an occupational hazard to healthcare workers and should always be handled using recommended engineering controls and PPE, regardless of their formulation (IV, intramuscular, subcutaneous, intradermal, topical, transdermal, tablet, or capsule), cytotoxic drugs used for cancer treatment are especially hazardous. These drugs damage cells and DNA and may lead to an increased risk of leukemia and other cancers.

Some drugs on the *List* have known reproductive or developmental hazards. They represent a potential occupational hazard to those who are actively trying to conceive, to the fetus of a pregnant worker, or to the baby who is breastfed (because hazardous drugs may enter breast milk of exposed workers). Protecting workers during the period of conception and pregnancy may be difficult, for reasons such as these:

- About 45% of pregnancies in the United States are unplanned [Finer and Zolna 2016].
- Employees who are pregnant and their partners may not realize they are pregnant.
- Not all employees who are pregnant may announce their pregnancy to their supervisors.
- Some hazardous drugs may pass into the semen and sperm, providing a route of exposure that could affect the health of offspring [Connor et al. 2014].

Therefore, although some drugs may be listed as only a reproductive or developmental hazard, facilities should consider risk management (including PPE use) for those drugs, to protect not only those who are known to be pregnant or planning pregnancy but for all staff members.

Intact tablets and capsules may not pose the same potential for occupational exposure as liquid or mixed injectable drugs, which usually require extensive preparation. However, cutting, crushing, or otherwise manipulating tablets and capsules will increase the potential for exposure of workers. Most drugs used for cancer treatment are accompanied by MSHI, which is typically in Section 16 of the drug package insert. The MSHI should be consulted before handling any drug.

Table of Control Approaches for Safer Handling of Hazardous Drugs, by Activity and Formulation

Activity	Control Approaches						Respiratory protection*
	Engineering Controls			Personal Protective Equipment			
Formulation	Ventilated engineering control (BSC or CACI)*	Closed system drug transfer device	Other	Double chemo-therapy gloves (ASTM rated)	Protective gown (impervious, single use)	Eye, face, hair, sleeve, and shoe protection	
Receiving, unpacking, and placing in storage	All types of hazardous drugs	NA*	NA*	No (Single pair of gloves)	No, unless a leak is observed or suspected	Consider protective sleeves; add additional protection if a leak is observed or suspected	No, unless a leak is observed or suspected
Transportation within facility	Intact tablets or capsules, manufacturers' prefilled syringes	NA*	Transport in containers that minimize the risk of breakage or leakage; Double-bag or place in a sealed container	No (Single pair of gloves)	No	No	No
	Cut or crushed tablets or capsules (in containers); powders, liquids, or creams; in-house filled syringes	NA*	Transport in containers that minimize the risk of breakage or leakage; Double-bag or place in a sealed container	Yes	No	No	No

(Continued)

Table of Control Approaches for Safer Handling of Hazardous Drugs, by Activity and Formulation

Activity	Control Approaches						
	Engineering Controls			Personal Protective Equipment			
Formulation	Ventilated engineering control (BSC or CACI)*	Closed system drug transfer device	Other	Double chemotherapy gloves (ASTM rated)	Protective gown (impervious, single use)	Eye, face, hair, sleeve, and shoe protection	Respiratory protection†
Compounding‡	Oral liquid drug	Yes§	NA*	Yes¹	Yes	Hair and shoe covers; Add eye and face protection, if not done in a ventilated engineering control	Yes, if not using a ventilated engineering control
Topical drug	Yes§ (Note: some drugs such as carmustine, thiotepa, and mechlorethamine are volatile)	NA*	NA*	Yes¹	Yes	Hair and shoe covers. Add eye and face protection, if not done in a ventilated engineering control	Yes, if not done using a ventilated engineering control
Injections withdrawn from a vial	Yes§	Yes, when dosage form allows	NA*	Yes¹	Yes	Hair and shoe covers; Add eye and face protection, if not done in a ventilated engineering control	Yes, if not using a ventilated engineering control
Mixing injections from a vial	Yes§	Yes, when dosage form allows	NA*	Yes¹	Yes	Hair and shoe covers; Add eye and face protection, if not done in a ventilated engineering control	Yes, if not using a ventilated engineering control

(Continued)

Table of Control Approaches for Safer Handling of Hazardous Drugs, by Activity and Formulation

	Control Approaches							
	Engineering Controls			Personal Protective Equipment				
Activity	Formulation	Ventilated engineering control (BSC or CACI)*	Closed system drug transfer device	Other	Double chemotherapy gloves (ASTM rated)	Protective gown (impermeable, single use)	Eye, face, hair, sleeve, and shoe protection	Respiratory protection†
	Solution for irrigation	Yes§	Yes, when dosage form allows	NA*	Yes*	Yes	Hair and shoe covers; Add eye and face protection, if not done in a ventilated engineering control	Yes, if not using a ventilated engineering control
	Powder/solution for aerosol treatments	Yes§	Yes, when dosage form allows	NA*	Yes*	Yes	Hair and shoe covers; Add eye and face protection, if not done in a ventilated engineering control	Yes, if not using a ventilated engineering control
	Administering							
	Intact tablets or capsules from unit dose package	NA*	NA*	NA*	No (Single glove)	No	Eye and face protection if vomit potential**	No
	Crushing or manipulating tablets or capsules	Yes§	NA*	Consider crushing tablets in a pill pouch	Yes*	Yes	Hair and shoe covers; Add eye and face protection, if not done in a ventilated engineering control	Yes, if not using a ventilated engineering control
	Cut, crushed, or uncoated tablets or capsules	NA*	NA*	NA*	Yes	Yes	Eye and face protection if vomit potential**	No

(Continued)

Table of Control Approaches for Safer Handling of Hazardous Drugs, by Activity and Formulation

Activity	Engineering Controls					Control Approaches			Respiratory protection†
	Ventilated engineering control (BSC or CACI)*	Closed system drug transfer device	Other	Double chemotherapy gloves (ASTM rated)	Protective gown (impermeable, single use)	Eye, face, hair, sleeve, and shoe protection			
Subcutaneous or intramuscular injections from manufacturer's supplied prefilled syringe or injector	NA*	NA*	NA*	No (Single glove)	Yes	Eye and face protection if liquid likely to splash**	No		
Subcutaneous or intramuscular injections from a prepared syringe or injector	NA*	NA*	NA*	Yes	Yes	Eye and face protection if liquid likely to splash**	No		
Intravenous injections from prepared syringes††	NA*	Yes, when dosage form allows	NA*	Yes	Yes	Eye and face protection if liquid that could splash**	No		
Intravenous solution for infusion	NA*	Yes, when dosage form allows	NA*	Yes	Yes	Eye and face protection if liquid that could splash**	No		
Ophthalmologic applications	NA*	Yes, when dosage form allows	NA*	Yes	Yes	Eye and face protection if liquid likely to splash**	No		

(Continued)

Table of Control Approaches for Safer Handling of Hazardous Drugs, by Activity and Formulation

Activity	Control Approaches						
	Engineering Controls			Personal Protective Equipment			
Formulation	Ventilated engineering control (BSC or CACI)*	Closed system drug transfer device	Other	Double chemotherapy gloves (ASTM rated)	Protective gown (impervious, single use)	Eye, face, hair, sleeve, and shoe protection	Respiratory protection†
Oral liquid drug; PO*/feeding tube/NG* tube	NA*	NA*	NA*	Yes	Yes	Eye and face protection if liquid likely to splash**	Yes, if inhalation potential
Topical drug (ointment, cream)	No (Note: some drugs such as carmustine, thiotepa, and mechlorethamine are volatile and may need to be administered in an enclosure)	NA*	NA*	Yes	Yes	Eye and face protection if liquid likely to splash**	Yes, if inhalation potential
Irrigation solution, bladder instillation, HIPEC*, limb perfusion	NA*	Yes, when dosage form allows	NA*	Yes	Yes	Eye and face protection	Yes

(Continued)

Table of Control Approaches for Safer Handling of Hazardous Drugs, by Activity and Formulation

		Control Approaches						
		Engineering Controls			Personal Protective Equipment			
Activity	Formulation	Ventilated engineering control (BSC or CACI)*	Closed system drug transfer device	Other	Double chemo-therapy gloves (ASTM rated)	Protective gown (impervious, single use)	Eye, face, hair, sleeve, and shoe protection	Respiratory protection*
	Powder/solution for inhalation/aerosol treatment	Yes, when applicable; Note that some treatments may need to be administered in an enclosure	Yes, when dosage form allows	NA*	Yes	Yes	Eye and face protection if liquid that could splash**	Yes, full facepiece or PAPR* with combination particulate/chemical cartridges if inhalation potential
Disposal and Cleaning	Drugs and metabolites in body fluids	NA*	NA*	Fold soft materials (sheets, hygiene care products) inward to prevent leakage Place in sealed bags	Yes	Yes	Eye and face protection if liquid could splash	Yes, if inhalation potential

(Continued)

Table of Control Approaches for Safer Handling of Hazardous Drugs, by Activity and Formulation

		Control Approaches						
		Engineering Controls			Personal Protective Equipment			
Activity	Formulation	Ventilated engineering control (BSC or CACI)*	Closed system drug transfer device	Other	Double chemotherapy gloves (ASTM rated)	Protective gown (impermeable, single use)	Eye, face, hair, sleeve, and shoe protection	Respiratory protection†
	Drug-contaminated waste	NA*	NA*	Avoid creating dust; Place in sealed bags; Use caution when closing bags; Pushing waste down may force hazardous drug dust up into face.	Yes	Yes	Eye and face protection if liquid could splash	Yes, if inhalation potential
Routine Cleaning	All types of hazardous drugs	NA*	NA*	Use wet wiping methods; Avoid creating dust; Disinfection, deactivation, or decontamination agents may be necessary; Place in sealed bags for disposal	Yes	Yes	As needed##	As needed##

(Continued)

Table of Control Approaches for Safer Handling of Hazardous Drugs, by Activity and Formulation

Activity	Engineering Controls				Control Approaches			Personal Protective Equipment	
	Ventilated engineering control (BSC or CACI)*	Closed system drug transfer device	Double chemo-therapy gloves (ASTM rated)	Double chemo-therapy gloves (imper-vious, single use)	Yes	Yes	Yes, as needed	Eye, face, hair, sleeve, and shoe protection	Respiratory protection†
Spill cleanup	All types of hazardous drugs	NA*	NA*	Limit access to area. Use absorbent pads for liquid spills; Disinfection, deactivation, or decontami-nation agents may be nec-essary; Avoid creating dust; Place in sealed bags	Yes	Yes	Yes, as needed	Yes, full facepiece or PAPR* with combination particulate/chemical car-tridges may be needed	Yes, full facepiece or PAPR* with combination particulate/chemical car-tridges may be needed

Note. The Table of Control Approaches provides general approaches that should be adapted to facility-specific conditions. For more detailed information on safe handling practices, see the reference list for this table [ASHP 2006; NIOSH 2004a, 2008; ONS 2011, 2018; OSHA 2016; Power and Cyne 2018].

***Abbreviations:** BSC: biological safety cabinet; CACI = compounding aseptic containment isolator; CSTD = closed system drug-transfer device; CVE = containment ventilated enclosure; HIPEC = hyperthermic intraperitoneal chemotherapy; NA = not applicable; NG = nasogastric; PAPR = powered air-purifying respirator; PO = per os (by mouth).

†Respiratory protection must be selected on the basis of the hazardous drug and its physical form (particulate, vapor, etc.) and other exposure factors. For general activities, a N95 may suffice. Use a surgical N95 respirator if there is potential for splashes of bodily fluids or liquid drugs. When performing activities such as cleaning the BSC or CACI or responding to large spills, a combination particulate/chemical cartridge respirator may be needed.

‡Compounding is the process of combining, mixing, or altering ingredients by or under the direct supervision of a licensed pharmacist or physician to create a prescribed medication tailored to the needs of an individual patient. See FDA: <https://www.fda.gov/drugs/human-drug-compounding/section-503a-federal-food-drug-and-cosmetic-act> and <https://www.fda.gov/drugs/human-drug-compounding/comounding-and-fda-questions-and-answers>.

§For nonsterile preparations, a ventilated engineering control such as a fume hood, Class I BSC or CVE is sufficient if the ventilated engineering control exhaust is either (1) HEPA filtered and appropriately exhausted to the outside of the building (preferred) or (2) filtered with redundant HEPA filters in series and recirculated back into the C-SCA. Although these activities are recommended in ventilated engineering controls, they may not be possible under some treatment scenarios (e.g., time-sensitive activities in the emergency department). If the activity is performed in a ventilated engineering control that is used for sterile intravenous preparations, a thorough cleaning and disinfecting is required following the activity.

*Sterile gloves are required for aseptic drug preparation in a BSC or CACI.

***Needed if the patient might resist (infant, unruly patient, patient predisposed to spitting, patient with difficulty swallowing, or veterinary patient) or if the formulation is hard to swallow.

††Intravenous tubing already attached and primed.

#Activities such as cleaning floors may not require eye or respiratory protection but cleaning a BSC or CACI may require it.

8.2 Control Approaches by Activity and Formulation

This section restates the information found in the previous Table of Control Approaches that should be adapted to facility-specific conditions. For more detailed information on safe handling practices, see the reference list for the table [ASHP 2006; NIOSH 2004a, 2008; ONS 2011, 2018; OSHA 2016; Power and Coyne 2018].

Receiving, unpacking, and storing all types of hazardous drugs

Controls: Use a designated area and restrict access to only authorized personnel. No controls necessary unless a leak or spill is observed or suspected. Open damaged containers inside of a fume hood, Class 1 BSC, or HEPA-filtered enclosure.

PPE: Single pair of chemotherapy gloves. Consider the use of sleeve covers. Add a protective gown, shoe covers, eye protection, and respiratory protection (N95 or combination particulate/chemical cartridge respirator) if a leak or spill is suspected.

Transportation within facility

Intact tablets or capsules, manufacturers' prefilled syringes

Controls: Transport in containers that minimize the risk of breakage or leakage. Double-bag or place in a sealed container.

PPE: Single pair of chemotherapy gloves.

Cut or crushed tablets or capsules, powders, liquids, creams, or in-house filled syringes

Controls: Transport in containers that minimize the risk of breakage or leakage. Double-bag or place in a sealed container.

PPE: Double chemotherapy gloves.

Compounding

Oral liquid drugs

Controls: Ventilated engineering control (fume hood or Class 1 BSC, CVE, or CACI).

PPE: Double chemotherapy gloves and a protective gown. Add eye and face protection and respiratory protection (N95) if compounding is done outside of the ventilated engineering control. Hair and shoe covers should be worn.

Topical drugs

Controls: Ventilated engineering control (fume hood or Class 1 BSC, CVE, or CACI). Note that carmustine, thiotepa, and mechlorethamine are volatile.

PPE: Double chemotherapy gloves and a protective gown. Add eye and face protection and respiratory protection (N95) if compounding is done outside of the ventilated engineering control. Hair and shoe covers should be worn.

Preparation of subcutaneous/intramuscular injections from a vial

Controls: Ventilated engineering control (Class II or III BSC or CACI). Use a CSTD when the dosage form allows.

PPE: Double chemotherapy gloves and a protective gown. Add eye and face protection and respiratory protection (N95) if not handling in a ventilated engineering control. Hair and shoe covers should be worn.

Preparation of intravenous solutions by withdrawing or mixing from a vial or ampule

Controls: Ventilated engineering control (Class II or III BSC or CACI). Use a CSTD when the dosage form allows.

PPE: Double chemotherapy gloves and a protective gown. Add eye and face protection and respiratory protection (N95) if not handling in a ventilated engineering control. Hair and shoe covers should be worn.

Irrigation solutions

Controls: Ventilated engineering control (Class II or III BSC or CACI). Use a CSTD if the dosage form allows.

PPE: Double chemotherapy gloves, a protective gown, and sleeve covers. Add eye and face protection and respiratory protection (N95) if not handling in a ventilated engineering control. Hair and shoe covers should be worn.

Powder/solution for aerosol treatments

Controls: Ventilated engineering control (Class II or III BSC or CACI). Use a CSTD if the dosage form allows.

PPE: Double chemotherapy gloves and a protective gown. Add eye and face protection and respiratory protection (N95) if not handling in a ventilated engineering control. Hair and shoe covers should be worn.

Administering

Intact and coated tablets and capsules

PPE: Single pair of chemotherapy gloves. Add eye and face protection if there is the potential to contact vomit or if patient may resist or is predisposed to spitting.

Crushing or manipulating tablets or capsules

Controls: Ventilated engineering control (fume hood or Class 1 BSC or CVE). Consider crushing tablets in a tablet (pill) pouch.

PPE: Double chemotherapy gloves and a protective gown. Add eye and face protection and respiratory protection (N95) if compounding is done outside of the ventilated engineering control. Hair and shoe covers should be worn.

Cut or crushed tablets or capsules or uncoated tablets

PPE: Double chemotherapy gloves and a protective gown. Add eye and face protection if there is the potential to contact vomit or if patient may resist or is predisposed to spitting.

Subcutaneous/intramuscular injections from a manufacturer's prefilled syringe or injector

PPE: Single pair of chemotherapy gloves and a protective gown. Add eye and face protection if administering a liquid that is likely to splash.

Subcutaneous/intramuscular injections from a prepared syringe or injector

PPE: Double chemotherapy gloves and a protective gown. Add eye and face protection if administering a liquid that is likely to splash.

Intravenous injections from a prepared syringe

Controls: Use a CSTD when the dosage form allows.

PPE: Double chemotherapy gloves and a protective gown. Add eye and face protection if administering a liquid that is likely to splash.

Intravenous solutions for infusion

Controls: Use a CSTD when the dosage form allows.

PPE: Double chemotherapy gloves and a protective gown. Add eye and face protection if administering a liquid that is likely to splash.

Ophthalmologic applications

Controls: Use a CSTD when the dosage form allows.

PPE: Double chemotherapy gloves and a protective gown. Add eye and face protection if administering a liquid that is likely to splash.

Oral liquid drugs by mouth/feeding tube/nasogastric tubes

PPE: Double chemotherapy gloves and a protective gown. Add eye and face protection if there is the potential for the liquid to splash, to contact vomit, or if patient may resist or is predisposed to spitting. Add respiratory protection (N95) if there is an inhalation potential.

Topical drugs

Controls: Volatile compounds may need to be administered in an enclosure.

PPE: Double chemotherapy gloves and a protective gown. Add eye and face protection if administering a liquid that is likely to splash. Add respiratory protection (N95) if inhalation is possible from volatile drugs.

Irrigation solution administration via bladder/HIPEC/limb profusion

Controls: Use a CSTD when the dosage form allows.

PPE: Double chemotherapy gloves, protective gown, eye and face protection, and respiratory protection (N95).

Powder/solution for inhalation/aerosol treatment

Controls: Some treatments may need to be administered in an enclosure. If patient is not intubated, use a demistifier or other air purification system. Use a CSTD if the dosage form allows.

PPE: Double chemotherapy gloves and a protective gown. Add eye and face protection if the liquid could splash, and respiratory protection with combination particulate/chemical cartridges, full facepiece, or PAPR if there is an inhalation potential.

Disposal and cleaning of body fluids

Controls: Fold soft materials (linens, hygiene care products) inward to prevent leakage. Use absorbent pads for liquids. Place in sealed bags.

PPE: Double chemotherapy gloves and a protective gown. Add eye and face protection if a liquid could splash and respiratory protection (N95) if there is an inhalation potential.

Disposal and cleaning of drug-contaminated waste

Controls: Dispose of contaminated wastes in a sealed and labeled container. Avoid creating dust. Place in sealed bags for disposal. Use caution when closing bags; pushing waste down may force hazardous drug dust up into the face.

PPE: Double chemotherapy gloves and a protective gown. Add eye and face protection if a liquid could splash and respiratory protection (N95) if there is an inhalation potential.

Routine cleaning

Controls: Use wet wiping methods. Avoid creating dust. Disinfection, deactivation, or decontamination agents may be necessary. Place in sealed bags for disposal.

PPE: Double chemotherapy gloves and a protective gown. Add eye and face protection and a combination particulate/chemical cartridge respirator when cleaning the BSC or CACI.

Spill cleanup

Controls: Limit access to spill area. Use absorbent pads for liquids. Disinfection, deactivation, or decontamination agents may be necessary. Avoid creating dust. Place in appropriate sealed bags for disposal.

PPE: Double chemotherapy gloves, protective gown, eye and face protection, and respiratory protection (N95 or combination particulate/chemical cartridge respirator).

9 Additional Considerations for Handling Hazardous Drugs

No single approach can protect healthcare workers against all hazardous drugs in all tasks. These steps, however, can lessen the chance of exposure to hazardous drugs:

- Label, tag, or mark all containers of hazardous drugs with the identity of the material and hazard warnings.
- Use unopened, intact tablets and capsules whenever possible and clinically appropriate.
- Do not cut or crush tablets or capsules, or otherwise manipulate them, if possible. This might produce powder that can contaminate workplace surfaces.
 - When such manipulations are necessary, perform them within a ventilated enclosure or augment the control of generated aerosols by using supplementary controls such as glove bags or tablet (pill) pouches that contain the hazardous drug during and after the crushing process.
 - When clinically appropriate, add liquid or moist products to crushed hazardous drug products as soon as possible after crushing to avoid the potential of subsequent aerosol dissemination.
 - Use drugs in liquid forms when possible to avoid crushing tablets or opening capsules [ONS 2018].
 - Wear PPE and use exposure controls as appropriate for the task.

The information provided herein applies to healthcare facilities such as hospitals and clinics and to nontraditional settings such as homes and veterinary clinics.

9.1 Home Healthcare

Although only limited experimental studies on home healthcare have been done, here are additional considerations for handling hazardous drugs in home settings:

- Provide overall basic education and related precautions to protect home healthcare workers, patient family members, and caregivers from indirect or direct exposure to hazardous drugs, including during spill management.
- Use gloves when caring for patients.
- Suggest that family members use gloves when handling laundry or cleaning within or around toilets [Meijster et al. 2006].

- Close the lid before flushing the toilet after each use by patient, for 48 hours after receipt of chemotherapy. If available, have the patient use a separate bathroom from family members [ONS 2014].
- Conduct double washing of linens and wash them separately from other family laundry [ONS 2018].

9.2 Veterinary Clinics

A 2014 study showed that veterinary medicine and animal care workers were exposed to hazardous drug concentrations 15 times higher than human healthcare personnel, partly because of how chemotherapy is administered in animals versus humans. Cost, time, inconvenience, and discomfort are just some of the barriers veterinary medicine and animal care workers report for not using safety measures in their practices [Klahn 2014]. Chemical contamination of hazardous drugs on surfaces were observed from NIOSH field evaluations in seven veterinary hospitals and clinics visited during 2017–2018 [NIOSH 2019, 2021 a,b,c,d,e,f]. The NIOSH Workplace Solutions document *Safe Handling of Hazardous Drugs for Veterinary Healthcare Workers* provides considerations for the administration of hazardous drugs in a veterinary setting [NIOSH 2010]. The Workplace Solutions document suggests the same hierarchy of controls (engineering controls, administrative controls, and PPE), with some specific suggestions such as these:

Engineering Controls

- Use dedicated cages, kennels, or stalls with dedicated drains for animals undergoing treatment with hazardous drugs. Avoid the use of sprayers or pressure washers to clean the cages, kennels, or stalls of treated animals to minimize the aerosolization of hazardous wastes.
- Place single-use disposable pads beneath animals receiving hazardous drug injections/infusions.

Administrative Controls

- Ensure that hazardous drugs are prepared or administered only by trained personnel in designated areas that are limited to authorized personnel.
- Post a sign to warn employees that they are working in an environment where hazardous drugs are handled.
- Warn employees who are pregnant, breastfeeding, or of reproductive age of the potential health effects of hazardous drugs, especially during the first trimester when a person may not know they are pregnant.
- Clean scissors and other tools, such as razors, after each use with animals receiving chemotherapy.

- Ensure dedicated cleaning supplies (e.g., mops, disposable wipes, buckets) used within chemotherapy treatment areas are not used in other areas of the veterinary facility.
- Clean the cages and kennels of treated animals with disposable towels if possible and use disposable towels to clean bodily waste from treated animals.
- Identify animals who receive chemotherapy drugs, such as with color-coded neckbands on animals and signs on kennels.
- Wash clothing and blankets that could be contaminated with a hazardous drug separately from items with no anticipated drug contamination. Use disposable blankets or color-coded blankets for animals who receive chemotherapy drugs.

PPE

- Wear gloves during all procedures involving administration of chemotherapeutics (including insertion of catheters).

Animal Owners

- Advise owners not to sleep with animals that are undergoing treatment without taking proper precautions against contamination from urine and feces.
- Educate animal owners how to handle waste from animals that are undergoing treatments and advise them to keep children away from the animals and waste until the drugs are eliminated.

10 Summary

The risk of adverse health effects from handling hazardous drugs depends on the hazards of the drugs and the exposure of workers when handling them. The drugs usually cannot be eliminated or substituted for, so reducing risk depends on reducing exposures. Occupational exposures are dependent on several factors unique to each work setting, such as the dosage form of the drug; routes of exposure; frequency, duration, and magnitude of exposure; work practices; and presence or absence of controls such as engineering controls, administrative controls, and PPE.

A comprehensive risk management program and a positive safety culture within the organization should be of paramount importance in the workplace. A continuous review of hazardous drugs is needed for each facility. A supervisor should be assigned to ensuring that compliance and risk assessments are kept up to date with the latest information available. Guidelines recommend reviewing and training annually, but training effectiveness can benefit from frequent reminders.

A recent study of 40,000 nurses found that despite longstanding recommendations for the safe handling of antineoplastic and other hazardous drugs, many of the nurses in the study—including those who were pregnant—reported not wearing protective gloves and gowns [Lawson et al. 2019]. A 2011 NIOSH survey of healthcare workers examined factors associated with adherence to safe handling practices among 1,094 hospital nurses who administered antineoplastic drugs. The study found that adherence to safe handling practices was not universal, and familiarity with safe handling practices and training in safe handling were associated with more reported PPE use. These results suggest that a positive safety culture, training, and familiarity with practices for safe handling of hazardous drugs, in addition to providing adequate time to adhere to guidelines and availability of PPE and certain engineering controls, are key to ensuring adherence to safe handling practices [Silver et al. 2016].

Employers must provide a safe workplace. The information in this document should be used as a helpful starting point for developing a facility-specific risk management plan. The written risk management plan should be part of an overall Safety Management System. Adherence to safe work practices can reduce potential occupational exposures to hazardous drugs and reduce possible adverse outcomes of exposure.

Resources

NIOSH (National Institute for Occupational Safety and Health)

NIOSH topic page on hazardous drugs, <https://www.cdc.gov/niosh/topics/hazdrug/antineoplastic.html>.

NIOSH topic page on reproductive health and the workplace: antineoplastic (chemotherapy) drugs, <https://www.cdc.gov/niosh/topics/repro/antineoplastic.html>.

NIOSH (2004). NIOSH Alert: preventing occupational exposures to antineoplastic and other hazardous drugs in health care settings, <https://www.cdc.gov/niosh/docs/2004-165/>.

NIOSH (2008). Personal protective equipment for health care workers who work with hazardous drugs, <https://www.cdc.gov/niosh/docs/wp-solutions/2009-106/>.

NIOSH topic page on the health and safety practices survey of healthcare workers, <https://www.cdc.gov/niosh/topics/healthcarehsps/default.html>.

NIOSH (2020). Sequence for putting on and removing personal protective equipment, infographic, <https://www.cdc.gov/niosh/npptl/pdfs/PPE-Sequence-508.pdf>.

OSHA (Occupational Safety and Health Administration)

OSHA (2016). Controlling occupational exposure to hazardous drugs, https://www.osha.gov/SLTC/hazardousdrugs/controlling_occex_hazardousdrugs.html.

ASHP (American Society of Health-System Pharmacists)

Power L, Coyne J (2018). ASHP guidelines on handling hazardous drugs, <https://www.ashp.org/-/media/assets/policy-guidelines/docs/guidelines/handling-hazardous-drugs.ashx?la=en&hash=E0DF626948227B0F25CAED1048991E8E391F2007>.

ONS (Oncology Nursing Society)

ONS safe handling resources learning library, <https://www.ons.org/learning-libraries/safe-handling-hazardous-drugs>.

Joint position statement from ONS and the Hematology/Oncology Pharmacy Association ensuring healthcare worker safety when handling hazardous drugs (2019), <https://www.ons.org/make-difference/ons-center-advocacy-and-health-policy/position-statements/ensuring-healthcare>.

USP (U.S. Pharmacopeial Convention)

USP General Chapter <800>, hazardous drugs handling in healthcare settings, <https://www.usp.org/compounding/general-chapter-hazardous-drugs-handling-healthcare>.

USP <800> HazRx, a phone app for 1000 HD drugs with monthly updates, <https://www.usp.org/hazrx-app>.

USP, know your exposure to hazardous drugs: help minimize your risk with the USP <800> HazRx phone app [wall chart], <https://www.usp.org/sites/default/files/usp/document/our-work/healthcare-quality-safety/800-know-your-exposure-to-hazardous-drugs.pdf>.

ACVIM (American College of Veterinary Internal Medicine)

ACVIM, small animal consensus statement on safe use of cytotoxic chemotherapeutics in veterinary practice, <https://onlinelibrary.wiley.com/doi/epdf/10.1111/jvim.15077>.

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