Managing Hazardous Drug Exposures: Information for Healthcare Settings

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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 who administer these drugs and inadvertently come into contact with them, and to their fetuses or breastfed offspring. In order to help healthcare facilities manage hazardous drugs in their formularies, the National Institute for Occupational Safety and Health (NIOSH) has developed a suite of tools designed to assist with the identification of hazardous drugs and their handling. NIOSH has provided an updated *List of Hazardous Drugs in Healthcare Settings (List)*, and *Procedures for Developing the NIOSH List of Hazardous Drugs in Healthcare Settings (Procedures)*, in addition to this document, *Managing Hazardous Drug Exposures: Information for Healthcare Settings*, which contains a table of Control Approaches. All of these documents are available on the NIOSH Hazardous Drugs topic page, https://www.cdc.gov/niosh/topics/hazdrug.html.

Executive Summary

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

A. Approved for use in humans by the FDA's Center for Drug Evaluation and Research (CDER);

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

C. Either:

1. Accompanied by prescribing information in the "package insert" that includes a manufacturer's special handling information (MSHI); 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; or 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.

This document, *Managing Hazardous Drug Exposures: Information for Healthcare Settings,* is derived from a table included in earlier versions of the *List*, titled *Personal Protective*

Equipment and Engineering Controls for Working with Hazardous Drugs in Healthcare Settings (often referred to as "Table 5").

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, or risk to the ability of men or women to successfully conceive and have healthy babies [NIOSH 2004a, NTP 2019, ONS 2018]. Some drugs 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 women who may become pregnant, or they could put the health of the fetus at risk. Some drugs handled or used in the healthcare workplace by women who are breastfeeding can also harm their children because drugs women are exposed to in the workplace can enter breast milk. Some drugs can affect either men's or women's fertility and make it harder to conceive.

Occupational risks are defined as the potential for and severity of adverse effects in workers from their exposure to workplace hazards [AIHA 1997]. Risk results from the combination of the hazard (potential harm from a substance) and the exposure (whether and how a worker comes in contact with a substance) [AIHA 1997]. These risks can be reduced by development and implementation of a risk 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 described in the risk assessment. Risk management also includes periodic exposure assessments and medical surveillance that should be conducted to determine the degree of control that has been obtained.

Approaches to protect workers from occupational exposure to hazardous drugs have been developed by several organizations [OSHA 1999, 2016; NIOSH 2004a; ASHP 2006, 2018; ONS 2018]. In general, they adhere to the hierarchy of controls for standard industrial hygiene practice that include elimination or substitution (when feasible), and the use of engineering controls, administrative controls, and PPE [NIOSH 2015].

Because the use of drugs that are hazardous to healthcare workers who handle them is often unavoidable, the most effective methods of decreasing employee exposure to hazardous drugs are the implementation of engineering controls, administrative controls, and PPE [ONS 2018].

Engineering controls prevent or reduce exposures by removing 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 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 aren't practical. 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 C.F.R. § 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 hazardous drug exposure [NIOSH 2004a, 2004b].

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 but are not limited to 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 may be encountered in healthcare settings where hazardous drugs are handled.

Efforts should be made to reduce all worker exposures to hazardous drugs. Occupational exposure to hazardous drugs should not be assumed to be harmless as workers may be exposed to multiple hazardous drugs daily over many years. Careful precautions and safeguards are suggested to protect workers, fetuses, and breastfed infants.

Periodic exposure assessment is needed to assess whether the risk management plan is effectively preventing healthcare worker exposures.

Contents

Acronyms

ACGIH	American Conference of Governmental Industrial Hygienists
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)
ASLs	acceptable surface limits
BSC	biological safety cabinet
CACI	compounding aseptic containment isolator
C.F.R.	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
DNA	deoxyribonucleic acid
FDA	Food and Drug Administration
GAO	Government Accountability office
HEPA	high efficiency particulate air
HIPEC	heated intraperitoneal chemotherapy
HVAC	heating, ventilation, and air conditioning
IARC	International Agency for Research on Cancer
ISO	International Organization for Standardization
IV	intravenous
NG	nasogastric
NIOSH	National Institute for Occupational Safety and Health

NSF	National Science Foundation
NTP	National Toxicology Program
OELs	occupational exposure limits
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
SDS	safety data sheet (formerly material safety data sheet)
U.S.	United States

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 glovebox isolator that operates under negative pressure 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 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 C-SEC is 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 are components of the secondary control strategy).

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

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

Engineering controls: Devices 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 the uncertainties in the assessment. It is often used to: compare exposures to established exposure limits; develop exposure-response relationships; inform risk assessment studies; and to evaluate the effectiveness of risk management plans.

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

Hazardous Drug: The NIOSH definition of a hazardous drug is a drug that is:

A. Approved for use in humans[1] by the 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] Although only drugs approved by the 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.

[2] Although biological products, such as vaccines, blood and blood components, allergenics, somatic cells, gene therapy, tissues, 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 Biologic Evaluation and Research (CBER), not by FDA's CDER.

[3] 10 C.F.R. 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*.

1. 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; organ toxicity at low doses;[6] or 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 property[8] that may limit the

[4] *See* 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 the 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."

[5] MSHI 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.

[6] All 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 mg/ day or a dose of 1 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 µg/m3 after applying appropriate uncertainty factors [Sargent and Kirk 1988; Naumann and Sargent 1997; Sargent et al. 2002]. OELs in this range are typically established for potent or toxic drugs in the pharmaceutical industry.

[7] NIOSH [2004]. 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, Public Health Service, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2004-165.

[8] Properties 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. *Molecular Pharmacology.* Hoboken, NJ: Wiley & Sons;2015; Di L, Kerns EH. *Drug-Like Properties: Concepts, Structure, Design, and*

potential for adverse health effects in healthcare workers from exposure to the drug.

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.

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, and/or delivery.

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

Sharps injury: A penetrating stab wound 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 cause malformation of an embryo.

Methods. Oxford, UK: Elsevier;2016; Mattson P, Kihlberg J. How big is too big for cell permeability. J Med Chem. 2017;60:1662-1664. https://doi.org/10.1021/acs.jmedchem.7b00237 .

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1.0 Purpose and Scope

This document contains risk management information and a table which describes some of the possible scenarios that may be encountered in healthcare settings where hazardous drugs are handled. The potential exposure of workers from handling a hazardous drug depends on several factors unique to each work setting. Such factors include but are not limited to the following: 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 PPE. NIOSH encourages healthcare settings to conduct a facility-specific assessment to determine the most effective strategy to control the risks identified in the assessment.

2.0 Background

2.1 History of the NIOSH Hazardous Drug List

To increase awareness of the potential adverse health effects from occupational exposure to antineoplastic and other hazardous drugs, the National Institute for Occupational Safety and Health (NIOSH) published an Alert *Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings* (Alert) in 2004. The Alert contained information for reducing exposures to antineoplastic and other hazardous drugs for all healthcare workers, and a list of drugs determined to be hazardous to workers' health [NIOSH 2004a]. The list of hazardous drugs from the Alert has been updated approximately every two years since 2010. The list includes drugs that meet the NIOSH definition of a hazardous drug that is either accompanied by prescribing information in the package insert[9] that includes a manufacturer's special handling information (MSHI);[10] or 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

[9] *See* 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 the 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."

[10] MSHI 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.

doses;[11] or structure; and toxicity profile that mimics existing drugs, 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.

In response to stakeholders' need to better understand how to manage risks when handling hazardous drugs in the workplace, the 2014 and 2016 NIOSH lists of hazardous drugs also provided a table titled *Personal Protective Equipment and Engineering Controls for Working with Hazardous Drugs in Healthcare Settings* (often referred to as Table 5). That 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 has been revised, now titled *Control Approaches for Safe Handling of Hazardous Drugs by Activity and Formulation*, and is presented in Chapter 8 of this document. The new table along with this document *Managing Hazardous Drug Exposures: Information for Healthcare Settings,* the *NIOSH List of Hazardous Drugs in Healthcare Settings (List)*, and *Procedures for Developing the NIOSH List of Hazardous Drugs in Healthcare Settings* (*Procedures*), are all available on the NIOSH Hazardous Drugs topic page, https://www.cdc.gov/niosh/topics/hazdrug.html.

This document is relevant to places of employment where hazardous drugs are handled. Workers potentially exposed to hazardous drugs in these settings may include, but are not limited to, pharmacists and pharmacy technicians, oncology nurses, infusion nurses and hematology/oncology nurses, advanced-practice registered nurses, licensed practical/vocational nurses, nurses' aides, home healthcare nurses, home healthcare nursing assistants, physicians, dentists, physicians' assistants, operating room personnel, shipping and receiving personnel, waste handlers, maintenance workers, laundry workers, environmental services workers, laboratory personnel, veterinarians, veterinary

[11] All 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 mg/ day or a dose of 1 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 µg/m3 after applying appropriate uncertainty factors [Sargent and Kirk 1988; Naumann and Sargent 1997; Sargent et al. 2002]. OELs in this range are typically established for potent or toxic drugs in the pharmaceutical industry.

technologists and other veterinary care workers. The current number of healthcare workers in the United States potentially exposed to hazardous drugs exceeds 8 million (BLS 2017).

2.2 Addressing the Risks of Hazardous Drugs

Occupational risks are defined as the potential for and severity of adverse effects in workers from their exposure to workplace hazards. Risk results from the hazard (or potential harm from an agent) and the exposure (whether a worker interacts with an agent)[AIHA 1997]. These risks can be mitigated by safeguards that are derived via 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 hazardous drugs are identified and exposures are assessed, the next step is to conduct a risk assessment that involves the 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 plan (Figure 1).

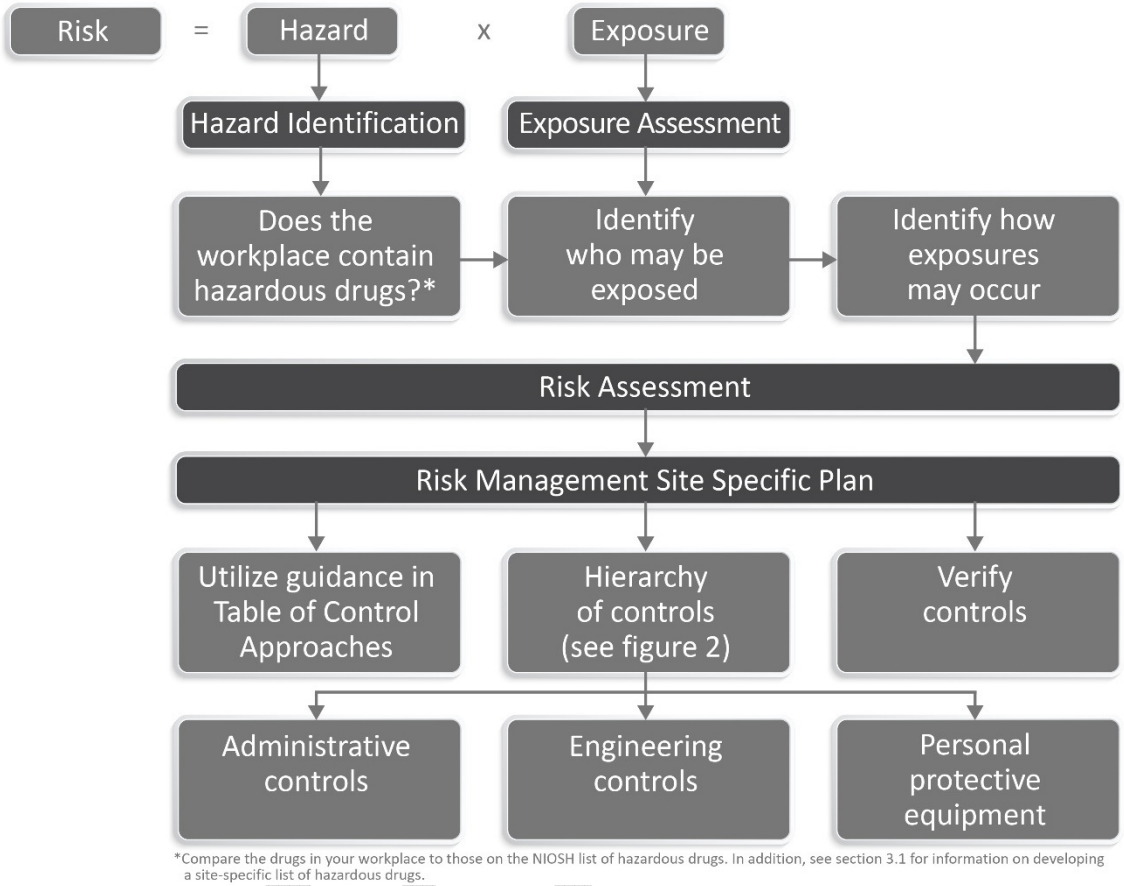

Figure 1. Elements of risk assessment provide the focus for a risk management program.

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. Steps to control potential exposures to minimize the risk are addressed in Chapter 6, Risk Management Plan.

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 how the drugs are formulated:

- **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 can 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, pills, powders, liquids, creams, or prefilled syringes.
- **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.
- **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.

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, or risk to the ability of men and women to successfully conceive and have healthy babies [NIOSH 2004a; ASHP 2006, 2018; Connor and McDiarmid 2006; ONS 2011; Connor et al. 2014; NTP 2019]. Some drugs can damage DNA in cells, leading to an increased risk of many types of cancer. Some drugs may cause damage to organs or organ systems, such as the liver or nervous system. Some drugs could harm women who may become pregnant, or they could put the health of the fetus at risk. Some drugs handled or used in the healthcare workplace can also be a concern for women who breastfeed because breast milk can contain drugs used in a workplace. Some drugs could affect either men's or women's fertility and make it harder to conceive. For drugs that are known carcinogens many have no known safe levels of exposure.

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

3.0 Hazard Identification

NIOSH uses a procedural approach for assessing and interpreting scientific information to determine whether a drug approved by the FDA CDER meets the NIOSH definition of a hazardous drug [NIOSH 2020]. Drugs considered hazardous include those accompanied by prescribing information in the package insert that includes a manufacturer's special handling information (MSHI) or is 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 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.

Healthcare workers who handle, compound, administer, or dispose of hazardous drugs; handle drug waste; or clean equipment used with hazardous drugs are at risk for adverse health effects, including reproductive harm and possibly leukemia and other cancers [NIOSH 2004a; ASHP 2006, 2018; Connor and McDiarmid 2006; ONS 2009; Connor et al. 2014; NTP 2019].

3.1 Developing a Facility-Specific Hazardous Drug List

Hazardous drug evaluation needs to be a continuous process completed on a routine basis. Employers can develop a facility-specific list that identifies the hazardous drugs in their workplace by comparing the drugs in their workplace to those on the NIOSH List of hazardous drugs. In addition, they should assess the hazards of new drugs as they are added to the workplace's formulary and/or as new information on the potential hazards of a drug become available and reassess whether a drug's presence on the facility-specific list is appropriate.

The *Procedures for Developing the NIOSH List of Hazardous Drugs in Healthcare Settings* [NIOSH 2020] provides information on how NIOSH creates a list of hazardous drugs; other

organizations have also developed various approaches to identify and classify hazardous drugs [Chaffee et al. 2010; Badry et al. 2014; Kaestli et al. 2013]. Information about the toxicity, carcinogenicity, and other hazards associated with a particular drug may be obtained from the drug product insert or from authoritative sources such as National Toxicology Program (NTP) or International Agency for Research on Cancer (IARC). Facilities may need to consider factors that affect them specifically, such as product formulation, 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.

4.0 Exposure Assessment

All of the drugs on the NIOSH List are considered hazardous, but the risk to the worker depends upon exposure. Exposure can occur through inhalation, skin or mucous membranes 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, vomitus, 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 Gieseker 2011], administration of the drugs in the operating room [Muehlbauer et al. 2006; Mellinger et al. 2010; Villa et al. 2015], aerosolization [Darwiche et al. 2013], or administration by inadequately trained healthcare professionals [ONS 2011; Menonna-Quinn 2013]. These activities can create aerosols or generate dust, thereby increasing exposure [OSHA 1999, 2016; NIOSH 2004a; ASHP 2006, 2018; ONS 2009]. Skin absorption and inhalation are the most common ways a healthcare worker may be exposed to hazardous drugs, although ingestion (from hand-to-mouth contact) or accidental injection through a needle stick or other sharps injury also is possible [NIOSH 2004a, 2016]. In addition to possible worker exposure during the course of patient treatment with these drugs, spills, and other events including 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 treatment of animals in the veterinary setting [Couch et al. 2013; Meijster et al. 2006; NIOSH 2010a].

NIOSH recommends an initial exposure assessment be conducted in any facility where hazardous drugs are handled and that periodic follow-up assessments be conducted, such as when operating procedures are modified, controls are put in place, and new drugs enter the workplace. 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 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 or making solutions from them outside a ventilated cabinet [Simmons 2010; Goodin et al. 2011]. Uncoated tablets may present a potential exposure from dust by skin contact and/or inhalation when the tablets are handled [Shahsavarani et al. 1993; Ahmad et al. 2015].

Exposure factors that should be assessed include, but are not necessarily limited to, the following:

- Agents used during work including hazardous drugs
- 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 (i.e., ventilated cabinets, CSTDs, glovebags, needleless systems, and PPE)
- Effectiveness of controls
- Physical layout of work areas
- Equipment maintenance procedures
- Decontamination and cleaning procedures
- Waste handling procedures
- Routine operations
- Spill response procedures

Comprehensive and facility-specific exposure assessment guidance specific to any particular healthcare setting is beyond the scope of this informational document. However, information on exposure assessment strategies can be found from other sources, such as in

the American Industrial Hygiene Association's (AIHA) *A Strategy for Assessing and Managing Occupational Exposures* [AIHA 2015].

5.0 Risk Assessment

Upon completing hazard identification and assessing the exposure factors, NIOSH recommends that employers 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:

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

For this document, the hazards are those associated with the hazardous drugs identified in the exposure assessment step described above.

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 may include consideration of dosage form and packaging of the material in the workplace, activities undertaken, 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 using 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, but is not limited to, consideration of worst-case scenarios such as identifying a maximum dose that a worker may be exposed to and the potential resulting health effects when considering dose-

response. This step helps to identify which scenarios require risk mitigation, given the hazards and likelihood of exposures. [AIHA 2015; NIOSH 2003].

This risk assessment should be used 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 utilizing the hierarchy of controls, verification of controls (Chapters 6 and 7), and information presented in the Table of Control Approaches (Chapter 8).

6.0 Risk Management Plan

The risk management plan is informed by the hazard identification, exposure assessment, and risk assessment, and identifies points of intervention to mitigate exposures and reduce risks to workers. A risk management plan is typically comprised of a plan to implement engineering controls, administrative controls, PPE, periodic exposure assessment, and medical surveillance based on the sources of exposure and the risks determined in the risk assessment. The elements of a risk management plan and factors that should be considered in addressing those elements are described in general in this chapter.

Occupational exposure to individual drugs should not be assumed to be harmless as workers may be exposed to multiple hazardous drugs, sometimes daily over many years. Careful precautions and safeguards to prevent exposures should be implemented. Because the combined effects of hazardous drugs are rarely studied, efforts should be made to reduce all worker exposures to hazardous drugs to protect workers, fetuses, and breastfed infants.

Recommendations on how to protect workers from occupational exposure to hazardous drugs have been developed by several organizations, including OSHA, American Society of Health-System Pharmacists (ASHP), and the Oncology Nursing Society (ONS) (see Additional 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]. 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 health care costs to care for injured workers but also to improved operational efficiency, improved employee morale, decreased employee absenteeism, and turnover [AIHA 2008]. Physicians should be made aware of issues with hazardous drugs and asked to consider substituting when prescribing treatments. Because the use of drugs that are hazardous to healthcare workers who handle them is often unavoidable, the most effective methods of decreasing employee exposure to hazardous

drugs are the implementation of engineering controls, administrative controls, and PPE [ONS 2018].

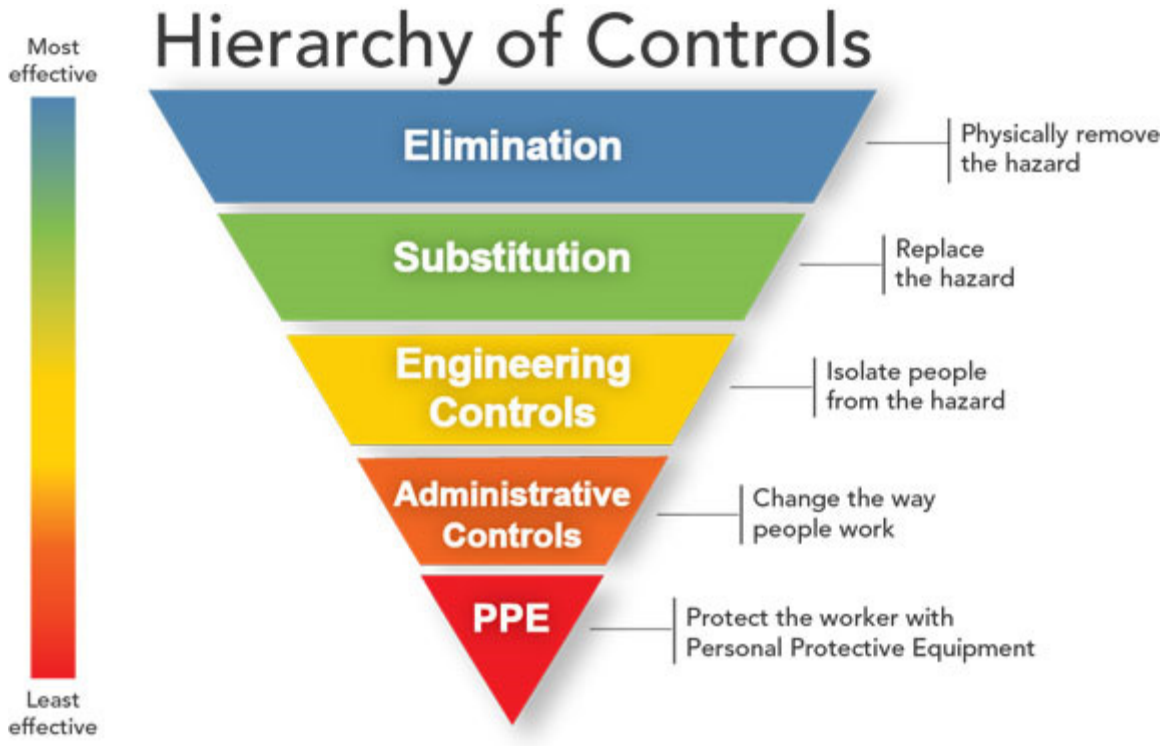

Figure 2. Hierarchy of Controls, NIOSH [2015], https://www.cdc.gov/niosh/topics/hierarchy/

6.1 Written Program

The risk management plan should be written and be 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, be developed using a collaborative effort including all affected departments, and specify measures that the employer is taking to ensure employee protection [OSHA 2016]. Since hazardous drugs are hazards that are identified in the Hazard Communication standard, the requirements of the Hazard Communication standard must also be met for some forms of

the drugs [29 CFR 1910.1200]. The written risk management plan should be part of an overall Safety Management System.

6.2 Engineering Controls

Engineering controls are used when elimination is not possible and less hazardous substitutes for the hazardous drug are not available or practical to implement. Engineering controls are implemented to reduce exposures by removing 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 to prevent it from entering the work environment. Well-designed engineering controls are typically independent of 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 only be used in combination with primary engineering controls (i.e., BSCs and CACIs) to further protect against worker exposures to hazardous drugs.

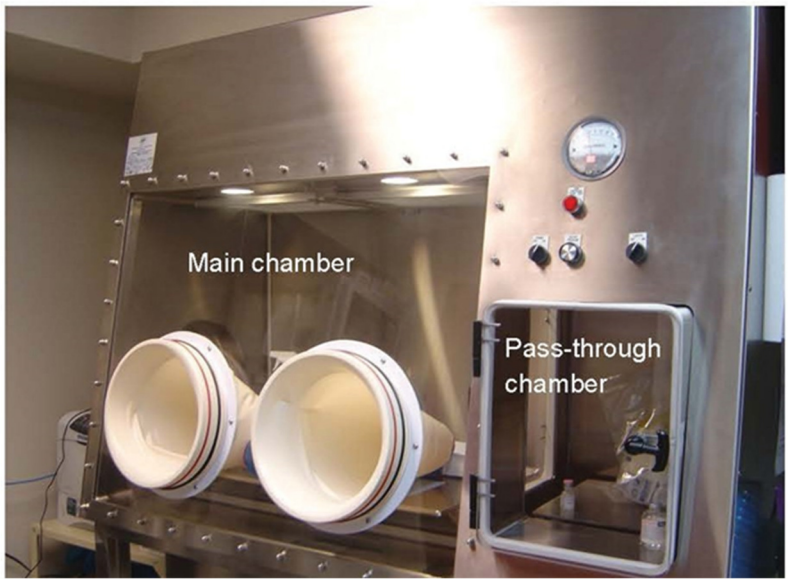

Figure 3. Compounding aseptic containment isolator (CACI) cabinet. (Photo by NIOSH.)

Figure 4. CSTD bag or infusion adapter attached to an IV bag. To learn more about CSTDs, please visit https://www.cdc.gov/niosh/topics/hazdrug/CSTD.html.

Figure 5. A robotic drug preparation system. Photo courtesy of Equishield.

The introduction of Class II BSCs for the preparation of hazardous drugs in the 1980s substantially reduced the potential for worker exposure, but not as efficiently as expected [Anderson et al. 1982, Connor et al. 1999]. CACIs have been introduced more recently, but their use has not been widespread. Additionally, CACIs have not been demonstrated to provide more protection for workers than BSCs [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 does not eliminate them [Connor et al. 2002; Wick et al. 2003; Harrison et al. 2006; Sessink et al. 2011, 2013].

Devices such as CSTDs, glovebags, 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 workers to sharps. The literature demonstrates a decrease in drug contaminants inside a Class II BSC when a CSTD is used [Sessink et al. 1999; Vandenbroucke and Robays 2001; Connor et al. 2002; Nygren et al. 2002; Spivey and Connor 2003; Wick et al. 2003]. However, a CSTD is not an acceptable substitute for a ventilated cabinet, and hazardous drugs should be prepared within a ventilated cabinet.

Formulations of hazardous drugs, including pills, powders, and liquid, should be compounded inside a BSC or CACI designed to prevent releases into the work environment.

Pharmacy personnel should prime the IV tubing and syringes inside the ventilated cabinet or prime them in-line with non-drug solutions.

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 assure 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 individual State boards of pharmacy [Pickard et al. 2016].

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

- Class II BSC (Type B2 is preferred, but Types A2 and B1 are allowed under certain conditions, such as when the presence of volatiles is expected to be minimal or non-existent)
- Class III BSC
- Isolators intended for asepsis and containment (aseptic containment isolators) [NSF/ANSI 2002; PDA 2001].

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

Certain areas may be well served to have negative pressure from 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 control" (C-PEC). A containment-secondary engineering control (C-SEC) is the room in which the C-PEC is placed. The C-SEC should be externally vented, have fixed walls and doors that separate it from other areas, and maintain a negative pressure to adjacent spaces [ASHP 2006, 2018].

A separate "doffing" area should be instituted 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 outside the compounding area.

Installation, Air Flow, and Exhaust of Ventilated Cabinets

Proper use of ventilated cabinets includes:

- Install, maintain, and routinely clean each 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].
- 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) or, if conducting non-sterile 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 sampling data.
- Seek additional information about placement of the cabinet, exhaust system, and stack design from NSF/ANSI 49–2002 [NSF/ANSI 2002]. Incorporate their recommendations regardless of the type of ventilated cabinet selected.

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. Make sure that workers performing maintenance are 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.

- 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.
- Seal used filtration media in plastic immediately upon removal, and tag it for disposal as chemotherapy waste; or 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 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 a worker's potential exposure.

Administrative controls include, but are not limited to, the following:

- Education and training of employers and employees.
- Limiting the time workers handle the material.
- Limiting access to the areas where hazardous drugs are used.
- Implementing good housekeeping practices (such as wet wiping cleanup and use of HEPA-filtered vacuums).
- Prohibiting the use of automated counting machines for hazardous drugs.
- Implementing signage, labeling, and storage of materials.
- Hand washing before eating, drinking, smoking, or leaving the workplace.
- Prohibiting consumption of food and drink in the areas where hazardous drugs are handled.
- Providing training on spill response and use of spill kits in areas where hazardous drugs are used.
- Continuous monitoring of compliance to policies and procedures.

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 cleaned with a deactivation agent (if available) and cleaning agent before and after each activity, and at the end of the work shift. Cleaning materials should be disposed of following the facility SOPs.

Tablet and capsule forms of hazardous drugs should not be placed in automated counting machines, which subject them to stress and may introduce powdered contaminants into the work area [Fent and Durgam 2012; Fent et al. 2014]. Counting and pouring of hazardous drugs should be done carefully, 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.

The ability of employees to translate training into work practices that reduce risks and that promote safe working conditions should be evaluated regularly by supervisors working in partnership with health and safety professionals. Measures of employee understanding, actions, and feedback can then be used to determine the frequency of training, the need for retraining, or the need to revise training methods.

6.4 Personal Protective Equipment

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

It is important to understand the attributes 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 the exposure of the worker. 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 PPE and to reduce the spread of contamination. All PPE should be inspected for defects or damage prior to use.

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

Gloves

Surfaces in areas where hazardous drugs are present and external parts (e.g., syringes, tubes, and bottles) 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 with 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 it provides and may make work activities more difficult. To the extent possible, gloves should be selected based on test information provided by the glove manufacturer that demonstrates permeation resistance to specific hazardous drugs. Currently, guidelines are only available for testing "chemotherapy gloves" [ASTM 2005] and information may not be available for other types of hazardous drugs.

Suggested work practices when using gloves (see also Table of Control Approaches):

- Review the gloving advice in the 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, but generally accepted practice is that gloves should not be used for more than 30 minutes [NIOSH 2004a; ASHP 2006,2018]. Whenever gloves are damaged or contact with a drug is known or suspected, carefully remove and dispose of them following SOPs.
- Use powder-free gloves since the powder can contaminate the work area and might adsorb and retain hazardous drugs.
- A single pair of chemotherapy gloves may be adequate when administering intact tablets or capsules or manufacturer's 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., cutting or crushing tablets or capsules; withdrawing injections from a vial; administering topical drugs, irrigation solutions, or aerosol treatments; spill cleanup) [NIOSH 2008].
- 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, 2018; ONS 2011].
- When compounding sterile preparations, sanitize gloves with sterile 70% alcohol spray or gel and allow them to dry; ensure that the selected gloves are not degraded by the alcohol [NIOSH 2008].
- Use double gloves for administering syringes that were filled in-house as they may have contamination on the external syringe.
- When removing gloves, turn gloves inside-out so that contaminated surfaces do not touch uncontaminated surfaces.
- Discard used gloves in a hazardous waste labeled, covered, and sealed disposal container.
- Wash hands thoroughly with soap and water after removing and disposing of gloves.

Gowns

Gowns protect workers from spills and splashes of hazardous drugs and waste materials. Gowns must be disposable and shown to resist permeation by the types of hazardous drugs being used [NIOSH 2008]. Gowns should not have seams or closures that could allow drugs to pass through and 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 of non-coated materials [NIOSH 2004a; 2009, ASHP 2006, 2018]. Cloth laboratory coats, surgical scrubs, or other absorbent

materials permit the penetration of hazardous drugs and can hold spilled drugs against the skin and increase exposure.

Suggested work practices when wearing gowns (see also Table of Control Approaches):

- Wear gowns whenever there is a possibility of splash or spill such as in compounding or administration of hazardous drugs.
- Avoid spreading drug contamination by not wearing gowns outside the compounding or administration area.
- Dispose of gowns after each use in a hazardous waste labeled, covered, and sealed disposal container. 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 may be inhaled by personnel 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 on the box or respirator. 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 the FDA as a surgical mask. A surgical N95 respirator provides the respiratory protection of an N95 respirator and the splash protection provided by a surgical mask. Surgical masks that are not labeled as N95 are not NIOSH-approved, do not provide

respiratory protection, and should not be used to compound or administer fine powders which may result from handling hazardous drugs [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, therefore it may be necessary to work with the respirator manufacturer to identify the types of filtration needed in a facility.

Suggested work practices when using respiratory protection (see also Table of Control Approaches):

- If there is an inhalation potential of fine powders, a N95 respirator should be used for routine handling of antineoplastic and other hazardous drugs. [NIOSH 2008].
- If there is an inhalation potential of fine powders and possible splashes from bodily fluids or liquid drugs, a surgical N95 respirator should be used for handling of antineoplastic and other hazardous drugs. [NIOSH 2008].
- A full-facepiece combination particulate/chemical cartridge-type respirator [42 C.F.R. Part 84; NIOSH 2004b] should be used for events such as large spills when an IV bag breaks or a line disconnects and leaks, or where there is known or suspected airborne exposure to volatile drugs, vapors, or gases.
- Use a full-facepiece combination particulate/chemical cartridge-type respirator or a powered air-purifying respirator (PAPR) whenever aerosolizing hazardous drugs for inhalation or nebulized therapy (Figure 6) [ONS 2018].
- Provide medical evaluation, fit-testing, and training of workers who use respiratory protection. Follow all requirements in the OSHA respiratory protection standard [29 C.F.R. § 1910.134] (www.osha.gov/SLTC/etools/respiratory/index.html).

Figure 6. An example N95 disposable respirator, a full-facepiece combination particulate/chemical cartridge-type respirator and a powered air-purifying respirator (PAPR). Images courtesy of 3M, Honeywell International and MaxAir.

Eye and Face Protection

Eye and face protection are needed whenever hazardous drugs may splash since many hazardous drugs are irritating to eyes and may be absorbed through the eyes or mucous membranes.

Suggested work practices when 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, 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 as 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 eye glasses or safety glasses with side shields, as glasses with side shields do not provide adequate protection to the eyes from splashes [NIOSH 2008].

Head, Hair, Shoe, and Sleeve Covers

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

- When compounding hazardous drugs, use sleeve covers constructed of coated materials to provide additional protection for the areas of the arms that may come in contact with the drug.
- Use hair and shoe covers constructed of coated materials to reduce the possibility of particulate or microbial contamination in compounding areas, clean rooms and other sensitive areas.
- Remove hair, shoe and sleeve covers before exiting drug compounding areas to avoid spreading drug contamination to other areas and possibly exposing non-protected workers.
- When compounding hazardous drugs, a second pair of shoe covers should be donned before entering the C-SEC and removed when exiting the C-SEC [ASHP 2018].
- Discard used head, hair, shoe and sleeve covers in a hazardous waste labeled, covered, and sealed disposal container.

PPE Disposal

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

- Contain and dispose of such PPE either as trace or bulk contaminated waste [NIOSH 2004a].
- Hazardous waste should be stored in a secure area in covered, leak-proof, containers or drums with distinct labels including the words, *hazardous waste*.

- To prevent contamination of the clean areas (e.g., offices, breakrooms, and common areas) of the facility, remove PPE at the entrance to the compounding areas, and after administration of the drug.
- Do not reach into hazardous waste containers when discarding PPE.
- Seal waste containers when three-fourths full.
- Wash hands thoroughly with soap and water after removing and disposing of PPE.

7.0 Exposure Control Evaluations

Measurement of surface contamination is currently the best indication of the level of environmental contamination 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]. Workplace contamination with hazardous drugs continues to be an issue in the United States [Connor et al. 1999, 2010; Wick et al. 2003; Harrison et al. 2006; Davis et al. 2011; Sessink et al. 2011, 2013]. 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 [Pethran et al. 2003; Connor et al. 2010; Villarini 2011]. A U.S. study reported nurses had exposure to the skin or eyes 17% of the time when handling antineoplastic drugs [Friese at 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 [Schierl et al. 2009; Connor et al. 2010; Siderov et al. 2010; Yoshida et al. 2010; Sessink et al. 2011, 2013, 2015; Turci et al. 2011; Chu et al. 2012; Sottani et al. 2012; Hon et al. 2013, 2014b, 2015; Kopp et al. 2013; Merger et al. 2014; Odraska et al. 2014; Viegas et al. 2014; Berruyer et al. 2015].

In the pharmaceuticals industry, acceptable surface limits (ASLs) are used for protection against 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 housekeeping 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

lunch rooms or offices, or on the outside surfaces of packaging materials) [Kimmel et al. 2011]. Commercial test kits are available to assess hazardous drug surface contamination and some industrial hygiene analytical laboratories are capable of analyzing for some hazardous drug contamination using specified types of surface wipe media.

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

7.1 Medical Surveillance

NIOSH and OSHA recommend the use of a medical surveillance program as an additional approach to protect the health of workers [NIOSH 2012; OSHA 2016]. 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 and identify where improvements in primary prevention are needed.

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. The second is to provide medical surveillance that focuses on detecting the adverse health effects caused by the classes of hazardous drugs in use. Because healthcare workers are typically exposed to numerous hazardous drugs [Boiano et al. 2014; Boiano et al. 2015; NIOSH 2004a, 2012], no single biomarker of effect is suitable for all of these drugs. Organizations should use the information obtained through medical surveillance to treat 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:

- A plan to provide initial baseline clinical evaluation, including targeted medical history, physical examination, and laboratory testing for workers potentially exposed to hazardous drugs that addresses their potential toxicities.
- Health questionnaires administered by a healthcare professional and completed 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 because their occurrence may go unreported. Opportunities to identify patterns of occurrence implying insufficient engineering controls, technique, or other preventive measures may be similarly missed.
- 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 for workers who have shown health changes consistent with known adverse effects of the hazardous drugs they are exposed to or who have experienced an acute exposure (e.g., substantial skin, mucosal or ocular contact or inhalation exposure or cleaning a large spill). This follow-up should include evaluation of current engineering and administrative controls and PPE to ensure that all systems are appropriately and accurately implemented [NIOSH 2012]. The physical examination of the worker should focus on the involved area of the body as well as other organ systems commonly affected (for a spill, the skin and mucous membranes of the affected area; for aerosolized hazardous drugs, the pulmonary system) [OSHA 2016].

8.0 Control Approaches for Safe Handling of Hazardous Drugs by Activity and Formulation

8.1 Introduction to Table of Control Approaches

The Table of *Control Approaches for Safe Handling of Hazardous Drugs by Activity and Formulation* provides information for some of the possible scenarios that may be encountered in healthcare settings where hazardous drugs are handled, but it cannot address all possible situations. Given the variety of drugs, addition 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 with use of recommended engineering controls and PPE, regardless of their formulation (IV, subcutaneous, topical, 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 NIOSH List are known reproductive or developmental hazards. They represent a potential occupational hazard to men or women who are actively trying to conceive, to the fetus of a pregnant woman or to the baby who is breastfed as hazardous drugs may be present in breast milk. Protecting workers during the period of conception and pregnancy may be difficult. Approximately 45% of pregnancies in the United States are unplanned [Finer and Zolna 2016], women 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, and some hazardous drugs may pass into the sperm providing a route of exposure for their partners. Therefore, while some drugs may only be listed as a reproductive or developmental hazard, risk management, including PPE use, for those drugs may be recommended for all staff, not just those who are known to be pregnant or known to be planning to become pregnant.

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 have MSHI which is typically in Section 16 of the drug package insert. The MSHI should be consulted prior to handling any drug.

Table. Control Approaches for Safe Handling of Hazardous Drugs by Activity and Formulation (to be formatted at publication, currently allowing header on each page)

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

		Control Approaches					
Activity	**Formulation**	**Ventilated engineering control (BSC or CACI)**	**Closed system transfer device**	**Double chemo-therapy gloves**	**Protective gown**	**Eye, face hair, sleeve, and shoe protection**	**Respiratory protection[1]**
	liquids, or creams. In-house filled syringes.						
Compounding[3]	Crushing or manipulating tablets or capsules	Yes[4] Consider crushing tablets in a pill pouch.	N/A	Yes[5]	Yes	Hair, sleeve and shoe covers. Add eye and face protection, if not done in a ventilated engineering control.	Yes, if not using a ventilated engineering control
	Oral liquid drug	Yes[4]	N/A	Yes[5]	Yes	Hair, sleeve and shoe covers. Add eye and face protection, if not done in a ventilated	Yes, if not using a ventilated engineering control

		Control Approaches					
Activity	**Formulation**	**Ventilated engineering control (BSC or CACI)**	**Closed system transfer device**	**Double chemo-therapy gloves**	**Protective gown**	**Eye, face hair, sleeve, and shoe protection**	**Respiratory protection[1]**
						engineering control.	
	Topical drug	Yes[4] (Note: some drugs such as carmustine, thiotepa, and mechloretha-mine are volatile)	N/AN/AN/A	Yes[5]	Yes	Hair, sleeve 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
	Withdrawing injections from a vial	Yes[4]	Yes	Yes[5]	Yes	Hair, sleeve and shoe covers. Add eye and face protection, if not done in a ventilated	Yes, if not using a ventilated engineering control

		Control Approaches					
Activity	**Formulation**	**Ventilated engineering control (BSC or CACI)**	**Closed system transfer device**	**Double chemo-therapy gloves**	**Protective gown**	**Eye, face hair, sleeve, and shoe protection**	**Respiratory protection[1]**
						engineering control.	
	Mixing injections from a vial	Yes[4]	Yes	Yes[5]	Yes	Hair, sleeve and shoe covers. Add eye and face protection, if not done in a ventilated engineering control.	Yes, if not using a ventilated engineering control
	Solution for irrigation	Yes[4]	N/A	Yes[5]	Yes	Hair, sleeve and shoe covers. Add eye and face protection, if not done in a ventilated	Yes, if not using a ventilated engineering control

		Control Approaches					
Activity	**Formulation**	**Ventilated engineering control (BSC or CACI)**	**Closed system transfer device**	**Double chemo-therapy gloves**	**Protective gown**	**Eye, face hair, sleeve, and shoe protection**	**Respiratory protection[1]**
						engineering control.	
	Powder/solutions for aerosol treatments	Yes[4]	Yes, when dosage form allows	Yes[5]	Yes	Hair, sleeve 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	N/A	N/A	Single glove	No	Eye and face protection if vomit potential[6]	No
	Cut, crushed or uncoated tablets or capsules	N/A	N/A	Yes	Yes	Eye and face protection if	No

		Control Approaches					
Activity	**Formulation**	**Ventilated engineering control (BSC or CACI)**	**Closed system transfer device**	**Double chemo-therapy gloves**	**Protective gown**	**Eye, face hair, sleeve, and shoe protection**	**Respiratory protection[1]**
						vomit potential[6]	
	Subcutaneous or intramuscular injections from a manufacturers' supplied pre-filled syringe or injector	N/A	N/A	Single glove	No	Eye and face protection if liquid likely to splash[6]	No
	Subcutaneous or intramuscular injections from a prepared syringe or injector	N/A	N/A	Yes	Yes	Eye and face protection if liquid likely to splash[6]	No
	Intravenous injections from prepared syringes[7]	N/A	Yes	Yes	Yes	Eye and face protection if liquid that could splash[6]	No
	Intravenous solutions for infusions	N/A	Yes, when dosage form allows	Yes	Yes	Eye and face protection if liquid that	No

		Control Approaches					
Activity	**Formulation**	**Ventilated engineering control (BSC or CACI)**	**Closed system transfer device**	**Double chemo-therapy gloves**	**Protective gown**	**Eye, face hair, sleeve, and shoe protection**	**Respiratory protection[1]**
						could splash[6]	
	Oral liquid drug: PO/feeding tube/nasogastric (NG) tube	N/A	N/A	Yes	Yes	Eye and face protection if liquid likely to splash[6]	Yes, if inhalation potential
	Topical drug (ointments, creams	No (Note: some drugs such as carmustine, thiotepa, and mechloretha-mine are volatile and may need to be administered in an enclosure.	N/A	Yes	Yes	Eye and face protection if liquid likely to splash[6]	Yes, if inhalation potential

		Control Approaches					
Activity	**Formulation**	**Ventilated engineering control (BSC or CACI)**	**Closed system transfer device**	**Double chemo-therapy gloves**	**Protective gown**	**Eye, face hair, sleeve, and shoe protection**	**Respiratory protection[1]**
	Irrigation solutions, bladder instillation, HIPEC, limb perfusion	N/A	Yes, when dosage form allows	Yes	Yes	Eye and face protection	Yes
	Powder/solution for inhalation/aerosol treatment	Yes, when applicable. Note that some treatments may need to be administered in an enclosure.	CSTD recommended when dosage form allows	Yes	Yes	Eye and face protection if liquid that could splash[6]	Yes, full facepiece or PAPR with combination particulate/ chemical cartridges if inhalation potential
Disposal and Cleaning	Drugs and metabolites in body fluids	Fold soft materials (sheets, hygiene care products) inward to prevent	N/A	Yes	Yes	Eye and face protection if liquid could splash	Yes, if inhalation potential

		Control Approaches					
Activity	**Formulation**	**Ventilated engineering control (BSC or CACI)**	**Closed system transfer device**	**Double chemo-therapy gloves**	**Protective gown**	**Eye, face hair, sleeve, and shoe protection**	**Respiratory protection[1]**
		leakage. Place in sealed bags.					
Disposal and Cleaning	Drug-contaminated waste	Avoid creating dusts. Place in sealed bags. Use caution when closing bags as pushing waste down may force hazardous drug dusts up into the user's face.	N/A	Yes	Yes	Eye and face protection if liquid could splash	Yes, if inhalation potential
Routine Cleaning	All types of hazardous drugs	Use wet wiping methods. Avoid creating	N/A	Yes	Yes	As needed[8]	As needed[8]

		Control Approaches					
Activity	**Formulation**	**Ventilated engineering control (BSC or CACI)**	**Closed system transfer device**	**Double chemo-therapy gloves**	**Protective gown**	**Eye, face hair, sleeve, and shoe protection**	**Respiratory protection[1]**
		dusts. Disinfection, deactivation or decontamination agents may be necessary. Place in sealed bags for disposal.					
Spill clean up	All types of hazardous drugs	Limit access to area. Use absorbent pads for liquid spills. Disinfection, deactivation or decontamination agents may be necessary Avoid creating	N/A	Yes	Yes	Yes	Yes, full facepiece or PAPR with combination particulate/ chemical cartridges may be needed

		Control Approaches					
Activity	**Formulation**	**Ventilated engineering control (BSC or CACI)**	**Closed system transfer device**	**Double chemo-therapy gloves**	**Protective gown**	**Eye, face hair, sleeve, and shoe protection**	**Respiratory protection[1]**
		dusts. Place in sealed bags.					

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

[1] Respiratory protection must be selected based on the hazardous drug and its physical form (particulate, vapor, etc.) and other exposure factors. For general activities, a N95 may suffice. When performing activities such as cleaning the BSC or CACI or responding to large spills, a combination particulate/chemical cartridge respirator may be needed.

[2] N/A Not applicable.

[3] 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; https://www.fda.gov/drugs/human-drug-compounding/compounding-and-fda-questions-and-answers.

[4] For nonsterile preparations, a ventilated engineering control such as a fume hood, Class I BSC or a CVE is sufficient if the ventilated engineering control exhaust is HEPA filtered and appropriately exhausted to the outside of the building (preferred) or it is filtered with redundant HEPA filters in series and recirculated back into the C-SCA. It is recommended that these activities be carried out in a ventilated engineering control, but it is recognized that under some treatment scenarios (e.g. time-sensitive activities in the emergency department), it is not possible. 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.

[5] Sterile gloves required for aseptic drug preparation in BSC or CACI.

[6] Needed if patient may resist (infant, unruly patient, patient pre-disposed to spitting out, patients with difficulty swallowing, veterinary patient) also needed if the formulation is hard to swallow.

[7] Intravenous tubing already attached and primed.

[8] Activities such as cleaning floors may not require eye or respiratory protection, while 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 the facility-specific conditions. For more detailed information on safe handling practices, see the reference list for this table [NIOSH 2004a, 2008; ASHP 2006, 2018; ONS 2011, 2018; OSHA 2016].

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 suspected. Open damaged containers inside of a fume hood, Class 1 BSC, or HEPA-filtered enclosure.

PPE: Double chemotherapy gloves and 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 pills 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 chemotherapy glove.

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

Crushing or manipulating tablets or capsules

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

PPE: Double chemotherapy gloves, protective gown and sleeve covers. Add eye/face protection and respiratory protection [N95] if compounding is

done outside of the ventilated engineering control. Hair and shoe covers should be worn.

Oral liquid drugs

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

PPE: Double chemotherapy gloves, protective gown and sleeve covers. Add eye/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, theotipa, and mechlorethamine are volatile.

PPE: Double chemotherapy gloves, protective gown and sleeve covers. Add eye/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.

PPE: Double chemotherapy gloves, protective gown and sleeve covers. Add eye/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 (withdrawing and/or mixing from a vial or ampoule)

Controls: Ventilated engineering control (Class II or III BSC or CACI). Use a CSTD.

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

Solutions for inhalation or 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, protective gown and sleeve covers. Add eye/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 chemotherapy gloves. Add eye and face protection if there is the potential to contact vomit or if patient may resist or is pre-disposed to spitting out.

Cut or crushed tablets or capsules or uncoated tablets

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

Subcutaneous/intramuscular injections from a manufacturers' prefilled syringe or injector

PPE: Single chemotherapy gloves. 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 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.

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

Intravenous Solutions for infusion

Controls: Use a CSTD.

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

Oral liquid drugs via po (by mouth)/feeding tube/neogastric tubes

PPE: Double chemotherapy gloves and 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 pre-disposed to spitting out.

Topical drugs

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

PPE: Double chemotherapy gloves and 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 solutions a**dministration via bladder/HIPEC/ limb profusion**

Controls: Use a CSTD if the dosage form allows.

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

Inhalation/aerosol treatments

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

PPE: Double chemotherapy gloves and 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 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 dusts. Place in sealed bags for disposal. Use caution when

closing bags as pushing waste down may force hazardous drug dusts up into the user's face.

PPE: Double chemotherapy gloves and 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 dusts. Disinfection, deactivation or decontamination agents may be necessary. Place in sealed bags for disposal.

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

Spill clean up

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

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

8.3 Steps to reduce potential exposure to hazardous drugs

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

- All containers of hazardous drugs must be labeled, tagged, or marked 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 pills 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 and/ or augment the control of generated aerosols using supplementary controls such as glovebags or 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 product 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.
- 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 the home or veterinary clinic.

Home Healthcare

Additional considerations for handling hazardous drugs in the home setting include:

- Providing overall basic education and related precautions to protect home healthcare workers, patient family members, and caregivers from indirect or direct exposure to hazardous drugs.
- Using gloves when caring for patients.
- Suggesting that family members use gloves when handling laundry or cleaning within or around toilets [Meijster et al. 2006].
- Closing the lid before flushing the toilet and flush twice after each use by patient, for 48 hours after receiving chemotherapy. If available, use separate bathroom from family members [ONS 2014].
- Conducting double washing of linens and washing them separately from other family laundry [ONS 2018].

Veterinary Clinics

Considerations for administration of hazardous drugs in a veterinary setting are provided in the NIOSH Workplace Solutions document *Safe Handling of Hazardous Drugs for Veterinary Healthcare Workers* [NIOSH 2010a]. The Workplace Solutions document suggests the same hierarchy of controls (engineering controls, administrative controls and PPE) with some specific suggestions such as:

- 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 woman may not know she is pregnant.
- 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.
- Clean the cages and kennels of treated animals with disposable towels if possible and use disposable towels to clean bodily waste from treated animals.
- Place single-use disposable pads beneath animals receiving hazardous drug injections/infusions.
- Clean scissors and other tools, such as razors, after each use with animals receiving chemotherapy.
- Ensure dedicated cleaning supplies (e.g., mops, rags, buckets) used within chemotherapy treatment areas are not used in other areas of the veterinary facility.
- Identify animals who receive chemotherapy drugs, such as 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 and/or color-coded blankets for animals who receive chemotherapy drugs.

9.0 Summary

The risk of adverse health effects from handling hazardous drugs is dependent on the hazards of the drugs and the exposure of workers when handling them. The drugs usually cannot be eliminated or substituted for, so the reduction of risk is dependent on reducing exposures. Exposures are dependent on several factors unique to each work setting. Such factors include, but are not limited to, the following: 1) dosage form of the drug; 2) routes of exposure; 3) frequency, duration, and magnitude of exposure; 4) work practices; and 5) presence or absence of any exposure controls such as engineering controls, administrative controls, or PPE.

A comprehensive risk management program and a positive safety culture within the organization should be of paramount importance in the workplace. One 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 1094 hospital nurses who administered antineoplastic drugs. That 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. The results suggest that a positive safety culture, training and familiarity with practices for safe handling of hazardous drugs, 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 have a responsibility to provide a safe workplace. This document offers information that should be used as a helpful starting point for developing a facility-specific risk management plan. Adherence to safe work practices can reduce potential occupational exposures and possible adverse outcomes from hazardous drugs.

Additional Resources

NIOSH

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

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NIOSH Topic page: Health and Safety Practices Survey of Healthcare Workers
https://www.cdc.gov/niosh/topics/healthcarehsps/default.html

OSHA

OSHA [2016] Controlling Occupational Exposure to Hazardous Drugs.
http://www.osha.gov/SLTC/hazardousdrugs/controlling_occex_hazardousdrugs.html.

OSHA Topic page on hazardous drugs
https://www.osha.gov/SLTC/hazardousdrugs/index.html

ASHP

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10 C.F.R. § 20.1003, Standards for Protection against Radiation, Definitions.

29 C.F.R. § 1910.132, General Requirements , Personal Protective Equipment.

29 C.F.R. § 1910.134, Respiratory Protection.

29 C.F.R. §1910.1200 Hazard Communication.

42 C.F.R. Part 84, Approval of Respiratory Protective Devices.

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