Best Practice Safety Tools for Pharmacy Personnel Handling Hazardous Drugs

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Best Practice Safety Tools for Pharmacy Personnel Handling Hazardous Drugs

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BEST PRACTICE SAFETY TOOLS FOR PHARMACY PERSONNEL HANDLING HAZARDOUS DRUGS

Presented by Larry Lee

Introduction

Best Practice Safety Tools

Best Practice Safety Tools for Pharmacy Personnel Handling Hazardous Drugs (Best Practice Safety Tools) was written to provide pharmacists and pharmacy managers with tools that they can use to identify hazardous drugs, assign hazardous drugs to appropriate risk categories, evaluate and select appropriate engineering controls, make personal protective equipment and respiratory protection determinations, safely address spills, and dispose of hazardous drug waste.

Pharmacists and pharmacy personnel are potentially exposed to a variety of hazardous drugs in nearly all practice settings, encompassing community, hospital, compounding, and long-term care alike. Hazardous drugs are commonly understood in pharmacy to include cytotoxic chemotherapy and antineoplastic drugs; however, other drugs may present hazards in terms of reproductive, cancer, toxicity, and other risks that may not be fully recognized in practice. Furthermore, the work practices and engineering controls used in the sterile compounding of hazardous drugs are fundamentally designed to protect the preparation from contamination but may be in conflict with the need to protect the preparer from exposure.

NIOSH published a sample list of antineoplastic and other hazardous drugs in 2004, updated the list in 2010, 2012, and the 2014 updates are pending at this writing. The NIOSH definition for hazardous drugs includes those drugs that exhibit one or more of the following characteristics: Carcinogenicity, Teratogenicity (or other developmental toxicity), Reproductive toxicity, Organ toxicity at low doses, Genotoxicity, and Structure and toxicity profiles of new drugs that mimic existing hazardous drugs.

Guidelines for the safe handling of hazardous drugs in pharmacy and healthcare have been developed nationally and internationally, and the following guidelines were reviewed, evaluated, and used in developing the *Best Practice Safety Tools for Pharmacists Handling Hazardous Drugs:*

- American Society of Health-System Pharmacists, Compounding Sterile Preparations – 3rd Ed. (2009)
- BC Cancer Agency: Care & Research, Safe Handling of Hazardous Drugs, Module 1 (2008)
- Institut de recherché Robert-Sauvé en santé et sécurité du travail (IRSST), Working Committee on the Safe Handling of Hazardous Drugs established by the Association paritaire pour la santé et la sécurité du travial du secteur affaires

sociales (ASSTAS), Prevention Guide: Safe Handling of Hazardous Drugs (2008)

- International Society of Oncology Pharmacy Practitioners, ISOPP Standards of Practice, Safe Handling of Cytotoxics (2006)
- NIOSH Alert, Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings (2004)
- NIOSH Workplace Solutions, Personal Protective Equipment for Health Care Workers Who Work with Hazardous Drugs (2008)
- The Society of Hospital Pharmacists of Australia, SHPA Standards of Practice for the Safe Handling of Cytotoxic Drugs in Pharmacy Departments (2004)
- University HealthSystem Consortium, UHC Consensus Statement: Model Hazardous Drug Safety Plan for Institutions (2009)

The Algorithm provided in Best Practice Safety Tools is intended to be used by pharmacists and pharmacy managers to make hazardous drug determinations by assigning each drug to an appropriate risk category based on the drug's hazard profile, physical characteristics, and level of manipulation. Individual drugs may be moved from one risk category to another based on its' physical characteristics (e.g. bulk powder v. coated tablet), manipulation (e.g. manipulated v. unmanipulated oral liquid), or packaging (e.g. multi-dose vial v. single dose vial). Each risk category includes recommendations for engineering controls and personal protective equipment.

Best Practice Safety Tools also includes detailed sections on receiving and storing hazardous drugs, hazardous drug compounding, personal protective equipment, respiratory protection, engineering controls, closed system transfer devices, spill cleanup, and waste handling procedures. Best Practice Safety Tools also identifies gaps in current knowledge and practice.

It is important to recognize that Best Practice Safety Tools is based on what is currently known and understood about hazardous drugs. Over time practices will be changed and refined as more research is conducted and technology improves. For example, it is likely that environmental surface contamination levels may eventually be correlated with occupational illness and risk of disease, but it is not known at this time. Closed system transfer device technology is expected to improve and show promise with regard to preventing environmental contamination in and outside the pharmacy.

There are also gaps in our current knowledge base and lack of evidence with regard to several pertinent issues, including potential exposure to vapor from some hazardous drugs and the protective capability of commonly recommended respiratory protection to prevent exposure, and the untested assertion that non-recirculating biological safety cabinets provide an increased level of safety for users over cabinets that circulate some

air. These issues are discussed in Best Practice Safety Tools and the rationale for the recommendations made is provided.

Best Practice Safety Tools is intended to provide a framework for pharmacists and pharmacy personnel to recognize and assess their risks; make informed choices concerning the selection of personal protective equipment, respiratory protection, and engineering controls; and implement work practices in order to reduce environmental contamination to the pharmacy and reduce potential exposure and illness risk to staff.

LIMITATIONS

Best Practice Safety Tools

Best Practice Safety Tools for Pharmacy Personnel Handling Hazardous Drugs (*Best Practice Safety Tools*) is intended to reflect the best practices available based on national and international guidance documents, current practices, and the practical application of industrial hygiene and pharmacy principles. *Best Practice Safety Tools* reflects the current body of knowledge available at the time it was written and acknowledges that the body of knowledge will continue to grow and develop, necessitating a continual and careful review of new and existing guidelines, the peer reviewed literature, and technological advances. *Best Practice Safety Tools* is not intended to be in conflict with USP 797, USP 800, or future iterations of sterile compounding and hazardous drug rules nor is it intended as a compliance document for OSHA, the Washington Department of Labor & Industries, or other OSHA State Programs. Best Practice Safety Tools does not preclude the use of additional administrative controls, engineering controls, personal protective equipment (PPE), or respiratory protection.

Commercially available products and systems are mentioned in *Best Practice Safety Tools* to provide the reader with examples. *Best Practice Safety Tools* was not intended to provide a comprehensive review of all applicable products and systems and the omission of other similar products and systems does not constitute and endorsement or condemnation.

1a

HANDLING HAZARDOUS DRUG EXPOSURE RISK ALGORITHM

The risk of potential exposure to hazardous drugs is a function of the drug's form as well as the handling and manipulation of the drug. For example, a cytotoxic chemotherapy agent in a parenteral form presents a greater risk than the same agent contained in a coated tablet, hazardous drugs in a bulk powder present greater risk of exposure when compared to the same agents contained in capsules, and handling intact packaging presents less risk than open packages. As a result, administrative and engineering controls, and the personal protective equipment (PPE) selected to limit the risk of exposure are based on risk.

Using the Algorithm

The Handling of Hazardous Drugs Exposure Risk Algorithm (Algorithm) is provided as a tool to assist pharmacists and pharmacy managers with assigning hazardous drugs to exposure risk categories that are used to select engineering controls and PPE. The Algorithm is designed for use for NIOSH listed and non-listed hazardous drugs, investigational new drugs, and for drugs developed in the future that exhibit carcinogenicity, teratogenicity, reproductive toxicity, organ toxicity, genotoxicity, and hazardous drug mimics.

Exposure Risk Categories

The Algorithm assigns hazardous drugs and drug manipulations in the following six exposure risk categories:

- Cytotoxic chemotherapy high exposure risk
- High hazard high exposure risk
- High exposure risk
- Moderate exposure risk
- Low exposure risk
- Existing precautions

The Algorithm is dichotomous with yes and no responses. The green arrows indicate "yes" and the red arrows indicate "no." The black arrows are used to determine specific routes or drug formulation and direct the user to that subcategory. For example, there are two black arrows for "Cytotoxic chemotherapy?". One arrow leads to "Parenteral, splash risk or inhalant?" and the other arrow leads to "Oral Solid, Topical,

Oral Liquid?". The drug in question is assigned by the user to one of these subcategories and proceeds until a risk category is reached.

The user then refers to the engineering controls and PPE summary for the selected risk category in the Algorithm and refers to the specific references in the text of this document.

Example drugs processed through the algorithm:

Drug A NIOSH-listed Antineoplastic Chemotherapy Agent – Antineoplastic Chemotherapy High Exposure Risk

Drug B NIOSH-listed Category D or X Reproductive Agent – High Hazard High Exposure Risk

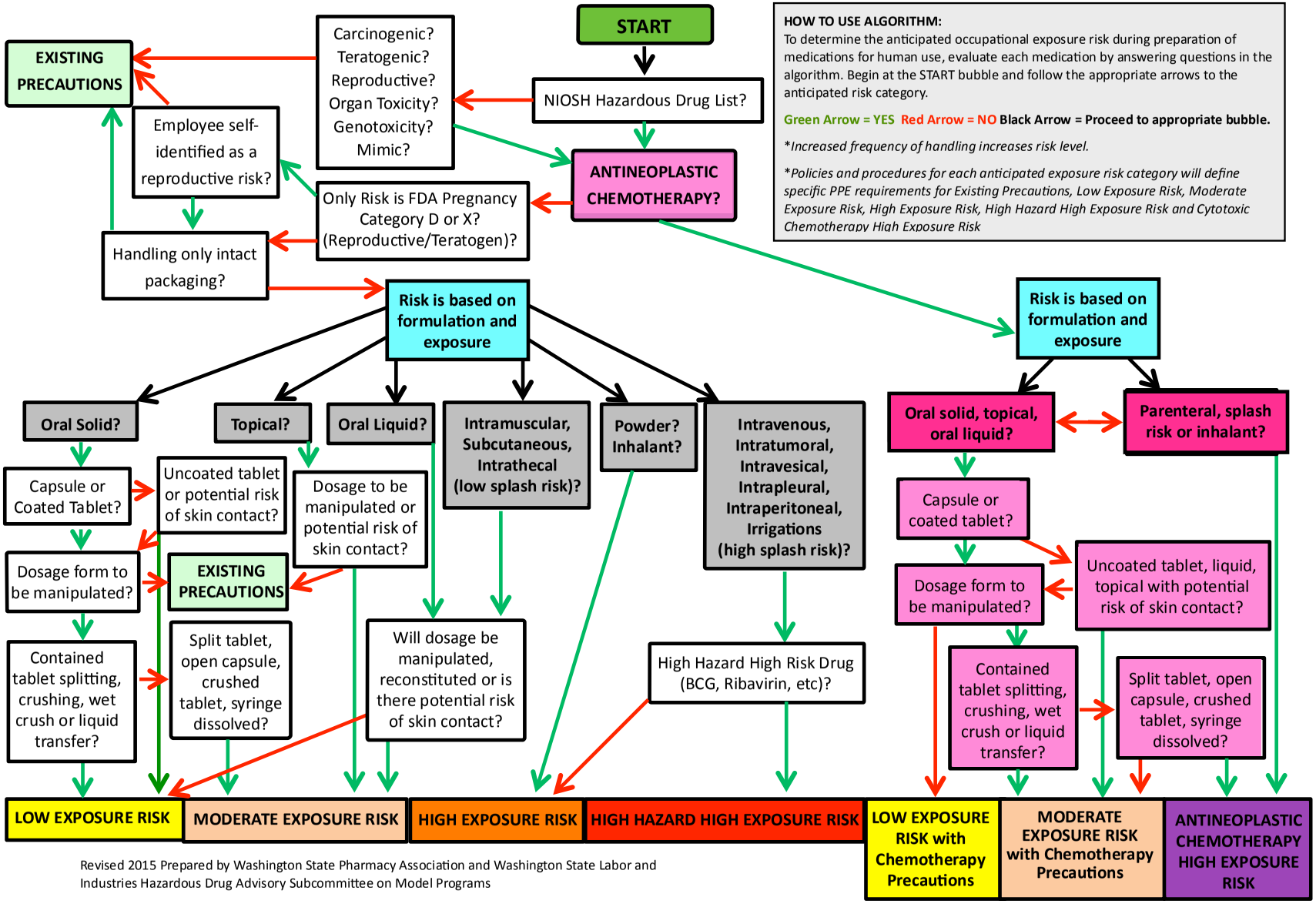
Drug C NIOSH-listed Moderate Risk

Drug D NIOSH-listed Antineoplastic Chemotherapy Agent – Low Exposure Risk with Chemotherapy Precautions

Drug E NIOSH-listed Existing Precautions

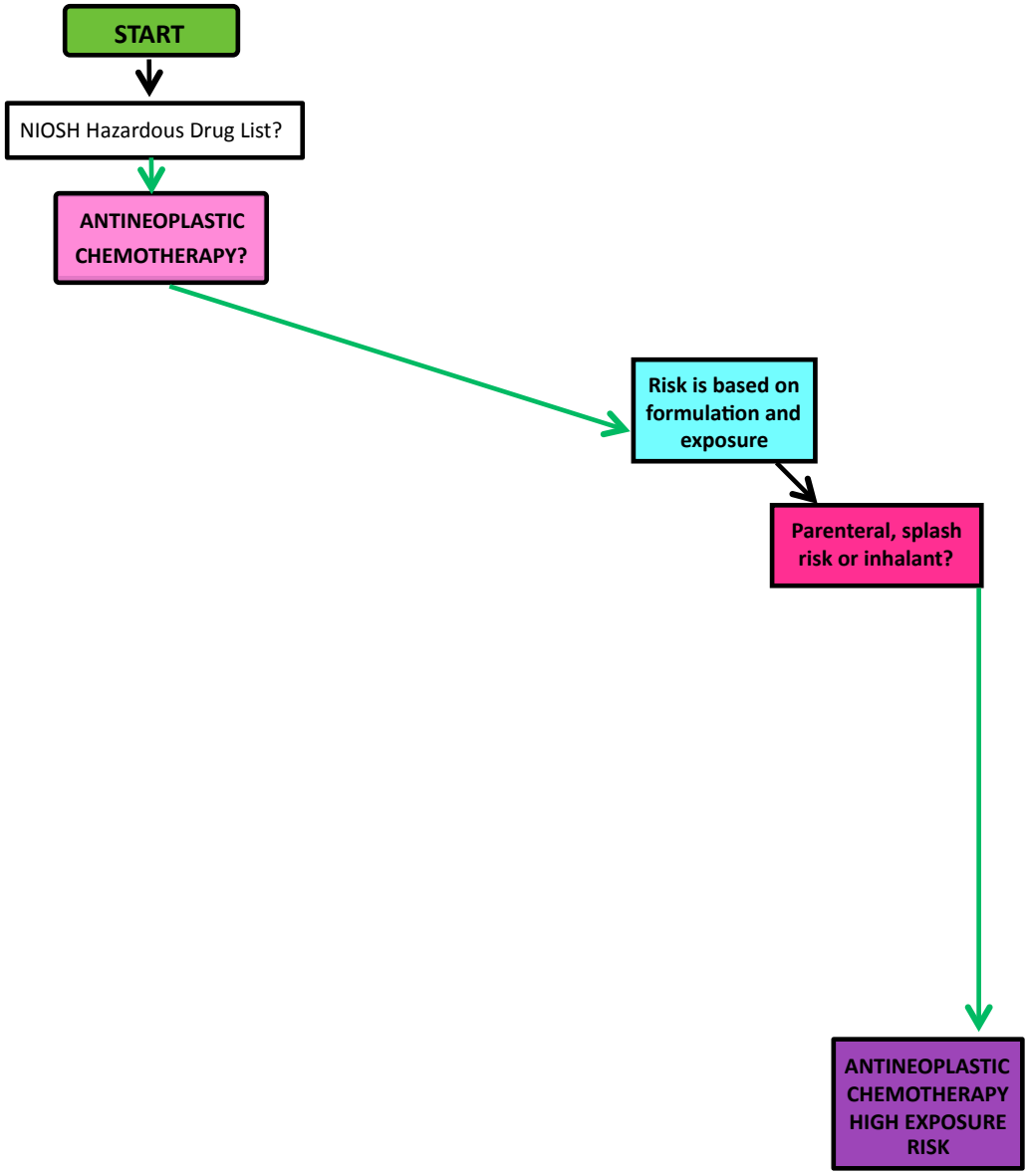
Handling of Hazardous Drugs Exposure Risk Algorithm

For Use in Assessing Risk During Preparation of Human Use Medications

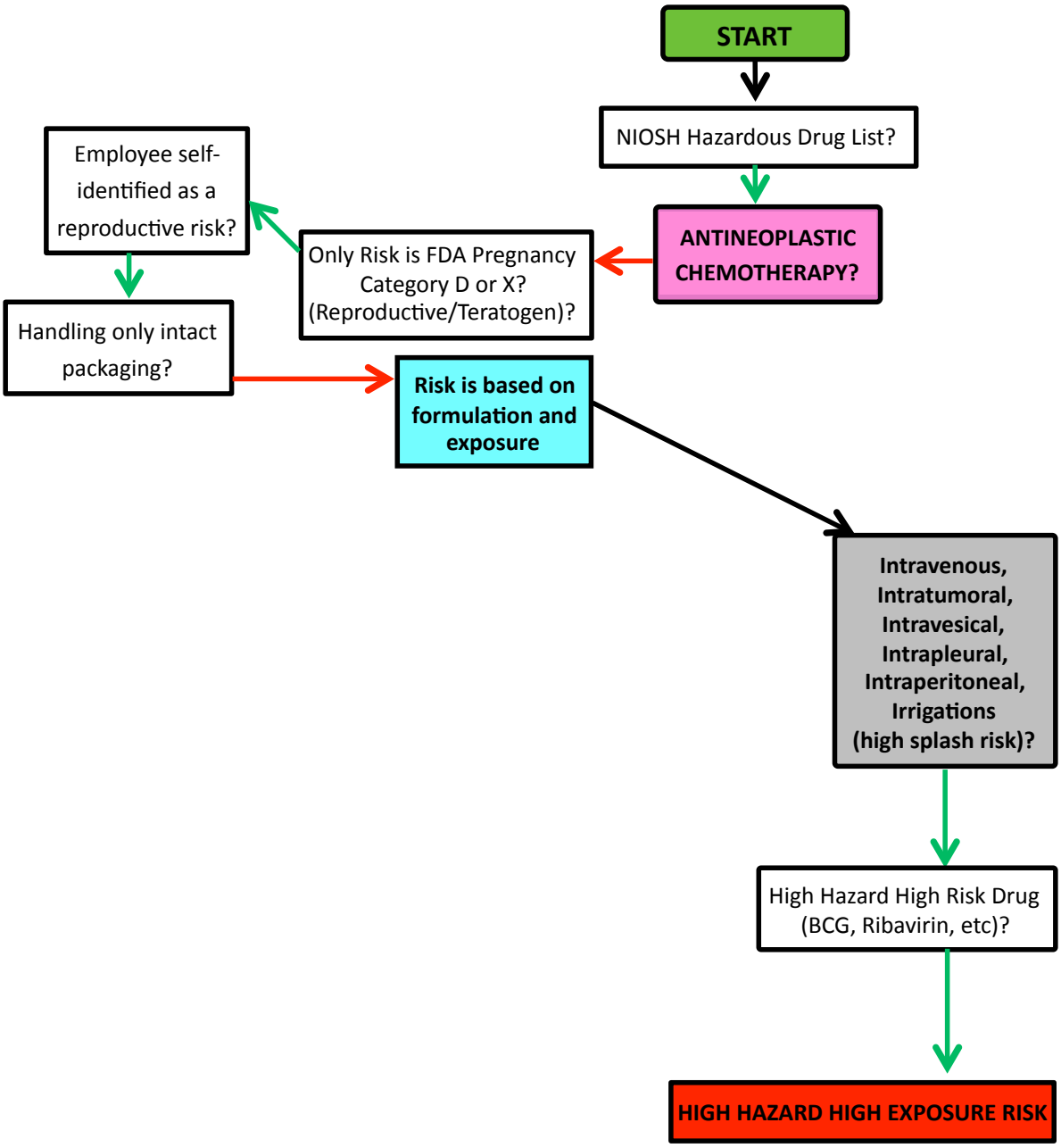


Revised 2015 Prepared by Washington State Pharmacy Association and Washington State Labor and Industries Hazardous Drug Advisory Subcommittee on Model Programs

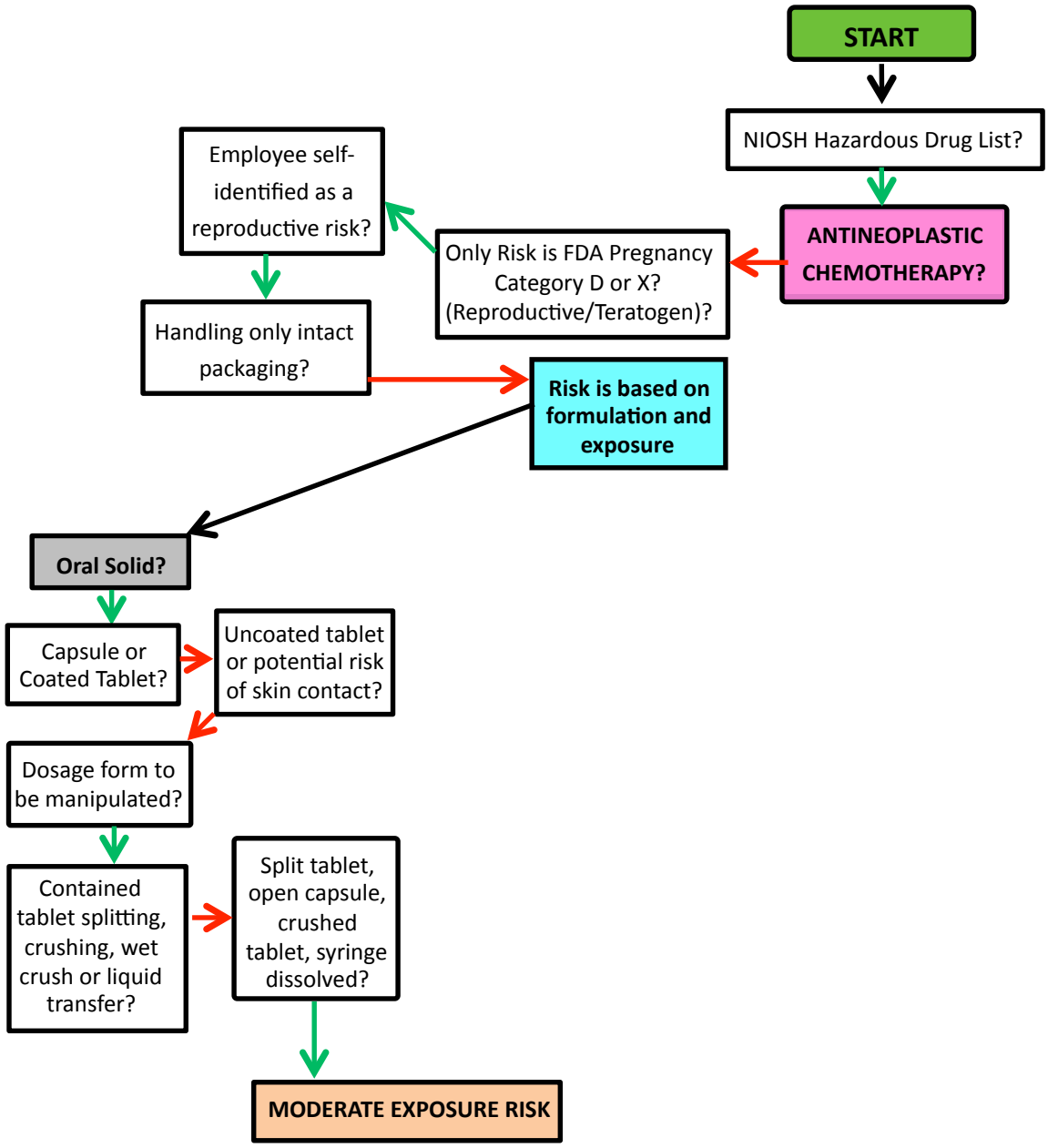
Drug A Intravenous Cisplatin



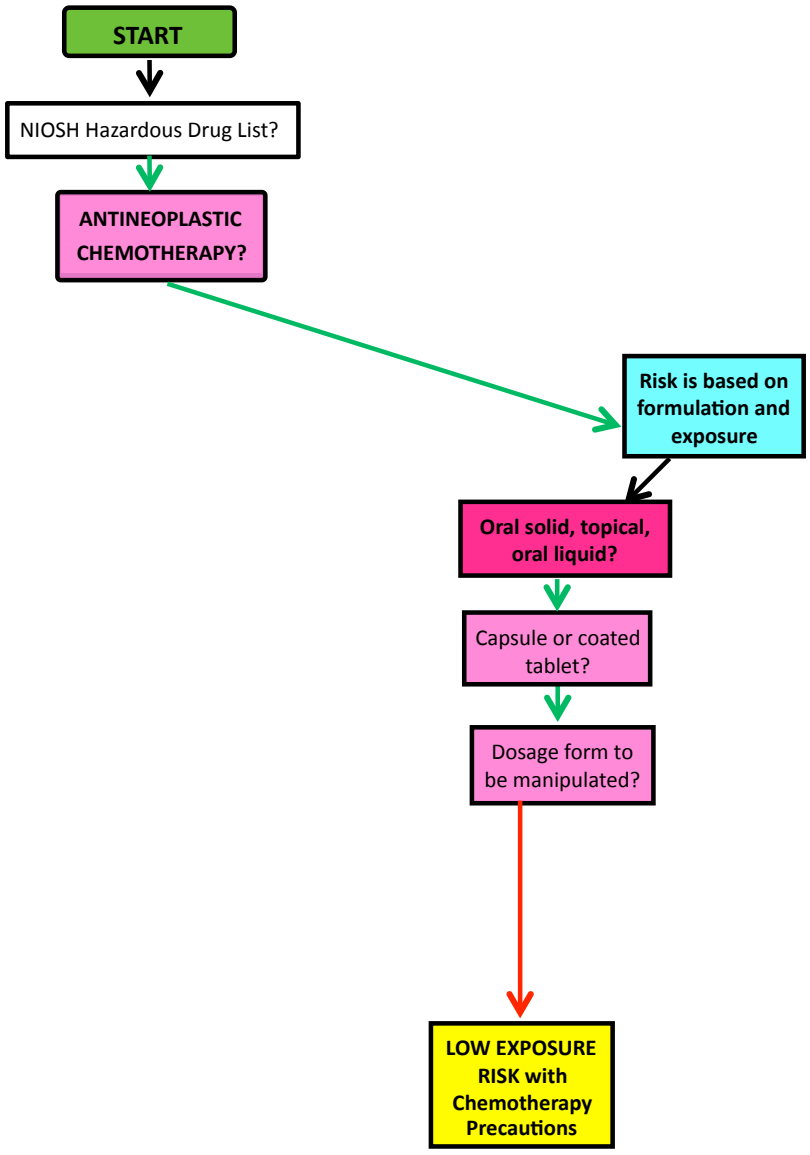
Drug B NIOSH-listed Category D or X Reproductive Agent Ribavirin



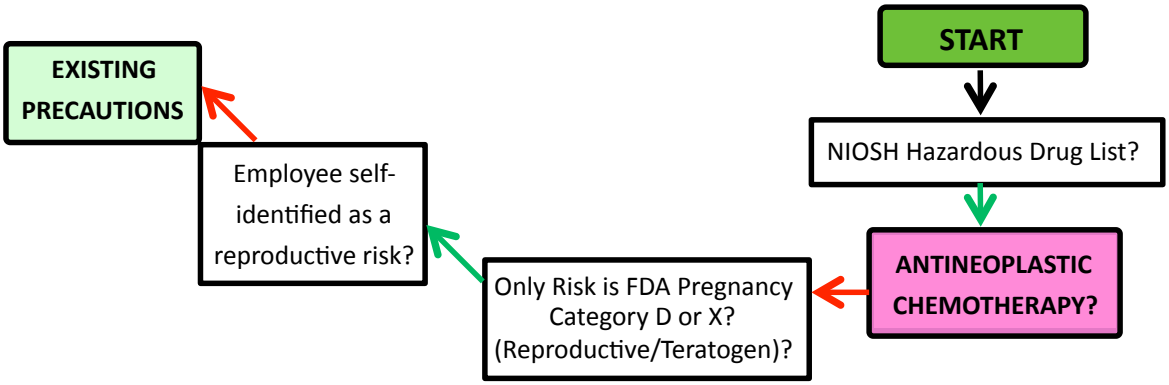
Drug C Clonazepam 1mg tablets to be split to make 0.5mg tablets



Drug D Letrozole 2.5mg Oral Tablets in 30 count bottle



Drug E Paroxetine prepared by employee without reproductive risk



1b

HANDLING HAZARDOUS DRUG EXPOSURE RISK ALGORITHM DEFINITIONS

Antineoplastic: inhibiting or preventing the growth and spread of neoplasms or malignant cells.

Antineoplastic Chemotherapy High Exposure Risk Drug: an antineoplastic chemotherapy medication that poses a high hazard risk to the safety of health care workers if exposure occurs requiring extensive person al protective equipment and engineering controls to minimize chance of exposure (e.g. cyclophosphamide).

Biological Safety Cabinet: a ventilated cabinet for compounding pharmaceutical ingredients, personnel, product, and environmental protection having an open front with inward airflow for personnel protection, downward high-efficiency air (HEPA)-filtered laminar airflow for product protection, and HEPA-filtered exhausted air for environmental protection. For a complete description of the different types of biological safety cabinets see the Centers for Disease Control and Prevention (CDC)/National Institutes of Health (NIH) document Primary Containment for Biohazards: Selection, Installation and Use of Biological Safety Cabinets.

Bulk Powders: an Active Pharmaceutical Ingredient (API) or excipient intended for pharmaceutical compounding and provided by a manufacturer as an unfinished drug formulation.

Carcinogenic: producing or tending to produce cancer.

Chemotherapy: for use within this algorithm, chemotherapy is a cytotoxic drug agent.

Chemotherapy Glove: a medical glove that has been approved by the Food and Drug Administration (FDA) and meets the permeability standards of the American Society for Testing Materials (ASTM) Standard D6978 - 05.

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 of the system. This includes drugs for preparation or administration.

Conditions for Exposure: employment activities that may result in healthcare worker exposure through inhalation, skin and mucosal contact, ingestion or injection.

Contained Crush: use of an engineering control while crushing a solid.

Cytotoxic: detrimental or destructive to cells.

Engineering Controls: devices designed to eliminate or reduce worker exposure to hazards. Examples include biological safety cabinets, laboratory fume hoods, containment isolators, safer sharps devices, safety interlocks, closed system transfer devices/administration sets and contained tablet splitters and crushers.

Existing Precautions: current exposure precautions or discretionary additional PPE or engineering controls.

Exposure Factors: factors that affect a workers potential exposure to a hazardous drug. Examples include: drug handling circumstances (preparation, administration, or disposal), formulation, packaging, amount of drug prepared, frequency and duration of drug handling, potential for absorption, PPE, work practices/safety programs and use of engineering controls such as ventilated cabinets.

FDA Pregnancy Category D: FDA medication designation stating positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks.

FDA Pregnancy Category X: FDA medication designation stating studies in animals or humans have demonstrated fetal abnormalities and/or there is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits.

Genotoxicity: capable of damaging DNA and leading to mutations.

Gloves: medical grade or other chemically protective glove appropriate for the task.

Hazard Assessment: as defined in Washington State rule (WAC-296-62-50020):

1) Each health care facility must conduct hazard assessments in order to determine the appropriate precautions to be taken. These assessments may be limited to the hazardous drugs for which there is reasonably anticipated occupational exposure.

2) Assessments must include the following elements as appropriate:
   (a) Personal protective equipment.
   (b) Engineering controls (e.g., ventilated cabinets, closed-system drug transfer devices, glove bags, and needleless systems).
   (c) Physical layout of work areas.
   (d) Types of hazardous drugs being handled.
   (e) Volume, frequency, packaging, and form of hazardous drugs handled (tablets, coated versus uncoated, powder versus liquid).
   (f) Equipment maintenance.
   (g) Decontamination and cleaning.
   (h) Waste handling.

(i) Potential hazardous drug exposures during work operations, such as drug preparation and administration.
(j) Spill response.

3) Conduct a hazard assessment as part of the hazardous drugs control program update and whenever changes that affect occupational exposure occur, such as introduction of a new hazardous drug or a change in handling practices.

Hazardous Drugs Control Program: as defined in Washinton State rule (WAC 296-62-50015), each health care facility covered under the scope of this chapter must develop and implement a written hazardous drugs control program. Elements of the hazardous drugs control program may be located in other documents such as the employer's accident prevention program or other policies and procedures as long as they are referenced in the program. The hazardous drugs control program must, at a minimum, include the following:

(a) A written inventory of hazardous drugs in the workplace.
(b) A current hazard assessment for hazardous drugs for which there is reasonably anticipated occupational exposure.
(c) Hazardous drugs policies and procedures including, but not limited to:
    (i) Engineering controls (equipment use and maintenance).
    (ii) Personal protective equipment.
    iii) Safe handling practices (receiving and storage, labeling, preparing, administering, and disposing of hazardous drugs).
    (iv) Cleaning, housekeeping, and waste handling.
    (v) Spill control.
    (vi) Personnel issues (such as exposure of pregnant workers).
    (vii) Training.

Hazardous Drugs: any drug identified as hazardous by the National Institute for Occupational Safety and Health (NIOSH) at the Centers for Disease Control (CDC) or any drug that meets at least one of the following six criteria:

- Carcinogenicity.
- Teratogenicity or developmental toxicity.
- Reproductive toxicity in humans.
- Organ toxicity at low doses in humans or animals.
- Genotoxicity.
- New drugs that mimic existing hazardous drugs in structure and toxicity.

High Exposure Risk Drug: A medication that poses a high risk to the safety of health care workers if high frequency or high volume exposure occurs requiring substantial personal protective equipment and

engineering controls to minimize chance of exposure. For example, increased exposure due to high frequency or high volume such as Estrogen as a bulk powder.

High Hazard High Exposure Risk Drug: a medication that poses a high hazard risk to the safety of healthcare workers in any exposure occurs requiring extensive personal protective equipment and engineering controls to minimize chance of exposure (e.g. Ribavirin).

Inhalant: a medication that is inhaled.

Intact Packaging: medication packaging that does not expose a healthcare worker directly to the medication.

Intramuscular: administered by entering a muscle.

Intraperitoneal: administered by entering the peritoneum.

Intrapleural: administered by entering the pleura or pleural cavity.

Intrathecal: introduced into or occurring in the space under the arachnoid membrane of the brain or spinal cord.

Intratumoral: administered into a tumor.

Intravenous: administered by entering a vein or vascular access device.

Intravesical: administered within the bladder.

Irrigation: to flush (a body part) with a stream of liquid.

Isolator: a device that is sealed or is supplied with air through a microbially retentive filtration system (HEPA minimum) and may be reproducibly decontaminated. When closed, an isolator uses only decontaminated interfaces (when necessary) or rapid transfer ports (RTPs) for materials transfer. When open, it allows for the ingress and/or egress of materials through defined openings that have been designed and validated to preclude the transfer of contaminants or unfiltered air to adjacent environments. An isolator can be used for aseptic processing, for containment of potent compounds, or for simultaneous asepsis and containment. Some isolator designs allow operations within the isolator to be conducted through attached rubber gloves without compromising asepsis and/or containment.

- **Aseptic Isolator:** a ventilated isolator designed to exclude external contamination from entering the critical zone inside the isolator.
- **Aseptic Containment Isolator:** a ventilated isolator designed to meet the requirements of both an aseptic isolator and a containment isolator.
- **Containment Isolator:** a ventilated isolator designed to prevent the toxic materials processed inside it from escaping to the surrounding environment.

Liquid Transfer: general term that includes the transfer of liquids in the absence of a secondary engineering control where there is a splash or spill potential i.e. pouring .

Low Exposure Risk Hazardous Drug: a medication that poses a lower risk to the safety of health care workers if exposure occurs. Inclusion criteria for this category are:

1. Solid dosage forms of antineoplastic, cytotoxic, or hormonal medications in an unaltered state (not crushed, opened, aerosolized, or manipulated other than for the purposes of administration directly from their current container, that is, as a capsule or tablet).

2. Parenteral dosage forms where there is limited evidence of toxicity, but the mechanism of action or drug class is conducive to potential toxicity or the molecular size of the product is large enough that the risk of transdermal or transmucosal absorption is unlikely if the drug aerosolizes or droplets are released during preparation and if proper post preparation hand-washing and work space cleaning occurs.

Manipulation/Manipulated: repackaging of a medication from the original dosage form supplied by the manufacturer for patient administration to another dosage form.

1. Oral tablets and capsules: includes crushing, dissolving, suspending, opening capsules, or splitting tablets; excludes repackaging small amounts of bulk-supplied tablets into unit-dose packaging.

2. Oral liquids: includes mixing from powders or diluting; excludes repackaging small amounts of bulk-supplied liquid into oral unit-dose cups, bottles, or syringes.

3. Injectable products: includes drawing up the ready-to administer dose into a syringe.

Moderate Exposure Risk Drug: a medication that poses a moderate risk to the safety of health care workers if exposure occurs (e.g. Cyclosporine as an oral liquid).

NIOSH: National Institute for Occupational Safety and Health with the Department of Health and Human Services under the Centers for Disease Control and Prevention (CDC). NIOSH is the U.S. federal agency responsible for conducting research and making recommendations for the prevention of work-related injury and illness. NIOSH is not a regulatory or enforcement agency.

NIOSH Alert: a document published by CDC NIOSH warning health care workers about the risks of working with hazardous drugs and recommends methods and equipment for protecting their health titled Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings published September 2004 and updates published 2010 and 2012.

NIOSH Hazardous Drug List: a sample list of potentially hazardous drugs included in the NIOSH Alert and subsequent updates. Sample List can be found at: http://www.cdc.gov/niosh/topics/hazdrug/

Non-Antineoplastic chemotherapy: targeted drug agent that is not antineoplastic.

Occupational Exposure: reasonably anticipated inhalation, skin, ingestion, or injection contact with hazardous drugs as a result of the performance of an employee's duties. Some drugs defined as hazardous may not pose a significant risk of occupational exposure because of their dosage formulation (for example, coated tablets or capsules that are administered to patients without modifying the formulation). However, they may pose a risk if altered (for example, if tablets are crushed or dissolved, or if capsules are pierced or opened).

Organ Toxicity: evidence of serious organ or other toxicity at low doses in animal models or treated patients.

Parenteral: administration by a route other than the mouth, nose, eye, rectum, urethra or vagina including but not limited to intravenous, intramuscular, or subcutaneous injection.

PPE: personal protective equipment utilized when there is reasonably anticipated exposure to hazardous drugs through occupational exposure in accordance with each health care facility's PPE assessment including but not limited to gloves, protective clothing, face protection, and respiratory protection etc.

Reconstituted: restored or constituted anew by adding liquid.

Reproductive Category Employees: women and men who are trying to conceive, women who are pregnant, and women who are breast-feeding.

Reproductive-Risk Hazardous Drug: a medication that has a specific warning for women and/or men who are trying to conceive, women who are pregnant, or women who are breast-feeding (reproductive category employee). The reproductive-risk hazardous drug category includes medications that have the potential to impair fertility; medications that are teratogenic, genotoxic, or cause developmental toxicity; or medications with existing recommendations for women who are pregnant or lactating. Examples are agents classified as Pregnancy Category X and D by the Food and Drug Administration (FDA), where the risk incurred is relative to the level of exposure to the agent and its intrinsic toxicity. Please note some Category C agents may have pertinent reproductive risks or hazards.

Subcutaneous: administered under the skin.

Syringe Dissolved: dissolving a solid within a syringe as a secondary engineering control.

Teratogenic: of, relating to, or causing developmental malformations.

Ventilated Cabinet: a type of engineering control designed for purposes of worker protection. These devices are designed to minimize worker exposures by controlling emissions of airborne contaminants through the following:

- The full or partial enclosure of a potential contaminant source.
- The use of airflow capture velocities to capture and remove airborne contaminants near their point of generation.

- The use of air pressure relationships that define the direction of airflow into the cabinet.

Examples of ventilated cabinets include biological safety cabinets and containment isolators.

Wet Crush: crushing a solid medication while introducing a liquid.

2

HAZARDOUS DRUG COMPOUNDING ENVIRONMENT

Hazardous drugs are compounded as sterile and non-sterile preparations. Sterile preparations are regulated under USP 797, and as such, are required to be prepared in an ISO Class 5 environment (i.e. biological safety cabinet or aseptic isolator), using engineering controls, and aseptic technique.

Compounding room physical environment

Compounding areas, room finishes and furnishings need to be readily cleanable to remove contamination and promote cleaning efficacy. Carpet, fleece, and upholstered finishes and furnishing (e.g. fabric covered cubicle dividers) are not appropriate. Finishes and furnishing constructed of smooth, stainless steel; rolled sheet vinyl flooring; and melamine, fiberglass reinforced paneling, and other similar hard, non-porous coverings are suitable.

Sterile preparation room ante chamber entrance with “ball in tube” directional air flow indicator confirms positive pressure.

Compounded sterile hazardous drug preparations are required to be prepared in a biological safety cabinet (BSC) that provides an ISO Class 5 environment. The BSC is required to be located inside an ISO Class 7 room environment, sometimes referred to elsewhere as a buffer area. The ISO Class 7 room environment ventilation system must maintain the room under negative pressure (<0.01” w.c.) and provide at least 12 air changes per hour.

Sterile compounding of hazardous drugs is also allowed by USP 797 using compounding aseptic isolators (CAI) and compounding aseptic containment isolators (CACI). CAIs protect the preparation by maintaining positive pressure inside the isolator. A leak in the CAI has the potential for a hazardous drug or vapor to escape and infiltrate the surrounding area. CACIs are under negative pressure, like BSCs, but are cumbersome to use, more difficult to clean, and reduce productivity and efficiency. Best Practice Safety Tools prefers the use of BSCs for compounding hazardous drugs due to their ease of use, cleaning, and decontamination, and familiarity with the technology by technicians and pharmacists by virtue of training and experience. For these reasons, Best Practice Safety Tools will not provide further detail on the use of CAIs and CACIs.

Biological safety cabinets

A biological safety cabinet (BSC) is the preferred primary engineering control to minimize worker exposure for sterile compounding, and sterile and non-sterile manipulation of high exposure risk, high hazard high exposure risk, and antineoplastic chemotherapy high exposure risk drugs. The purpose of the BSC is threefold: to protect the preparation from microbiological and other contamination, to protect the worker from exposure, and to protect the surrounding environment. These purposes can be in conflict with one another.

BSC fundamentals

BSCs intended for use with hazardous drugs provide a clean air field that "washes" over the drug preparation (prep) inside the cabinet and maintains negative pressure within the cabinet in order to prevent the escape of drug or vapor outside the cabinet. The cabinet provides vertical, laminar flow HEPA-filtered air that washes over the prep from the top of the cabinet. The BSC's high efficiency particulate air (HEPA) filter is capable of removing 99.97% of 0.3 micron-sized particles from the air stream. The prep area inside the cabinet is under negative pressure (in relation to the room environment where the BSC is located) and "make-up" air from the room area (ISO Class 7 buffer area) enters the cabinet at the open sash (work position) and mixes with the HEPA-filtered air stream. The mixed air passes around and through the grill vents located around the perimeter of the prep surface and is either exhausted entirely out of the BSC or partially exhausted and recirculated, depending on the cabinet Class and Type (see below).

A well-organized biological safety cabinet preparation space with pad, waste bags, and sharps container.

Class II Biological safety cabinets

A Class II BSC is defined by NSF/ANSI Standard 49 as "a ventilated cabinet for personnel, product, and environmental protection having an open front with inward air flow for personnel protection, downward HEPA-filtered airflow for product protection, and HEPA-filtered exhausted air for environmental protection." Best practice dictates that BSCs exhaust outdoors and for that reason Class II BSCs that vent outdoors are considered appropriate for compounding and manipulating hazardous drugs.

Class II Type A2

Class II Type A2 (A2) cabinets have HEPA-filtered downward flow air that mixes with make-up air from outside the cabinet via the sash/work position. At the sash/work position, inflowing air enters the cabinet at a rate of 100 feet per minute (FPM). All potentially contaminated cabinet plenums and ducts in an A2 cabinet are required to be under negative pressure. If the cabinet were to leak, the surrounding air would leak in toward the cabinet and not out into the room. A2 cabinets re-circulate and HEPA-filter 70% of the cabinet air, and exhaust the remaining 30%.

A2 cabinets are exhausted into a separate, designated exhaust system (i.e. ducting and exhaust fan) inside

the room. The A2 cabinet exhausts independently into the exhaust system via an open "thimble" or "canopy" connection. This means that the HEPA-filtered exhaust air is vented under positive pressure into a designated exhaust duct that is under negative pressure from its' own exhaust fan. The A2 cabinet exhaust and the designated exhaust ducting must be carefully balanced such that the cabinet exhaust doesn't "over power" the designated exhaust system and vent into the room. The purpose of the open "canopy" connection is to allow for the A2 cabinet to be shut down when not in use for energy savings and continuously operate the designated exhaust ducting without altering the room air balancing and pressurization.

Class II Type B1

Class II Type B1 (B1) cabinets differ from A2 cabinets in that B1 cabinets HEPA-filter the mixed air (where it is ducted beneath the prep surface) in addition to HEPA-filtering the down flow and exhaust air. B1 cabinets re-circulate 30% and exhaust 70% of the cabinet air and are hard-ducted/connected to the dedicated exhaust duct system. At the sash/work position, inflowing air enters the cabinet at a rate of 100 feet per minute (FPM). B1 cabinets must run continuously.

Class II Type B2

Class II Type B2 (B2) cabinets differ significantly from A2 and B1 cabinets in that they HEPA-filter air directly from the room, exhaust 100% of the cabinet air, and are hard ducted/connected to the dedicated exhaust system ducting. At the sash/work position, inflowing air enters the cabinet at a rate of 100 FPM. B2 cabinets must run continuously.

Class III

Class III cabinets are designed for the most extreme levels of biological containment needed for pathogenic biological warfare agents and other pathogens. Class III cabinets are completely enclosed, ventilated, and leak tight. Down flowing air is HEPA-filtered and exhaust air is double HEPA-filtered. A minimum negative pressure differential of 0.5" water column (w.c.) is maintained at all times. Class III cabinets can be used for sterile and non-sterile preparations, however, they are not suitable or appropriate for this purpose.

BSC evaluation and selection

A2, B1, and B2 cabinets all maintain an internal HEPA-filtered environment that protects the drug preparation, maintain a negative pressure environment that prevents exposure to the pharmacist or technician at the work position, and HEPA-filter the exhaust air. All three types of cabinets have been used for sterile compounding of hazardous drugs, however, A2 cabinets are the predominant choice for pharmacies currently.

NIOSH Alert

The NIOSH Alert (2004) directs pharmacies away from compounding volatile hazardous drugs (e.g. cyclophosphamide, fluorouracil, cisplatin, and carmustine) in A2 and B1 cabinets (except in the case of compounding minute quantities) in favor of B2 cabinets. The argument appears to be that air exhausted into the room (via the "canopy" connection) in the case of the A2, and re-circulating air that may contain concentrations of volatilized drug vapor in A2 and B1 cabinets have the potential to cause exposure at the work position.

Class II Type A2 exhaust evaluation

It is important that the positioning of the A2 exhaust duct as well as the "canopy" connection and the air flow balancing between the A2 exhaust and dedicated exhaust duct system are properly aligned so that the

exhaust air from the cabinet does not escape and enter the room and result in potential exposure. Improper alignment and balancing is possible, but unlikely, due to the cabinet verification testing at installation and performed twice per year thereafter as a USP 797 requirement. It is also important to note that BSCs are located in a negative pressure room and that "escaped" cabinet exhaust air would be directed to the exhaust grills (typically located at the ceiling) and away from the breathing zone.

An unlikely potential exposure scenario exists in a case where the dedicated exhaust duct system exhaust fan fails and the A2 fan continues to run. Assuming that a volatile hazardous drug had been spilled in the hood at the same time, it becomes more likely that there could be a potential exposure to volatilized hazardous drug vapor as the A2 cabinet vents into the room. The room is, however, under negative pressure and the vapor would be vented toward the exhaust grills as described above, and the concentration of hazardous drug vapor in the room at large would continue to be diluted.

This unlikely scenario also exists for the B1 and B2 cabinets. The potential exposure would be greater with the B1 and B2 cabinets as compared to the A2 because the cabinet exhaust would be blown back directly at the worker via the open sash. The A2 appears to be the "safer" cabinet in this scenario. For any of the cabinets, dedicated exhaust system alarms and cabinet alarms are recommended.

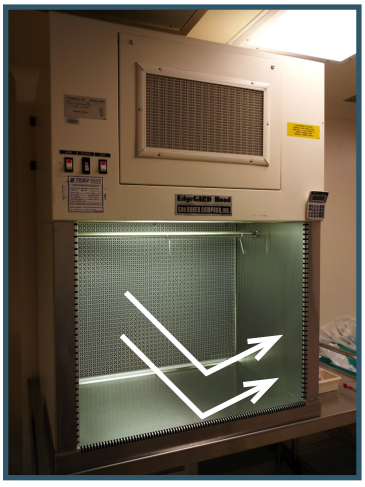
A2 & B1 re-circulation evaluation

The re-circulation of air in the A2 and B1 cabinets does not appear to have any impact on exposure at the work position because the cabinets are maintained under negative pressure and cabinet air cannot leak out of the cabinet. The work position is maintained outside the cabinet and is physically removed from the preparation area. Exposure is only possible when the pharmacy technician or pharmacist opens the sash and physically enters the hood in order to clean up a spill or for some other purpose. Exposure in this scenario would be the same for A2, B1 and B2 cabinets.

Working inside the hood requires PPE and respiratory protection in order to prevent potential exposure (see Spills).

BSC recommendations

There is no perfect BSC for the sterile compounding of hazardous drugs. A2, B1, and B2 cabinets all maintain an internal HEPA-filtered environment that protects the drug preparation, maintain a negative pressure environment that prevents exposure to the pharmacist or pharmacy technician at the work position, and HEPA-filter the exhaust air. A2, B1, and B2 cabinets are acceptable for sterile compounding of hazardous drugs in pharmacies. CAIs, CACIs, and Class III cabinets are also acceptable, but are generally impractical. Sterile compounding of hazardous drugs outside a Class II A2, B1, B2, Class III cabinets, or CAI and CACI is unacceptable.



Laminar flow hoods are not appropriate for preparing and manipulating hazardous drugs because the air flow is toward the preparer.

3

PERSONAL PROTECTIVE EQUIPMENT

Hazardous drug contact, handling, manipulation and cleanup requires the use of personal protective equipment (PPE) when administrative and engineering controls are not sufficient to prevent exposure. The use of PPE is familiar in pharmacy practice especially with regard to sterile compounding and the requirements of USP 797. PPE is intended to prevent exposure to hazardous drugs by preventing contact with skin, eyes, and clothing.

Respiratory protection differs from PPE in that its primary purpose is to prevent the inhalation of hazardous drug particles and vapors. It is important to distinguish respiratory protection from PPE in that they serve different intended purposes and address different potential routes of exposure. PPE is regulated by the Washington State Department of Labor & Industries in WAC 296-800 and by OSHA in 29 CFR 1910.132.

Algorithm

The Handling of Hazardous Drugs Exposure Risk Algorithm (algorithm) assigns risk to the various types of hazardous drugs and the manipulation of those drugs, both in preparation and administration. In terms of drug categories, cytotoxic chemotherapy agents are considered separate from non-chemotherapy drugs. The algorithm also categorizes non-carcinogenic, teratogenic, reproductive, organ toxic, genotoxic, and mimic drugs. In addition, the algorithm categorizes drug agents by form. For example, an antineoplastic chemotherapy agent in a parenteral form presents a greater risk than the same agent in a coated tablet.

The algorithm assigns hazardous drugs and drug manipulations in the following six risk categories:

- Antineoplastic chemotherapy high exposure risk drug
  Example: Cyclophosphamide

- High hazard high exposure risk
  Example: Ribavirin

- High exposure risk
  Example: Estrogen as a bulk powder

- Moderate exposure risk
  Example: Cyclosporine as an oral liquid

- Low exposure risk
  Example: Risperidone as a contained, crushed tablet

- Existing precautions/additional PPE is optional
  Example: oral contraceptives as a non-manipulated uncoated tablet

The use of engineering controls and biological safety cabinets is prescribed only for the top three risk categories: Antineoplastic Chemotherapy High Exposure Risk Drug, High Hazard Exposure Risk, and High Exposure Risk. Engineering controls and biological safety cabinets can be used to prepare and manipulate the three lesser risk categories (Moderate Exposure Risk, Low Exposure Risk, and Existing Precautions) but it is not necessary according to the algorithm. Please refer to "Chapter 2, Hazardous Drug Compounding Environment" for more information on engineering controls and biological safety cabinets.

The algorithm also assigns PPE for each of the risk categories. In general, the PPE requirements are more extensive for the higher risk categories. However, pharmacies are not precluded from using higher levels of PPE or engineering controls.

PPE Selection

PPE selection is based on an assessment of the hazard. The hazardous drugs processed in pharmacy present risk to pharmacy personnel as a result of contact, as do the disinfection and sanitizing agents used to clean surfaces and equipment. For example, repeated or frequent contact with sanitizing agents (e.g. alcohol, bleach) can limit the useful life of gloves and require that they be changed more frequently than gowns. Matching the PPE to the hazard and work processes is important in order to prevent accidental exposure.

Gloves
The hands come into direct contact with drug containers, product, and devices during preparation, handling, manipulation, and clean up. Gloves serve to protect the wearer from contact with hazardous drugs and contaminated surfaces, equipment, and devices. They also serve to protect the preparation from biological contamination.

There are a significant number of choices with regard to glove selection and purchasing. Gloves are available in latex, neoprene, nitrile, polyester, polyethylene, polyurethane, and vinyl. The most common gloves used in pharmacies are latex, neoprene, nitrile, and vinyl. Gloves are also available in powdered, non-powdered, sterile, and non-sterile forms. There are pros and cons associated with all PPE and gloves are no exception. In particular, latex gloves contain allergens and my cause dermatitis or other allergic-type reactions (e.g. asthma, anaphylaxis) to the wearer and others. Alternatives to latex gloves are required for all pharmacy workers that have allergic sensitivities to latex.

Non-powdered gloves are recommended for work in pharmacy because the powder in powdered gloves increases the level of particulate overall and may contaminate the preparation. Powder can also spread and contaminate supplies, product and product containers, and hands. Powdered latex gloves are particularly

problematic because the powder can contain allergen and both the powder and latex are persistent in the environment.

Work with chemotherapy agents requires the use of chemotherapy gloves that meet the Food and Drug Administration (FDA) definition and meet the testing standards of the American Society for Testing and Materials (ASTM) Standard ASTM D6978-05 for permeation. It is important to note that gloves are typically tested against select chemotherapy agents that are most commonly prescribed currently (e.g. cisplatin, cyclophosphamide, doxorubicin, etoposide, fluorouracil, and paclitaxel). The glove manufacturers can be contacted directly with queries about other specific agents.

It is recommended that gloves are changed frequently under actual working conditions and be worn no longer than 30 minutes. Gloves that are damaged should be immediately discarded and replaced.

It is important to note that diligent hand hygiene practices are an integral component with regard to wearing gloves. Hand washing with soap and water immediately after removing the gloves is critical to removing potential contamination on the hands from inadvertent contact with contaminated surfaces, materials, or PPE. Further, alcohol-based hand gels, sanitizer, or wipes are not soaps, and as such, are not designed to, and do not necessarily, remove foreign objects from the skin. Alcohol gels, wipes, and sanitizers are not a recommended substitute for hand washing with soap and water.

The use of double gloves is recommended in the algorithm for Antineoplastic Chemotherapy High Exposure, High Hazard High Exposure, and High Exposure Risk drugs. It is recommended, for work performed in a biological safety cabinet (e.g. IV hood) to remove the outer pair of gloves inside the hood and dispose of the used gloves be placed in a waste bag or container located in the hood to prevent contamination of the surrounding work area.

Lastly, used gloves should not be re-used. As a result of use, used gloves may be contaminated with hazardous drugs, or have experienced damage that could lead to exposure. Gloves are for single use only.

Gowns

Gowns are worn during sterile compounding and preparation to protect the preparation from contamination by the preparer and to protect the preparer from the preparation. Gowns are also worn when cleaning up spills of hazardous drugs. Gowns are typically worn over scrubs and lab coats. As with gloves, the FDA considers gowns that are marketed as having been tested against hazardous drugs to be medical devices. It is important to note that some brand names include the word Chemo or Chemotherapy and that this does not necessarily mean that the gowns have been tested or protect against exposure. It is critical to confirm that the gowns selected are appropriate for the drugs being handled.

Disposable gowns are required to provide protection against hazardous drugs, to be non-shedding/lint free, and have a solid front, long sleeves, and tight fitting elastic or knit cuffs. Gowns constructed of coated polypropylene or coated vinyl perform best in terms of providing adequate splash protection and preventing penetration by hazardous drugs. The useful life of a chemotherapy gown ranges between 2 and 4 hours. Gowns that are damaged or have spilled material on them should be immediately discarded and replaced.

As with gloves, gowns are not intended for re-use. As a result of use, used gowns may be contaminated

with hazardous drugs from contact with the drug or contaminated gloves if the gown was not removed properly (i.e. from the inside out), or been otherwise damaged that could, in turn, lead to exposure by the wearer. Gowns are for single-use or single-shift only.

Eye protection

Eye protection is not necessary when preparation occurs in a BSC with the sash lowered. However, eye protection is required when cleaning a BSC or hazardous drug spills, or when there is a splash hazard. The use of contact lenses is not recommended because they do not provide protection and can absorb hazardous drugs which can lead to additional exposure.

Splash shields that cover the entire face, worn in conjunction with safety glasses or goggles, are preferred over safety glasses alone because they provide additional face protection. Disposable splash shields integral to surgical masks are available, but integral splash shields for N95 respirators are not yet available. Disposable splash shields are preferred because it removes the cleaning step required of rigid, re-usable face shields and eliminates another potential exposure to hazardous drug residues.

Disposable continuous protective eyewear (i.e. one continuous lens protects both eyes) does not provide face protection but is preferred over rigid, re-usable eyewear for the reasons described above, and there are no hinges or hard to reach areas to clean. It is important that disposable or not, the eyewear extend past the side of the eye to protect against eye contact from all angles.

Regular, normal prescription eye wear cannot be used as a substitute for appropriate eye and splash protection.

Shoe and shoe covers

Dedicated shoes and disposable shoe covers are typically worn to prevent tracking in dust, particulate, and biological contaminants to the compounding/prep area, and prevent tracking out potential drug contamination from the compounding/prep area. Dedicated shoes and shoe covers are not worn outside the compounding/prep/buffer area and shoe covers are discarded at the end of the work shift or when damaged.

Hair and facial hair covers

Hair and facial hair covers are worn to protect the preparation from the preparer and are a USP 797 requirement for sterile preparations. They are not considered PPE per se, but it is important to reinforce their importance in terms of aseptic compounding and good pharmacy practice.

Surgical masks

Surgical masks are worn as a USP 797 requirement to protect the preparation from biological contaminants generated by the preparer during talking, sneezing, and coughing. The concern is that these contaminants can be generated at velocities that can overcome the velocity of the HEPA-filtered protected air flow in a BSC or a horizontal laminar air flow workbench. Surgical masks are not respirators and do not provide protection for the wearer from hazardous drugs or vapor (note that N95 surgical masks do provide respiratory protection and are discussed in the Respiratory Protection chapter).

Recommended PPE by Hazard Category

The following PPE and engineering controls are recommended for the following risk categories:

Antineoplastic chemotherapy high exposure risk drugs – parenteral, splash risk, inhalant, or manipulated oral

- Biological safety cabinet
- Double pair chemotherapy gloves
- Chemotherapy gown
- Dedicated shoes and shoe covers
- Hair cover (in BSC or sterile areas only)
- Eye and face protection for splash hazards
- Surgical mask

High hazard high exposure risk – BCG, ribavirin, etc.

- Biological safety cabinet
- Double pair medical gloves
- Gown
- Dedicated shoes and shoe covers
- Hair cover (in BSC or sterile areas only)
- Eye and face protection for splash hazards
- Surgical mask

High exposure risk – Intravenous and other high splash risk liquids, bulk powders, and inhalants

- Appropriate engineering controls or biological safety cabinet
- Double pair medical gloves
- Gown
- Dedicated shoes and shoe covers

- Hair cover (in BSC or sterile areas only)
- Eye and face protection for splash hazards
- Surgical mask (aseptic technique)

Moderate exposure risk – oral liquids and IM, SQ, intrathecal (low splash risk)

- Single pair medical gloves
- Gown
- Dedicated shoes and shoe covers
- Hair cover (sterile areas only)

Moderate risk antineoplastic chemotherapy – Uncoated tablet or contained manipulation, and liquid transfer

- Single pair chemotherapy gloves
- Chemotherapy gown
- Dedicated shoes and shoe covers
- Hair cover (sterile areas only)

Low exposure risk – topical and oral solids that are manipulated

- Single pair medical gloves
- Dedicated shoes and shoe covers
- Hair cover (in BSC or sterile areas only)

Low risk antineoplastic chemotherapy – capsule and coated tablet

- Single pair chemotherapy gloves
- Dedicated shoes and shoe covers
- Hair cover (in BSC or sterile areas only)

Existing precautions

- Current exposure precautions and PPE use is acceptable
- Additional PPE use is optional and at the discretion of the pharmacy personnel
- Additional PPE use is not precluded

Gowning Sequence

It is important that a proper gowning sequence take place in order to protect the preparation and prevent contamination by the preparer. It should be noted that there are conflicting opinions with regard to gowning sequences among various guidance documents and publications. It is important for the pharmacist and pharmacy to consider the gowning practices recommended by their respective accrediting agencies, professional practice standards, safety and health regulatory agencies, and guidelines when making their policy and procedure decisions regarding the gowning sequence they select based on their specific need.

Donning PPE - Double gloving and removal sequence
The following gowning sequence is specific to gowning up when using double gloves.

- Enter the designated gowning area (i.e. outer/clean area of the ante room)
- Remove street clothes and don scrubs
- Wash and dry hands with soap and water only (alcohol hand gels and wipes are not acceptable)
- Don dedicated shoes and shoe covers one at a time and enter dirty/change area of ante room one foot at a time
- Don hair and facial covers
- Apply alcohol-based hand gel to hands and allow to dry
- Don inner pair of gloves
- Don gown and keep inner pair of gloves underneath the gown cuffs
- Don eye/face protection (if necessary)
- Don outer gloves and pull up over top of cuffs (Note: outer gloves may be put on in sterile work area)
- Enter sterile work area

The following gown removal sequence is specific to double gloving.

- Remove outer pair of gloves in sterile prep room and discard
- Enter dirty/change area of ante room
- Remove eye/face protection and discard (if necessary)
- Remove hair and facial hair covers and mask and discard
- Remove gown and discard
- Remove inner gloves and discard
- Remove shoe covers and designated shoes one after the other and enter outer/clean area of ante room one foot at a time
- Wash hands in clean area with soap and water only (Alcohol hand gels and wipes are not acceptable)

Ante room showing well-marked dirty/clean floor delineation, seat for changing into clean and out of dirty areas, sink and hand sanitizing station, and gown and glove storage area.

Training

Staff is required to receive training on the selection, proper use, and care and maintenance of the PPE provided. Documentation of training is required under WAC 296-800-16035 and documentation must include:

- Written documentation that each employee using PPE has received and understood their training.
- The employee's name, the training date(s), and the name of the subject/topic taught.

At a minimum, annual re-training is recommended. Traiing should be conducted immediately when it is recognized that staff do not understand appropriate PPE procedures and use, when there has been a change in PPE and/or use, and when the previous training has become obsolete. It is recommended that training records be kept and maintained for documentation purposes.

4

RESPIRATORY PROTECTION

Respiratory protection is used to protect the wearer from exposure to airborne contaminants. Contaminants exist in different physical forms: solid, liquid, vapor, and gas. Hazardous drugs are manufactured as solids and liquids. Some hazardous drugs volatilize (evaporate) at room temperature and produce vapor. These drugs include carmustine, cisplatin, cyclophosphamide, etoposide, and fluorouracil, for example. Hazardous drug gases are not typically produced in most pharmacies; however, some specialty pharmacies may handle anesthetic gases such as nitrous oxide, sevoflurane, and isoflurane.

Airborne exposure to hazardous drugs during handling and manipulation is controlled by the use of engineering controls such as biological safety cabinets, compounding aseptic isolators, and closed system transfer devices; substitution of a less challenging drug form instead of a more challenging drug form such as single-dose tablets for bulk powder, coated tablets for uncoated tablets, and manufacturer prepared single-dose vials for multi-dose vials; and work practice techniques such as wet crushing of tablets versus dry crushing. Despite the use of these controls, there are foreseeable instances where pharmacy and other (e.g. spill response, environmental services) staff can be potentially exposed to aerosolized hazardous drugs and may include cleaning the inside and outside of a biological safety cabinet or cleaning up spills inside and outside of a biological safety cabinet. The use of respiratory protection in these instances can further reduce the potential exposure to hazardous drugs. It is important to note that respirators are worn and designed to protect the wearer, and, with few exceptions, are not intended to protect the preparation.

Regulations

The use of respiratory protection is regulated in Washington State by the Department of Labor & Industries (WAC 296-842) and by OSHA at the federal level (29 CFR 1910.134). These regulations require the following:

- A written Respiratory Protection Program and Program Administrator
- The Program is required to have the following program elements:

    Respirator selection, use, and care procedures

    Medical evaluations for wearers

    Fit testing procedures

Wearer training

- Hazards
- Care and maintenance
- Donning, doffing and limitations of use
- Emergency use

Employee respirator use for routine, infrequent, and emergencies

Respirator maintenance

- Cleaning and disinfection
- Storage
- Inspection and repair
- Removal from service
- Filter/chemical change out schedule and rationale
- Supplied air respirator air delivery and quality procedures

Program efficacy evaluation procedures

Please refer to 29 CFR 1910.134 (federal) or WAC 296-842 (Washington State) for specific regulatory requirements.

It is important to emphasize the importance of having a written and detailed respiratory protection program to insure that staff is trained, the respirator fit tested, the appropriate respirator is selected and used correctly, and the equipment is properly maintained. The equipment and training is specialized and requires a level of expertise above and beyond what can be provided by a retail building supply store.

Respirator categories

Respirators are categorized according to their performance and physical characteristics.

Positive and negative pressure respirators
Respirators deliver breathing air to the wearer by either positive pressure or negative pressure. Positive pressure respirators deliver or "push" air into the respirator. Positively pressurized air is "pumped" into the respirator from a motor/fan, compressor, or pressurized tank via a tube, or in some cases, the motor/fan is attached directly to the respirator. There is minimal exertion required by the wearer to receive air and the

respirator is designed to maintain positive pressure as the wearer breathes. Airborne contaminants are not able to reach the wearer when the respirator is under constant positive pressure because air will flow out of the respirator wherever it may leak.

The wearers of negative pressure respirators use the power of their own breathing to draw air into the respirator. The physical exertion required of the wearer is greater for negative pressure respirators. Airborne contaminants may be able to infiltrate the respirator and reach the wearer via leaks in the respirator sealing surface due to inward air flow because the respirator will be under negative pressure each time the wearer inhales.

Respirator styles

There are four basic respirator "styles" and they include filtering face piece respirators, half-face respirators, full-face respirators, and loose fitting hoods.

Filtering face piece respirators

Filtering face piece respirators are typically constructed almost entirely of the actual filter media with support material that allows the respirator to cover the nose, mouth, and chin, and is attached around the wearer's head using elastic straps. The outer edge of the respirator's sealing surface may have additional material (e.g. foam rubber) to improve the seal and a bendable, metal reinforcing strip may be installed over the bridge of the nose to improve the fit and seal of the respirator over the nose. They are commonly, but inappropriately, referred to as "dust masks" in retail building supply stores. Some specialized filtering face piece respirators come equipped with face shields for splash protection. All filtering face piece respirators are negative pressure respirators.

Half face respirators

Half face respirators are made from rubber, silicon, or other flexible, elastomeric material that typically provide a tighter and improved face seal as compared to filtering face piece respirators. Half face respirators cover the wearer's mouth and nose and are attached around the wearer's head using elastic straps. Half face respirators are typically used as negative pressure respirators when they are equipped with filter cartridges. Half face respirators may also be used as positive pressure respirators when used in a supplied air system and/or used as a face piece option in a powered air purifying respirator.

Full face respirator

Full face respirators are made from rubber, silicon, or other flexible, elastomeric material that typically provides a tighter and improved face seal as compared to filtering face piece and half face respirators. Full face respirators cover the wearer's entire face (mouth, nose, and eyes), have a clear shield to provide vision and eye protection, and are attached around the wearer's head using elastic straps. Full face respirators are typically used as negative pressure respirators when they are equipped with filter cartridges, but may also be used as a face piece option for positive pressure respirators when used in a supplied air system and or used as a face piece option for a powered air purifying respirator.

Loose fitting hood

Loose fitting hoods are simply that, a loose fitting hood that is put on over the head, may or may not have a supporting interior head band, and has a clear viewing shield. They are only available for use in combination with a supplied air system or as part of a powered air purifying respirator, and as such, loose fitting hoods are always under positive pressure.

Air purifying respirators

Air purifying respirators "clean" or "purify" the air source by using filter cartridges. Dust, solid particulate matter, and liquid aerosols (mists) are captured and removed from the breathing air by mechanical filters. Chemical vapors and gases are removed by filters made from absorbent filter media that is used to capture specific contaminants (e.g. mercury) or broad classes of vapors and gases. For example, filters that contain activated charcoal are used to capture and remove organic vapors from the air stream. Filters are rated and tested against a variety of chemical compounds and those compounds are listed by the manufacturer. Filters also have a useful life span that varies with use, filter loading, and the chemical compound. Most filters are now equipped with an "End of Life" indicator that informs the wearer when the filter is no longer effective and needs to be changed. However, there are not "End of Life" indicators for all filter cartridges or for all chemical compounds and it becomes incumbent on the pharmacy and their safety department to make its' best estimate regarding filter change out policies. Air purifying respirators are used in both negative and positive pressure respirators.

Powered air purifying respirators

Powered air purifying respirators (PAPRs) are unique in that they maintain positive pressure and deliver filtered air for the wearer. PAPRs provide filtered air to the wearer using a battery-powered motor and fan. The motor and fan are intended to maintain positive pressure within the respirator through a constant flow of air. PAPRs are available for use with a half face, full face, or loose-fitting hood attachment. The fan and motor are typically attached to the wearer using a belt; however, the motor and fan may be affixed directly to full face piece in some models.

In terms of functional PAPR operation, breathing air is drawn by negative pressure through the filter, passes the motor and fan where the air becomes positively pressurized, and is directed to the face piece via a tube.

Supplied air respirators

Supplied air respirators bring air from some other source to the wearer. The respirator source air may be purified at an air compressor where is it either distributed to the wearer(s) via a panel or used to fill air tanks for storage purposes that is utilized later by the wearer. Supplied air respirator systems are complicated, require significant training to use and maintain, and are expensive to own and operate.

Solids and liquid aerosols

Exposure by inhalation to solid and liquid forms of hazardous drugs requires that the drug particles or droplets be small enough to be inhaled (approximately </= 50 microns). Inside and outside of pharmacy, potential aerosolization is expected to occur during activities that include handling or weighing bulk powders, tablet crushing, liquid transfers, mixing (e.g. topical creams and food), and accidental spills. Aerosolization requires a physical action that plays upon the drug. Potential exposure to solid aerosol exposure from solid crushing can be mitigated by using a closed crushing device; however, it is important to recognize that the transfer or pouring of the crushed drug can become aerosolized and contaminate hands, clothing, and surfaces.

Filtration

Air filtering respirators are typically used to prevent exposure to aerosols and N95 rated filters are the most commonly used in industry. N95 and P95 filters can remove small particulate from atmospheric breathing air at an efficiency of 95%. The N designation refers to respirators that are not resistant to oil and the P designation refers to filters that are resistant to oil. N95 filter cartridges are available for tight-fitting elastomeric half face, full face, and powered air purifying respirators, as well as filtering facepiece and surgical face masks. Higher efficiency filter cartridges such as HEPA-filters (High Efficiency Particulate Air) are available and are classified as either N100 or P100; however, they are not available as filtering facepiece respirators or surgical masks at this time. N100/P100/HEPA filters are capable of removing particulate matter from breathing air at an efficiency of 99.97%.

Standard mechanical air filter media is designed to remove aerosols and particulates but is not capable of removing vapor or gases unless the media is specifically treated to do so.

Respirator selection

The inhalation hazards presented to pharmacists, pharmacy technicians, and other staff from hazardous drugs is likely limited to the following scenarios:

- Spilled drug in packages at Receiving/Processing
- Spilled drug in the BSC
- Spilled drug outside the BSC

Selecting respiratory protection for non-volatile hazardous drug solid and liquid aerosols is straightforward. Properly fitted half-face and full-face negative pressure air purifying respirators equipped with N95/P95 or N100/P100 filter cartridges are acceptable for the cleanup of spilled solids and liquids, as are fitted N95 filtering face piece respirators and N95 surgical masks. They do not, however, provide protection from hazardous drug vapor.

Selecting respiratory protection for the cleanup of volatile hazardous drugs is more challenging because there is no data available that shows that the filter cartridges typically used for organic vapors are effective for these drugs.

Powered air purifying respirator

Powered air purifying respirators (PAPRs) equipped with combination HEPA/organic vapor cartridges and a loose fitting hood are preferred for use in pharmacy for cleaning up hazardous drug spills inside and outside of biological safety cabinets. PAPRs have several advantages over negative pressure air purifying respirators and they include the following:

- Source air does not originate in the breathing zone (face). The motor/fan and filter unit is belted to the waist and situated on the small of the back or hip. Cleaning and wiping up spilled drug using hands means that the face and breathing zone are close to the drug. Air provided by a PAPR is further away

and not in the breathing zone.

- Positive pressure is maintained within the hood. Air is forced outward from the hood and that prevents the infiltration of aerosols and vapor. Infiltration can occur in negative pressure respirators that have leaks around the face seal because they are under negative pressure when the wearer inhales.

- Loose fitting hoods designed to fit all head sizes. Negative pressure respirators come in a variety of sizes and can accommodate most, but not all, people.

- Loose fitting hoods provide splash protection whereas filtering face piece and half face respirators do not.

- Training on the use of PAPRs is generally simpler because of its ease of use as compared to negative pressure respirators. Hospital-affiliated pharmacies benefit by the hospital having a PAPR program in place that they use for TB patients, and other patients placed under respiratory precautions.

- Fit testing is not required for PAPRs with loose fitting hoods.

PAPRs have the following advantages over supplied air respirators:

- Less expensive, easier to use, and require less expertise to operate and maintain.

- More portable and convenient to use.

Combination HEPA/organic vapor filter cartridges are recommended for use in PAPRs used for cleaning up hazardous drugs for the following reasons:

- The combination filter cartridge allows the wearer to clean up spills of both non-volatile and volatile hazardous drugs.

- The organic vapor component, while not proven, is expected to limit potential exposure to volatile hazardous drugs to some degree.

- The location of the motor/filter unit on the hip or small of the back typically provides cleaner air because it is further away from the spilled hazardous drug.

5
RECEIVING AND STORAGE

Intro

Hazardous and non-hazardous drugs are typically delivered at the receiving dock and may be unpacked at the dock location or transferred for unpacking at the pharmacy. Hazardous and non-hazardous drug deliveries may, or may not, arrive segregated from one another, and mixed shipments are common.

Inspection and acceptance

Visual inspection of the outer packaging and segregation of the hazardous drugs from the non-hazardous drugs is best performed by trained pharmacy personnel at the receiving dock. It is recommended that the pharmacy be notified as drug shipments arrive in order to minimize the opportunity for contact and handling of the drug packages by unauthorized or untrained personnel.

It is recommended that personnel engaged in receiving and sorting wear one pair of chemotherapy gloves when unloading, processing, and inspecting hazardous drug deliveries. Chemotherapy gloves are recommended because chemotherapy agents can be shipped mistakenly with other drug orders and it cannot be known until inspection if a chemotherapy drug container has leaked. Leaking or stained packages should be immediately rejected, placed in a plastic, leak proof bin or tub, and isolated. The shipper should be informed that the rejected package contains hazardous drugs and will be held, sorted, and the leaking container and waste disposed of by the receiver. The damaged package and any leaked or spilled solid, powder, or liquid product at the receiving dock should be isolated, removed, and cleaned in accordance with the spill cleanup policies and procedures. It is a best practice to segregate hazardous drugs within a HEPA-filtered negative pressure hood or negative pressure room for the purpose of isolating the area in the event of a spill or release.

Undamaged, segregated hazardous drug packages should be delivered to the pharmacy on a designated hazardous drug cart or container for unpacking in a dedicated hazardous drug processing area.

Unpacking

Packaging, wrapping, stuffing, and cartons have the potential of being contaminated with hazardous drugs from residual contamination on the drug vials and containers by either the manufacturer or distributor. There may also be breakage of vials and containers during transport that have contaminated the interior packages. For these reasons, it is safer to assume that the materials and product inside the shipping package are contaminated and pharmacy personnel processing hazardous drug packages should wear chemotherapy gloves.

Hazardous drugs should be unpacked/processed at a dedicated work table. The table should be covered with, and packages placed on, a disposable, plastic-backed, absorbent pad that will absorb contamination from the outer cardboard packaging, the package exteriors, and leaking vials or containers.

Packages with broken, spilled, or leaking vials or containers should be isolated, removed, and cleaned in accordance with spill cleanup policies and procedures. Undamaged packages and contents should be unpacked and appropriately stored. Hazardous drug containers and vials can be pre-cleaned to remove potential contamination using disposable, microfiber wipes containing a surfactant (e.g. Wet Ones® - see IRSST reference) or water and a mild detergent, and placed in dedicated, leakproof storage bins. The wipes or wiping material should be disposed as drug contaminated waste. In the event that hazardous drug containers and vials are not cleaned at this stage, they should be placed in dedicated, leakproof storage bins or bags and marked or flagged in such a way that indicates that they have not yet been cleaned. Note that some drug vials may arrive with a plastic covering. These coverings are typically added at the end of the manufacturing cycle and are intended to provide an uncontaminated surface for safe handling and prevent breakage. The covering does not have to be removed.. The bins should then be relocated using a dedicated safe cart (i.e. has raised sides to prevent falls and breakage) and stored in dedicated hazardous drug areas (e.g. cabinets, shelves, refrigerators, etc.) in the pharmacy.

Storage

The hazardous drug storage area should be separate from the unpacking area. Counters and shelving should have guarded sides to prevent drug container falls and breakage. Storing hazardous drugs in plastic, leakproof bins on counters and shelving is preferred for stability and containment of leaks or spills. Maintaining separation of hazardous drugs from non-hazardous drugs is important to prevent cross-contamination. Segregated and designated hazardous drug refrigerators and freezers are preferred, however, hazardous and non-hazardous drugs can be stored within the same refrigerator and freezer provided they are on different shelves.

For Antineoplastic Chemotherapy High Exposure Risk, High Hazard High Exposure Risk, and High Exposure Risk drugs, the hazardous drug storage room or area should be under negative pressure and the ventilation system should provide both general exhaust ventilation and at least 12 air changes per hour to dilute and remove potential hazardous drug vapors/contamination.

6

SPILL CLEANUP

Exposure to spilled hazardous drugs to pharmacists, pharmacy technicians, and other staff is likely limited to the following scenarios:

- Spilled drug in packages at Receiving/Processing
- Spilled drug outside the BSC
- Spilled drug in the BSC

The cleanup of a spilled hazardous drugs requires the use of PPE and respiratory protection, the isolation of the drug and immediate area, the cleanup of the spilled drug, and the disposal of the cleanup and waste materials.

All drugs, hazardous or not, and drug forms can be spilled, and spills can happen anytime they are handled, transferred, manipulated, or stored. The degree and type of PPE and respiratory protection necessary to safely cleanup hazardous drugs varies with regard to the drug's exposure risk and the size and location of the spill. Exposure risk, as presented in the algorithm is based on hazard (e.g. cytotoxicity, carcinogenicity, teratogenicity, reproductive, organ toxicity, genotoxicity, and mimicry), and formulation (e.g. liquid, powder, uncoated tablet, capsule) and potential exposure. For example, the cleanup of antineoplastic chemotherapy high exposure risk drugs requires the use of more extensive PPE and respiratory protection than cleanup of low exposure risk drugs.

In terms of size, small liquid spills of moderate and low exposure risk drugs (</= 30 ml inside the BSC and </= 5 ml outside the BSC), will require less PPE and respiratory protection than large spills (> 30 ml inside the BSC and > 5 ml outside the BSC). In terms of formulation, the PPE and respiratory protection necessary for coated tablet and capsule spills will be less than that needed for bulk powders.

It is important to emphasize that all staff need to be aware of how to manage a hazardous drug spill and to understand that only those staff members that are trained in spill response and cleanup are allowed to proceed with the cleanup. It is important for staff to recognize that there can be significant risk involved during the cleanup of even small spills of antineoplastic chemotherapy agents. Staff should not conduct cleanup beyond their level of training no matter how seemingly insignificant a spill may appear. Improper cleanup can cause more contamination and potential for exposure than the original spill.

PPE and respiratory protection

The cleanup of a spilled hazardous drug involves direct contact with undiluted or diluted drug with potential exposure via inhalation, skin and mucous membrane contact, and ingestion. The following PPE and respiratory protection represents best practice for hazardous drug cleanup given the broad spectrum of drug agents, the amount of drug spilled, and the number of potential cleanup environments.

PPE

Antineoplastic chemotherapy high exposure risk drugs – parenteral, splash risk, inhalant, or manipulated oral

- Double pair chemotherapy gloves
- Chemotherapy gown
- Dedicated shoes and shoe covers
- Hair cover (in BSC or sterile areas only)
- PAPR equipped with combination HEPA/acid gas/organic vapor cartridges and loose fitting hood

High hazard high exposure risk – BCG, ribavirin, etc.

- Double pair medical gloves
- Gown
- Dedicated shoes and shoe covers
- Hair cover (in BSC or sterile areas only)
- PAPR equipped with combination HEPA/acid gas/organic vapor cartridges and loose fitting hood

High exposure risk – intravenous and other high splash risk liquids, bulk powders, and inhalants

- Double pair medical gloves
- Gown
- Dedicated shoes and shoe covers
- Hair cover (in BSC or sterile areas only)
- PAPR equipped with combination HEPA/acid gas/organic vapor cartridges and loose fitting hood

Moderate exposure risk – oral liquids and IM, SQ, intrathecal (low splash risk)

- Single pair medical gloves
- Gown

- Dedicated shoes and shoe covers
- Hair cover (sterile areas only)

Moderate risk antineoplastic chemotherapy – uncoated tablet, or contained manipulation, and liquid transfer

- Single pair chemotherapy gloves
- Chemotherapy gown
- Dedicated shoes & shoe covers
- Hair cover (sterile areas only)
- Large spill requires PAPR equipped with combination HEPA/acid gas/organic vapor cartridges and loose fitting hood

Low exposure risk – topical and oral solids that are manipulated

- Single pair medical gloves
- Gown
- Dedicated shoes and shoe covers
- Hair cover (in BSC or sterile areas only)

Low risk antineoplastic chemotherapy – capsule and coated tablet

- Single pair chemotherapy gloves
- Chemotherapy gown
- Dedicated shoes and shoe covers
- Hair cover (in BSC or sterile areas only)

Existing precautions

- Single pair medical gloves

Spilled Drug at Receiving/Processing

Spilled or leaking drugs are most likely to be discovered when the shipment arrives because the outer package is stained, discolored, or leaking, or during unpacking the shipping container. Recall that receiving and sorting personnel should wear one pair of chemotherapy gloves when handling hazardous drug packages (see Chapter 5, Receiving and Storage).

Leaking or stained packages
Leaking or stained packages should be immediately rejected, isolated, and marked (e.g. warning cones or tape). Leaking, stained, or broken packages discovered inside the shipping container should be left inside the shipping container and the container similarly staged and isolated.

Don appropriate PPE and respiratory protection, place package in plastic leak proof bin/tub/overpack container or on absorbent pad(s) as necessary (to contain leaking drug), and inspect package exterior. Place the package in an appropriate waste container or waste bag for return to shipper or disposal when the exterior shows signs of staining or liquid breakthrough, and assume package contents are contaminated. If the package is returned to the shipper, inform the driver and shipping company by phone and in writing that the package contains spilled hazardous drug and that the package is contaminated. Clean the area (described below) and return area to service. Place all spilled hazardous drug, cleanup materials, and used, disposable PPE in an appropriate waste container or waste bag for disposal.

Broken containers or spilled drug in shipping package
Secure and isolate the package as described above and inspect package interior and contents when spilled drug or broken containers are observed during unpacking and storage. Assume contents are contaminated until proven otherwise. Put on appropriate PPE and respiratory protection prior to inspecting package contents.

If readily accessible, remove the broken or damaged container(s) from the package and place on absorbent pad or in an appropriate waste container or waste bag for return to shipper or disposal. Assume packing material (e.g. foam, bubble wrap, plastic peanuts) is contaminated and place in an appropriate waste container or waste bag for disposal. Remove and segregate drug packages on absorbent pad from the container for inspection and cleaning. Place shipping container in an appropriate waste container or waste bag for disposal.

Visually inspect hazardous drug containers for signs of obvious contamination and place in an appropriate waste container or waste bag for disposal. Clean and wipe visibly non-contaminated drug containers with disposable wipes (e.g. Wet Ones®) to remove exterior contamination and segregate on an absorbent pad. Remove and replace gloves with a single pair of chemotherapy outer gloves. Remove drug container from secondary packaging, if any, and place in appropriate storage bin or container for use.

Place all spilled hazardous drug, cleanup materials, and used, disposable PPE in an appropriate hazardous drug waste container or waste bag for disposal.

Spilled drug outside the BSC

The procedures for cleaning up spilled drug in areas outside a BSC are similar to those described for shipping and receiving; however, the difference is that the spills are generally more “out in the open” as compared to being inside a shipping package. Hazardous drug spill kits are typically used to clean spilled drugs in open, uncontrolled environments.

Hazardous drug spill kits
Hazardous drug spill kits are available commercially and can also be assembled individually. Hazardous drug spill kits should be readily available wherever hazardous drugs are handled. Hazardous drug spill kits

typically contain the following components:

- Respiratory protection (not typically provided in a commercial kit)
- PPE (gown, shoe covers, gloves, hair cover, faceshield/safety glasses)
- Warning pop-up signs
- Absorbent pads/towels to cover and remove drug from surfaces (i.e. simple towels or pads that contain a solidifier that congeals in the presence of liquid or water. Congealing products are preferred for hard surfaces and application for both solid and liquid spills)
- Solidifying/congealing absorbent pads
- Solidifier
- Waste bags/containers
- Disposable scoop and scraper
- Cleaning wipes

Kits may also include:

- Hazardous drug warning signs or cones

Best Practice Safety Tools recommends disposable cleaning wipes containing a surfactant (e.g. Wet Ones) for final cleaning purposes once the bulk drug has been removed from the surface, and a loose-fitting PAPR equipped with combination organic vapor, acid gas, and HEPA/N or P100 filters for respiratory protection, and a gown (or chemotherapy gown as appropriate), 2 pairs of gloves (or chemotherapy gloves as appropriate), and polyethylene coated shoe covers for PPE when cleaning up large quantity hazardous drug spills outside a biological safety cabinet.

Large quantity spilled drug

No matter the size of a hazardous drug spill, it is important to stay calm and proceed carefully and methodically. A large quantity liquid spill is considered to be >5 ml outside the BSC, and >30 ml inside the BSC.

A large quantity solid spill is >5 tablets or capsules with visible residue present, and >5 mg of bulk powder, for the purpose of this Best Practice Safety Tool. The absence of visible residue from a tablet or capsule spill defaults to a small spill.

Liquids
Spilled hazardous drugs and leaking or broken containers should first be isolated. The person attending the spill should direct people away and out of the immediate area so that they do not expand the footprint of the

spill. If absorbent pads are immediately available, the spill should be covered directly and at the spill perimeter to prevent the spill from spreading. Next, the attendant should direct someone to bring the spill kit (if not immediately available) and/or notify the spill team members. Upon arrival of the kit or team, the warning cones or tape should be placed at all potential access points to the spill to keep unauthorized personnel away.

The individuals that intend to follow through with the clean up should locate themselves in a clean area away from the immediate spill area, and don their PPE and respiratory protection accordingly:

1. Wash hands
2. Inner gloves
3. Shoe covers
4. PAPR belt and motor/filter unit (Do not don the hood)
5. Gown (sleeves should cover inner gloves and be over the PAPR belt and motor/filter unit)
6. Outer gloves
7. PAPR hood (and turn on)

Prepare the bag(s) by rolling down the sides outwardly in order to make it easier to deposit waste materials inside and/or open/remove the lid from the waste container. Prepare separate waste and disposable PPE waste bags/containers. Approach the spill carefully in order to avoid contact and maintain balance. Use the disposable scoop(s) and scraper(s) to remove and lift the pads, drug, and drug container into the waste bag or waste container. Take care to remove any and all glass fragments from the surface in order to prevent damaging the gloves or cutting the fingers or hands during final cleaning.

Wipe the spill area three times using individual disposable wipes for each cleaning and place in waste bag or container. Roll up waste bag and seal with zip tie or internal drawstring/closure mechanism.

Remove outer glove and place in PPE waste bag/container. Remove gown and shoe covers and place in waste bag/container. Remove inner gloves and respirator. Wash hands and face thoroughly and repeatedly with soap and water.

Solids

Spilled hazardous drugs and leaking or broken containers should first be isolated. The person attending the spill should direct people away and out of the immediate area so that they do not expand the footprint of the spill. If absorbent pads are immediately available, the spill should be covered directly and at the spill perimeter to prevent the spill from spreading. Next, the attendant should direct someone to bring the spill kit (if not immediately available) and/or notify the spill team members. Upon arrival of the kit or team, the warning cones or tape should be placed at all potential access points to the spill to keep unauthorized personnel away.

The spilled material should be covered with an absorbent pad (if it hasn't already been covered) and additional pads placed at the perimeter of the spill to prevent the spill from spreading. The individuals that intend to follow through with the clean up should locate themselves in a clean area away from the immediate spill area don their PPE and respiratory protection accordingly:

1. Wash hands
2. Inner gloves
3. Shoe covers
4. PAPR belt and motor/filter unit (Do not don the hood)
5. Gown (sleeves should cover inner gloves and be over the PAPR belt and motor/filter unit
6. Outer gloves
7. PAPR hood (and turn on)

Prepare the waste bag(s) by rolling down the sides outwardly in order to make it easier to deposit waste materials inside and/or open/remove the lid from the waste container. Prepare separate waste and disposable PPE waste bags/containers. Approach the spill carefully in order to avoid contact and maintain balance.

For solidifying/congealing absorbent pads, apply water to absorbent pad and allow pad to break down and congeal over the spilled solid. For non-solidifying or non-congealing pads, lift pad off of spilled solid and gently sprinkle and completely cover spilled drug with solidifying granules. Cover granules and drug with non-plastic-backed, absorbent pad and apply water to the pad. Soak/saturate the pad and solidifier and wait approximately 3 to 5 minutes for the solidifier to congeal with the drug.

Use the disposable scoop(s) and scraper(s) to remove and lift the pads, drug, and drug container into the waste bag or waste container. Take care to remove any and all glass fragments from the surface in order to prevent damaging the gloves or cutting the fingers or hands during final cleaning. Wipe the spill area three times using individual disposable wipes for each cleaning and place in waste bag or container. Roll up waste bag and seal with zip tie or internal drawstring/closure mechanism.

Remove outer glove and place in PPE waste bag/container. Remove gown and shoe covers and place in waste bag/container. Remove inner gloves and respirator. Wash hands and face thoroughly and repeatedly with soap and water.

Small quantity spilled drug

A small quantity liquid spill is considered to be </=5 ml outside the BSC, and </= 30 ml inside the BSC. A small quantity solid spill is </= 5 tablets or capsules with no visible residue present, and </= 5 mg of bulk powder, for the purpose of this Best Practice Safety Tool. Small quantity spilled drugs should be cleaned up using the same techniques as described above; however, less PPE is necessary due to the size of the spill and the limited amount of time expected to clean up the spill. A single pair of chemotherapy or medical

gloves and gown, as appropriate, is all that is needed to be worn for PPE for most small spills. The exception to this is the use of a single pair of medical gloves when existing precautions are warranted.

Spilled drug in the BSC

Hazardous drugs spilled in a BSC present different challenges to those spilled outside a BSC. The BSC is a controlled environment and the immediate risk of a spill is minimized because the BSC is under negative pressure and the drug cannot exit the BSC. It is likely that for this reason that the ASHP Guidelines recommend using a spill kit if the volume of the spill exceeds 30 ml or the contents of one drug vial or ampule. However, cleaning large and small spills may require the pharmacist or technician to open the sash which reduces negative pressure in the BSC, or they may need to reach inside the hood, and possibly break the plane of the sash with their head. Both of these conditions can increase the risk of exposure.

The PPE used for sterile prep at the BSC doesn't change; however, respiratory protection (PAPR equipped with combination HEPA/organic vapor cartridges and loose fitting hood) is necessary whenever the sash is raised and when the pharmacist or technician's head may break the plane of the sash during clean up. The cleanup procedures are similar to spilled drug cleanup conducted outside the BSC.

Liquids
Cover large and small liquid spills with non-solidifying/non-congealing absorbent pad if the spill has extended beyond the bottom pad where the drug is compounded. Dispose of the absorbent pad(s) in an appropriate waste container or waste bag and repeat application of absorbent pads until all liquid is removed. Wipe the clean up area and materials/containers/instruments/etc. with a disposable wipe containing a surfactant (e.g. Wet Ones®) and discard wipe in waste container or waste bag. Repeat wiping two additional times for a total of three cleanings. Place all spilled hazardous drug, cleanup materials, and used, disposable PPE in an appropriate waste container or waste bag for disposal. Discard PPE used for cleanup and don new change of PPE for BSC disinfection. Perform hood disinfection in accordance with USP 797 and pharmacy policy and return BSC to service.

Solids
Use disposable wipes containing a surfactant (e.g. Wet Ones®) to remove all bulk drug from surfaces and place in appropriate waste container or waste bag. Wipe up cleaned surfaces and materials/containers/instruments/etc. with additional disposable wipe and dispose of wipe in waste container or waste bag. Repeat wiping two additional times for a total of three cleanings. Place all spilled hazardous drug, cleanup materials, and used, disposable PPE in an appropriate waste container or waste bag for disposal. Discard PPE used for cleanup and don new change of PPE for BSC disinfection. Perform hood disinfection in accordance with USP 797 and pharmacy policy and return BSC to service.

Carpet and upholstery spills

Hard surface flooring materials such as vinyl tile and sheeting, and rolled flooring are typical of pharmacy floor finishes because they do not generate dust and particulate matter, and cleaning spills off of solid surfaces is much easier than cleaning spills from fleecy surfaces such as carpet. The same holds true for pharmacy furniture and solid surface (e.g. plastic/vinyl covered) furniture is typically used for the same reason.

However, hazardous drugs spills can occur outside the pharmacy during transport in carpeted and furnished corridors and waiting areas, for example, and cleanup of spills on carpet, upholstered furniture, and fleecy surfaces (e.g. room dividers) presents different challenges.

Carpet cleanup
It is extremely difficult to completely remove spilled solid or liquid hazardous drug from fleecy surfaces. Removing the affected carpet is the only way to be sure that no drug residue or contamination remains.

Carpet removal
Isolate the spill area, and the person attending the spill should direct people away and out of the immediate area so that they do not expand the footprint of the spill. If absorbent pads are immediately available, the spill should be covered directly and at the spill perimeter to prevent the spill from spreading. Next, the attendant should direct someone to bring the spill kit (if not immediately available) and/or notify the spill team members. Upon arrival of the kit or team, the warning cones or tape should be placed at all potential access points to the spill to keep unauthorized personnel away.

The spilled material, solid or liquid, should be covered with a non-solidifying or non-congealing absorbent pad (if it hasn't already been covered) and additional pads placed at the perimeter of the spill to prevent a liquid spill from spreading. The individuals that intend to follow through with the clean up should locate themselves in a clean area away from the immediate spill area don their PPE and respiratory protection accordingly:

1. Wash hands
2. Inner gloves
3. Shoe covers
4. PAPR belt and motor/filter unit (Do not don the hood)
5. Gown (sleeves should cover inner gloves and be over the PAPR belt and motor/filter unit)
6. Outer gloves
7. PAPR hood (and turn on)

Prepare the bag(s) by rolling down the sides outwardly in order to make it easier to deposit waste materials inside and/or open/remove the lid from the waste container. Prepare separate waste and disposable PPE waste bags/containers. Approach the spill carefully in order to avoid contact and maintain balance.

Apply tape over the absorbent pad edges and seal to the carpet to prevent aerosolization of the spilled material. Outline and cut through the carpet approximately 3 or more inches or more from the taped perimeter using a razor knife. Use a metal scraper to help peel back the carpet from the floor surface below and lift and place the carpet section, pad, and drug into the waste bag.

If spilled solid or liquid drug is observed on the solid floor underneath the removed carpet section, place a solidifying/congealing pad over the drug, apply water, and allow it to break down and congeal. If solidifying/congealing pads are not available, gently sprinkle and completely cover spilled drug with solidifying granules. Cover granules and drug with non-plastic backed, absorbent pad and apply water to the pad. Soak/saturate the pad and solidifier and wait approximately 3 to 5 minutes for the solidifier to congeal with the drug.

Use the disposable scoop(s) and scraper(s) to remove and lift the pads, drug, and drug container into the waste bag or waste container. Take care to remove any and all glass fragments from the surface in order to prevent damaging the gloves or cutting the fingers or hands during final cleaning. Wipe the spill area three times using individual disposable wipes for each cleaning and place in waste bag or container. Roll up waste bag and seal with zip tie or internal drawstring/closure mechanism.

Remove outer glove and place in PPE waste bag/container. Remove gown and shoe covers and place in waste bag/container. Remove inner gloves and respirator. Wash hands and face thoroughly and repeatedly with soap and water.

Carpet and upholstery cleaning

It is assumed that the purpose of cleaning hazardous drug from carpet and upholstered furniture is to re-use them. A dedicated, HEPA-filtered vacuum cleaner is required for this purpose for both solid and liquid drugs.

Isolate and secure the spill area as described above but cover the spill with a non-/solidifying or non-congealing absorbent pad. The individuals that intend to follow through with the clean up should locate themselves in a clean area away from the immediate spill area, and don their PPE and respiratory protection accordingly:

1. Wash hands
2. Inner gloves
3. Shoe covers
4. PAPR belt and motor/filter unit (Do not don the hood)
5. Gown (sleeves should cover inner gloves and be over the PAPR belt and motor/filter unit)
6. Outer gloves
7. PAPR hood (and turn on)

Prepare the bag(s) by rolling down the sides outwardly in order to make it easier to deposit waste materials inside and/or open/remove the lid from the waste container. Prepare separate waste and disposable PPE waste bags/containers. Approach the spill carefully in order to avoid contact and maintain balance.

For solid spills, HEPA-vacuum the carpet gently to remove the solid drug from the surface and prevent spreading the drug due to recoil from the carpet or furniture. Continue vacuuming until no more visible solid is present, or no more visible solid can be removed. Seal the HEPA-vacuum opening with a piece of duct tape with the vacuum running, immediately shut off the vacuum once the opening is sealed, and wipe the surface of the vacuum with a disposable wipe (e.g. Wet Ones) and discard the wipe in a waste bag.

Wipe the carpet surface with an alkaline detergent (pH 8 to 9) and sponge, repeat wiping two additional times, and dry carpet by repeatedly applying non-solidifying or non-congealing absorbent pads until dry. Allow the carpet to air dry for an additional 20 to 30 minutes, conduct a final HEPA-vacuuming, and return the area to service.

For liquid spills, repeatedly apply non-solidifying/non-congealing pads until the drug has been sufficiently removed. Wipe the surface with an alkaline detergent (pH 8 to 9) and sponge, repeat wiping two additional times, and dry carpet by repeatedly applying non-solidifying/non-congealing absorbent pads until dry. Allow the surface to air dry for an additional 20 to 30 minutes, conduct a final HEPA-vacuuming, and return to service.

Accidental personnel exposure and cleanup

Accidental exposure to hazardous drugs can occur almost any time hazardous drugs are handled. Leaking packages, broken vials, leaking IV bags, syringe malfunctions, and other accidents can occur. This can result in hazardous drugs making contact with clothing, skin, eyes, or being injected through intact skin via needle sticks or broken glass. It is important to seek medical attention following an accidental personal exposure.

Clothing, linen, and skin contact

It is important to immediately remove contaminated clothing after it has become in contact with a hazardous drug. The clothing can be placed in a plastic waste bag for disposal or for temporary holding pending laundering. Wash the affected skin area with soap and water and repeat washing as many as three times in order to be confident that the drug has been removed. If the contact area is large or in an awkward area (e.g. back, waist, head), taking a series of showers may be necessary.

Keep the wash sink or shower off limits to others while waiting for it to dry, and once it is dry, don a single pair of chemotherapy gloves and completely wipe with disposable wipes (e.g. Wet Ones®). Place the used wipes and gloves in a plastic waste bag or container, seal, and discard appropriately. Return the sink or shower to service following wiping.

Contaminated clothing and linen can be laundered and re-used if desired. It is important to notify the laundry personnel that the clothing submitted is contaminated with hazardous drugs and what form the drug is in (i.e. liquid or solid) so they can take precautions and choose appropriate PPE. Gowns and a single pair of gloves are appropriate for liquid-contaminated clothing. Gowns, gloves, and a properly fitted particle-filtering respirator (e.g. filtering face piece N/P95 respirator, half-face N/P95 air purifying respiratory, or PAPR equipped with N/P95 filter cartridges) are appropriate for solid-contaminated clothing. The washing machine should be run a second time without a load for rinsing purposes following the initial cleaning.

Eye contact

It is important to immediately begin flushing a person's eyes when they come into contact with hazardous drugs. An emergency eyewash station that can provide warm potable water is preferable to a portable

station in that warm water is more tolerable on the person whereas flushing with cold water can be a less desirable experience. It is also important to remove contact lenses, if worn. Contact lenses do not offer protection and can increase exposure if the drug is trapped between the lenses and eyes, or is adhered to the lenses. Contaminated contact lenses should be discarded because there is no known or validated way to clean and remove hazardous drugs from them. Please note that it will be difficult for the person to keep their eyes open. During the flushing and assistance from another person may be needed to hold the eyes open. The assistant should wear a pair of chemotherapy gloves for their protection. The eyes should be flushed for at least 15 minutes.

The affected person should wash their face and hands with soap and water following flushing. The person assisting should also wash their hands following flushing. Keep the eye wash sink/eye wash area off limits to others while waiting for it to dry, and once it is dry, don a single pair of chemotherapy gloves and completely wipe with disposable wipes (e.g. Wet Ones®). Place the used wipes and gloves in a plastic waste bag or container, seal, and discard appropriately. Return the eye wash sink/eye wash area to service following wiping.

Injection

Hazardous drugs can be injected through intact skin via needle sticks and broken glass (e.g. glass vial). In order to limit the absorption of drug, don a clean pair of chemotherapy gloves and massage in the direction of the wound to make it bleed. Be careful to avoid pinching the wound because it can cause suction and restricts the flow of blood. Remove and discard gloves in a plastic waste bag or container and proceed to wash the wound with soap and water. Repeat washing three times and cover the wound with a bandage.

Keep the wash sink off limits to others while waiting for it to dry, and once it is dry, don a single pair of chemotherapy gloves and completely wipe with disposable wipes (e.g. Wet Ones®). Place the used wipes and gloves in a plastic waste bag or container, seal, and discard appropriately. Return the wash sink to service following wiping.

Report all accidental exposures by injection to management.

7

CLOSED SYSTEM TRANSFER DEVICES

Closed system transfer devices (CSTDs), in the simplest terms, are mechanical devices that are used to prevent the release of a hazardous drug, and protect against its' contamination, when it is removed or added from one container to another container (e.g. vial to syringe to vial, vial to syringe to IV bag). Similarly, CSTDs are used for the same purpose during the introduction of a diluent into a hazardous drug vial for reconstitution.

CSTD technology continues to develop and evolve as manufacturers attempt to perfect a CSTD that is easy to use, protective, and cost effective. CSTDs, in general, have been shown to reduce hazardous drug releases that occur during transfer with some CSTDs being more efficient and effective than others. Recent studies of some CSTDs have reported extraordinary results where contamination of the pharmacy and clinic was all but eliminated over a short period of time following their introduction and use. It is important, however, to recognize that all CSTDs have limitations, and understanding and adapting to their limitations will be critical to their success in reducing contamination. As such, it is recommended herein and by ASHP, USP 797, ISOPP, and NIOSH, that CSTDs always be used inside a BSC that provides an ISO Class 5 Environment.

Theory of operation

CSTDs are intended to establish a fully enclosed "system" where the changing internal pressure of vials, syringes, and receiving containers (e.g. IV bags) during drug withdrawal and reconstitution does not result in environmental releases and contamination.

Air exchange occurs when a liquid drug is withdrawn from a rigid vial using a syringe. The withdrawal of the liquid from a vial using a syringe causes the vial to become negatively pressurized and atmospheric air can be drawn into the vial via leaks in the seal and/or when the syringe is removed. Positive pressurization occurs in rigid glass vials when diluent is introduced during drug reconstitution. Drug can escape from the vial as the pressure inside the vial overcomes the seal. Drug can also escape a vial during transfer on the surface of the syringe needle, at the interfacing connection/mating/sealing surfaces (e.g. vial seal, Luer Lok connections), and from rebound of the rubber seal when the syringe is withdrawn.

Connections

The connecting unit system between the vial and syringe, and syringe IV bag/administration port is a key component of all CSTDs. Needleless enclosed systems are variations on the male/female locking system (e.g. Luer Lok & Clave) where the syringe can interface with both the vial and and the IV bag interchangeably via elastomeric sealing surfaces. There are also enclosed systems for securing needles. There are systems

that utilize a separate connecting/sealing device that is directly attached to the vial. Attaching these devices to the vial also simultaneously spikes the vial. The potential release of drug during the attachment and spiking of the vial has not been studied in the peer reviewed literature. This is an important reason why CTSDs need to be used within a BSC.

Systems vary with regard to the number and degree of their safety features that include: needle stick prevention, spill prevention, autolocking features when not engaged/attached, and critical sealing surface integrity. Challenges the connecting systems pose for users include drug residue on the connecting system mating/sealing surfaces, disinfection and cleaning of mating surfaces, and seal integrity.

Locking systems, like other CSTDs, have limitations and it is important to evaluate their strengths, limitations, and fit with regard to selecting the most appropriate system for each pharmacy and institution. Further development and improvement in locking systems and CSTDs is expected as market demand increases and the technologies improve.

Pressure relief

All CSTDs address both positive and negative pressurization differences that occur during drug transfer. The two most common approaches use either pressure equalization or venting systems.

Pressure equalization

Pressure equalization systems are intended to allow drug transfers without generating significant pressure changes between the source container and syringe, or syringe and receiving container that could result in the introduction of environmental contaminants to the drug or prep, and the release of drug into the environment. All pressure equalization systems are dependent on the locking mechanism connection seal. The equalization system will not work as intended if the seal fails.

The PhaSeal diaphragm (PhaSeal Protector) is spiked into the vial using an attachment device and becomes permanently connected to the vial. The diaphragm fills when air or fluid is injected into the vial and contracts when the syringe is removed from the vial. Contamination of the attachment device is a concern for all CTSDs and the obstruction of airflow in the BSC is a concern for this system specifically.

The Genie Vial Access device utilizes a sterile, internal balloon that is spiked by hand into the vial. The balloon fills with external environmental air when the vial becomes negatively pressurized during drug transfer. The air remains inside the balloon and does not make contact with the vial contents. Both the PhaSeal and Genie Vial Access equalization systems can be used with multi-dose vials.

The Equashield system uses dual needles and a sealed air chamber to equalize pressure between the vial and syringe. Similar to the above systems the vial is spiked by hand with an adapter. The syringe unit is attached to the adapter, and the sealing surface membrane on the vial adapter and the syringe unit make contact as the syringe is depressed. The dual needles then penetrate both membranes. One needle is connected to the drug transfer chamber and the other is connected to the sealed sterile air chamber behind the piston. As one needle withdraws drug the other supplies sterile air to the vial, thereby equalizing pressure. During reconstitution, diluent is added through a syringe into the vial while the other needle extracts air from the vial that is stored in the back of the syringe to equalize pressure. The system can be used with multi-dose vials.

Each of the above examples of pressure equalization systems are fully enclosed.

Venting

Venting is another method used to equalize pressure in CSTDs. The venting systems employ a vented vial adapter that is hand spiked into the vial. Air pressure between the syringe and vial is equalized by the introduction of environmental air via a filter during withdrawal when the system becomes negatively pressurized. The filter is also used to prevent the escape of drug when the vial becomes positively pressurized when a diluents is added during drug reconstitution, for example.

The mechanical filter media used typically has a pore size of 0.2 microns and is intended to capture aerosols. The mechanical filter is often paired with a charcoal impregnated membrane that is intended to capture hazardous drug vapor. There are needle and needleless systems available and most can be used with both single- and multi-dose vials.

Alarmed manometers can warn staff of improper pressurization conditions.

Evaluation and selection considerations

CSTDs have been shown to reduce environmental contamination in pharmacy and clinical areas; however, all devices have limitations. The evaluation and selection of CSTDs is pharmacy specific given the differences in types and volumes of hazardous drugs processed, the physical layout of the facility, and the patients served. Pharmacists should consider the ease of use, ergonomic factors, work flow and production impacts, additional training and labor costs, waste generation, and CSTD cost when evaluating CSTDs.

An economic argument has been put forth regarding an assertion that spiking vials with a CSTD can prolong the sterility of the vial which can result in longer expiration dating which can lead to considerable cost savings. However, the evaluation of this claim is beyond the scope of the Best Practice Safety Tools. Pharmacists are advised to consult the peer reviewed literature, USP 797, and the FDA with regard to evaluating this claim.

Pharmacists are urged to confer with peers that use or have trialed a device, consult with nursing regarding CSTD compatibility with drug administration, research the peer reviewed literature about a specific CSTDs, and review the FDA adverse events reports as devices are selected for trial. Consult with staff during and after the trial period for feedback on ease of use, complexity, productivity, and ergonomic issues. Tracking events such as spills, needlesticks, waste volume changes, etc. during the trial period can be used for comparison with other CSTDs, and current practices.

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AUTOMATED DISPENSING SYSTEMS

Automated dispensing systems are in commonly used by the pharmacy to fill individual patient prescriptions and unit-dose orders, filling prescriptions in "remote" locations outside the main pharmacy (e.g. clinical unit), and for other purposes. Automated dispensing systems offer benefits that include improved inventory control, reduced labor costs, responsive delivery times, and tracking.

Background

Automated dispensing systems typically store drugs in bins, hoppers, drawers, or hooks, and the drugs are loaded by hand. The drugs may be loaded as bulk stock (e.g. coated or uncoated tablets, capsules), packaged (e.g. blister packaged or vial), or as administration ready (e.g. loaded syringe). Automated dispensing systems may withdraw drugs using a robotic arm that deposits the drug package into a receiving bin/hopper, fill a vial/bottle placed underneath a drug bin/hopper using gravity, deliver a drug bin/hopper to a receiving window via a conveyor, unlock a secured drawer, or by some other method.

Potential Hazardous Drug Contamination

The potential for hazardous drug contamination exists for automated dispensing systems as it does for human systems. The challenge for automated dispensing systems is recognizing and limiting contamination without the benefit of human interface and judgment in real time.

Contamination can take place during almost every phase of use. Bin loading, internal equipment failure (e.g. hopper fails to close), and transfer (unloading) to the receiving vial (e.g. misalignment between the bin/hopper and the receiving vial) can result in spills or contamination that may not be immediately recognized. Pharmacy technicians may not be able to recognize or diagnose a problem unit equipment maintenance and service, or routine cleaning is performed.

To this end, the technology is not sufficiently developed to be compatible with hazardous drugs. Best Safety Practice Tools agrees with ASHP Guidelines on the Safe Use of Automated Dispensing Devices that hazardous drugs are not appropriate for Automated Dispensing Systems.

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