Evidence-Based Series #16-3 Version 2 - REQUIRES UPDATING

A Quality Initiative of the Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

Safe Handling of Cytotoxics

June 22, 2018

Evidence-based Series (EBS) 16-3 Version 2 was reviewed in 2017/18 and determined to REQUIRE UPDATING. See Section 4: Document Assessment and Review for details.

Evidence-Based Series #16-3v2 is available on the CCO Oncology Nursing page and is comprised of 4 sections:

- **Section 1:** Guideline Recommendations
- **Section 2:** Evidentiary Base
- **Section 3:** Development Methods, Recommendations Development and External Review Process
- **Section 4:** Document Assessment and Review

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Evidence-Based Series #16-3 Version 2

A Quality Initiative of the Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

Safe Handling of Cytotoxics

Guideline Report History

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<th>NOTES and KEY CHANGES</th>
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<td>Current Version 2</td>
<td>July 2006 to January 2013</td>
<td>New data added to original Full Report</td>
<td>Updated web publication. Peer review publication.</td>
</tr>
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<td>Reviewed June 2018</td>
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A Quality Initiative of the Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

Safe Handling of Cytotoxics: Guideline Recommendations


Report Date: December 16, 2013

The 2013 guideline recommendations REQUIRE UPDATING

This means that the recommendations require additional evidence but are still relevant for decision-making.

GUIDELINE OBJECTIVES
The original guideline objective was: to provide recommendations regarding the safe handling of parenteral cytotoxics by health care workers.

The objective of this update is: to update and address new issues in cytotoxic handling that have developed since the previous guideline, including the use of oral cytotoxics, selection and use of personal protective equipment, and treatment in diverse settings including in the home setting.

TARGET POPULATION
Health care workers who may come into contact with cytotoxic drugs at any point in the medication circuit. The medication circuit includes all steps through which the drug travels, from the receiving dock to the storage facility, as well as its preparation, administration and disposal. Exposure is possible throughout the medication circuit in the hospital or in the home setting.

INTENDED USERS
Hospital Administrators, Educators and Managers, Occupational Health and Safety Services, Pharmacy and Health Care Workers.

SUMMARY OF GUIDELINE DEVELOPMENT METHODS
This guideline was developed primarily by adaptation and endorsement of the guideline “Prevention Guide: Safe Handling of Hazardous Drugs,” developed by the Association paritaire
pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS), and the Institut de recherche Robert-Sauvé en santé et en sécurité du travail (IRSST) (1), as described in Section 3 of this document. This adaptation/endorsement process was supplemented with additional searches for evidence in the medical literature on some specific topics as described in Section 2 of this document. The recommendations below reflect the consensus of the expert panel on how best to adapt and endorse the recommendations in the “Prevention Guide: Safe Handling of Hazardous Drugs,” as well as the assessment and interpretation of the identified evidence.
APPLICABLE OCCUPATIONAL HEALTH AND SAFETY LEGISLATION
The overarching legislation that applies to all provincially governed workplaces is the Occupational Health and Safety Act (2). The goal is to achieve safe and healthy workplaces. The Act sets out the rights and duties of all parties in the workplace and establishes procedures for dealing with workplace hazards, including employers taking all reasonable measures necessary to protect workers from exposure to hazardous biological or chemical agents. A number of regulations under the Act also apply, including the Regulation for Health Care and Residential Facilities, the Needle Safety Regulation and the Control of Exposure to Biological or Chemical Agents Regulation.

Health care workplaces are required to comply with applicable provisions of the Occupational Health and Safety Act (OHSA), R.S.O. 1990, c.0.1 and its Regulations. Employers, supervisors and workers have rights, duties and obligations under the OHSA. To see what the specific requirements are under the OHSA go to: http://www.elaws.gov.on.ca/html/statutes/english/elaws_statutes_90o01_e.htm

A guide to the requirements of the Occupational Health and Safety Act may be found at: http://www.labour.gov.on.ca/english/hs/ohsaguide/index.html

Specific requirements for certain health care and residential facilities may be found in the Regulation for Health Care and Residential Facilities, which can be found at: http://www.elaws.gov.on.ca/html/regs/english/elaws_regs_930067_e.htm. Requirements for antineoplastic drugs are found in Section 97.

Requirements for the use of safety-engineered needles may be found in the Needle Safety Regulation which can be found at: http://www.elaws.gov.on.ca/html/regs/english/elaws_regs_070474_e.htm

Requirements for the Control of Exposure to Biological or Chemical Agents can be found at: http://www.elaws.gov.on.ca/html/regs/english/elaws_regs_900833_e.htm

HIERARCHY OF CONTROLS
“Controlling exposures to occupational hazards is the fundamental method of protecting workers,” as stated by The Centres for Disease Control and Prevention in the NIOSH Engineering Controls Program Portfolio. It describes the Hierarchy of Controls used to implement feasible and effective controls. In descending order, they are Elimination, Substitution, Engineering controls; Administrative controls and the use of Personal Protective Equipment. “Engineering controls are used to remove the hazard or place a barrier between the worker and the hazard (3).” In health care, examples of engineering controls include the use of biosafety cabinets and safety-engineered medical devices (SEMDs): particularly, safety-engineered needles help protect the worker from blood borne pathogen exposures. Administrative controls include policies and procedures and staff education and training. Although Personal Protective Equipment is the last control between the hazard and the worker, it really is the primary control on which we rely. It is very important that health care workers are educated in the appropriate selection and use of Personal Protective Equipment for protection against exposure to cytotoxic drugs. This usually consists of the use of gloves, gowns and eye protection as appropriate.
DEFINITION OF TERMS
Airlock: An enclosed space with two or more doors that is interposed between two or more rooms, usually of differing classes of cleanliness, for the purpose of controlling the airflow between those rooms when either people or goods need to enter or leave them (4).

Biological Monitoring: Biological monitoring is the systematic collection and analysis of a biological specimen for the presence of an indicator of exposure or response in the worker.

Biological Safety Cabinet (BSC): A ventilated containment cabinet with an inflow of air to protect the worker and a down-flow of HEPA-filtered air to protect the product. The exhaust is HEPA filtered to protect the environment.

**Class II, Type B1 Biological Safety Cabinets (5)**
- Hard-ducted through a dedicated duct exhausted to the atmosphere after passage through a HEPA filter; contain negative-pressure plena.
- Maintain a minimum average face velocity of 0.5 m/s (100 ft/min).
- Recirculate 30% of the air within the cabinet.
- Suitable for work with low levels of volatile toxic chemicals and trace amounts of radionuclides.

**Class II, Type B2 Biological Safety Cabinets (5)**
- Does not recirculate air within the cabinet.
- Maintain a minimum average face velocity of 0.5 m/s (100 ft/min).
- Hard-ducted through a dedicated duct exhausted to the atmosphere, 100% of cabinet air, after passage through a HEPA filter; contain negative-pressure plena.
- Suitable for work with volatile toxic chemicals and radionuclides.

The exhaust canopy must allow for proper Biological Safety Cabinet (BSC) certification. An alarm should be provided that is audible at the cabinet to indicate loss of exhaust flow from the building exhaust system. The cabinet internal fan should also be interlocked to shut down when the building exhaust system fan fails to prevent pressurization of the cabinet.

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 outside the system, and the escape of hazardous drug or vapour concentrations outside the system (6).

Cytotoxic: An agent that possesses a specific destructive action on certain cells or that may be genotoxic, oncogenic, mutagenic, teratogenic, or hazardous to cells in any way and includes most anti-cancer drugs (7).

Cytotoxic Waste: Any material that comes into contact with cytotoxic drugs during their storage, handling, preparation, administration and disposal (e.g., packaging material, protective equipment, preparation supplies (such as syringes, tubing, drug bags), soiled disposable incontinent briefs of patients who have received cytotoxic drugs during the previous 48 hours, hood prefilters and HEPA filters, etc.).

Extravasation: Passage or escape into tissue of (cytotoxic) drugs. Signs and symptoms may be sudden onset of localized pain at an injection site, sudden redness or extreme pallor at an
injection site, or loss of blood return in an IV needle. Tissue slough and necrosis may occur if the condition is severe. Treatment depends on the causative agent.

**HEPA Filter**: High-efficiency particulate air filter. A type of filter that is composed of a mat of dense fibres arranged in folds, designed according to trap at least 99.97% of airborne particles measuring 0.3 microns in diameter.

**Leak**: Refers to fluid that escapes from a medication delivery system or container such as IV tubing, medication port, or connection.

**Packaging**:
- External packaging = outer cardboard box or shrink-wrap.
- Secondary packaging = manufacturer’s cardboard box. It directly contains the vials.
- Primary packaging = the vials.

**Spill**: Refers to a significant amount of escaped liquid or powder that requires control and containment to avoid further exposure.

**RECOMMENDATIONS**

In the recommendations that follow, the following action verbs are used to help the intended user determine the level of variation one might expect from following that recommendation. These are:

- **Legislation/regulation requires** - A recommendation that is supported by law, regulation or standard. All centres and users would be expected to implement this recommendation with little variation.

- **Strongly recommend** - A recommended course of action or practice based on evidence in the medical literature and/or a strong consensus of the expert panel. Variation from this course of action or practice should be based on a considered judgment of how the local circumstances may vary from those typically found in practice.

- **Recommend** - A course of action or practice which, in the consensus of the expert panel, is sound and worth considering, but whose implementation may vary according to local circumstances.

**RECOMMENDATION 1: GENERAL MEASURES**

**Committee Responsible for Policy and Procedures for Cytotoxic Drugs**
It is strongly recommended that all institutions administering cytotoxic drugs form such a committee. It is also strongly recommended that this committee include, but not be limited to, representatives from various departments and services such as: occupational health and safety, joint health and safety committee, pharmacy, nursing, medical oncology (physician), environmental services and risk management.

This committee would be responsible for clear processes of developing, reviewing and revising policies and procedures related to cytotoxic drugs. In addition, this committee is responsible to ensure that there is a process in place for orientation and ongoing education for the identified target population.
This committee is responsible for implementation and follow-up of the Risk Prevention Management Program related to the use of cytotoxic drugs.

**Continuing Education and Orientation Program**

It is legislated that initial and ongoing hospital-approved education be provided to all staff involved with cytotoxic drugs throughout the medication circuit including safe handling and spill or leak management (8). It is strongly recommended that all staff have initial and ongoing training to best practice standards in place at the time.

It is legislated that there is documentation that annual training of safe handling of cytotoxic drugs has occurred (8).

**Identification and Safety**

It is strongly recommended that each institution maintain a list of cytotoxic drugs.

It is legislated that Cytotoxic drugs and their waste be properly identified with the symbol capital “C” and, under it, the words “CYTOTOXIC/CYTOTOXIQUE” in capital letters (9, 10). It is legislated that all cytotoxic waste under the Ministry of Environment regulation (guideline C4) include bilingual wording and both the words and the symbol appear on a dark grey rectangle (9, 10).

**Purchasing of Drugs**

When purchasing cytotoxic drugs, it is strongly recommended that institutions consider vendors that include safe handling measures such as pre-wiped or protective containers, or smaller receptacles to decrease volume of potential spills.

**Spills Kit**

It is strongly recommended that a spill-management kit be available in all areas where cytotoxic drugs are stored, transported, handled and administered.

**Precautionary Reassignment**

It is strongly recommended that all staff be fully informed of the potential reproductive hazards of cytotoxic drugs (11). It is strongly recommended that the facility consider alternative duties for women who are pregnant or breast feeding.

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**RECOMMENDATION 2: PERSONAL PROTECTIVE EQUIPMENT (PPE)**

It is legislated that a worker work in compliance with the Occupational Health and Safety Act and regulations and use or wear the equipment, protective devices or clothing that the
employer requires to be used (2).

It is legislated that the appropriate personal protective equipment for the task (as described in Table 1) be worn throughout the medication circuit (2). It is the employer’s responsibility to provide the necessary protective equipment and training on how to use the equipment.

**Gloves**
The gloves used to handle cytotoxic drugs are strongly recommended to comply with ASTM standard D-6978-(05)-13 and be powder free (12). Gloves are recommended to be nitrile, polyurethane, neoprene or latex (12). Latex is a known allergen, therefore it is strongly recommended that this be taken into consideration for glove selection. It is strongly recommended that vinyl gloves not be used. It is strongly recommended that the frequency of glove changes be adjusted according to the level of exposure at each step in the medication circuit. For example, when administering reconstituted medications, it is strongly recommended that workers change gloves immediately if torn, punctured, or visibly contaminated with a cytotoxic drug, and to ensure following Routine Practices (13). It is strongly recommended that great care be taken in the removal of gloves to not contaminate the skin. When two pairs of gloves are required, put on the first pair before putting on the gown. See Appendix F for the donning and doffing of one pair of gloves and Appendix G for the donning and doffing of two pairs of gloves.

**Gown**
It is strongly recommended that the gowns used for handling cytotoxic drugs be disposable, made of lint-free, low-permeability fabric, have long sleeves with tight-fitting cuffs and fasten in the back. Gowns need to be changed in the event of contamination, spillage, rips, and at the end of the procedure. For medication preparation, gowns need to be changed halfway through a shift or every 3.5 hours (14). It is strongly recommended that the supplier be able to certify that the gown protects against cytotoxic drugs.

It is strongly recommended that care be taken to avoid contamination of the hands by avoiding touching the outside of the gown when removing the gown.

**Facial Protection**
Surgical/procedure masks are required while handling and preparing medications in a biological safety cabinet and, in this instance, are worn to prevent microbial contamination of the sterile field.

It is strongly recommended that full-facial protection be worn whenever there is a risk of splashing (e.g., during certain drug administration procedures). The use of a full-facial shield is preferred. If goggles are used, they need to be worn in conjunction with a fluid-resistant mask. For further information, see *CSA standard Z94.3-07 - Eye and Face Protectors* (15).

**Respiratory Protection Apparatus (RPA)**
It is strongly recommended that fit-tested respirators such as NIOSH certified N95 or N100 be used when there is a risk that airborne powder or aerosol will be generated. It is legislated that respirators be used in accordance with a respiratory protection program such as that outlined in *CSA Standard Z94.4-11 “Selection, Use and Care of Respirators”* (16).
Caps are only required in the sterile preparation room and are worn to prevent microbial contamination of the sterile field.

**Shoe Covers**
Disposable shoe covers are worn to prevent contamination of the health care workers shoes, and it is strongly recommended that they be worn when in the sterile preparation room or in the event of a spill. It is strongly recommended that shoe covers be removed immediately when leaving the sterile prep room to avoid contamination of other areas.

### Table 1. Personal Protective Equipment to be worn throughout the medication circuit.

<table>
<thead>
<tr>
<th>Medication circuit steps</th>
<th>Gloves</th>
<th>Gown</th>
<th>RPA</th>
<th>Face protection</th>
<th>Cap</th>
<th>Shoe covers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unpacking and cleaning</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(2 pairs)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sterile preparations</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>(2 pairs)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-sterile preparations:</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>- Counting of solid oral forms</td>
<td>(1 pair)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Preparing creams, ointments, oral solutions and crushing tablets</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Routes of administration (intravenous, subcutaneous, intramuscular, intravesical, intraperitoneal, intrathecal, liquid oral)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>(1 pair)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solid oral administration (tablets)*</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>(1 pair)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Topical administration (creams, ointments)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>(2 pairs)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aerosolized administration (e.g., ribavirin, pentamidine)*</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>(1 pair)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient care</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>(1 pair)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Management of extravasation</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>(1 pair)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Handling of</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>
### Medication Circuit Steps

<table>
<thead>
<tr>
<th>Steps</th>
<th>Gloves</th>
<th>Gown</th>
<th>RPA</th>
<th>Face Protection</th>
<th>Cap</th>
<th>Shoe Covers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contaminated bedding on the wards</td>
<td>(1 pair)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Waste management (collection and transport)</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Spill or damaged or broken container</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓ (if suspicion of powder or aerosolization is generated)</td>
<td>✓</td>
<td>✓ (if on the floor)</td>
</tr>
<tr>
<td>Cleaning of sterile preparation room and airlock</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Cleaning of preparation cabinets (hoods)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Cleaning of other oncology pharmacy rooms and care units/clinics</td>
<td>✓ (1 pair)</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* NG = nasal gastric tube, G = gastric tube, J = jejunostomy tube.

* Although the risk of contamination with oral medications is minimal, the working group believes that consistency of practice for any handling of cytotoxic drugs is of primary importance, and the preference is to wear a standard chemotherapy glove.

† Although cytotoxic, they are not neoplastic.

### RECOMMENDATION 3: RECEIVING AND TRANSPORT

**Handling Cytotoxic Drug Delivery Containers**

It is strongly recommended that all receiving-dock workers receive training in the proper handling of cytotoxic drugs. It is strongly recommended that the receiving-dock workers check the integrity of the external packaging upon receipt; in the event of breakage or a damaged parcel likely to cause a spill, apply the Spill Protocol from your institution.

It is strongly recommended that delivery containers be taken immediately to the Pharmacy Department by the receiving-dock workers or the distributor.

It is strongly recommended that the receiving-dock or storeroom workers not open the delivery containers. It is strongly recommended that the delivery containers be handled with care to avoid breakage of the cytotoxic drug containers and not be left unattended in a corridor. Only trained workers (e.g., pharmacy technicians) are to proceed with the unpacking and subsequent steps.

**Damaged Containers/Spill**

It is strongly recommended that damaged containers be handled like spills. It is strongly recommended that the manufacturer or distributor be notified if the container is received in a damaged state. To limit exposure, it is strongly recommended that a damaged container never be returned to the manufacturer or distributor. Notify the pharmacy if any damaged containers are suspected.
RECOMMENDATION 4: UNPACKING AND STORAGE

Packaging can have high levels of contamination. It is strongly recommended that there be an unpacking area in the pharmacy limiting exposure risks. It is strongly recommended that the unpacking area be a separate dedicated space, separate from eating areas, preferably a separate room. It is regulated that there be adequate ventilation in the area, negative pressure and preferably vented to the outside (17). It is strongly recommended that there be a receptacle for cytotoxic waste in the unpacking area, for the disposal of secondary packaging (8, 18).

It is strongly recommended that workers at risk of exposure wear a protective gown and two (2) pairs of gloves when unpacking and cleaning cytotoxic drugs, from the opening of the external packaging to the placing of the secondary and/or primary packaging in their storage space. It is strongly recommended that workers check the integrity of all packaging at every step of the unpacking process. In the event of breakage or leaking, it is strongly recommended that the damaged contents be treated as a spill. It is strongly recommended that the primary and or secondary packaging be cleaned prior to being placed in storage.

It is strongly recommended that a regular cleaning protocol be in place either at this stage or prior to storage in the clean room. It is strongly recommended that all drug containers be cleaned to reduce external contamination. An example is the use of pre-moistened towelettes. It is important to ensure that the procedure does not damage the container or interfere with the reading of the label. It is also important to ensure than any product that is used will not further contaminate. However, it is strongly recommended that this procedure not increase the risk of incidents/accidents due to damage to the cytotoxic drug container or label.

It is strongly recommended that procedures be in place to minimize the risk of contamination of surfaces during the cleaning of vials (e.g., use of a disposable, plastic-backed, absorbent pad). It is strongly recommended that all surfaces be cleaned when the task is complete.

Establish a dedicated negative-pressure storage area for cytotoxic drugs that minimizes the risk of contamination (17).

When removing or transporting drugs out of the storage area, it is strongly recommended that one pair of gloves and a gown be worn.

RECOMMENDATION 5: CYOTOXIC DRUG PREPARATION

Planning the Oncology Pharmacy

It is strongly recommended that the oncology pharmacy be in compliance with relevant guidelines from the Canadian Society of Hospital Pharmacists (CSHP) and Accreditation Canada standards. While the specific details of oncology pharmacy planning is beyond the scope of this document, details and some important considerations may be found in the Canadian Standard Association document CSA Z8000-11 (19).

It is strongly recommended that special requirements for heating, ventilation and air-conditioning (HVAC) systems in health care facilities be taken into consideration (18).
A class II type B biological safety cabinet is required with preference for the type B2, because it ensures that there is no recirculation of air within the cabinet (5).

There is emerging evidence suggesting some robotic devices that prepare cytotoxics improve the accuracy of medication preparation and reduce potentially harmful staff safety events. Further studies are required to establish the cost effectiveness of these robotic implementations. Each health care facility will need to assess the need for such devices in their environment (20).

It is strongly recommended that all mixing, and preparation of administration sets with a cytotoxic drug be performed in one centralized area in a specially designated class II type B biological safety cabinet that (18):

(a) is exhausted through a HEPA filter to the outside atmosphere in a manner that prevents recirculation into any inside area;

(b) has exhaust and ventilation systems that remain in operation for a sufficient period of time to ensure that no contaminants escape from the biological safety cabinet into the workplace; and

(c) is equipped with a continuous monitoring device to permit confirmation of adequate airflow and cabinet performance.

It is recommended that airlocks be considered if there are particular concerns about the propagation of airborne cytotoxic drugs.

It is strongly recommended that priming of administration sets be prepared in the manner mentioned above.

It is strongly recommended that the layout allow and facilitate the unimpeded cleaning of all surfaces (walls, floors, ceilings, doors, diffusers, windows). It is strongly recommended that the furniture and equipment in the sterile preparation room be kept to a bare minimum. It is strongly recommended that there be a visual link, for example, a window and a way to communicate between the sterile preparation room and the pharmacy, in order to view the work in progress. It is strongly recommended that access to the sterile room be limited to trained and authorized workers.

Limit worker traffic, particularly near unpacking and storage areas (to avoid accidental breakage) and near preparation cabinets (to avoid interfering with their proper operation).

It is legislated that the facilities include an emergency eyewash that may or may not be hooked up to the airlock sink (2). As a minimum, it is strongly recommended that emergency eyewash be able to provide 15 minutes of flushing to both eyes (21). It is strongly recommended that a full shower be accessible nearby (e.g., in the oncology units/clinics).

Closed-drug transfer systems (e.g., PhaSeal®) are not a substitute for class II type B biological safety cabinets. There is evidence from studies (22-27) that closed-drug transfer-systems can reduce contamination during preparation. Further emerging evidence suggests that when these devices are not used as specified, they could become open to the environment. Further research is needed to evaluate this possibility.
It is strongly recommended that the biological safety cabinets remain in operation 24 hours a day, 7 days a week, as recommended by the manufacturers.

In the non-sterile drug preparation process (e.g., oral preparations), it is strongly recommended that the same level of worker protection be adhered to.

**Pharmacy Policies and Procedures**
Establish policies and procedures regarding preventive maintenance, monitoring, certification and the optimal use of facilities and equipment (28).

### RECOMMENDATION 6: DRUG PREPARATION

The following recommendations apply to the preparation of all cytotoxic medications including parenteral, oral and topical, both sterile and non-sterile preparations. It is strongly recommended that policies and procedures include the use of appropriate personal protective equipment, the equipment for preparation including appropriate ventilation, and other automated equipment for packaging and a dedicated work area.

**Personal Protective Equipment**
It is strongly recommended that workers (pharmacists or pharmacy technicians) wear a cap, surgical/procedure mask, shoe covers, a protective gown and two (2) pairs of gloves (see Table 1) to make sterile preparations of cytotoxic drugs in preparation cabinets.

**Organization of the Work**
Organize the work to limit microbial and environmental contamination.

For both sterile and non-sterile preparations, it is strongly recommended that workers cover the work surface with a disposable, absorbent, sterile, plastic-backed pad to absorb any liquid contamination that may occur during handling. It is strongly recommended that the pad not cover the front and rear grilles of the preparation cabinet. It is strongly recommended that it be changed after 3.5 hours of continuous work or for a new batch of preparations (e.g., a set of vials of a given drug) or in the event of a spill or contamination. It is legislated that the pad be disposed of in a cytotoxic waste receptacle (10).

Limit the quantity of supplies and cytotoxic drugs in the cabinet, to avoid adversely affecting the laminar flow and to facilitate regular cleaning of the work surface; place the sterile products in the centre and the non-sterile products (e.g., waste receptacle) along the sides of the cabinet.

**Removal of Packaging**
Remove the packaging, when applicable, and clean all of the drug containers before taking them into the preparation cabinet. For sterile preparations, adhere to aseptic technique for sterility.

**Handling Techniques**
Use handling techniques that limit the risk of injury or accidental exposure.

It is strongly recommended that spiking of bags and priming of tubing occur before the addition of the cytotoxic drug unless the clinical protocol requires otherwise.
Preparation, Priming and Removing Air from the Tubing
It is strongly recommended that cytotoxic drugs be reconstituted in the pharmacy environment as described above. It is strongly recommended that the drug containers not be overfilled to avoid compromising the integrity of the container. It is strongly recommended that the techniques used for priming and removal of air minimize the exposure risks. It is strongly recommended that air never be removed from the IV tubing with a solution containing the drug. It is strongly recommended that IV tubing is primed and air removed in the pharmacy, prior to adding the cytotoxic drug(s) to the infusion solution. Glass containers are not recommended due to increased risk of breakage and exposure.

Labeling and final packaging
It is legislated that cytotoxic drugs be labeled to inform those handling these preparations of the nature of the drugs and the precautions to be taken. It is legislated that cytotoxic drugs display the “Cytotoxic” hazard symbol or the word “Cytotoxic” (9, 10).

It is strongly recommended that the outside surface of the cytotoxic drug containers (e.g., syringes, infusion bags, tubing) in the preparation cabinet be cleaned in the cabinet.

Place each cytotoxic drug container (e.g., syringe, bag), as well as the administration supplies (e.g., tubing), in a clear, leak-proof plastic bag (e.g., Ziploc® type) to facilitate identification by the nurse without having to remove the container from the bag.

Following final verification, it is strongly recommended that the plastic bags containing the cytotoxic drugs be placed in a rigid transport container (ideally opaque), properly identified with the “Cytotoxic” hazard symbol.

Waste
It is strongly recommended that everything that comes out of the cabinet be wiped clean.

It is strongly recommended that all contaminated waste be disposed of in the chemotherapy waste stream.

RECOMMENDATION 7: TRANSPORT AND STORAGE FOLLOWING PREPARATION

On-site Transport of Cytotoxic Drugs
Transport cytotoxic drugs using a method that will prevent contamination of the environment in the event of breakage.

It is strongly recommended that cytotoxic drugs be placed in a closed, leak-proof plastic bag (e.g., Ziploc® type).

It is strongly recommended that transport of the cytotoxic drug in a closed, leak-proof plastic bag from the pharmacy to an area not adjacent to the preparation area (e.g., care unit, outpatient clinic), be done in a rigid, shock-resistant, leak-proof container made of a material that can be easily cleaned and decontaminated in the event of a drug leak. It is strongly recommended that the bottom be covered with an absorbent, plastic-backed cloth.

It is legislated that the transport container be identified with the “Cytotoxic” hazard symbol and be cleaned regularly (9, 10).

It is strongly recommended that mechanical transport systems, such as pneumatic tubes, not be used because of the stress they put on the contents, and the whole transport system would be compromised if a leak occurred.
It is strongly recommended that prepared medications be stored in a designated area prior to administration. It is strongly recommended that this area be cleaned regularly.

**Off-site Shipping and Transport of Cytotoxic Drugs**
Establish policies and procedures regarding the shipping of cytotoxic drugs (29).

In the event that cytotoxic drugs are shipped off-site (e.g., from one institution to another), it is strongly recommended that they be packed separately from other drugs, according to the recommendations from the manufacturer and distributor. It is strongly recommended that pharmacy be consulted in the packaging of cytotoxic drugs.

It is strongly recommended that Cytotoxic drugs be packed in a double plastic bag and placed in a box that is properly identified with the "Cytotoxic" hazard symbol. If necessary, immobilize the drug with packing material (30). It is legislated that the "Cytotoxic" hazard symbol be visible on the outside of the delivery container (30). It is strongly recommended that reusable delivery containers be cleaned regularly.

Ensure that the courier company will handle cytotoxic drugs.

**RECOMMENDATION 8: DRUG ADMINISTRATION**

It is strongly recommended that safe handling and administration techniques be used to minimize possible exposure to individuals and the environment when administering cytotoxic drugs.

- It is legislated that appropriate personal protective equipment be made available to all healthcare workers and be worn as prescribed by the employer, please refer to Table 1 (2).
- It is strongly recommended that Luer-Lock connectors and needleless administration systems be used to administer any intravenous medications.
- Closed systems may offer additional protection.
- It is strongly recommended that disposable plastic-backed absorbent pads be used over work surfaces and placed under tubing or bag connections and ports when attaching any tubing, bag or syringe that have been exposed to a cytotoxic drug.
- Unless a closed system is used, never disconnect tubing from cytotoxic drug bags. Discard bag with attached tubing into an appropriate waste container as a single unit.
- It is legislated that safety engineered needles be used as per Needle Safety Regulation 474/07 made under the Occupation Health and Safety Act Labour, 2010 (31). Do not purge air from the needle before administration.
- It is strongly recommended that oral cytotoxics be handled in a manner that avoids skin contact, liberation of aerosols or powdered medicine into the air, and cross-contamination with other medicines (32).
- It is strongly recommended that solid oral preparations (tablets) of cytotoxic drugs be crushed or cut within the biological safety cabinet. If patients are unable to take in the solid format, it is strongly recommended that the pharmacy provide these drugs in an oral syringe, in a ready-to-administer, liquid oral form.
- It is strongly recommended that application of topical cytotoxic drugs be done using appropriate personal protective equipment and in a way that prevents contamination of the environment. Between applications, it is strongly recommended that the cytotoxic
medication (i.e., tube or jar) be kept in a safe container (i.e., Ziploc) and in a secure place that prevents contamination of the surrounding environment.

- With any intravesical administration, e.g., bladder instillation, ensure there are detailed procedures in place to avoid risks of splashing.
- Use caution when administering intrathecal cytotoxic drugs, as there is risk of splashing due to increased intrathecal pressures.

**RECOMMENDATION 9: HOME CARE**

**Home Care of Patients who Have Received Cytotoxic Drugs**

It is strongly recommended that all cytotoxic drugs preparations be compounded in pharmacies meeting the requirements for cytotoxic drug preparation.

It is strongly recommended that cytotoxic drugs be transported, administered and disposed of by individuals who have received appropriate training. It is strongly recommended that cytotoxic drug transport containers are not reused by patients for domestic purposes, which may expose the family to cytotoxic drugs (e.g., toy box, sewing basket, etc.).

It is legislated that the health care provider who administers cytotoxic drugs in the home wear Personal Protective Equipment as outlined in Table 1 (2).

It is strongly recommended that health care providers follow the same recommendations outlined in Recommendation 8 - Drug Administration.

It is strongly recommended that a spill kit be readily available in the home in case of accidental spills.

It is strongly recommended that patients be informed of and be provided with written instructions for the safe handling of cytotoxic drugs.

It is strongly recommended that contact information be provided for home care patients who require assistance with safe handling of cytotoxics.

**Cytotoxic Drug Waste in the Home**

It is strongly recommended that the institution have a clear process to address the issue of cytotoxic waste from patients in their homes, in compliance with municipal or local cytotoxic waste rules. It is strongly recommended that this process include patient and caregiver education.

It is strongly recommended that caregiving staff provide the patients/caregivers involved in administering cytotoxic drugs in the home with a process for appropriate disposal of cytotoxic waste, including left-over drugs.

**RECOMMENDATION 10: MANAGEMENT OF WASTE**

**Bodily-Fluid Waste**

It is strongly recommended that workers who handle the biological fluids, excreta, contaminated bedding and soiled equipment of patients who have received cytotoxic drugs wear one (1) pair of gloves and a protective gown. It is strongly recommended that face protection be worn when there is a risk of splashing.
**Cytotoxic Drug Waste**

Establish policies and procedures as per provincial legislation regarding cytotoxic waste management.

The term “cytotoxic waste” includes any material that comes into contact with cytotoxic drugs during their storage, handling, preparation, administration and disposal (e.g., packaging material, protective equipment, preparation supplies, such as syringes, tubing, drug bags), soiled disposable incontinent briefs of patients who have received cytotoxic drugs during the previous 48 hours or longer depending on the drug [e.g., it is known that cyclophosphamide may persist for several days], hood pre-filters and HEPA filters, etc.).

It is legislated that cytotoxic waste be placed in a waste container clearly identified with the “Cytotoxic” hazard symbol. It is legislated that cytotoxic waste be disposed of in the appropriate containers (10).

It is legislated that sharps be placed in rigid containers with a leak proof lid; CSA standard Z316.6-07 specifies the use of the colour red for the rigid containers (33). If the containers are another colour, follow the instructions of the company ensuring the final disposal (10).

It is strongly recommended that other waste (soft items, such as tubing, protective equipment, etc.) be placed in leak-proof and tear-resistant containers, identified with the “Cytotoxic” hazard symbol.

For final disposal outside the institution, it is legislated that all cytotoxic waste be in a rigid, leak proof, container identified with the “Cytotoxic” hazard symbol and scheduled for transport outside the institution (10).

It is legislated that any excess fluid from cytotoxic drugs (e.g., drug loss) be disposed of in a sealed container and placed in a rigid container, the bottom of which is to be covered with an absorbent pad. This rigid container will be handled like other cytotoxic waste (10).

It is recommended that disposable/incontinent briefs soiled by patients who have received cytotoxic drugs be placed in a cytotoxic waste container.

It is legislated that cytotoxic waste be incinerated at a high temperature (i.e., 800°C to 1200°C, depending on the product) (10).

It is legislated that cytotoxic waste not be disposed of in the receptacles used for infectious biomedical waste (which may be autoclaved and then sent to a landfill site) (10).

It is legislated that every area where cytotoxic drugs are handled will have an appropriate cytotoxic waste receptacle as close as possible to the work area (10).

The lids of cytotoxic drug receptacles must remain closed, except when depositing waste. Bins with foot pedals and lids, which lock automatically when full, are recommended to minimize exposure.

It is strongly recommended that workers be careful to avoid contaminating the outside of the receptacle when depositing waste.
It is legislated that the transport of cytotoxic waste receptacles be assigned to properly trained workers (2).

It is strongly recommended that workers who handle cytotoxic waste receptacles wear one pair of disposable gloves and have a spill kit at their disposal. It is strongly recommended that the waste go through as few care units, public areas and areas containing food or linens as possible.

It is legislated that the final storage areas for cytotoxic waste receptacles be secure. Refer to Ontario storage requirements (9, 10).

**RECOMMENDATION 11: ACCIDENTAL EXPOSURE**

Be aware of any mandatory reporting requirements under the Occupational Health and Safety ACT and report requirements to WSIB (2).

Establish policies and procedures regarding accidental worker exposure.

If a cytotoxic drug accidentally comes into contact with a worker’s skin or clothing, it is strongly recommended that the worker immediately remove the contaminated clothing and thoroughly wash the skin of the affected area with soap and water and continue to rinse for 15 minutes. If appropriate, it is strongly recommended that the contaminated worker take a shower. It is strongly recommended that a deluge shower be made available in the vicinity (e.g., in the oncology clinics/units). It is strongly recommended that all contaminated clothing be discarded in cytotoxic waste.

If a cytotoxic drug comes into contact with a worker’s eyes, it is strongly recommended that the worker flush their eyes at an eye wash station. Alternatively, it is recommended that the workers use an isotonic solution to flush their eyes (e.g., sterile NaCl 0.9%). It is strongly recommended that eyes be flushed for at least 15 minutes (21). It is strongly recommended that if contact lenses are worn, they be removed immediately prior to flushing.

In the event of a needlestick or sharps injury, let the wound bleed freely. Under running water, gently and thoroughly wash the area with soap. Contact Occupational Health. Ensure that facility policies for needlestick or sharps injury are followed including completion of an incident report and reporting to WSIB if indicated.

**RECOMMENDATION 12: SPILLS MANAGEMENT**

It is strongly recommended that the facility develop policies and procedures for spills management that take into account the types of spills (i.e., amount, location, concentration, powder vs. liquid, etc.). It is strongly recommended that a spill management kit be readily available within the work area.

It is legislated that items from the clean-up of spills be placed in the cytotoxic waste receptacle (10).

Most spills can be contained and managed by the trained health care worker (e.g., leaking IV
tubing).

When a spill is not contained or easily managed (e.g., exposure to large volume of fluid that is a risk to the environment or a large crate of vials filled with powder broken in the receiving area), it is strongly recommended that a Code Brown or equivalent be called.

**RECOMMENDATION 13: ENVIRONMENTAL CLEANING**

Establish environmental cleaning policies and procedures for all surfaces where contact with cytotoxic drugs may occur. Examples may include: unpacking and storage, preparation, administration and disposal areas. Pharmacy counters are among the most contaminated surfaces.

It is strongly recommended that cleaning of the biological safety cabinets be performed by trained personnel following manufacturer’s guidelines (34).

**Use of Pumps to Administer Cytotoxic Drugs**

Make sure there is an appropriate policy to clean and inspect the equipment between uses.

**Laundry**

Ensure the facility complies with the Occupational Health and Safety Act - Ontario Regulation for Health Care and Residential Facilities (8).

**RECOMMENDATION 14: MEDICAL SURVEILLANCE AND ENVIRONMENTAL MONITORING**

**Medical Surveillance**

Methods used to investigate potential health effects of exposure to cytotoxic drugs are inconclusive and difficult to interpret. The ideal test should meet several requirements — it should be sensitive, specific, quantitative, rapid, and reproducible. Importantly, the procedures for taking a sample should be non-invasive and should not cause unnecessary duress or anxiety to the individual. Unfortunately, there is currently no suitable test to meet these requirements. As a consequence, there is conflicting information and opinion about the value of routine biological monitoring for employees handling cytotoxic drugs.

Employers do have a responsibility to ensure that they remain aware of and apply any future developments for monitoring the health of employees in the handling of cytotoxic drugs.

The panel supports further research to determine if there are adverse health effects that result from exposure to cytotoxic drugs.

Adherence to agreed standard operating procedures with sufficient initial and regular ongoing training in safe handling/administration is paramount to reducing potential for exposure and risk.

There is evidence in the literature of a higher rate of spontaneous abortion among women working in roles that expose them to cytotoxic drugs (35, 36). There are no other identified medical conditions known to result from chronic exposure of health care workers to cytotoxic drugs, no exposure limits set for cytotoxic drugs, and no standards for interpretation of test results of exposed health care workers to enable meaningful interpretation or action based on biological monitoring results.
Environmental Monitoring
It is recommended that the facility consider implementing an environmental monitoring program. Surface testing would audit contamination of the environment (e.g., pharmacy counters, patient bedside tables) and provide a quality indicator of cleaning effectiveness and adherence to recommended work practices.
REFERENCES


RELATED GUIDELINES


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Evidence-Based Series #16-3 Version 2: Section 2

A Quality Initiative of the Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

Safe Handling of Cytotoxics: Evidentiary Base


The 2013 guideline recommendations

REQUIRE UPDATING

This means that the recommendations require additional evidence but are still relevant for decision-making.

Report Date: December 16, 2013

INTRODUCTION

As described in Section 3 of this document, the Safe Handling of Cytotoxics Expert Panel chose the “Prevention Guide: Safe Handling of Hazardous Drugs,” developed by the Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS), and the Institut de recherche Robert-Sauvé en santé et en sécurité du travail (IRSSST) (1), as the basis for creating an Ontario guideline on safe handling of cytotoxics. As part of the adaptation/endorsement process, the working group determined that there were three areas where the evidence base found in the “Prevention Guide: Safe Handling of Hazardous Drugs” was insufficient to fully inform the necessary recommendations. These areas were:

- Closed-system transfer devices,
- pregnancy outcomes in healthcare workers who handle cytotoxic drugs, and
- general health outcomes in health care workers who handle cytotoxics.

All of these areas had been reviewed in the 2006 Ontario guideline, and the working group believed that it was necessary to update the evidence in these three areas to fully support the adaptation/endorsement process of the “Prevention Guide: Safe Handling of Hazardous Drugs.” Therefore, the working group conducted a systematic review of the medical literature in these three areas.

QUESTIONS

1. Do closed-system transfer devices reduce contamination when used to prepare chemotherapy?
2. What are the risks in pregnancy for women health care workers who work or have worked with cytotoxic agents?
3. Are there any adverse health outcomes for health care workers who handle cytotoxics?

METHODS
This evidentiary base was developed using a planned two-stage method, summarized here and described in more detail below:

1. Search for and evaluation of existing guidelines. If one or more existing guidelines are identified that address the research questions and are of reasonable quality, then those guidelines will form the core of the evidentiary base.
2. Systematic review of the primary literature focusing on those areas not covered by existing and accepted guidelines.

The PEBC is supported by the Ontario Ministry of Health and Long-Term Care. All work produced by the PEBC and any associated Programs is editorially independent from the Ministry.

Search for Existing Systematic Reviews
Systematic reviews for the safe handling of cytotoxics were searched for using MEDLINE, EMBASE and the Cochrane Database of Systematic reviews (2006 to September 2011).
Identified systematic reviews that required further consideration based on the criteria above would be assessed using the AMSTAR tool (2). The results of the AMSTAR assessment would be used to determine whether or not an existing review could be incorporated as part of the evidentiary base.

Any identified reviews that did not meet the criteria above, whose AMSTAR assessment indicated important deficiencies in quality, or that were otherwise not incorporated as part of the evidence base would be reported in the reference list, but not further described or discussed.

Primary Literature Systematic Review
Assuming that no existing systematic reviews were identified, or that identified guidelines were incomplete in some fashion, a systematic review of the primary literature was also planned. This review would be reduced in scope, such as a reduction in subject areas covered, time frames covered, etc., based on the scope of incorporated existing reviews. The criteria described below are written assuming no existing reviews would be incorporated.

Literature Search Strategy
As the 2006 Ontario Guideline had already addressed the three topic areas, the new search was limited to articles published from 2007 onward. The MEDLINE (2007 to November 2012), EMBASE (2007 to December 2013), and Cochrane Library (2013, Issue 3) databases were searched for technology assessments, systematic reviews, clinical trials and studies investigating the safe handling of cytotoxics. Reference lists of papers and review articles were scanned for additional citations. Search terms indicative of cytotoxic drugs were used. The full search strategy is available in Appendix A.

Study Selection Criteria and Protocol
Inclusion Criteria
1) Technology assessments, systematic reviews, clinical trials and studies investigating the safe handling of cytotoxics.

Exclusion Criteria
1) Review articles
2) Letters and editorials that reported clinical trial outcomes.

One author did a review of the titles and abstracts that resulted from the search. For those items that warranted full-text review, one author reviewed each item in collaboration with the working group.

Data Extraction and Assessment of Study Quality and Potential for Bias
Data extraction was done independently by NC. An audit of the extracted data was conducted by staff at the PEBC. Ratios, including hazard ratios, were expressed with a ratio <1.0 indicating that subjects exposed to the intervention experienced a lower probability of an event compared to the control. All extracted data and information were audited by an independent auditor.

Important quality features, such as potential bias by study sponsor, for each study were extracted.

Synthesizing the Evidence
When clinically homogenous results from two or more trials were available, a meta-analysis would be conducted using the Review Manager software (RevMan 5.1) provided by the Cochrane Collaboration (3). For time-to-event outcomes, hazard ratios (HRs), rather than the number of events at a certain time point, would be the preferred statistic for meta-analysis, and would be used as reported. If the HR and/or its standard error were not reported, they would be derived from other information reported in the study, if possible, using the methods described by Parmar et al (4). For all outcomes, the generic inverse variance model with random effects, or other appropriate random effects models in RevMan would be used.

Statistical heterogeneity would be calculated using the $X^2$ test for heterogeneity and the $I^2$ percentage. A probability level for the $X^2$ statistic less than or equal to 10% ($p \leq 0.10$) and/or an $I^2$ greater than 50% would be considered indicative of statistical heterogeneity.

RESULTS

Primary Literature Systematic Review
Three searches for primary literature were done due to incompleteness of the subject area in the Quebec guideline, as described above. Articles were selected for consideration in this systematic review if they were published technology assessments, systematic reviews, clinical trials or studies. As the 2006 version of the guideline included the same three literature searches, the updated literature searches only included studies published since the 2006 searches.

The literature search for closed-system transfer devices yielded 808 results. Fifty-four of the documents were chosen for full-text review and 16 met the inclusion criteria for the systematic review. The literature search on pregnancy outcomes on health care workers yielded 27 articles, of which 2 were relevant. The literature search on general health outcomes yielded 83 articles, and 1 of them was relevant.

Study Design and Quality
The working group was aware a priori that the quality of the literature would be poor. Due to the nature of the topics, no randomized clinical trials can be performed for ethical reasons. The literature consisted of before and after studies and technical reports. Reports from professional associations such as NIOSH (The National Institute for Occupational Health and Safety) were not considered evidenced based without references to studies.
Outcomes
Closed-System Handling Devices

Fifty-four of 808 documents on closed-system transfer devices had a full-text review. Of these, 16 met the inclusion criteria. The results of these documents can be seen in Table 1. In nine of these studies, authors declared no conflict of interest (5-10, 13, 14, 19). The other seven studies had authors who were affiliated with the device manufacturer (11, 12, 15-18, 20).

The 2006 version of this guideline found seven studies of closed systems (21). These studies measured surface contamination, and two measured cytotoxics in the urine of pharmacy staff. These studies were descriptive in nature, and while five of the studies compared open and closed systems, none were designed to evaluate differences between groups. No studies were randomized or included statistical analysis of the results (21). In summary, there were no data to support or refute the value of closed systems.

In the current version of this guideline, 14 documents reviewed the PhaSeal system. Eight studies reviewed the PhaSeal system in isolation (7, 8, 11-15, 18) and six studies compared the PhaSeal system to other systems (5, 10, 16, 17, 19, 20). One study reviewed the Tevadaptor system alone (9), and one study examined the EquaShield (5). The quality of these studies was not high, as most were observational studies, and there were not randomized trials. The one multi-centre trial only assessed product sterility (15). The other five studies examined areas such as microbacterial contamination and validation to NIOSH and ISOPP standards, and they will not be discussed any further (15-18, 20). Ten studies examined levels of contamination after the use of a closed system (5, 7-14, 19). One study examined leakages in three devices (6). The study by Nygren (9) examined the Tevadaptor system. While this system showed a reduction in spills, this is not a true closed system according to the NIOSH 2004 guidelines as air can still pass in and out of the system during preparation. The study by Odou (19) is a descriptive review and provides no study data.

The studies by De Ausen, Favier, Nyman, Queruau Lamerie, Sessink, Siderov and two studies by Yoshida all examined the Phaseal system and found that it reduced contamination (6-8, 10-14). The study by Nyman showed that surface contamination decreased to 21% for cyclophosphamide and to 12% for ifosfamide from 33% and 71%, respectively, after a closed-system transfer device was used for 6 months. However, this system cannot be used for all chemotherapy drugs, and it is very costly (8). The study by Favier (7) showed that after preparing 10 chemotherapy preparations using the standard procedure and then 10 using the PhaSeal system, contamination was reduced by 93%. Sessink (11) demonstrated that contamination levels in 22 hospitals were significantly reduced after the implementation of the closed-system transfer device (p<0.0001 for cyclophosphamide, p<0.001 for ifosfamide and p<0.01 for 5-flourouracil). Siderov tested samples taken from two Australian hospitals at baseline and then 5 and 12 months after the introduction of a closed-system transfer device. One hospital withdrew after 5 months due to the cost of the closed-system transfer device. At 5 months, contamination was reduced in 13 of the 22 sites sampled: this was a 24% reduction for both hospitals. After 12 months, contamination was reduced by 75% in the one remaining hospital. The total contamination of the surfaces sampled was reduced by 68% (12).

The 2009 study by Yoshida demonstrated that contamination from wipe samples were lowered by 25% when using a closed-system transfer device. The level of contamination in glove samples was undetectable when using the closed-system transfer device (p=0.004) (13). In the second study by Yoshida in 2011, wipe samples, air samples and urine samples were collected and analyzed. Three of the hospitals used closed systems and two did not. The conclusions were that the contamination level was related to the skill level of the staff using the devices, the amount of drugs that were handled in the centre and cleaning methods used. Contamination was not necessarily reduced with the use of closed-system devices.
Contamination was still found on the outside of the BSC (Biological Safety Cabinet) and on other equipment in the room. Yoshida states that in order to reduce the contamination to zero, adequate mixing and cleaning methods must be used, as well as a biological safety cabinet (14). The study by Querau Lamerie did various contamination tests comparing six devices: Kis 1, Tevadaptor, PhaSeal, Codan Connect Z, Pchimx, Clave extension set 011-H1225 with or without Spiros. Some of these devices are not true closed systems and were included for reference. In the contamination test, Phaseal, Tevadaptor, Clave extension set with Spiros, Connect Z and Pchimx with cap all had a contamination volume of <0.200 (10). The study by Clark evaluated the EquaShield device. Wipe samples in the hospital were taken three times. During the first two times, the level of contamination was found to be very low and mostly just above the detection limit. The CSTD was introduced after the second sampling. When tested a year after the implementation of EquaShield, no contamination was found (5). The study by De Ausen et al examined leakages from CSTD detected by radioactive tracer. PhaSeal had the lowest geometric mean leak 0.1 nL (95%CI 0-0.2nL), Onguard had a leak of 1.5nL (95%CI 1.1-1.9nL) and ChemoClave a leak of 35.6nL (95%CI 29.1-43.6nL) (6).

Compared with the studies found in the previous version of this guideline (21), there is evidence from studies found in this guideline search that closed drug-transfer systems can reduce contamination during preparation (7, 8,11-14).

Table 1. Comparison of Closed System Transfer Devices.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Purpose/Scope</th>
<th>Product(s) Tested</th>
<th>Method</th>
<th>Results</th>
<th>Disclosures re: Conflicts of Interest</th>
<th>Test Environment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clark et al (2013) (5)</td>
<td>To evaluate the system at reducing surface contamination</td>
<td>EquaShield</td>
<td>Observational</td>
<td>Results after the use of EquaShield showed no contamination in any area.</td>
<td>No conflict of interest disclosed.</td>
<td>Pharmacy, infusion suite and offices</td>
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<tr>
<td>De Ausen et al (2013) (6)</td>
<td>To study leakages from selected CSTDs</td>
<td>ChemoClave, OnGuard and PhaSeal</td>
<td>Comparative/Observational</td>
<td>PhaSeal had the lowest geometric mean leak 0.1 nL (95%CI 0-0.2nL) Onguard 1.5nL (95%CI 1.1-1.9nL) ChemoClave 35.6nL (95%CI 29.1-43.6nL)</td>
<td>No conflict of interest disclosed.</td>
<td>Medical Centre</td>
</tr>
<tr>
<td>Nyman et al (2007) (8)</td>
<td>Determine levels of chemotherapy contamination using a closed system.</td>
<td>PhaSeal</td>
<td>Observational</td>
<td>Levels of chemotherapy contamination lower but not eliminated.</td>
<td>No conflict of interest disclosed.</td>
<td>Pharmacy, nursing unit, patient rooms, employee exposure</td>
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<tr>
<td>Nygren et</td>
<td>Test a drug.</td>
<td>Tevadaptor</td>
<td>Observational</td>
<td>System has</td>
<td>No conflict of interest disclosed.</td>
<td>Laboratory</td>
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<td>Reference</td>
<td>Purpose/Scope</td>
<td>Product(s) Tested</td>
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<td>al (2008) (9)</td>
<td>handling system for spill and leakage of chemotherapy during preparation.</td>
<td></td>
<td></td>
<td>similar performance to other drug preparation systems. Comparison is made between studies and not within this study.</td>
<td>interest disclosed.</td>
<td></td>
</tr>
<tr>
<td>Queruau Lamerie et al (2012) (10)</td>
<td>To evaluate CSTD in protecting workers against contamination</td>
<td>Kis 1 Tevadaptor PhaSeal Codan Connect Z Pchimx Clave extension set 011-H1225 with or without Spiros</td>
<td>Comparative/ Observational</td>
<td>No contamination was detected while using Phaseal, Tevadaptor or the Clave extension set with Spiros or Pchimx with a cap or Connect Z devices.</td>
<td>No conflict of interest disclosed.</td>
<td>Laboratory</td>
</tr>
<tr>
<td>Sessink et al (2010) (11)</td>
<td>Compare surface cytotoxic contamination with standard drug preparation or the use of a closed system.</td>
<td>PhaSeal</td>
<td>Comparative/ Observational</td>
<td>Significant reduction in levels of contamination noted with use of the PhaSeal system.</td>
<td>Financial support for study provided by Carmel Pharma (PhaSeal).</td>
<td>Pharmacy</td>
</tr>
<tr>
<td>Siderov et al (2010) (12)</td>
<td>Determine the impact of a closed system on cytotoxic surface contamination.</td>
<td>PhaSeal</td>
<td>Pre/post intervention/ Observational</td>
<td>Total contamination of surfaces reduced by 24% after 5 months and by 68% after 6 months.</td>
<td>Some financial support provided by Carmel Pharma (PhaSeal).</td>
<td>Pharmacy</td>
</tr>
<tr>
<td>Yoshida et al (2009) (13)</td>
<td>Evaluate ability of a closed system to protect against chemotherapy contamination.</td>
<td>PhaSeal</td>
<td>Comparative/ Observational</td>
<td>Use of a closed system can reduce environmental contamination and exposure to chemotherapy.</td>
<td>No conflict of interest disclosed.</td>
<td>Pharmacy</td>
</tr>
<tr>
<td>Yoshida et al (2011) (14)</td>
<td>Evaluate the measurement of contamination by antineoplastic drugs for safer handling.</td>
<td>PhaSeal</td>
<td>Observational</td>
<td>Contamination level related to amount of drugs handled, cleaning methods and skill level. Adequate cleaning and mixing required in addition to safety cabinets</td>
<td>No conflict of interest identified.</td>
<td>Pharmacy</td>
</tr>
</tbody>
</table>
Pregnancy outcomes on health care workers handling cytotoxics
The literature search on pregnancy outcomes on health care workers yielded 27 articles, and 2 of these were relevant (22, 23). In addition, one article was not listed in the online databases but found in BMC Nursing, which is an online open access journal (24). One of the
articles was a meta-analysis of occupational exposure and adverse pregnancy outcomes in nurses (23). The other two studies were cohort studies that looked at adverse pregnancy outcomes in nurses who had been potentially exposed to antineoplastic drugs (22, 24). The working group was interested in recent studies that showed if current preventative measures have shown a decrease in adverse pregnancy outcomes, but no studies were found that addressed this question.

In the 2006 version of this guideline, 10 studies were identified that examined spontaneous abortions and congenital malformation in health care workers exposed to cytotoxics. Several of these studies reported on both topics (21). Nine studies examined spontaneous abortions in health care workers who handle cytotoxics. Data from five of these studies was pooled in a meta-analysis. There was no statistically significant heterogeneity among the five studies that were pooled (p=0.14; I² = 42%). Very similar results were obtained from pooling raw data to obtain crude odds ratios (overall OR, 1.45; 95%CI, 1.12-1.88) and reported adjusted odds ratios (overall OR, 1.46; 95%CI, 1.11-1.92), with both indicating an excess of spontaneous abortions among subjects exposed to cytotoxic drugs (21). Six studies reported on congenital malformations. Four of the studies were pooled in a meta-analysis. There was heterogeneity among the four studies (p=0.07, I² = 59.8%), but no obvious association between observed effect size and study design. The 95%CI for the pooled OR contains 1.0 (OR, 1.64; 95%CI, 0.91-2.94), indicating no statistically significant incremental risk (21).

In the current search, the meta-analysis by Quansah and Jaakkola (23) examined occupational exposure and adverse pregnancy outcomes in nurses. This study specifically looked at spontaneous abortions. PubMed and EMBASE were searched from 1996 to August 2009. Four cross-sectional studies, one case-control study and one cohort study provided data for this analysis. The meta-analysis showed moderate heterogeneity I² = 32.8%. The analysis was not statistically significant (p=0.190) (23).

The cohort study by Ratner et al identified nurses that were registered with a professional body for 1 year between 1974 and 2000. The results showed that the risk for all congenital anomalies was not statistically significant: OR, 1.42; 95%CI, 0.86-2.36. There was also no statistically significant risk of congenital abnormalities in the first trimester with mothers who were exposed to antineoplastic drugs: OR, 0.93; 95%CI, 0.72-1.21. There was also no increased risk of stillbirths related to antineoplastic drug exposure in the first trimesters (OR, 0.67; 95%CI, 0.21-2.13) (24). Statistical significance was only discussed in this study, and no p values were given.

In the study by Lawson et al, nurses who were part of the Nurses’ Health Study II responded to a supplemental questionnaire that was sent to nurses who had at least one pregnancy since 1993. Nurses who were potentially exposed to antineoplastic agents were at an increased risk for having spontaneous abortions: OR, 0.94; 95%CI, 1.32-2.86. Nurses exposed to antineoplastic agents were also at an increased risk for having spontaneous abortions early in their pregnancy: OR, 2.13; 95%CI, 1.39-3.27. (22).

General outcomes on health care workers handling cytotoxics
The literature search on general health outcomes in health care workers who handle cytotoxics yielded 83 articles, of which one was relevant. In the initial literature search for this topic, there were numerous studies that examined the DNA of health care workers and found DNA changes. However, these studies did not compare the health outcomes of health care workers who handled cytotoxics to those who did not, and were therefore excluded.

Three studies on general outcomes of health care workers were identified in the previous version of this guideline. One of these was an unpublished thesis that collected survey data from 3627 members of the Oncology Nursing Society in 2002 and found a higher
probability of cancer (OR, 3.27; 95%CI, 1.11-9.58) for health care nurses who handled cytotoxics (21). A case-control study by Gunnarsdottir had an odds ratio of 1.22 (95%CI, 0.41-3.62) (21), and a comparative study by Skov had an odds ratio of 1.20 (95%CI, 0.65-2.01) (21).

In the current version of this guideline, one study was found in the literature search. This study by Ratner discussed above included a section on incidence of cancer among nurses who handle cytotoxics (24). Nurses who had ever worked in a cancer agency had an increased risk for cancer: RR = 1.83; 95%CI, 1.03-3.23 (24). It should be noted that this was based on two cases. When estimated weighted duration of exposure was done by surveys, nurses had an increased risk of cancer to the rectum: RR = 1.87; 95%CI, 1.07-3.29. This was based on 14 cases (24).

**DISCUSSION**

Three systematic reviews were completed on three areas: closed-transfer systems, pregnancy-related outcomes, and general health outcomes. The searches were done from 2007 to 2013, as they were updated from the previous version of this guideline. The corporate sponsors heavily influenced the literature on closed systems, as they subsidized numerous tests and comparisons. Therefore, the group interpreted the results of these studies cautiously. The other systematic reviews on pregnancy and general health outcomes did not identify many studies. Most of the research on this topic was done before 2006 and is, therefore, captured in the previous version of this guideline.

Previous data on closed-system handling devices was similar to what we found in this update. Most studies were observational, and few were comparative. Studies on pregnancy from the previous guideline showed that there is a slightly elevated risk for spontaneous abortion among health care workers who handle cytotoxics, but not for congenital malformations. The previous version of this guideline also found a slight risk for cancer in health care workers exposed to cytotoxics.

In addition, the articles that were retrieved, while published recently, used older study data. While there are numerous studies about wipe sampling where cytotoxics are handled, those data neither translate into general health outcomes nor show if the preventative measures currently used will prevent adverse health effects in the future to those who handle them. Due to insufficient evidence, the group cannot state whether workers handling cytotoxics are at an increased risk of cancer and other acute toxic effects.
REFERENCES


Evidence-Based Series #16-3 Version 2: Section 3

A Quality Initiative of the
Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

Safe Handling of Cytotoxics:
Development Methods, Recommendations Development
And External Review Process

The 2013 guideline recommendations

REQUIRE UPDATING

This means that the recommendations require additional evidence but are still relevant for decision-making.


Report Date: December 16, 2013

THE PROGRAM IN EVIDENCE-BASED CARE

The Program in Evidence-Based Care (PEBC) is an initiative of the Ontario provincial cancer system, Cancer Care Ontario (CCO) (1). The PEBC mandate is to improve the lives of Ontarians affected by cancer through the development, dissemination, and evaluation of evidence-based products designed to facilitate clinical, planning, and policy decisions about cancer care.

The PEBC supports a network of disease-specific panels, termed Disease Site Groups (DSGs), as well as other groups or panels called together for a specific topic, all mandated to develop the PEBC products. These panels are comprised of clinicians, other health care providers and decision makers, methodologists, and community representatives from across the province.

The PEBC produces evidence-based and evidence-informed guidelines, known as Evidence-Based Series (EBS) reports, using the methods of the Practice Guidelines Development Cycle (1, 2). The EBS report consists of an evidentiary base (typically a systematic review), an interpretation of and consensus agreement on that evidence by our Groups or Panels, the resulting recommendations, and an external review by Ontario clinicians and other stakeholders in the province for whom the topic is relevant. The PEBC has a formal standardized process to ensure the currency of each document, through the periodic review and evaluation of the scientific literature and, where appropriate, the integration of that literature with the original guideline information.

This EBS is comprised of the following sections:
Section 1: Guideline Recommendations. Contains the clinical recommendations derived from a systematic review of the clinical and scientific literature and its interpretation by the Group or Panel involved and a formalized external review in Ontario by review participants.

Section 2: Evidentiary Base. Presents the comprehensive evidentiary/systematic review of the clinical and scientific research on the topic and the conclusions reached by the Group or Panel.

Section 3: Development Methods, Recommendations Development, and External Review Process. Summarizes the EBS development process, the recommendations development process and the results of the formal external review of the draft version of the EBS.

FORMATION OF GUIDELINE DEVELOPMENT/WORKING GROUP

The Systemic Treatment and Nursing clinical programs asked the PEBC to update the guideline on cytotoxic handling. In consultation with the systemic treatment and nursing groups, a Working Group was identified. This Working Group has representation from a research scientist and a human factors specialist, a pharmacist, an occupational health physician, a nurse, a medical oncologist and a methodologist. The Working Group and Systemic Treatment and Nursing clinical programs also formed the Cytotoxic Handling Guideline Development Group (GDG). This group would take responsibility for providing feedback on the guideline as it was being developed and acted as the Expert Panel for the document at Internal Review, reviewing the document and requiring changes as necessary before approving it.

OBJECTIVES

This Working Group developed the following objective(s) for this guideline in consultation with Systemic Treatment and Nursing clinical programs.

- To update and address new issues that have developed since the previous guideline on the handling of cytotoxics, such as oral cytotoxics, appropriate personal protective equipment and treatment in diverse settings such as in the home.

GUIDELINE REVIEW

Almost all PEBC document projects begin with a search for existing guidelines that may be suitable for adaptation. The PEBC defines adaptation, in accordance with the ADAPTE Collaboration, as, “the use and/or modification of (a) guideline(s) produced in one cultural and organizational setting for application in a different context” (3). This includes a wide spectrum of potential activities from the simple endorsement, with little or no change, of an existing guideline, to the use of the evidence base of an existing guideline with de novo recommendations development.

Guidelines from 2007 to 2012 were searched for using the following databases.

Inventory of Cancer Guidelines (SAGE):


CMAJ Infobase: http://www.cma.ca/index.php/ci_id/54316/la_id/1.htm

NICE (UK) - http://www.nice.org.uk/guidance/index.jsp

SIGN (UK) - http://www.sign.ac.uk/guidelines/index.html

ASCO (US) - http://www.asco.org/ASCO/Quality-Care+%26+Guidelines/Practice+Guidelines

NCCN (US) - http://www.nccn.org/ (consensus-based)
In addition, the websites of several, known, high-quality guideline developers were searched:
NIOSH - http://www.cdc.gov/niosh/
ISOPP - http://www.isopp.org/
ASHP - www.ashp.org/
HSE - www.hse.gov.uk/
OSHA - www.osha.gov/

In addition, the MEDLINE (2007 to September 2011) and EMBASE (2007 to November 2011) databases were searched for guidelines.

Only guidelines published after 2007 were considered. Guidelines that were considered relevant to the objectives and the research questions were then evaluated by the working group for quality using the AGREE II instrument.

Twenty-nine guidelines were identified for current review. Of those, 20 were given to the working group for further consultation. Only five of those guidelines were found to be relevant and underwent a further review by the working group. The five guidelines included the “Prevention Guide: Safe Handling of Hazardous Drugs,” developed by the Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS), and the Institut de recherche Robert-Sauvé en santé et en sécurité du travail (IRSST) (4). Four documents from the BC cancer agency were considered as one guideline, and they comprise the second guideline that was considered. They are as follows: Cytotoxic agents - Safe handling standards (5); Summary of BCCA Pharmacy Practice Standards for Hazardous drugs (6); Employee Health; Management of risks related to cytotoxic agents (7); and Spill management of cytotoxic agents (8). The third guideline for consideration was “The standards of practice from ISOPPP” (The International Society of Oncology Pharmacy Practitioners) (9). The fourth guideline was “Quality Standards for the Oncology Pharmacy Service with Commentary - 4” (Quapos4) from the German Society of Oncology Pharmacy (10), and the final guideline was “Cytotoxic and Hazardous Products Training Manual from Alberta Health Services (11). These guidelines were scored using the AGREE instrument (12). Details of the scores can be found in Appendix C.

Each guideline was assessed using the following categories that were formulated by the working group: policies and procedures, personal protective equipment (PPE), ventilated cabinets, closed systems, syringes and IV sets, transport and labeling, education and training, pregnancy, surveillance, medical surveillance, spills, homecare, nursing administration and handling of waste. Details of those results can be found in Appendix D. The “Prevention Guide: Safe Handling of Hazardous Drugs” guideline covered all areas of the above categories and was decided by the working group to be the most comprehensive and was, therefore, used as the basis for the new cytotoxic handling guideline. The ISOPPP, Quapos4 and the Alberta Health Services document were more pharmacy and nursing focused. The BC guidelines covered the categories well, but they were not as encompassing as was the “Prevention Guide: Safe Handling of Hazardous Drugs.” The working group also liked the fact that the “Prevention Guide: Safe Handling of Hazardous Drugs” looked at the whole medication circuit and not just individual components of it.
The working group believed that a guideline was needed that addressed the safe handling of cytotoxic drugs from the point that they enter the centre to when they leave as either waste or in the patient. One of the challenges that the working group faced was that some of the guidelines were too narrow in that they only discussed one aspect of the medication circuit (e.g., pharmacy) in great detail (9, 10). The group settled on the “Prevention Guide: Safe Handling of Hazardous Drugs” document since it was current, broad and detailed enough. Nonetheless, a significant amount of work was required to tailor the content of that guide for the purpose of this document. For example, there were some recommendations in the “Prevention Guide: Safe Handling of Hazardous Drugs” document that were too detailed and prescriptive for the purpose of this document; in these instances, the recommendations were re-worded to convey the underlying principles in order to give centres some flexibility when developing their own policy and procedures. Occasionally a recommendation did not exist in an area when it was required. In these circumstances, the working group agreed by consensus to re-word or create a recommendation. Another reason the working group needed to re-word a recommendation was that some of the “Prevention Guide: Safe Handling of Hazardous Drugs” recommendations were ambiguous when they were translated into English. These were re-worded to clarify their meaning.

The working group went through each one of the “Prevention Guide: Safe Handling of Hazardous Drugs” recommendations in detail and checked off the following boxes: Endorse, Endorse with reservation, Needs further consideration, Recommendations not supported in Ontario context, and Abstain. Since the results of this exercise varied between individuals and were not unanimous, it was decided that the working group would go through each recommendation as a group. The working group in consultation with the guideline sponsor realized that many of these recommendations were far too prescriptive for the purpose of this Ontario Guideline update. Recommendations were then agreed upon and reduced to high-level statements. The original recommendations in the “Prevention Guide: Safe Handling of Hazardous Drugs” document can be found at: https://www.irsst.qc.ca/media/documents/PubIRSST/CG-002.pdf.

The working group met 10 times from March 2012 to April 2013 to work on the recommendations. The recommendations still have the same group structure as the original “Prevention Guide: Safe Handling of Hazardous Drugs” guideline, but the wording has been changed. Some recommendations were deleted, because they were not applicable to Ontario, and others were collapsed into a single recommendation. In instances where the group needed more information than was provided, a search of the primary literature was done. This was done in three instances and is described in Section 2. The working group relied on the expertise of a member of the expert panel when there were specific questions about the handling of cytotoxic waste in Ontario that could not be answered by the working group. While this guideline was adapted, recommendations that are backed by law, regulation or standard are footnoted and written using the term “legislation requires.” All users would be expected to implement this recommendation with little variation.

EVIDENTIARY BASE DEVELOPMENT

Using the research questions described above, a search for existing systematic reviews and a systematic review of the primary literature was conducted, as described in Section 2 of this EBS.

INITIAL RECOMMENDATIONS

Using the “Prevention Guide: Safe Handling of Hazardous Drugs” guideline and the evidentiary base in Section 2, the Working Group developed a set of initial recommendations. These initial recommendations were developed through a consideration of the aggregate
evidence quality, the potential for bias in the evidence, and the likely benefits and harms of the potential interventions. Because the initial recommendations were substantial in length, they are not summarized here but can instead be found at https://www.irsst.qc.ca/media/documents/PubIRSST/CG-002.pdf. The Working Group considered the values they used in comparing benefits to harms, and then made a considered judgment.

Key Evidence for Benefits and Harms
The evidence in the medical literature for both harms of improper handling of cytotoxics and the benefits of appropriate handling practices and procedures is sparse. There is some evidence that the handling of cytotoxics without proper precautions can lead to teratogenic effects in health care workers (13, 14). There is little evidence regarding the value of specific handling practices, with the exception of closed-transfer systems. This is not surprising, as developing studies to specifically measure the effectiveness of many of the practices and procedures considered to be standard would be difficult and resource intensive.

Aggregate Evidence Quality and Potential for Bias
While only one guideline was used as the basis of the recommendations, the “Prevention Guide: Safe Handling of Hazardous Drugs” was evidence informed and used data from other guidelines produced by government and health agencies, Canadian federal standards and laws, and technical reports that were found during the initial guideline search when it was available. Also, the consensus group that developed “Prevention Guide: Safe Handling of Hazardous Drugs” was broad and thorough. Therefore, the working group believes this guideline to be authoritative and worthwhile as the basis for an Ontario Guideline.

Values of the Working Group
Decreasing the likelihood of accidental exposure to cytotoxic agents within the medication circuit was the main objective of the working group. Preventing accidental exposure is a goal that is worth prudent effort on the part of institutions that handle these agents.

The working group believed strongly that safe handling practices should take place throughout the medication circuit to limit exposure: that is, the recommendations could not be limited to just the point of care, but must cover the entire chain of handling of cytotoxics from the time they enter the institution until they leave in the patient or as waste.

Considered Judgment
The working group advocates for no accidental exposure to cytotoxic agents anywhere along the medication circuit, and recognizes that this goal requires close attention to every aspect of the recommendations contained within this report. The recommendations represent a reasonable and practical set of procedures that the intended users of this guideline should implement to minimize the opportunity for accidental exposure.

INTERNAL REVIEW
PEBC documents undergo internal review. This review is conducted by the Expert Panel and the Report Approval Panel. The Working Group was responsible for incorporating the feedback and required changes of both of these panels, and both panels had to approve the document before it could be sent to External Review.

Expert Panel Review and Approval
The Cytotoxic Handling Expert Panel acted as the Expert Panel for this document. The members of this group were required to submit conflict of interest declarations prior to reviewing the document. These declarations are described in Appendix B. The document must be approved by formal vote. In order to be approved, 75% of the Cytotoxic Handling Expert Panel membership must cast a vote or abstain, and of those that vote, 75% must approve the document. At the time of the voting, Cytotoxic Handling Expert Panel members could suggest changes to the document, and possibly make their approval conditional on those changes. In those cases, the Working Group was responsible for considering the changes, and if those changes could be made without substantially altering the recommendations, the altered draft would not need to be resubmitted for approval again.

The Cytotoxic Handling Expert Panel reviewed the document through May and June 2013, which was sent to members of the panel through email. During this review the Cytotoxic Handling Expert Panel provided the following key feedback.

A comment was made regarding some of the new biological agents, targeted therapy, antibodies, and viral therapy.
Response: This guideline can be applied to other drugs that are considered cytotoxic. The same general precautions can be applied to other drugs.

A general definition of biological safety cabinet was suggested.
Response: The working group approved this change, and it is reflected in the document.

The definition of closed-system drug-transfer system to be expanded.
Response: The working group approved this change, and it is reflected in the document.

Comment about why the term “antineoplastic cytotoxic drugs” is used several times in the document.
Response: “Antineoplastic” was used throughout the Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS), and the Institut de recherche Robert-Sauvé en santé et en sécurité du travail (IRSST) document and a few instances were not removed. This has now been fixed, and the terminology is now consistent throughout the document.

Comment was made about regional committees responsible for policy and procedures in level 4 facilities.
Response: There is nothing in this document that would prevent centres from being part of regional committees if they wish.

Comment about the use of the French term “Cytotoxique” appearing next to cytotoxic in labeling drugs and their waste and also including a symbol.
Response: The working group approved this change, and it is reflected in the document.

Comment was made about the purchasing of cytotoxics and should consider the maximum adult dose and not purchase vials that are larger than this maximum dose (e.g., Vincristine 5 mg).
Response: The working group believes that this is outside the scope of the document.

Several comments were made about re-assigning male and females who are trying to conceive.
Response: The working group believed that re-assigning workers trying to conceive was not
pragmatic and difficult for the institutions. There is also not enough evidence on this topic.

Several comments were made about gloves including referencing a new standard, how to remove them and when to change them. 
Response: The working group approved these changes, and they are reflected in the document.

A comment was made about why gowns should be changed if they are not soiled. 
Response: The group did not change this recommendation as it is legislation.

Several comments were made about respirators. 
Response: The working group approved this change, and is reflected in the document.

Comments were made about a new standard for eye protection. 
Response: The working group approved these changes, and they are reflected in the document.

A comment was made about wearing facial protection for sterile preparation. 
Response: The working group approved this change, and it is reflected in the document.

Several comments were made about fit-tested and NIOSH-certified respirators: 
Response: The working group approved these changes, and they are reflected in the document.

A comment was made about using non-chemotherapy gloves to deliver oral medications. 
Response: The working group added some clarification in the document about this matter. They believed that for consistency, chemotherapy gloves should be used.

Several comments were made about the ventilation in the chemotherapy unpacking and storage rooms, including adding references to newer legislation. 
Response: The working group approved these changes, and they are reflected in the document.

Several comments were made about a need for a regular cleaning protocol including naming of household wipes. 
Response: The working group approved these changes, and they are reflected in the document.

A comment was made about including the reference for a new standard for dedicated storage areas for cytotoxic drugs. 
Response: The working group approved this change, and it is reflected in the document.

A comment was made to change the language to avoid confusion between open and closed systems. 
Response: The working group approved this change, and it is reflected in the document.

A comment and a change in wording were made about safety-engineered needles. 
Response: The working group believed that the new wording did not add to the recommendation, and the old wording was retained.
A comment was made about whether the statement, “do not purge air from the needle before administration,” was clear enough.  
Response: The group decided that it was clear as stated.

A comment was made about who will handle home care waste and medicines.  
Response: The wording in the recommendations was changed to clarify that only individuals with specific training can handle, administer and transport home care medicines.

A comment was made the use of bed pans as an example of contaminated biological fluids.  
Response: The working group removed the example, as it did not further the recommendation and could confuse the readers.

A suggestion was made to add a reference to the Ministry of the Environment guideline for handling of biomedical waste.  
Response: The working group approved this change, and it is reflected in the document.

A comment was made about the type of containers for soft waste items.  
Response: The working group changed the wording of this recommendation so that there is no confusion.

Several comments were made about handling disposable incontinent briefs that have been soiled by patients who have received cytotoxic drugs.  
Response: The language has been clarified and changed in this recommendation.

Several comments were made about needing references for the eye wash station.  
Response: The working group approved this change, and it is reflected in the document.

A comment was made about having a biological safety cabinet run for 24 hours a day, 7 days a week in smaller facilities.  
Response: This is standard operating procedure for these types of cabinets.

A comment was made about a reference for maintenance for biological safety cabinets.  
Response: The working group approved this change, and it is reflected in the document.

A comment was made about the optional use of a pad in preparing cytotoxics in the biological safety cabinet.  
Response: The group decided that the recommendation would stay as is.

A comment was made about only putting in one drug for one patient into the biological safety cabinet.  
Response: That is a patient safety issue and is addressed in other CCO guidelines. A link to these guidelines will be put in the document.

A comment was made about the wording of transfer of cytotoxics within the hospital.  
Response: The wording has now been changed to on-site and off-site transport of cytotoxics.

Several comments were made about using robot technologies.  
Response: The group added a statement to reflect the use of new and emerging technologies.
A comment was made about placing items from the clean-up of spills into cytotoxic waste containers.
*Response: The working group approved this change, and it is reflected in the document.*

A comment was made about whether the chemotherapy suites are being cleaned appropriately.
*Response: Each centre will have to look at their cleaning protocols in relation to this document to see if they are following the proper cytotoxic handling procedures.*

A comment was made about cleaning the vials prior to putting them away in the pharmacy, and that this could cause more contamination to enter the environment and that this recommendation should be dropped, as it is not recommended in any other place.
*Response: NIOSH recommends this procedure in their guideline and many other articles address this as well. The recommendation will stay.*

A comment was made about adding more detail to planning the oncology pharmacy.
*Response: A statement and references were added to find more information.*

A comment was made on the consistency of use of the terms: sterile or non-sterile.
*Response: Changes have been made to clarify these terms.*

A comment was made about the statement “more than one-way to prime lines”, and that our recommendations did not address that.
*Response: The working group approved this change, and it is reflected in the document.*

A comment was made about which pharmacies can prepare cytotoxic medications.
*Response: The working group changed the recommendation.*

A comment was made about whether the HEPA filters should go into the cytotoxic waste.
*Response: This seems like a reasonable course of action and is recommended by Cancer Care BC, ISOPP and ASHP. The recommendation was not changed.*

A comment was made suggesting the re-wording of biological monitoring for occupational diseases.
*Response: The language has been changed for clarification*

All comments regarding minor typographical errors have been fixed.

Through email in June and July 2013, the Cytotoxic Handling Expert Panel considered a draft of the document incorporating the changes described above. The group formally approved the document by vote on July 5, 2013. Of the 17 members of the Cytotoxic Handling Expert Panel, 13 members cast votes, for a total of 76% response. Of those that cast votes, 12 approved the document (92%).

**Report Approval Panel Review and Approval**
The purpose of the Report Approval Panel (RAP) review is to ensure the methodological rigour and quality of PEBC documents. The RAP consists of nine clinicians with broad experience in clinical research and guideline development, and the Director of the PEBC. For each document, three RAP members review the document: the Director and two others. RAP members must not have had any involvement in the development of the guideline prior to
Internal Review. All three RAP members must approve the document, although they may do so conditionally. If there is a conditional approval, the Working Group is responsible for ensuring the necessary changes are made, with the Assistant Director of Quality and Methods, PEBC, making a final determination that the RAP’s concerns have been addressed. Due to the nature of this report, only the Director of the PEBC reviewed this document. This document was adapted from another guideline and, therefore, had very little methodological matters that needed reviewing.

In July 2013 the Director of the PEBC reviewed this document. The Director approved the document on July 23, 2013. Key issues raised by the Director included the following:

To include the objective from the previous version of this guideline so that one can see the differences between the guidelines  
Response: The working group approved this change, and it is reflected in the document.

To keep the language and references consistent with shall, must and should. Sometimes shall was used with no reference to legislation. These terms should also be bolded or underlined.  
Response: The working group went through each term and reviewed its use, and added references to legislation where needed. The terms have also been underlined in the recommendations.

Some references are proper references, and some are legislation in brackets. This should be uniform throughout the document.  
Response: The working group approved this change, and it is reflected in the document.

In the Surveillance recommendation, there are some statements of fact. These should be removed.  
Response: The working group approved this change, and it is reflected in the document.

A comment was made about adding the difference found in studies of closed-system transfer devices from this guideline and the previous version.  
Response: The working group approved this change, and it is reflected in the document.

A comment was made to include why “shall” was used when this document was adapted from another guideline.  
Response: The working group approved this change, and it is reflected in the document.

A comment in the Evidence and Harms section that is contradictory should be removed.  
Response: The working group approved this change, and it is reflected in the document.

External Review by Ontario Clinicians and Other Experts  
The PEBC external review process is two-pronged and includes a targeted peer review that is intended to obtain direct feedback on the draft report from a small number of specified content experts and a professional consultation that is intended to facilitate dissemination of the final guidance report to Ontario practitioners.  
Following approval of the document at Internal Review, the Cytotoxic handling working group circulated the draft document with recommendations modified as noted under Internal Review, above, to external review participants for review and feedback. Appendix E summarizes the draft recommendations and supporting evidence developed by the Cytotoxic handling Expert Panel as submitted for External Review.
**Methods**

**Targeted Peer Review:** During the guideline development process, three targeted peer reviewers from Ontario and British Columbia considered to be clinical and/or methodological experts on the topic were identified by the working group. Several weeks prior to completion of the draft report, the nominees were contacted by email and asked to serve as reviewers. Three reviewers agreed and the draft report and a questionnaire were sent via email for their review. The questionnaire consisted of items evaluating the methods, results, and interpretive summary used to inform the draft recommendations and whether the draft recommendations should be approved as a guideline. Written comments were invited. The questionnaire and draft document were sent out on September 19, 2013. Follow-up reminders were sent at 2 weeks (email) and at 4 weeks (telephone call). The Cytotoxic handling working group reviewed the results of the survey.

**Professional Consultation:** Feedback was obtained through a brief online survey of health care professionals who are the intended users of the guideline. The survey was sent to all oncology nurses who administer systemic treatment, pharmacy workers, environmental service managers, occupational health professionals, and medical oncologists in the PEBC database were contacted by email to inform them of the survey. The survey was sent to 167 people: 159 from Ontario, 4 from British Columbia, 1 from Manitoba, 1 from Nova Scotia, 1 from Prince Edward Island and 1 from Newfoundland. Participants were asked to rate the overall quality of the guideline (Section 1) and whether they would use and/or recommend it. Written comments were invited. Participants were contacted by email and directed to the survey website where they were provided with access to the survey, the guideline recommendations (Section 1) and the evidentiary base (Section 2). The notification email was sent on September 20, 2013. The consultation period ended on November 1, 2013. The cytotoxic handling working group reviewed the results of the survey.

**Results**

**Targeted Peer Review:** Two responses were received from three reviewers. Key results of the feedback survey are summarized in Table 1.

Table 1. Responses to nine items on the targeted peer reviewer questionnaire.

<table>
<thead>
<tr>
<th>Question</th>
<th>Reviewer Ratings (N=2)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lowest Quality (1)</td>
</tr>
<tr>
<td>1. Rate the guideline development methods.</td>
<td>1</td>
</tr>
<tr>
<td>2. Rate the guideline presentation.</td>
<td>1</td>
</tr>
<tr>
<td>3. Rate the guideline recommendations.</td>
<td>1</td>
</tr>
<tr>
<td>4. Rate the completeness of reporting.</td>
<td>1</td>
</tr>
<tr>
<td>5. Does this document provide sufficient information to inform your decisions? If not, what areas are missing?</td>
<td>2</td>
</tr>
<tr>
<td>6. Rate the overall quality of the guideline report.</td>
<td>1</td>
</tr>
<tr>
<td>7. I would make use of this guideline in my professional</td>
<td>1</td>
</tr>
</tbody>
</table>
9. What are the barriers or enablers to the implementation of this guideline report?

A comment was made on the barriers of the facility design negative-pressure rooms which house biological safety cabinets.

*Response: While we understand this barrier, it is outside the scope of the document.*

A comment was made about the language of “shall must and may” being difficult to read and a set of posters or a flow chart being helpful.

*Response: The terms “shall must and may” have been changed. A flow chart or poster idea will be passed on the implementation team.*

**Summary of Written Comments**

The main points contained in the written comments were:

A comment was made about the proper removal of gloves.

*Response: A chart showing the donning and doffing of PPE will be added to Appendix F.*

A comment was made about changing the timing of changing the gown and wearing the gown while counting solid oral dosages.

*Response: The timing of the changing of the gown is supported by an ASTM standard (14). A gown is worn during the preparation of oral solid chemotherapy in the event that a tablet must be crushed.*

A comment was made about using respiratory protection when cleaning the BSC.

*Response: A change was made in the document based on this comment.*

A comment was made that Accreditation Canada requires all BSC 2 cabinets to have 100% exhaust.

*Response: Our guidelines states that we strongly recommend that the oncology pharmacy be in compliance with relevant guidelines from the Canadian Society of Hospital Pharmacists (CSHP) and Accreditation Canada standards. Since it is not legislation, we cannot use stronger language.*

A comment was made about the BSC being in a negative-pressure room.

*Response: No information could be found about this.*

A comment was made about the use of negative-pressure technique to reconstitute or withdraw from vials.

*Response: This is outside the scope of our guideline*.

A comment was made the length of time for flushing skin and needle-stick exposure.

*Response: This has been changed in the document.*

A comment was made that since this is an adaptation, it is only as good as the original.

*Response: We choose this guideline because it was comprehensive and evidence based. The rationale is available in Section 3.*
Professional Consultation: Forty responses were received. Key results of the feedback survey are summarized in Table 2.

Table 2. Responses to four items on the professional consultation survey.

<table>
<thead>
<tr>
<th>General Questions: Overall Guideline Assessment</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lowest Quality (1)</td>
</tr>
<tr>
<td></td>
<td>(2)</td>
</tr>
<tr>
<td>1. Rate the overall quality of the guideline report.</td>
<td>7.5%</td>
</tr>
<tr>
<td>2. I would make use of this guideline in my professional decisions.</td>
<td>5%</td>
</tr>
<tr>
<td>3. I would recommend this guideline for use in practice.</td>
<td>5%</td>
</tr>
</tbody>
</table>

4. What are the barriers or enablers to the implementation of this guideline report?

There were several comments about staff at the institution being barriers to implementing this guideline.  
Response: *This is beyond the scope of the document and should be addressed by each institution.*

There were several comments pertaining to costs of implementing this guideline.  
Response: *This is outside the scope of the document.*

There were many comments pertaining to the language used in the guideline.  
Response: *The use of “shall must and should” has been changed to make it clearer for the users of the guideline.*

There were several comments pertaining to the change from double gloving to using a single glove in drug administration.  
Response: *While this is a change in practice from the previous version of this guideline, the working group believes this to be current best practice. There is no evidence to suggest that a second pair of gloves for medication administration provides any additional protection over a single pair that is ASTM D-6978-(05)-13 certified. Double gloving was a common previous practice, particularly when latex gloves were used, prior to the use of certified nitrile chemotherapy gloves. Double gloves are still recommended in specific situations as outlined in Table 1. Note that there will also be a section on proper glove removal added to Appendices F and G.*

There were several comments about physical constraints such as structures being barriers to implementing this guideline.  
Response: *While the working group understands the problems with physical space in institutions, this is beyond the scope of the document.*
Summary of Written Comments
Modifications/Actions

The main points contained in the written comments were:

There were several comments on the language used in the document.  
Response: The language in the document has been changed to make it clearer for the users of the guideline.

There were several comments on the risk of dropping vials while cleaning them and thus leading to a spill.  
Response: The document states that care must be taken while wiping the vials so not to increase the risks of incidents or accidents. The document has also been changed to remove the wording “and a solution of detergent and water” to increase safety around this cleaning protocol.

A comment was made about whether or not lines primed in the hood would be contaminated or not.  
Response: If this was the case, then everything that was prepared in the hood would be deemed contaminated.

Various comments were made about CCAC and homecare having different standards and practices and how it is difficult to standardized staff practices.  
Response: This is outside the scope of the document.

A comment was made about adding more detail and information and making the recommendation stronger regarding closed-system transfer devices.  
Response: No changes were made in the document. The working group was satisfied with their wording of the recommendation and definition.

A comment was made about the use of one pair of gloves when handling patient excreta and if chemotherapy gloves should be used for longer than 48 hours as a few drugs remain in the system for longer.  
Response: The working group has struggled with this point. The majority of the group believed that one pair of chemotherapy gloves for 48 hours was sufficient. There was much discussion whether chemotherapy gloves should be used at all, for 48 hours or 7 days when handling patient excreta. For many of the chemotherapy drugs, there is no list that states how long they will be excreted in the patient. The risk is theoretical and not known. Therefore, it is a challenge to make a recommendation. Each day, less and less of the drug is excreted from the patient. The group understands it is a potential hazard, but we don’t know how that translates into a risk for workers, and therefore, the recommendation was not changed beyond wearing proper PPE for 48 hours when
handling patient excreta, unless you know the drug remains in the system for a longer time period.

A comment was made about crushing tablets and risk for aerosolization and should facemasks not be used.
   Response: *The guideline has been changed to state that the crushing of oral medicines should be done in the hood.*

CONCLUSION
This EBS report reflects the integration of feedback obtained through the external review process with final approval given by the Cytotoxic Handling Expert Panel and the Report Approval Panel of the PEBC. Updates of the report will be conducted in accordance with the PEBC Document Assessment and Review Protocol.

CONFLICT OF INTEREST
In accordance with the PEBC Conflict of Interest (COI) Policy, the guideline authors, Cytotoxic Guideline Development Group members, and internal and external reviewers were asked to disclose potential conflicts of interest.

   The working group members declared no conflicts of interest except for AE, who is president and owns a medical consulting company. This company is not engaged in any work related to cytotoxic handling.

   The guideline development group members and Targeted Peer Reviewers declared no conflicts of interest except for ER, who was a committee member on a CSA standard used in this guideline.

   The COI declared above did not disqualify any individuals from performing their designated role in the development of this guideline, in accordance with the PEBC COI Policy. To obtain a copy of the policy, please contact the PEBC office by email at ccopgi.mcmaster.ca.

ACKNOWLEDGEMENTS AND AUTHORSHIP
   The Cytotoxic Handling Expert Panel and the Working Group would like to thank the following individuals for their assistance in developing this report:

   - Melissa Brouwers, Roxanne Cosby, Adam Haynes, Sheila McNair, Hans Messersmith, Roxanne Dobish and Maureen Trudeau for providing feedback on draft versions.
   - Mark Gichuru for conducting a data audit.
   - Bruce Histed for copy editing.
   - Roxanne MacAskill, Project Coordinator, Princess Margaret Cancer Centre - University Health Network, for her help with closed-system transfer devices.

   A complete list of the members of the Cytotoxic Handling Expert Panel and the Working Group, with their affiliations and conflict of interest information, is provided in Section 3, Appendix B.
REFERENCES


APPENDICES

Appendix A. Literature Searches

Medline and Embase combined general search on cytotoxics and health care workers
1. exp occupational exposure/
2. exp health personnel/
3. oncologic nursing.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, ps, rs, ui]
4. oncology service, hospital.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, ps, rs, ui]
5. pharmacy.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, ps, rs, ui]
6. pharmacy service, hospital.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, ps, rs, ui]
7. nurs:.mp.
8. pharmac:.mp.
9. or/2-8
10. 1 and 9
11. exp antineoplastic agents/ad, ae, po, st, to
12. 10 and 11
13. exp epidemiologic study characteristics/
14. cohort.mp.
15. control.mp.
16. 13 or 14 or 15
17. 12 and 16
18. exp occupational diseases/
19. abnormalities, drug-induced.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, ps, rs, ui]
20. exp environmental exposure/
21. carcinogens.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, ps, rs, ui]
22. teratogens.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, ps, rs, ui]
23. exo drug toxicity.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, ps, rs, ui]
24. hazardous substances.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, ps, rs, ui]
25. or/1-24
26. 1 or 25
27. 26 and 9 and 11 and 16

Medline and Embase search on closed systems
1. phaseal.mp.
2. closed-system.ti.
3. antineoplastic agents.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, ps, rs, ui]
4. drug compounding.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, ps, rs, ui]
5. occupational exposure.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, ps, rs, ui]
6. 2 or 4 or 5
7. 3 and 6
8. chemoclave.mp.
10. onguard.ti.
11. baxa.mp.
12. phaseal.mp.
13. Tevadaptor.mp.
14. or/8-13
15. 7 or 14

Medline and Embase search on pregnancy
1. environmental monitoring/mt
2. occupational exposure/an
3. antineoplastic agents.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, ps, rs, ui]
4. pregnancy.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, ps, rs, ui]
5. exp pregnancy/
6. occupational exposure/ae
7. neoplasms/dt
8. neoplasms/nu
9. nurses.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, ps, rs, ui]
10. antineoplastic agents/ae
11. antineoplastic agents/pc
12. 1 or 2 or 6
13. 3 or 7 or 10 or 11
14. 8 or 9
15. 12 and 13
16. health care worker.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, ps, rs, an, ui]
17. pharmacist.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, ps, rs, an, ui]
18. pharmacy technician.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, ps, rs, an, ui]
19. pharmacy technician.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, ps, rs, an, ui]
20. 14 or 16 or 17 or 18
21. 12 and 20
22. 12 and 20
23. 13 and 22
24. 4 and 5
25. 23 and 24

Medline and Embase search on general effects of cytotoxics
1. environmental monitoring/mt
2. occupational exposure/an
3. antineoplastic agents.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, ps, rs, ui]
4. occupational exposure/ae
5. neoplasms/dt
6. neoplasms/nu
7. nurses.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, ps, rs, ui]
8. antineoplastic agents/ae
9. antineoplastic agents/pc
10. adverse outcome.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, ps, rs, ui]
11. cancer chemotherapy.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, ps, rs, ui]
12. nurses.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, ps, rs, ui]
13. healthcare worker.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, ps, rs, ui]
14. health care worker.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, ps, rs, ui]
15. pharmacist.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, ps, rs, ui]
16. chemotherapy.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, ps, rs, ui]
17. exp occupational exposure/
18. environmental monitoring/mt
19. occupational exposure/an
20. antineoplastic agents.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, ps, rs, ui]
21. occupational exposure/ae
22. neoplasms/dt
23. neoplasms/nu
24. nurses.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, ps, rs, ui]
25. antineoplastic agents/ae
26. antineoplastic agents/pc
27. health care worker.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, ps, rs, ui]
28. pharmacist.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, ps, rs, ui]
29. pharmacy technician.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, ps, rs, ui]
30. pharmacy technician.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, ps, rs, ui]
31. biological monitoring.mp.
32. 1 or 2 or 4 or 10 or 17 or 18 or 19 or 21 or 31
33. 7 or 12 or 13 or 14 or 15 or 24 or 27 or 28 or 29 or 30
Appendix B. Members of the Cytotoxic Handling Expert Panel

<table>
<thead>
<tr>
<th>Members</th>
<th>Affiliations</th>
<th>Conflict of Interest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carole Chambers</td>
<td>Alberta Health Services</td>
<td>No conflict</td>
</tr>
<tr>
<td>Flay Charbonneau</td>
<td>Odette Cancer Center</td>
<td>No conflict</td>
</tr>
<tr>
<td>Dr. Susan Dent</td>
<td>Ottawa Regional Cancer Center</td>
<td>No conflict</td>
</tr>
<tr>
<td>Dr. Leta Forbes</td>
<td>McLaughlin Durham Regional Cancer Center</td>
<td>No conflict</td>
</tr>
<tr>
<td>Diana Incekol</td>
<td>Princess Margaret Hospital</td>
<td>No conflict</td>
</tr>
<tr>
<td>Rita Kwong</td>
<td>Princess Margaret Hospital</td>
<td>No conflict</td>
</tr>
<tr>
<td>Marcia Langhorn</td>
<td>London Regional Cancer Program</td>
<td>No conflict</td>
</tr>
<tr>
<td>Ming Lee</td>
<td>Ming Lee and Associates</td>
<td>No Conflict</td>
</tr>
<tr>
<td>Sharon Meeke</td>
<td>Juravinski Cancer Center</td>
<td>No conflict</td>
</tr>
<tr>
<td>Daryl Roitman</td>
<td>North York General</td>
<td>No conflict</td>
</tr>
<tr>
<td>Edward Rubinstein</td>
<td>UHN</td>
<td>Former technical sub-committee member for the revision of SCA standard Z317.10.09, Handling of waste materials in health care facilities and veterinary health care facilities.</td>
</tr>
<tr>
<td>Dr. Xinni Song</td>
<td>Ottawa Regional Cancer Centre</td>
<td>No Conflict</td>
</tr>
<tr>
<td>Ted Vandenberg</td>
<td>London Regional Cancer Program</td>
<td>No conflict</td>
</tr>
<tr>
<td>Jeanette Van Norden</td>
<td>Juravinski Cancer Centre</td>
<td>No conflict</td>
</tr>
<tr>
<td>Dimitri Vergidis</td>
<td>Thunder Bay Regional Health Sciences Centre</td>
<td>No conflict</td>
</tr>
<tr>
<td>Cori Watson</td>
<td>Thunder Bay Regional Health Sciences Centre</td>
<td>No conflict</td>
</tr>
<tr>
<td>Dr. Lillian Wong</td>
<td>Ontario Ministry of Labour</td>
<td>No conflict</td>
</tr>
</tbody>
</table>
### Appendix C. Agree Scores

<table>
<thead>
<tr>
<th>Domain</th>
<th>Item</th>
<th>AGREE II Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Alberta</td>
</tr>
<tr>
<td><strong>Scope and Purpose</strong></td>
<td>1. The overall objective(s) of the guideline is (are) specifically described.</td>
<td>70%</td>
</tr>
<tr>
<td></td>
<td>2. The health question(s) covered by the guideline is (are) specifically described.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.</td>
<td></td>
</tr>
<tr>
<td><strong>Stakeholder Involvement</strong></td>
<td>4. The guideline development group includes individuals from all the relevant professional groups.</td>
<td>54%</td>
</tr>
<tr>
<td></td>
<td>5. The views and preferences of the target population (patients, public, etc.) have been sought.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6. The target users of the guideline are clearly described.</td>
<td></td>
</tr>
<tr>
<td><strong>Rigour of Development</strong></td>
<td>7. Systematic methods were used to search for evidence.</td>
<td>14%</td>
</tr>
<tr>
<td></td>
<td>8. The criteria for selecting the evidence are clearly described.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>9. The strengths and limitations of the body of evidence are clearly described.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10. The methods for formulating the recommendations are clearly described.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>11. The health benefits, side effects and risks have been considered in formulating the recommendations.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12. There is an explicit link between the recommendations and the supporting evidence.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>13. The guideline has been externally reviewed by experts prior to its publication.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>14. A procedure for updating the guideline is provided.</td>
<td></td>
</tr>
<tr>
<td><strong>Clarity of Presentation</strong></td>
<td>15. The recommendations are specific and unambiguous.</td>
<td>48%</td>
</tr>
<tr>
<td></td>
<td>16. The different options for management of the condition or health issue are clearly presented.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>17. Key recommendations are easily identifiable.</td>
<td></td>
</tr>
<tr>
<td><strong>Applicability</strong></td>
<td>18. The guideline describes facilitators and barriers to its application.</td>
<td>33%</td>
</tr>
<tr>
<td></td>
<td>19. The guideline provides advice and/or tools on how the recommendations can be put into practice.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>20. The potential resource implications of applying the recommendations have been considered.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>21. The guideline presents monitoring and/or auditing criteria.</td>
<td></td>
</tr>
<tr>
<td><strong>Editorial Independence</strong></td>
<td>22. The views of the funding body have not influenced the content of the guideline.</td>
<td>17%</td>
</tr>
<tr>
<td></td>
<td>23. Competing interests of guideline development group members have been recorded and addressed.</td>
<td></td>
</tr>
<tr>
<td><strong>Overall Guideline Assessment</strong></td>
<td>1. Rate the overall quality of this guideline.</td>
<td>50%</td>
</tr>
</tbody>
</table>
### Appendix D.: Guideline Comparison and Assessment Checklist
- Each colour represents a different working group member

<table>
<thead>
<tr>
<th>Quebec</th>
<th>BC</th>
<th>ISOPP</th>
<th>Quapos4</th>
<th>Alberta Health</th>
</tr>
</thead>
</table>
| **Policies and Procedures** | • Yes - guidelines/recommendations  
• Institutional action plan defined with recommendations included.  
• Yes  
• Section 4: Establishing a hazardous drug committee...etc., | • Yes - actually P&P not standards last revised in 2000!  
• Written policy revised 2009  
• Written as policies in the entire document. Relatively little detail given.  
• Yes  
• V-10: Section C outlined the responsibilities of various staff members Module 1, Section A - written policies and procedures must be developed | • Speaks specifically to Pharmacy staff - very much like Quapos4  
• Considers them to be standards of practice 1 1/8 page on administering medications  
• Wording use indicates that certain sections are obligatory or voluntary by using “must” and “should”.  
• Most pertain to pharmacy staff  
• Section 21.8: A paragraph about the requirement of procedure manual with description of what should be in the manuals. | • More Standards and recommendations  
• Basically for Pharmacy and those that support Pharmacy - housekeeping, receiving and transportation  
• Very detailed policies and procedures stated throughout, including great detail on pharmacy and treatment unit design. Document is very lengthy and is not always easy to navigate.  
• Yes - detailed  
• Section 1.3: Written operating procedures demanded. Content of the written procedure listed. | • No- Only for Pharmacy some areas are vague and give the reader options  
• Yes for pharmacy |
| **PPE** | • Yes - very clear for all individuals in the medication circuit  
• Defined in detail in Table 4.  
• Very clear  
• Table 4. Section 4.1.7 Mentioned throughout the document due to the unique structure of this document. The benefits of this structure are that  
• Yes, for preparing and administration  
• Defined in detail.  
• Yes- detailed  
• V-10: Section D, “Personal protective equipment” (no references cited)  
V-10: Table 2 (again, no sources cited)  
-
-Module 1, section C (other guidelines cited, no primary literature) | • Speaks to Hierarchical Order of protection  
• Speaks to only Pharmacy and associated personnel speaks to depending on what piece of equipment being used and grade of room  
• Very little on PPE with administration  
• More info and quite specific when handling pt’s bodily fluids  
• Good, clear descriptions of | • Speaks to Hierarchical Order of protection  
• Speaks to only Pharmacy and associated personnel speaks to depending on what piece of equipment being used and grade of room  
• Very little on PPE with administration  
• More info and quite specific when handling pt’s bodily fluids  
• Good, clear descriptions of  
• Speaks to any work duties and those associated with that task  
• Hierarchical design of protective measures remove, reduction, replacement, isolate, PPE etc Then very extensive chapters on gowns, gloves etc. but discussion only - still vague in recommendations and only | • -somewhat vague at first - “must be CE marked” again only for preparation related work duties and those associated with that task  
• Hierarchical design of protective measures remove, reduction, replacement, isolate, PPE etc | • Only for pharmacy not clear for RNs  
• Yes - only for pharmacy workers  
• Section II D: Referenced other guidelines and standards. |
<table>
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</thead>
</table>
|                              | the recommendations are tailored to the different levels of exposure depending on the role (e.g., drug preparation vs., drug transport...etc.) | Module 1, section E (other guidelines cited, no primary literature) | certain types of PPE.  
  • Yes - for pharmacy not for nursing  
  • Section 6. Referenced other guidelines and standards. | for the preparation of drugs  
  • Very detailed description of PPE requirements with a clear indication of when each component should be used, changed, etc.  
  • Yes  
  • Section 3.2, 3.2.1, 3.2.2, 3.2.3: Very detailed discussion with primary literature support. |                                                            |
| Ventilated Cabinets          | • Yes  
  • Preparation cabinets are required and are defined in detail.  
  • Yes  
  • Section 7: Different types of BSC discussed as well as its suitability.  
  Section 8: Cleaning procedures of ventilated cabinets. | • Yes - not detailed refers to another policy  
  • Defined in detail.  
  • Yes  
  • V-10: Section D Module 1: Section B, E (other guidelines cited, no primary literature) | • Yes - detailed not sure if not more textbook then recommendations  
  • Described in detail.  
  • Yes - detailed  
  • Sections 8: Very detail discussion re: different type of biological safety cabinets, testing and monitoring. | • Yes - very detailed pharmacy working area dimensions etc  
  • Extremely detailed description of laminar airflow hoods. The level of detail goes beyond the needs of most staff and would be relevant for facilities designers and builders.  
  • Yes very detailed  
  • Section 2.2. European classification of BSC different from US? | • Very detailed  
  • Yes - with detailed cleaning and admin procedures  
  • Section II B. Clear policy stated regarding BSC standard.  
  • Section IV: Working within a BSC. |
| Closed Systems               | • Yes - not enough evidence to support as yet  
  • These are discussed but no final recommendation is given. Further evaluative research on this topic is encouraged.  
  • No  
  • Section 8.1. Three paragraphs dedicated to | • No  
  • Specific guidance is included in this document, but we know from discussions that BCCA staff are currently studying the competing closed drug systems.  
  • No | Very vague, Clarifies that “closed system” should change the language to “contained system” speaks to protection for handlers, preparation and admin personnel but reads like a text book - not scientific evidence  
  • The types of closed systems are defined in | • Very vague recommendation under equipment - then lengthy description of what is available on the market but no scientific evidence or analysis regarding the evidence to support the use of the systems or the effectiveness of one system over the other and discussion of product only  
  • Speaks to them from a Pharmacy perspective yet - however not clear as to whether best practice recommendation -  
  • No  
  • Section III H. Discussed Spiros. Focus is on the proper |                                                            |
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</thead>
</table>
| closed systems discussion. Studies cited to support the relative effectiveness of different close systems. | great detail, but as far as I can tell, no specific guidance is given regarding their use.  
- A bit but no guidelines  
- Section 7. Some primary literature cited. | with respect to preparation  
- Detailed descriptions and illustrations of the common closed drug transfer systems are provided, but specific guidance on the use of these products is not provided, which is unfortunate, because it leaves the reader unclear as to how best to proceed.  
- No  
- Section 3.3.1: Provides a description of closed systems, but did not include its effectiveness | usage |

### Syringes and IV sets
- Yes  
- This topic is covered but just at a high level with no specifics given.  
- Yes - a bit  
- Section 10.3
- Yes does state leur lock but that is about all  
- These components are mentioned, but at a high level only.  
- A little bit no detail  
- V-10 Section D Module 1: Section D (other guidelines cited, no primary literature)
- Not really - speaks in general about a contained system versus closed system  
- This topic is briefly mentioned.  
- No  
- Section 12
- Yes - speaks to type of syringes eg. Single use, leur lock clear scale etc. Nothing really specific about admin sets  
- A very detailed description of all the components required for chemotherapy delivery is provided.  
- Yes - detailed
- Procedures in detail for pharmacy does not include RN administration  
- Yes  
- Section III, VI.

### Transport and Labeling
- Yes  
- Transport processes are defined in detail. Labeling recommendations are included.  
- Yes  
- Section 5: Receiving and transport: Good discussion.  
- Section 9: Transport after
- Yes - some information about labeling  
- High-level guidance is provided. The handling standards are more explicit.  
- Yes  
- V-10 Section D, Table 1
- Yes - quite general  
- Both topics are clearly discussed.  
- Yes  
- Section 2. Good discussion about transportation and labeling for external and internal transportation of chemo.
- Transportation and storage to and within the pharmacy - not clear about to administration areas  
- Labeling -yes to dispensed medication minimum requirements - not necessarily based on best practice per se?  
- Also labeling as per law in transporting out of building
- Very detailed including transportation via air/land/train  
- No transport within the hospital only the mailing of drugs  
- Section VIII. Policies and procedures described.
<table>
<thead>
<tr>
<th>Education and Training</th>
<th>Quebec</th>
<th>BC</th>
<th>ISOPP</th>
<th>Quapos4</th>
<th>Alberta Health</th>
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<tbody>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Very detailed for pharmacist and pharmacy technicians - not clear for any other profession or housekeeping - vague mother hood statements</td>
</tr>
<tr>
<td>Well-documented and embedded in recommendations. Yes - some 4.1.4. Listed the content of continuing education and orientation program.</td>
<td>No clear distinction between internal and external transportation.</td>
<td></td>
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<tr>
<td>Yes - states it should happen - no details This topic is mentioned at a high level. Yes - not very detailed Summary of BCCA Pharmacy Practice of Hazardous Drugs - Chemotherapy certification (Must demonstrate knowledge and competency, then recertify on a regular basis)</td>
<td></td>
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<tr>
<td>Yes - should have education and annual review. Reeducate for new drugs etc, every 2-3 years. Detailed outline for pharmacy - includes outline of content, skill set of trainers etc. Specific course requirements are laid out in this document. Yes - detailed Section 3.1, 4. Listed the content of training courses.</td>
<td></td>
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</tr>
<tr>
<td>Yes - &quot;law&quot; May work if pregnant - but employer must remove any risk - if not able to do so - offer another job - in not able to do so - exempt from work German laws are cited with regard to maternal exposure. They are generally aligned with approaches in other jurisdictions, but</td>
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<tr>
<td>Yes for pharmacy - but generic - up to individual to identify - organization will attempt to accommodate if individual requests - if nothing available suggests LOA without pay Yes a bit Section XIII: One</td>
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<tr>
<th>Pregnancy</th>
<th>Quebec</th>
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<th>ISOPP</th>
<th>Quapos4</th>
<th>Alberta Health</th>
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<tbody>
<tr>
<td>Yes - Employees The document simply states that pregnant employees must be fully informed of the risks. Employees responsibly to discuss desire in change of work because of pregnancy, breastfeeding, or planning to &quot;reproduce&quot; Another policy</td>
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<tr>
<td>Yes - &quot;Family Planning&quot; Pregnant, breastfeeding or planning imminent parenthood should be permitted to avoid working around cytotoxic agents and should be able to go to another job in pharmacy. Institution needs to make the policy does not speak to professionals administering</td>
<td></td>
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<tr>
<td>Yes - “law” May work if pregnant - but employer must remove any risk - if not able to do so - offer another job - in not able to do so - exempt from work German laws are cited with regard to maternal exposure. They are generally aligned with approaches in other jurisdictions, but</td>
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Section 3: Development Methods, Recommendations Development & External Review
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<tbody>
<tr>
<td>Section 15: Precautionary reassignment.</td>
<td>“Must make every effort to accommodate requests to change work assignments from staff who are pregnant, breast feeding or attempting to reproduce” The document simply states that pregnant employees. There does not appear to be a push to reassign them to other duties. Not much</td>
<td>States that pregnant workers should be permitted to avoid working with cytotoxics during their pregnancy. Not much</td>
<td>States that there is some degree of variability here, with some jurisdictions pressing hard for pregnant workers to be reassigned while others leave it to the personal decision of the worker. Yes</td>
<td>paragraph describing policy.</td>
</tr>
<tr>
<td>Surveillance</td>
<td>Yes - for surfaces in admin and prep areas. Environmental monitoring is reviewed with an appendix on the measurement of contamination. Very detailed Section 15. Provided clear guidelines. Appendix 5: Discussion of various tests for surface contamination.</td>
<td>Not clearly stated that I could see. - No</td>
<td>Speaks to Pharmacy only Record # hours worked with what equipment, # and names of drugs manipulated. Chapter 10 - Chemical contamination monitoring. Environmental surveillance approaches are discussed in detail. Yes</td>
<td>Section 8: BSC surveillance. Section 10: Good discussion regarding various aspects of surveillance (provided references for different surveillance tests)</td>
</tr>
<tr>
<td>Medical Surveillance</td>
<td>Speak to it – not recommended unless research study. The topic is discussed but no specific</td>
<td>Employees will have access to employee health/occupational health and safety services for the purpose</td>
<td>Imply “no” as state no direct measures to detect total exposure to cytotoxics - but it is actually yes...</td>
<td>Yes – Physical before employment - offered 12 -24 months after employment and prn - random bio-monitoring recommended</td>
</tr>
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<td>Quebec</td>
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<td>Alberta Health</td>
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<tr>
<td><strong>recommendations are given. Yes, but no recs</strong> Section 15.</td>
<td><strong>of a general health interview/risk assessment. It is recommended that newly hired employees who are at risk of exposure undergo an assessment with employee health services within 4-6 weeks after hire to review any questions/concerns related to risk of cytotoxic exposure.</strong> 3. <strong>Annually, employees are encouraged to arrange a routine medical examination with his/her family physician.</strong> 4. <strong>For health surveillance purposes, records of preparation and related handling activities must be maintained, as determined necessary by the Employee Health Unit and Workers’ Compensation Board Regulations. In another Policy - states “Ensure cytotoxic exposure records are maintained for the duration of employment of each employee plus 10 years, and training records for 3 years from the date training occurred (WCB).</strong></td>
<td>1. <strong>persons with abnormal pathology should not be preparing Chemo until pathology has been investigated.</strong> 2. <strong>As a baseline - then offered every six months Hospitals should have policies Regular monitoring is promoted with periodic blood tests.</strong> Yes</td>
<td><strong>Section 10.2.3: Biological monitoring: Discussed various tests, but did not mention the frequency of testing.</strong> Section 19.1.5: Listed the elements of a medical surveillance program</td>
<td><strong>with exams as a means of a “spot check” Regular workers check-ups are required, starting with an initial check followed by exams at either 12 or 24 months. Yes</strong></td>
</tr>
<tr>
<td><strong>Section 2.1: Discussion surveillance of work area (bacterial contamination)</strong></td>
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<td>Quebec</td>
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<td>ISOPP</td>
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<tr>
<td></td>
<td>Regulations Oct 99) These are covered in some detail under the Work safe BC regulations, which of course are province-specific. Yes detailed V-20 (encouraged routine medical examination with family physician, records of cytotoxic handling activities.)</td>
<td></td>
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<tr>
<td>Spills</td>
<td>Yes</td>
<td>Yes - revised 2009 The notion of contained and non-contained spills require different procedure rather than referring to a spill by volume. Detailed instructions for dealing with a spill are provided. Yes, but types of spills not defined. V-10 Section D, E V-30: A document focused on management of spills. Good step by step procedures provided.</td>
<td>Yes - in some detail The handling of spills is described in some detail, and there is also a discussion of extravasation. Yes, but details are lacking. Section 2 and 14.</td>
<td>Speak to contents of spill kit and organizations must have clear policies and procedures. Interesting this resource states “Studies on decontamination of primary packaging material showed that the following two-step procedure yields the best results: Clean 1. with 0.05 M NaOH solution and 2. with 98% isopropyl alcohol. Isopropyl alcohol must be handled carefully to avoid danger of explosions [1]” Very detailed description of the processes to be followed in dealing with a spill. A bit Section 4.2: Listed content of spill kit.</td>
</tr>
<tr>
<td>Home Care</td>
<td>Yes</td>
<td>No not that I could see/find</td>
<td>Yes A descriptive section on</td>
<td>Yes - fairly specific to pump and venous access education</td>
</tr>
</tbody>
</table>

Section 3: Development Methods, Recommendations Development & External Review

Page 61
<table>
<thead>
<tr>
<th>Quebec</th>
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<th>ISOPP</th>
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<th>Alberta Health</th>
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<tbody>
<tr>
<td>Yes 11.3.3.</td>
<td>-</td>
<td>home care is provided, and some specific issues of concern are addressed. Yes</td>
<td>to patients A very detailed section on home care is provided. Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

**Nursing Administration**

Yes, in some detail for all routes of administration. Discussion and recommendations regarding the reassignment of workers. Yes Section 10: Excellent discussion. Content tailored for nursing practice.

Yes very basic The responsibilities of a series of staff are spelled out. Yes V-10: Section D, E

Yes - 1 1/8 pages - No

Section 12: Not a complete discussion, only highlighted some points of interest.

Yes - 1 1/8 pages - No

Mentions P&P are important for admin of drugs from RNs, and Doctors with consideration of family as well Should be at least “coats, gloves and absorbent mats” -direct from texts “With regard to the wearing of gloves, it must be kept in mind that in many practices employees do not wish to «scare» their patients by wearing gloves. In this situation the attending pharmacist should strive to inform the staff and patients in agreement with the physician. The necessity is easily communicated 287 The Pharmacy as Coordination Center in Cytostatics Therapy by pointing out that gloves (even non-sterile ones) additionally serve to protect the immunosuppressed patient from nosocomial

Virtually little to none - not helpful in my opinion for nursing at all. No
<table>
<thead>
<tr>
<th>New: Handling of Waste Materials &amp; Human Waste</th>
<th>Quebec</th>
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<th>ISOPP</th>
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<tr>
<td>Detailed section on this topic. yes</td>
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<tr>
<td>Described in detail in this document. yes</td>
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<tr>
<td>Described in detail. yes</td>
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<tr>
<td>Described in detail. yes</td>
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<tr>
<td>Very detailed sections with good background. yes</td>
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<td>No</td>
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</table>

- Infections by staff and hence the protection of the patient.”
- Not really
Appendix E. Recommendations Submitted for External Review

RECOMMENDATION 1: GENERAL MEASURES

Committee responsible for policy and procedures for cytotoxic drugs
All institutions administering cytotoxic drugs must form such a committee. This committee should include, but not be limited to, representatives from various departments and services such as: occupational health and safety, pharmacy, nursing, medical oncology (physician), environmental services and risk management.

This committee would be responsible for clear processes of reviewing and revising policies and procedures related to cytotoxic drugs. In addition, this committee is responsible for the process of orientation and ongoing education for the identified target population.

This committee is responsible for implementation and follow-up of the Risk Prevention Management Program related to the use of cytotoxic drugs.

Continuing Education and Orientation Program
Initial and ongoing hospital-approved education must be provided to all staff involved with cytotoxic drugs throughout the medication circuit including safe handling and spill or leak management. All staff should have initial and ongoing training to best practice standards in place at the time.

There must be documentation that annual training of safe handling of cytotoxic drugs has occurred.

Identification and Safety
Antineoplastic drugs and their waste must be properly identified with the symbol described in CSA standard Z317.10: i.e., the symbol capital “C” and, under it, the words “CYTOTOXIC” in capital letters. Both the words and the symbol must appear on a dark grey rectangle.

Each institution should maintain a list of cytotoxic drugs.

Purchasing of Drugs
When purchasing cytotoxic drugs institutions should consider vendors that include safe handling measures such as pre-wiped or protective containers, or smaller receptacles to decrease volume of potential spills.

Spills Kit
A spill management kit must be available in all areas where cytotoxic drugs are stored, transported, handled and administered.

Precautionary Reassignment
All staff should be fully informed of the potential reproductive hazards of cytotoxic drugs. The facility should consider an alternative duty to women who are pregnant or breast-feeding.

RECOMMENDATION 2: Personal Protective Equipment (PPE)

A worker must work in compliance with the Occupational Health and Safety Act and
regulations and use or wear the equipment, protective devices, or clothing that the employer requires to be used (2).

The appropriate personal protective equipment for the task (as described in Table 1) must be worn throughout the medication circuit. It is the employer’s responsibility to provide the necessary protective equipment and training on how to use the equipment (2).

Gloves
The gloves used to handle cytotoxic drugs must comply with ASTM standard D-6978-05 and be powder free. Gloves may be latex, nitrile, polyurethane or neoprene (12). Latex is a known allergen, and this should be taken into consideration for glove selection. Vinyl gloves should not be used. The frequency of glove change should be adjusted according to the level of exposure of each step in the medication circuit. For example, when administering reconstituted medications, workers should change gloves every 30 minutes or less, and gloves must be changed immediately if torn, punctured, or visibly contaminated with a cytotoxic drug. Great care should be taken in removal of gloves to not contaminate the skin. Where two pairs of gloves are required, put on the first pair before putting on the gown.

Gown
a) The gowns used when handling cytotoxic drugs should be disposable, made of lint-free, low-permeability fabric, have long sleeves with tight fitting cuffs and fasten in the back. Gowns need to be changed in the event of contamination, spillage, rips, and at the end of the procedure. Gowns that are worn for medication preparation need to be changed halfway through a shift or every 3.5 hours. The supplier must be able to certify that the gown protects against cytotoxic drugs (14).

b) Care must be taken to avoid contamination of the hands by avoiding touching the outside of the gown when removing the gown.

Cap
Caps are only required in the sterile prep room and are worn to prevent microbial contamination.

Facial Protection
Full-facial protection must be worn whenever there is a risk of splashing (e.g., during certain drug administration procedures). The use of a full-facial shield is preferred. If goggles are used, they need to be worn in conjunction with a fluid-resistant mask. For further information, see CSA standard Z94.3.1-02: Protective Eyewear: A User’s Guide (15).

Respiratory Protection Apparatus (RPA)
Respirators should be used when there is a risk that airborne powder or aerosol will be generated.

Shoe Covers
Disposable shoe covers should be worn when in the sterile preparation room or in the event of a spill. Shoe covers must be removed immediately when leaving the sterile prep room to avoid contamination of other areas.

Table 1. Personal Protective Equipment to be worn throughout the medication circuit

<table>
<thead>
<tr>
<th>Medication circuit steps</th>
<th>Gloves</th>
<th>Gown</th>
<th>RPA</th>
<th>Face protection</th>
<th>Cap +</th>
<th>Shoe covers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication circuit steps</td>
<td>Gloves</td>
<td>Gown</td>
<td>RPA</td>
<td>Face protection</td>
<td>Cap +</td>
<td>Shoe covers</td>
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<tr>
<td>Unpacking and cleaning</td>
<td>✓</td>
<td>✓</td>
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<td></td>
<td>(2 pairs)</td>
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<tr>
<td>Sterile preparations</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td>✓</td>
<td>✓</td>
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<tr>
<td></td>
<td>(2 pairs)</td>
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<tr>
<td>Non-sterile preparations:</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
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<tr>
<td>- Counting of solid oral forms</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>(if risk of splashing, e.g., bladder installation or NG, G, or J tube*)</td>
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<tr>
<td>- Preparing creams, ointments, oral solutions and crushing tablets</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>(if risk of splashing, e.g., disposal of bodily fluids)</td>
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<tr>
<td>Routes of administration (intravenous, subcutaneous, intramuscular, vesical, intraperitoneal, intrathecal, liquid oral)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>(if risk of splashing)</td>
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<tr>
<td>Solid oral administration (tablets)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>(if risk of splashing)</td>
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<tr>
<td>Topical administration (creams, ointments)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>(if risk of splashing)</td>
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<tr>
<td>Aerosolized administration (e.g., ribavirin, pentamidine)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>(if risk of splashing)</td>
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<tr>
<td>Patient care</td>
<td>✓</td>
<td>✓</td>
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<td>✓</td>
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<td></td>
<td>(1 pair)</td>
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<tr>
<td>Management of extravasation</td>
<td>✓</td>
<td>✓</td>
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<td></td>
<td>(1 pair)</td>
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<tr>
<td>Handling of contaminated bedding on the wards</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>(if suspicion of powder or aerosolization is generated)</td>
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<td>(1 pair)</td>
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<tr>
<td>Waste management (collection and transport)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>(if on the floor)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(1 pair)</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Spill or damaged or broken container</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>(if suspicion of powder or aerosolization is generated)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(2 pairs)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cleaning of sterile preparation room and airlock</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>(if suspicion of powder or aerosolization is generated)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(1 pair)</td>
<td></td>
<td></td>
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</table>
### RECOMMENDATION 3: RECEIVING AND TRANSPORT

**Handling Cytotoxic Drug Delivery Containers**

All receiving-dock workers should receive training in the proper handling of cytotoxic drugs. The receiving-dock workers should check the integrity of the external packaging upon receipt; in the event of breakage or a damaged parcel likely to cause a spill, apply the Spill Protocol from your institution.

Delivery containers should immediately be taken to the Pharmacy Department by the receiving-dock workers or the distributor.

The receiving-dock or storeroom workers should not open the delivery containers. The delivery containers should be handled with care to avoid breakage of the cytotoxic drug containers and should not be left unattended in a corridor. Only trained workers (e.g., pharmacy technicians) are to proceed with the unpacking and subsequent steps.

**Damaged Containers/Spill**

Damaged containers should be handled like spills. The manufacturer or distributor must be notified if the container is received in a damaged state. To limit exposure, a damaged container should never be returned to the manufacturer or distributor. Notify the pharmacy if any damaged containers are suspected.

See recommendation 10: Management of Waste, Accidental Exposure, Spills and Returns

### RECOMMENDATION 4: UNPACKING AND STORAGE

Packaging can have high levels of contamination. There should be an unpacking area in the pharmacy limiting exposure risks. The unpacking area should be a separate dedicated space, separate from eating areas, preferably a separate room (O.Reg67/93,s.32) (8). There should be adequate ventilation in the area, preferably vented to the outside. There should be a receptacle for cytotoxic waste in the unpacking area for the disposal of secondary packaging.

Workers at risk of exposure must wear a protective gown and two (2) pairs of gloves when unpacking and cleaning cytotoxic drugs, from the opening of the external packaging to the placing of the secondary or primary packaging in their storage space. Workers should check the integrity of all packaging at every step of the unpacking process. In the event of breakage or leaking, the damaged contents should be treated as a spill. The primary and or secondary

---

**Medication circuit steps**

<table>
<thead>
<tr>
<th>Gloves</th>
<th>Gown</th>
<th>RPA</th>
<th>Face protection</th>
<th>Cap +</th>
<th>Shoe covers</th>
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</thead>
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<tr>
<td>Cleaning of preparation cabinets (hoods)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>(2 pairs)</td>
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<td></td>
</tr>
<tr>
<td>Cleaning of other oncology pharmacy rooms and care units/clinics</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1 pair)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

+ The wearing of a cap is related to sterile practices.

NG = Nasal gastric tube, G = Gastric tube, J = Jejunostomy tube

^ Although cytotoxic they are not neoplastic
Packaging should be cleaned prior to being placed in storage.

A regular cleaning protocol must be in place. All drug containers should be cleaned to reduce external contamination. Options include pre-moistened towelettes (e.g., Wet-Ones) or a disposable cloth and a solution of detergent and water. However, this procedure must not increase the risk of incidents/accidents due to damage to the cytotoxic drug container or label.

Procedures should be in place to minimize the risk of contamination of surfaces during the cleaning of vials (e.g., use of a disposable, plastic-backed, absorbent pad). All surfaces must be cleaned when the task is complete.

Establish a dedicated storage area for cytotoxic drugs that minimizes the risk of contamination.

When removing or transporting drugs out of the storage area, one pair of gloves and a gown should be worn.

**RECOMMENDATION 5: CYTOTOXIC DRUG PREPARATION**

**Planning the Oncology Pharmacy**

The oncology pharmacy should be in compliance with relevant guidelines from the Canadian Society of Hospital Pharmacists (CSHP) and Accreditation Canada standards.

Special requirements for heating, ventilation and air-conditioning (HVAC) systems in health care facilities should be taken into consideration (18).

A class II type B cabinet is required with preference for the type B2 since it ensures that there is no recirculation of air within the cabinet (5).

All mixing and preparation of administration sets with a cytotoxic drug must be performed in one centralized area in a specially designated class II type B biological safety cabinet that (18):

- (a) is exhausted to the outside atmosphere in a manner that prevents recirculation into any work area,
- (b) has exhaust and ventilation systems that remain in operation for a sufficient period of time to ensure that no contaminants escape from the biological safety cabinet into the workplace, and
- (c) is equipped with a continuous monitoring device to permit confirmation of adequate airflow and cabinet performance.

Airlocks may be considered if there are particular concerns about the propagation of airborne cytotoxic drugs.

Priming of administration sets should be prepared in the manner mentioned above.

The layout should allow and facilitate the unimpeded cleaning of all surfaces (walls, floors, ceilings, doors, diffusers, windows). The furniture and equipment in the sterile-preparation room should be kept to a bare minimum. There should be a visual link - for example, a
window and a way to communicate between the sterile-preparation room and the pharmacy in order to view the work in progress. Access to the sterile room should be limited to trained and authorized workers.

Limit worker traffic, particularly near unpacking and storage areas (to avoid accidental breakage) and near preparation cabinets (to avoid interfering with their proper operation).

The facilities must include an eye wash fountain, which may or may not be hooked up to the airlock sink. If this is not possible, a portable eye wash system may be used. A full shower should be accessible nearby (e.g., in the oncology units/clinics).

*Closed-drug transfer systems* (e.g., PhaSeal®) are not a substitute for class II type B preparation cabinets. There is evidence from studies (22-27) that closed drug-transfer systems can reduce contamination during preparation. Further, emerging evidence suggests that when these devices are not used as specified, they could become open to the environment. Further research is needed to evaluate this.

The biological safety cabinets should remain in operation 24 hours a day, 7 days a week, as recommended by the manufacturers.

In the non-sterile drug preparation process (e.g., oral preparations), the same level of worker protection must be adhered to.

**Pharmacy Policies and Procedures**

Establish policies and procedures regarding preventive maintenance, monitoring and the optimal use of facilities and equipment.

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**RECOMMENDATION 6: DRUG PREPARATION**

The following recommendations apply to the preparation of all cytotoxic medications including parenteral, oral and topical, both sterile and non-sterile preparations. Policies and procedures must include the use of appropriate personal protective equipment, the equipment for preparation including appropriate ventilation and other automated equipment for packaging and a dedicated work area.

**Personal Protective Equipment**

Workers (pharmacists or pharmacy technicians) must wear a cap, shoe covers, a protective gown and two (2) pairs of gloves (see Table 1) to make *sterile* preparations of cytotoxic drugs in preparation cabinets.

**Organization of the Work**

Organize the work to limit microbial and environmental contamination.

Preparation workers should cover the work surface with a disposable, absorbent, sterile, plastic-backed pad to absorb any liquid contamination that may occur during handling. The pad must not cover the front and rear grilles of the preparation cabinet. It should be changed after 3.5 hours of continuous work or for a new batch of preparations (e.g., a set of vials of a
given drug) or in the event of a spill or contamination. The pad must be disposed of in a cytotoxic waste receptacle.

Limit the quantity of supplies and cytotoxic drugs in the cabinet, to avoid adversely affecting the laminar flow and to facilitate regular cleaning of the work surface; place the sterile products in the centre and the non-sterile products (e.g. waste receptacle) along the sides of the cabinet.

Removal of Packaging
Remove the packaging, when applicable, and clean all of the drug containers before taking them into the preparation cabinet. Adhere to aseptic technique for sterility.

Handling Techniques
Use handling techniques that limit the risk of injury or accidental exposure.

Spiking of bags and priming of tubing should occur before the addition of the cytotoxic drug unless the clinical protocol requires otherwise.

Preparation, Priming and Removing Air from the Tubing
Cytotoxic drugs must be reconstituted in the pharmacy environment as described above. The drug containers must not be overfilled to avoid compromising the integrity of the container. The techniques used for priming and removal of air should minimize the exposure risks. Air should never be removed from the tubing with a solution containing the drug. The air must be removed and the tubes should be primed in the pharmacy, prior to adding the cytotoxic drug(s) to the infusion solution. Glass containers are not recommended due to increased risk of breakage and exposure.

Labeling and Final Packaging
Cytotoxic drugs must be labeled to inform those handling the preparations of the nature of the drugs and the precautions to be taken. Cytotoxic drugs must display the “Cytotoxic” hazard symbol or the word “Cytotoxic.”

The outside surface of the cytotoxic drug containers (e.g., syringes, infusion bags, tubing) in the preparation cabinet must be cleaned in the cabinet.

Place each cytotoxic drug container (e.g., syringe, bag), as well as the administration supplies (e.g., tubing), in a clear, leak-proof, plastic bag (e.g., Ziploc® type) to facilitate identification by the nurse without having to remove the container from the bag.

Following final verification, the plastic bags containing the cytotoxic drugs should be placed in a rigid transport container (ideally opaque), properly identified with the “Cytotoxic” hazard symbol.

Waste
Everything that comes out of the cabinet should be wiped clean.

All contaminated waste should be disposed of in the chemotherapy waste stream.

**RECOMMENDATION 7: TRANSPORT AND STORAGE FOLLOWING PREPARATION**
**Drug Transport**

Transport cytotoxic drugs using a method that will prevent contamination of the environment in the event of breakage.

Cytotoxic drugs should be placed in a closed, leak-proof plastic bag (e.g., Ziploc® type).

Transport of the cytotoxic drug in a closed, leak-proof plastic bag, from the pharmacy to an area not adjacent to the preparation area (e.g., care unit, outpatient clinic, home care), must be done in a rigid, shock-resistant, leak-proof container made of a material that can be easily cleaned and decontaminated in the event of a drug leak. The bottom should be covered with an absorbent, plastic-backed cloth.

The *transport container* must be identified with the “Cytotoxic” hazard symbol and be cleaned regularly.

Mechanical transport systems, such as pneumatic tubes, should not be used because of the stress they put on the contents, and the whole transport system would be compromised if a leak occurred.

Prepared medications should be stored in a designated area prior to administration. This area should be cleaned regularly.

**Shipping of Mixed Drugs**

Establish policies and procedures regarding the shipping of cytotoxic drugs (29).

In the event that cytotoxic drugs are shipped off-site (e.g., from one institution to another), they should be packed separately from other drugs, according to the recommendations from the manufacturer and distributor. Pharmacy should be consulted in the packaging of cytotoxic drugs.

Cytotoxic drugs should be packed in a double plastic bag placed in a box that is properly identified with the "Cytotoxic" hazard symbol. If necessary, immobilize the drug with packing material. The "Cytotoxic" hazard symbol must be visible on the outside of the delivery container. Reusable delivery containers should be cleaned regularly.

Ensure that the courier company will handle cytotoxic drugs. In most cases, the regulation regarding the transport of hazardous goods does not apply in these situations.

**RECOMMENDATION 8: DRUG ADMINISTRATION**

Safe handling and administration techniques must be used to minimize possible exposure to individuals and the environment when administering cytotoxic drugs.

- Appropriate personal protective equipment must be worn by all healthcare providers, please refer to Table 1.
- Luer-Lock connectors and needleless administration systems should be used to administer any intravenous medications.
- Closed systems may offer additional protection.
- Disposable plastic-backed absorbent pads should be used over work surfaces and placed under tubing or bag connections and ports when attaching any tubing, bag or syringe that have been exposed to a cytotoxic drug.
- Never disconnect tubing from cytotoxic drug bags. Discard bag with attached tubing into
appropriate waste container as a single unit.
- Safety-engineered needle devices must be used for subcutaneous and intramuscular injection as per Needle Safety Regulation 474/07 Occupation Health and Safety Act Labour, 2010 #28. Do not purge air from the needle before administration.
- Oral cytotoxic must be handled in a manner that avoids skin contact, liberation of aerosols or powdered medicine into the air, and cross-contamination with other medicines. (Australian doc).
- Solid oral preparations (tablets) of cytotoxic drugs should not be crushed or cut outside the pharmacy. The pharmacy should provide these drugs in an oral syringe, in a ready-to-administer, liquid oral form.
- Application of topical cytotoxic drugs should be done in a way that prevents contamination of the environment. Between applications, the cytotoxic medication (i.e., tube or jar) must be kept in a safe container (i.e., Ziploc) and in a secure place that prevents contamination of the surrounding environment.
- With any intravesical administration (e.g. bladder instillation), ensure there are detailed procedures in place to avoid risks of splashing.
- Caution should be taken when administering intrathecal cytotoxic drugs as risk of splashing due to increased intrathecal pressures.

RECOMMENDATION 9: HOME CARE

Home Care of Patients who have Received Cytotoxic Drugs
All cytotoxic drug preparations must be compounded in the pharmacy.

Cytotoxic drugs should be transported, administered and disposed of by properly trained workers. It should be ensured that the cytotoxic drug transport containers are not reused by patients for domestic purposes, which may expose the family to cytotoxic drugs (e.g., toy box, sewing basket, etc.).

The health care provider who administers cytotoxic drugs in the home must wear Personal Protective Equipment as outlined in Table 1.

Health care providers should follow the same recommendations outlined in Recommendation 8 - Drug Administration.

A spill kit should be readily available in the home in case of accidental spills.

Patients should be informed of and be provided with written instructions for the safe handling of cytotoxic drugs.

Contact information should be provided for home care patients who require assistance with safe handling of cytotoxics.

Antineoplastic-Type Cytotoxic Drug Waste in the Home
The institution should have a clear process to address the issue of cytotoxic waste from patients in their homes, in compliance with municipal or local cytotoxic waste rules. This process should include patient and caregiver education.

Caregiving staff must provide the patients/caregivers involved in administering antineoplastic-type cytotoxic drugs in the home with a process for appropriate disposal of
cytotoxic waste, including left over drugs.

**RECOMMENDATION 10: MANAGEMENT OF WASTE**

**Bodily Fluid Waste**
Workers who handle the biological fluids, excreta, contaminated bedding and soiled equipment (e.g., bedpans) of patients who have received cytotoxic drugs must wear one (1) pair of gloves and a protective gown. Face protection must be worn when there is a risk of splashing (e.g., when emptying and cleaning the bedpans of patients receiving antineoplastic type cytotoxic drugs).

**Cytotoxic Drug Waste**
Establish policies and procedures as per provincial legislation regarding cytotoxic waste management.

The term “cytotoxic waste” includes any material that comes into contact with cytotoxic drugs during their storage, handling, preparation, administration and disposal (e.g., packaging material, protective equipment, preparation supplies (such as syringes, tubing, drug bags), soiled disposable incontinent briefs of patients who have received antineoplastic-type cytotoxic drugs during the previous 48 hours, hood pre-filters and HEPA filters, etc.).

Cytotoxic waste must be placed in a waste container clearly identified with the “Cytotoxic” hazard symbol. Cytotoxic waste must be disposed of in the appropriate containers.

Sharps must be placed in rigid containers with a leakproof lid; CSA standard Z316.6-02 specifies the use of the colour red for the rigid containers (33). If the containers are another colour, follow the instructions of the company ensuring the final disposal.

Other waste (soft items, such as tubing, protective equipment, etc.) must be placed in leak-proof and tear-resistant plastic bags, identified with the “Cytotoxic” hazard symbol, under the anticipated conditions of use. For final disposal outside the institution, these bags must be placed in a rigid, leak-proof, container identified with the “Cytotoxic” hazard symbol and scheduled for transport outside the institution.

Any excess fluid from antineoplastic type cytotoxic drugs (e.g., drug loss) must be disposed of in a sealed container and placed in a rigid container, the bottom of which is to be covered with an absorbent pad. This rigid container will be handled like other cytotoxic waste.

Routine precautions should be used to handle disposable incontinent briefs soiled by patients who have received antineoplastic-type cytotoxic drugs.

Cytotoxic waste must be incinerated at a high temperature (i.e., 800°C to 1200°C, depending on the product).

Cytotoxic waste must not be disposed of in the receptacles used for infectious biomedical waste (which may be autoclaved and then sent to a landfill site).

Every area where cytotoxic drugs are handled must have an appropriate cytotoxic waste receptacle as close as possible to the work area.
The lids of cytotoxic drug receptacles must remain closed, except when depositing waste. Bins with foot pedals and lids that lock automatically when full are recommended to minimize exposure.

Workers must be careful to avoid contaminating the outside of the receptacle when depositing waste.

The transport of cytotoxic waste receptacles must be assigned to properly trained workers. Workers who handle cytotoxic waste receptacles must wear one (1) pair of disposable gloves and must have a spill kit at their disposal. The waste must go through as few care units, public areas and areas containing food or linens as possible.

The final storage areas for cytotoxic waste receptacles must be secure. Refer to Ontario storage requirements (10).

**RECOMMENDATION 1: ACCIDENTAL EXPOSURE**

Establish policies and procedures regarding accidental worker exposure.

If a cytotoxic drug accidentally comes into contact with a worker’s skin or clothing, the worker must immediately remove the contaminated clothing and thoroughly wash the skin of affected area with soap and water. If necessary, the contaminated worker should take a full shower. A full shower can be made available in the vicinity (e.g., in the oncology clinics/units).

If a cytotoxic drug comes into contact with a worker’s eyes, the worker should flush their eyes at an eye wash station. Alternatively, the workers may use an isotonic solution to flush their eyes (e.g., sterile NaCl 0.9%). Eyes should be flushed for at least 15 minutes. If contact lenses are worn, they must be removed immediately prior to flushing.

In the event of a needle-stick or sharps injury, let the wound bleed freely. Under running water, gently and thoroughly wash the area with soap. Contact Occupational Health. Ensure that facility policies for needle-stick or sharps injury are followed including completion of an incident report and reporting to WSIB if indicated.

**RECOMMENDATION 12: SPILLS MANAGEMENT**

The facility should develop policies and procedures for spills management that take into account the types of spills (i.e., amount, location, concentration, powder vs. liquid, etc.). A spill management kit must be readily available within the work area.

Most spills can be contained and managed by the trained health care worker (e.g., leaking IV, tubing).

When a spill is not contained or easily managed (e.g., exposure to large volume of fluid that is a risk to the environment or a large crate of vials filled with powder broken in the receiving area), a Code Brown or equivalent must be called.

**RECOMMENDATION 13: ENVIRONMENTAL CLEANING**
Establish environmental cleaning policies and procedures for all surfaces where contact with cytotoxic drugs may occur. Examples may include unpacking and storage, preparation, administration and disposal areas. Pharmacy counters are among the most contaminated surfaces.

Cleaning of the biological safety cabinets should be performed by trained personnel following manufacturer’s guidelines (34).

**Use of Pumps to Administer Cytotoxic Drugs**
Make sure there is an appropriate policy to clean and inspect the equipment between uses.

**Laundry**
Ensure the facility complies with the Occupational Health and Safety Act - Ontario Regulation for Health Care and Residential Facilities (8).

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**RECOMMENDATION 14: BIOLOGICAL AND ENVIRONMENTAL MONITORING**

**Biological Monitoring**
There is evidence in the literature of a higher rate of spontaneous abortion among women working in roles that expose them to cytotoxic drugs (35, 36).

There are no identified medical conditions known to result from exposure of health care workers to cytotoxic drugs, no exposure limits set for cytotoxic drugs, and no standards for interpretation of test results of exposed health care workers to enable meaningful interpretation or action based on biological monitoring results.

Biologic monitoring for occupational diseases requires an identified hazard and an accepted and detectable clinical outcome that can be reliably identified by clinical tests. All of these elements are lacking in the current research on health effects of cytotoxic drugs on exposed health care workers.

**Environmental Monitoring**
The facility may consider implementing an environmental-monitoring program. Surface testing would audit contamination of the environment (e.g., pharmacy counters, patient bedside tables) and provide a quality indicator of cleaning effectiveness and adherence to recommended work practices.
Appendix F: Technique for donning and doffing one pair of gloves (15)
Source: http://www.who.int/gpsc/5may/Glove_Use.Information_Leaflet.pdf

When the hand hygiene indication occurs before a contact requiring glove use, perform hand hygiene by rubbing with an alcohol-based handrub or by washing with soap and water.

I. HOW TO DON GLOVES:

1. Take out a glove from its original box
2. Touch only a restricted surface of the glove corresponding to the wrist (at the top edge of the cuff)
3. Don the first glove

4. Take the second glove with the bare hand and touch only a restricted surface of glove corresponding to the wrist
5. To avoid touching the skin of the forearm with the gloved hand, turn the external surface of the glove to be donned on the folded fingers of the gloved hand, thus permitting to glove the second hand
6. Once gloved, hands should not touch anything else that is not defined by indications and conditions for glove use

II. HOW TO REMOVE GLOVES:

1. Pinch one glove at the wrist level to remove it, without touching the skin of the forearm, and peel away from the hand, thus allowing the glove to turn inside out
2. Hold the removed glove in the gloved hand and slide the fingers of the ungloved hand inside between the glove and the wrist. Remove the second glove by rolling it down the hand and fold into the first glove
3. Discard the removed gloves

4. Then, perform hand hygiene by rubbing with an alcohol-based handrub or by washing with soap and water
Appendix G: Technique for donning and doffing two pairs of gloves (4).

**Figure 6**

Procedure for removing gloves if the gown is kept on and two pairs of gloves are worn.
Evidence-Based Series 16-3 Version 2: Section 4

Safe Handling of Cytotoxics

Document Review Summary

K. Kennedy, K. Vu, N. Coakley and Members of the Expert Panel on Safe Handling of Cytotoxics

The 2013 guideline recommendations

REQUIRE UPDATING

This means that the recommendations require additional evidence but are relevant for decision-making.

June 22, 2018

OVERVIEW

The original version of this guidance document was released by Cancer Care Ontario’s Program in Evidence-based Care in 2013.

In August 2017, this document was assessed in accordance with the PEBC Document Assessment and Review Protocol and was determined to require a review. As part of the review, a PEBC methodologist conducted an updated search of the literature. Two clinical experts (KK and KV) reviewed and interpreted the new eligible evidence and proposed that the existing recommendations should be updated.

DOCUMENT ASSESSMENT AND REVIEW RESULTS

Questions Considered

1. Do closed-system transfer devices reduce contamination when used to prepare chemotherapy?
2. What are the risks in pregnancy for women health care workers who work or have worked with cytotoxic agents?
3. Are there any adverse health outcomes for health care workers who handle cytotoxics?
Literature Search and New Evidence
The new search (January 2013 to November 2017) yielded 10 guidelines, and no new full text publications. Brief results of these publications are shown below in the Document Summary and Review Tool.

Impact on the Guideline and Its Recommendations
The handling of cytotoxics in Ontario is changing. As of Jan 1, 2019, Ontario will be following the National Association of Pharmacy Regulatory Authorities (NAPRA) guidelines for pharmacy. The current guideline does not conform to these standards. Furthermore, there are additional subjects covered by the new evidence that were not addressed in the original guideline. These include
- Beard covers
- Intravesical chemo (bladder in OR room)
- Washing of linens and clothes
- Environmental monitoring

As a result of this new information, an updated document should be prioritized.

Document Review Tool

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<th>Number and Title of Document under Review</th>
<th>16-3 Version 2 Safe Handling of Cytotoxics</th>
</tr>
</thead>
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<tr>
<td>Current Report Date</td>
<td>December 16, 2013</td>
</tr>
<tr>
<td>Date Assessed (by DSG or Clinical Program Chairs)</td>
<td>May 9, 2017</td>
</tr>
<tr>
<td>Health Research Methodologist</td>
<td>Nadia Coakley</td>
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<td>Clinical Expert</td>
<td>Kathy Vu and Kardi Kennedy</td>
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<td>Approval Date and Review Outcome (once completed)</td>
<td>UPDATE</td>
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<td></td>
<td>June 22, 2018</td>
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<tr>
<td>Original Question(s):</td>
<td>1. Do closed-system transfer devices reduce contamination when used to prepare chemotherapy?</td>
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<td>2. What are the risks in pregnancy for women health care workers who work or have worked with cytotoxic agents?</td>
</tr>
<tr>
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<td>3. Are there any adverse health outcomes for health care workers who handle cytotoxics?</td>
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<tr>
<td>Target Population:</td>
<td>Healthcare workers who may come into contact with cytotoxic drugs at any point in the medication circuit. The medication circuit includes all steps through which the drug travels, from the receiving dock to the storage facility, as well as its preparation, administration and disposal. Exposure is possible throughout the medication circuit in the hospital or in the home</td>
</tr>
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setting.

**Study Selection Criteria:**

**Inclusion Criteria**
- Technology assessments, systematic reviews, clinical trials and studies investigating the safe handling of cytotoxics.

**Exclusion Criteria**
- Review articles
- Letters and editorials that reported clinical trial outcomes.

**Search Details:**
- Search for and evaluation of existing guidelines. If one or more existing guidelines are identified that address the research questions and are of reasonable quality, then those guidelines will form the core of the evidentiary base.
- Systematic review of the primary literature focusing on those areas not covered by existing and accepted guidelines.

**Summary of new evidence:**
A separate search for guidelines was conducted. Guidelines from 2013 to November 2017 were searched for using the following databases.
- National Guideline Clearing House
- CMAJ Infobase
- NICE (UK):
- SIGN (UK)
- ASCO (US)
- NCCN (US)
- SIGN (UK)
- New Zealand Guidelines Group
- Provincial Cancer and Health Agencies in Canada

In addition, the websites of several high-quality guideline developers were searched:
- NIOSH
- ISOPP
- ASHP
- HSE
- OSHA

In addition, the MEDLINE (2013 to November 2017) and EMBASE (2013 to November 2017) databases were searched for guidelines. Ninety four results were found through the Medline and EMBASE search and none were retained. An additional 10 guidelines were found using the websites identified above.

**Results of the primary literature searches**

**Closed system transfer devices:** 591 records were found, 43 records were considered for a full text review and 13 were relevant.

**Pregnancy outcomes on health care workers:** 27 records were found, 2 records were considered for a full text review and 1 was relevant.

**General health outcomes in health care workers who handle cytotoxics:** 1424 records were found, 10 records were considered for a full text review and 3 were relevant.
Clinical Expert Interest Declaration:
KV has stocks, bonds, or stock options valued at $5,000 or more in a relevant business entity. KV has also published an article about the safe handling of oral chemotherapy in community pharmacies in the Ontario College of Pharmacists bulletin (http://www.ocpinfo.com/library/pharmacy-connection/download/OCP_PharmacyConnection_Summer2017.pdf).

KK and NC have nothing to declare

1. Does any of the newly identified evidence contradict the current recommendations? (i.e., the current recommendations may cause harm or lead to unnecessary or improper treatment if followed)
   No

2. Does the newly identified evidence support the existing recommendations?
   No

3. Do the current recommendations cover all relevant subjects addressed by the evidence? (i.e., no new recommendations are necessary)
   No
   - Beard covers Intravesical chemo (bladder in OR room)
   - Washing of linens and clothes
   - Environmental monitoring

Review Outcome as recommended by the Clinical Expert

If the outcome is UPDATE, are you aware of trials now underway (not yet published) that could affect the recommendations?
Ontario will be following the NAPRA guidelines for pharmacy as of Jan 1, 2019. This guideline currently is contradictory in places to the NAPRA guideline.

DSG/GDG Commentary

Evidence Tables See below (Starting on page 83)

References (page 190)
DEFINITIONS OF REVIEW OUTCOMES

1. **EDUCATION AND INFORMATION** - EDUCATION AND INFORMATION means that a Clinical Expert and/or Expert Panel has reviewed new evidence pertaining to the guideline topic and determined that the guideline is out of date or has become less relevant. The document will no longer be tracked or updated but may still be useful for academic or other informational purposes. The document is moved to a separate section of our website and each page is watermarked with the words “EDUCATION AND INFORMATION.”

2. **ENDORSED** - ENDORSED means that a Clinical Expert and/or Expert Panel has reviewed new evidence pertaining to the guideline topic and determined that the guideline is still useful as guidance for clinical decision making. A document may be endorsed because the Expert Panel feels the current recommendations and evidence are sufficient, or it may be endorsed after a literature search uncovers no evidence that would alter the recommendations in any important way.

3. **UPDATE** - UPDATE means the Clinical Expert and/or Expert Panel recognizes that the new evidence pertaining to the guideline topic makes changes to the existing recommendations in the guideline necessary but these changes are more involved and significant than can be accomplished through the Document Assessment and Review process. The Expert Panel advises that an update of the document be initiated. Until that time, the document will still be available as its existing recommendations are still of some use in clinical decision making, unless the recommendations are considered harmful.
RECOMMENDATION 1: GENERAL MEASURES

Committee Responsible for Policy and Procedures for Cytotoxic Drugs
It is strongly recommended that all institutions administering cytotoxic drugs form such a committee. It is also strongly recommended that this committee include, but not be limited to, representatives from various departments and services such as: occupational health and safety, joint health and safety committee, pharmacy, nursing, medical oncology (physician), environmental services and risk management.

This committee would be responsible for clear processes of developing, reviewing and revising policies and procedures related to cytotoxic drugs. In addition, this committee is responsible to ensure that there is a process in place for orientation and ongoing education for the identified target population.

This committee is responsible for implementation and follow-up of the Risk Prevention Management Program related to the use of cytotoxic drugs.

Continuing Education and Orientation Program
It is legislated that initial and ongoing hospital-approved education be provided to all staff involved with cytotoxic drugs throughout the medication circuit including safe handling and spill or leak management (8). It is strongly recommended that all staff have initial and ongoing training to best practice standards in place at the time.

It is legislated that there is documentation that annual training of safe handling of cytotoxic drugs has occurred (8).

Identification and Safety
It is strongly recommended that each institution maintain a list of cytotoxic drugs.

It is legislated that Cytotoxic drugs and their waste be properly identified with the symbol capital "C" and, under it, the words “CYTOTOXIC/CYTOTOXIQUE” in capital letters (9, 10). It is legislated that all cytotoxic waste under the Ministry of Environment regulation (guideline C4) include bilingual wording and both the words and the symbol appear on a dark grey rectangle (9, 10).

Purchasing of Drugs
When purchasing cytotoxic drugs, it is strongly recommended that institutions consider vendors that include safe handling measures such as pre-wiped or protective containers, or smaller receptacles to decrease volume of potential spills.

Spills Kit
It is strongly recommended that a spill-management kit be available in all areas where cytotoxic drugs are stored, transported, handled and administered.

Precautionary Reassignment
It is strongly recommended that all staff be fully informed of the potential reproductive hazards of cytotoxic drugs (11). It is strongly recommended that the facility consider alternative duties for women who are pregnant or breastfeeding.

**Saskatchewan (Sask health)** Employees who are pregnant, attempting to conceive or breastfeeding may refrain from administering chemotherapy drugs upon request. This must be communicated in writing as soon as possible to the Manager of the unit prior to commencement of their shifts.

**Saskatchewan (Regina, Feb 2016)** Pregnant, nursing females and individuals trying to conceive (male & female) should inform their manager if they wish to be excused from handling blood/body fluids and preparing or administering hazardous drugs.

**National Association of Pharmacy Regulatory Authorities (Nov 2016)**

The pharmacy manager or pharmacy department head is responsible for developing, organizing and supervising all activities related to pharmacy compounding of hazardous sterile preparations. This person may share or assign these responsibilities to a pharmacist or pharmacy technician, who will be designated as the sterile compounding supervisor. If the designated pharmacist or pharmacy technician chooses not to perform these activities, the pharmacy manager or pharmacy department head must assume the responsibilities of the sterile compounding supervisor and must therefore be qualified to perform compounding of hazardous sterile preparations in the pharmacy. If these responsibilities are assigned to a pharmacist or pharmacy technician, the pharmacy manager or pharmacy department head must ensure that the sterile compounding supervisor fulfills them adequately. In the pharmacy of a health care facility, a hazardous drugs committee should be established. The committee should comprise representatives of the employer, representatives of compounding and administration personnel, and representatives of cleaning and disinfecting personnel for the compounding areas. A pharmacist or pharmacy technician must be designated to support hazardous products management.

Sites shall be responsible for informing and training new and existing Staff about the potential hazards related to the risk of Exposure while Handling Hazardous Medications. Before compounding any hazardous sterile preparations, employees must receive specific training in the workplace and must undergo and pass an assessment of their competency, as described in section 5.1.2.3. An annual competency assessment program must also be put into place. All personnel (pharmacists, pharmacy technicians and pharmacy assistants) must know and apply safe-handling procedures for the receipt, storage, distribution and disposal of hazardous products and hazardous waste, as well as the procedures for dealing with accidental exposure and spills.
Manitoba (Oct 2015)
The WRHA Hazardous Medication List shall be published by the Pharmacy Safe Work Committee (WRHA, St. Boniface Hospital, and CancerCare Manitoba). Updates shall be provided as new information becomes available or as new drugs are brought into WRHA and CCMB facilities.

The procedures outlined in this Handling of Hazardous Medications (Cytotoxic and Non-Cytotoxic) Policy shall be used in conjunction with, not instead of, Infection Prevention and Control policies, operational directives, protocols, and best practice documents that can prevent or reduce the risk of transmission of microorganisms to health care providers, clients/patients/residents and visitors.

In accordance with the Manitoba Workplace Safety and Health regulations, Staff Handling Hazardous Medications shall discuss with their site Occupational Health Nurse or designate any information regarding pregnancy, breast-feeding or attempt to reproduce in order to discuss risks.

All diagnostic specimens and accompanying requisitions from patients receiving Cytotoxic Hazardous Medications and for the 48 hour time period following Cytotoxic Hazardous Medication administration shall be labeled as “Cytotoxic” before being submitted to the appropriate laboratory.

BC cancer agency (Sep 2016)
RESPONSIBILITIES
Senior Management
- Designate responsibility for the implementation and maintenance of the Hazardous Drug Safe Handling Standards.
- Ensure that all managers and supervisory staff are familiar with and adhere to the Hazardous Drug Safe Handling Standards.
- Ensure that health surveillance mechanisms are established for all staff that are at significant risk of exposure to hazardous drugs.

Directors/Managers and Supervisory Staff
- Ensure that all staff are fully familiar with the Hazardous Drug Safe Handling Standards and that they receive safe handling education and training.
- Ensure that staff comply with all workplace safe handling policies and procedures.
- Ensure that the health and safety of patients and staff are given primary consideration when implementing or altering processes, programs, or physical facilities related to hazardous drugs.
- Make every effort to accommodate requests to change work assignments for staff who are pregnant, breastfeeding or attempting to reproduce.

Ensure hazardous drug exposure records are maintained for duration of employment of each employee plus 10 years, and training records for 3 years from the date training occurred. (Work Safe BC Regulations).

All pharmacy staff involved in the preparation and delivery of hazardous drugs must demonstrate knowledge and competency for the duties that they are required to undertake. Re-evaluation of competency and knowledge must take place on a regular basis with documentation of results. A passing score of 85% or higher on the on-line test must be obtained by the pharmacy staff member to be eligible for participation in the on-site performance assessment.

Staff Education
- Education for the safe handling and exposure documentation of hazardous drugs is to be provided prior to working with hazardous drug.
• Information on the possible risks and necessary precautions to take when handling hazardous drugs must be made available to all relevant staff.
• Written procedures for handling hazardous drugs must be accessible to all relevant staff.
• Personnel handling hazardous drugs must receive education and training in the use of personal protective equipment, safe handling procedures and hazardous drug spill management to decrease risk of exposure to these agents. (Refer to Table 2)
• To ensure that safe handling procedures are being followed, work practices must be assessed at appropriate intervals with retraining provided as necessary.

Work safe BC (2015)
Workplaces where cytotoxic drugs are present must have an exposure control plan in place. See sections 5.54(1) and 6.43 of the Regulation. The employer must review the exposure control plan at least annually and update if required. See section 5.54(3) of the Regulation. An exposure control plan (ECP) describes how workers will be protected from hazardous drugs in the workplace. An ECP includes information on the nature of the hazard and the risk associated with exposure, as well as controls that the employer will use to protect workers. The ECP includes the following components, which are detailed in section 5.54(2) of the Regulation:
• Statement of purpose and responsibilities
• Risk identification and assessment
• Risk controls • Written safe work procedures
• Education and training
• Written records
• Hygiene facilities and decontamination procedures (when required)
• Health monitoring (when required)
The ECP should be reviewed at least annually and updated as necessary by the employer, in consultation with the joint occupational health and safety committee or the worker health and safety representative.

Some hazardous drugs may also be reproductive toxins. According to section 6.49 of the Regulation, where reproductive toxins are present in cytotoxic drugs, the employer must develop procedures to reduce the risk of exposure to workers who are pregnant or who are trying to conceive a child. An administrative control method of achieving this is protective reassignment. This is where the worker is assigned to alternative tasks that reduce the risk of their exposure to hazardous drugs. Some examples of protective reassignment include, but are not limited to:
• Moving the worker to a different area that does not involve exposure to hazardous drugs
• Assigning the worker to tasks where they won’t be exposed to hazardous drugs
• Reducing shift hours working in areas where hazardous drugs are handled

Where cytotoxic drugs are present in the workplace, information must be communicated to workers in the form of labels, signs, lists, education and training, and written records. See sections 6.45, 6.46, 6.47, 6.50, and 6.52 of the Regulation.

Alberta Health Services (June 2017)
Pregnancy and other Medical Conditions
1. Anyone can be at risk of adverse effects from occupational exposure to cytotoxic medications. It is important to limit exposure by following guidelines found in this manual. If you have a medical condition that you feel excludes you from handling these medications, consult with Occupational Health and notify your manager.

2. It is the responsibility of staff handling these drugs to discuss with their immediate supervisor any desired
change in work assignment as a result of their pregnancy, breastfeeding, or attempt to reproduce.

**United States Pharmacopeial Convention (Chapter to become official July 1, 2018.)**

Entities that handle HDs must incorporate the standards in this chapter into their occupational safety plan. The entity’s health and safety management system must, at a minimum, include:

- A list of HDs
- Facility and engineering controls
- Competent personnel
- Safe work practices
- Proper use of appropriate Personal Protective Equipment (PPE)
- Policies for HD waste segregation and disposal

Each entity must have a designated person who is qualified and trained to be responsible for developing and implementing appropriate procedures; overseeing entity compliance with this chapter and other applicable laws, regulations, and standards; ensuring competency of personnel; and ensuring environmental control of the storage and compounding areas. The designated person must thoroughly understand the rationale for risk-prevention policies, risks to themselves and others, risks of non-compliance that may compromise safety, and the responsibility to report potentially hazardous situations to the management team. The designated person must also be responsible for the oversight of monitoring the facility and maintaining reports of testing/sampling performed in facilities, and acting on the results. All personnel who handle HDs are responsible for understanding the fundamental practices and precautions and for continually evaluating these procedures and the quality of final HDs to prevent harm to patients, minimize exposure to personnel, and minimize contamination of the work and patient-care environment.

**Hazard Communication program:** Entities are required to establish policies and procedures that ensure worker safety during all aspects of HD handling. The entity must develop SOPs to ensure effective training regarding proper labeling, transport, storage, and disposal of the HDs and use of Safety Data Sheets (SDS), based on the Globally Harmonized System of Classification and Labeling of Chemicals (GHS).

Elements of the hazard communication program plan must include:

- A written plan that describes how the standard will be implemented
- All containers of hazardous chemicals must be labeled, tagged, or marked with the identity of the material and appropriate hazard warnings
- Entities must have an SDS for each hazardous chemical they use (29 CFR 1910.1200)
- Entities must ensure that the SDSs for each hazardous chemical used are readily accessible to personnel during each work shift and when they are in their work areas
- Personnel who may be exposed to hazardous chemicals when working must be provided information and training before the initial assignment to work with a hazardous chemical, and also whenever the hazard changes
- Personnel of reproductive capability must confirm in writing that they understand the risks of handling HDs

**PERSONNEL TRAINING** All personnel who handle HDs must be trained based on their job functions (e.g., in the receipt, storage, compounding, repackaging, dispensing, administrating, and disposing of HDs). Training must occur before the employee independently handles HDs. The effectiveness of training for HD handling competencies must be demonstrated by each employee. Personnel competency must be reassessed at least every 12 months. Personnel must be trained prior to the introduction of a new HD or new equipment and prior to a new or significant change in process or SOP. All training and competency assessment must be documented. The training must include at least the following:

- Overview of entity's list of HDs and their risks
- Review of the entity's SOPs related to handling of HDs • Proper use of PPE
• Proper use of equipment and devices (e.g., engineering controls)
• Response to known or suspected HD exposure
• Spill management
• Proper disposal of HDs and trace-contaminated materials

DOCUMENTATION AND STANDARD OPERATING PROCEDURES
The entity must maintain SOPs for the safe handling of HDs for all situations in which these HDs are used throughout a facility. The SOPs must be reviewed at least every 12 months by the designated person, and the review must be documented. Revisions in forms or records must be made as needed and communicated to all personnel handling HDs. The SOPs for handling of HDs should include:
• Hazard communication program
• Occupational safety program
• Designation of HD areas
• Receipt
• Storage
• Compounding
• Use and maintenance of proper engineering controls (e.g., C-PECs, C-SECs, and CSTDs)
• Hand hygiene and use of PPE based on activity (e.g., receipt, transport, compounding, administration, spill, and disposal)
• Deactivation, decontamination, cleaning, and disinfection
• Dispensing
• Transport
• Administering
• Environmental monitoring (e.g., wipe sampling)
• Disposal
• Spill control
• Medical surveillance
Personnel who transport, compound, or administer HDs must document their training according to OSHA standards (see OSHA Standard 1910.120 Hazardous Waste Operations and Emergency Response) and other applicable laws and regulations.

The National Institute for Occupational Safety and Health (NIOSH) maintains a list of antineoplastic and other HDs used in healthcare. An entity must maintain a list of HDs, which must include any items on the current NIOSH list that the entity handles. The entity's list must be reviewed at least every 12 months. Whenever a new agent or dosage form is used, it should be reviewed against the entity's list. The NIOSH list of antineoplastic and other HDs provides the criteria used to identify HDs. These criteria must be used to identify HDs that enter the market after the most recent version of the NIOSH list, or that the entity handles as an investigational drug. If the information available on a drug is deemed insufficient to make an informed decision, consider the drug hazardous until more information is available. Some dosage forms of drugs defined as hazardous may not pose a significant risk of direct occupational exposure because of their dosage formulation (e.g., tablets or capsules—solid, intact medications that are administered to patients without modifying the formulation). However, dust from tablets and capsules may present a risk of exposure by skin contact and/or inhalation. An assessment of risk may be performed for these dosage forms to determine alternative containment strategies and/or work practices. If an assessment of risk is not performed, all HDs must be handled with all containment strategies defined in this chapter. The assessment of risk must, at a minimum, consider the following:
• Type of HD (e.g., antineoplastic, non-antineoplastic, reproductive risk only)
• Dosage form
• Risk of exposure
• Packaging
• Manipulation
If an assessment of risk approach is taken, the entity must document what alternative containment strategies and/or work practices are being employed for specific dosage forms to minimize occupational exposure. If used, the assessment of risk must be reviewed at least every 12 months and the review documented.

**LABELING, PACKAGING, TRANSPORT AND DISPOSAL**

The entity must establish SOPs for the labeling, packaging, transport, and disposal of HDs. The SOPs must address prevention of accidental exposures or spills, personnel training on response to exposure, and use of a spill kit. Examples of special exposure-reducing strategies include small-bore connectors (such as Luer Lock) and syringes, syringe caps, CSTDs, the capping of container ports, sealed impervious plastic bags, impact-resistant and/or water-tight containers, and cautionary labeling. Labeling HDs identified by the entity as requiring special HD handling precautions must be clearly labeled at all times during their transport. Personnel must ensure that the labeling processes for compounded preparations do not introduce contamination into the non-HD handling areas.

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**ASCO and ONS 2015**

Organizations in which HDs are present will establish evidence-based policies and procedures for safe handling that comply with regulatory requirements.

- Organizations in which HDs are prepared and administered will provide and maintain primary engineering controls and evaluate the utility of supplemental engineering controls, such as closed-system transfer devices, to reduce worker exposure.
- Organizations in which HDs are present will ensure that appropriate PPE is available to all staff to minimize exposure.
- Organizations in which HDs are present will provide education and training specific to each worker’s role for staff who are potentially exposed; education and training will include the risks of exposure, including reproductive and developmental effects, recommended precautions for specific handling activities, safe handling of contaminated patient excreta, proper disposal of contaminated waste, and how to handle acute exposure.
- Organizations in which HDs are present will protect the right of staff who are trying to conceive, pregnant, or breast feeding to engage in alternative duties that do not require HD handling.
- Organizations in which HDs are present will ensure that patients who receive these drugs and their caregivers receive education about safe handling to minimize unintended exposure.
- Organizations will ensure that HD waste is disposed of according to regulatory guidelines and in a manner that protects staff and the environment.
- Our professional societies will continue to explore evidence-based strategies for mitigation of risk associated with
### RECOMMENDATION 2: PERSONAL PROTECTIVE EQUIPMENT (PPE)

It is legislated that a worker work in compliance with the Occupational Health and Safety Act and regulations and use or wear the equipment, protective devices or clothing that the employer requires to be used (2).

It is legislated that the appropriate personal protective equipment for the task (as described in Table 1) be worn throughout the medication circuit (2). It is the employer’s responsibility to provide the necessary protective equipment and training on how to use the equipment.

### Gloves

The gloves used to handle cytotoxic drugs are strongly recommended to comply with ASTM standard D-6978-(05)-13 and be powder free (12). Gloves are recommended to be nitrile, polyurethane, neoprene or latex (12). Latex is a known allergen, therefore it is strongly recommended that this be taken into consideration for glove selection. It is strongly recommended that vinyl gloves not be used. It is strongly recommended that the frequency of glove changes be adjusted according to the level of exposure at each step in the medication circuit. For example, when administering reconstituted medications, it is strongly recommended that workers change gloves immediately if torn, punctured, or visibly contaminated with a cytotoxic drug, and to ensure following Routine Practices (13). It is strongly recommended that great care be taken in the removal of gloves to not contaminate the skin. When two pairs of gloves are required, put on the first pair before putting on the gown. See Appendix F for the donning and doffing of one pair of gloves and Appendix G for the donning and doffing of two pairs of gloves.

### Gown

It is strongly recommended that the gowns used for handling cytotoxic drugs be disposable, made of lint-free, low-permeability fabric, have long sleeves with tight-fitting cuffs and fasten in the back. Gowns need to be changed in the event of contamination, spillage, rips, and at the end of the procedure. For medication preparation, gowns need to be changed halfway through a shift or every 3.5 hours (14). It is strongly recommended that the supplier be able to certify that the gown protects against cytotoxic drugs.

It is strongly recommended that care be taken to avoid contamination of the hands by avoiding touching the outside of the gown when removing the gown.

### Facial Protection

Surgical/procedure masks are required while handling and preparing medications in a biological safety cabinet and, in this instance, are worn to prevent microbial contamination of the sterile field.

It is strongly recommended that full-facial protection be worn whenever there is a risk of splashing (e.g., during certain drug administration procedures). The use of a full-facial shield is preferred. If goggles are used, they need to be worn in conjunction with a fluid-resistant mask. For further information, see CSA standard Z94.3-07 - Eye and Face Protectors (15).

### Respiratory Protection Apparatus (RPA)

It is strongly recommended that fit-tested respirators such as NIOSH certified N95 or N100 be
used when there is a risk that airborne powder or aerosol will be generated. It is legislated that respirators be used in accordance with a respiratory protection program such as that outlined in CSA Standard Z94.4-11 “Selection, Use and Care of Respirators” (16).

**Cap**
Caps are only required in the sterile preparation room and are worn to prevent microbial contamination of the sterile field.

**Shoe Covers**
Disposable shoe covers are worn to prevent contamination of the health care workers shoes, and it is strongly recommended that they be worn when in the sterile preparation room or in the event of a spill. It is strongly recommended that shoe covers be removed immediately when leaving the sterile prep room to avoid contamination of other areas.

| Table 1. Personal Protective Equipment to be worn throughout the medication circuit. |
|-----------------------------------------------|--|--|--|--|--|--|
| **Medication circuit steps** | **Gloves** | **Gown** | **RPA** | **Face protection** | **Cap** | **Shoe covers** |
| Unpacking and cleaning |  |  |  |  |  |  |
| Sterile preparations |  |  |  |  |  |  |
| Non-sterile preparations:  
- Counting of solid oral forms  
- Preparing creams, ointments, oral solutions and crushing tablets |  |  |  |  |  |  |
<p>| Routes of administration (intravenous, subcutaneous, intramuscular, intravesical, intraperitoneal, intrathecal, liquid oral) |  |  |  |  |  |  |
| Solid oral administration (tablets)* |  |  |  |  |  |  |
| Topical administration (creams, ointments) |  |  |  |  |  |  |
| Aerosolized administration (e.g., ribavirin, pentamidine)† |  |  |  |  |  |  |
| Patient care |  |  |  |  |  |  |</p>
<table>
<thead>
<tr>
<th>Medication circuit steps</th>
<th>Gloves</th>
<th>Gown</th>
<th>RPA</th>
<th>Face protection</th>
<th>Cap</th>
<th>Shoe covers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Management of extravasation</td>
<td>(1 pair)</td>
<td></td>
<td></td>
<td>(if risk of splashing, e.g., disposal of bodily fluids)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Handling of contaminated bedding on the wards</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Waste management (collection and transport)</td>
<td>(1 pair)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spill or damaged or broken container</td>
<td>(2 pairs)</td>
<td></td>
<td></td>
<td>(if suspicion of powder or aerosolization is generated)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cleaning of sterile preparation room and airlock</td>
<td>(1 pair)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cleaning of preparation cabinets (hoods)</td>
<td>(2 pairs)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cleaning of other oncology pharmacy rooms and care units/clinics</td>
<td>(1 pair)</td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

NG = nasal gastric tube, G = gastric tube, J = jejunostomy tube.
* Although the risk of contamination with oral medications is minimal, the working group believes that consistency of practice for any handling of cytotoxic drugs is of primary importance, and the preference is to wear a standard chemotherapy glove.
† Although cytotoxic, they are not neoplastic

**Saskatchewan (Regina, Feb 2016)** Vigilant use of personal protective equipment (PPE) must be used to prevent risk of exposure to hazardous drugs. See Appendix A.

- Gloves should be changed after each administration, if contaminated, or puncture occurs, or every 30 minutes.
- Gowns should not be shared and changed at minimum when leaving room or immediately if any contamination occurs.
- Discard all contaminated disposable material and disposable PPE in cytotoxic waste.

If assisting with drug aspiration, don PPE and N95 respiratory mask, place sterile gauze pad around vial during withdrawal of drug to reduce aerosolization.

**Quapos 5 (2016)**
Personnel assembling drug products for the cytostatic compounding process and personnel packaging the final product also need to wear personal protective equipment.

The personal protective equipment consists of:
- protective gown (possibly in combination with cuffs)
- protective gloves
and in special cases:
- respiratory protective equipment
- protective eyewear
- overshoes

The special cases are:
- cleaning tasks inside the safety workbench which extend beyond simply wiping the work surface
- clearing up spilled cytostatic materials
- filter replacement in the safety workbench

The kind of personal protective equipment is chosen based on the hazard evaluation of the work environment.

**Protective gown**

Protective gowns must be sufficiently long (covering the thighs) and closed up to the neck. They have long arms with close-fitting cuffs. They should repel liquids at especially exposed positions. For reasons of product protection they should at least be almost sterile and give off as few particles as possible.

**Disposable gloves for protection during the production of cytostatic solutions**

Suitable gloves or glove combinations must be worn, which are changed regularly and also in the event of contamination.

**Breathing protection, protective eyewear, overshoes**

In special cases the avoidance of contamination when dealing with cytostatics requires the wearing of breathing protection, protective eyewear and overshoes in addition to a protective gown and protective gloves. These additional measures are mandatory for cleaning the safety workbench, clearing up spillages of cytostatics and during filter replacement at the safety workbench. Breathing protection must consist of a half mask particle filter complying with DIN EN 149. The protective eyewear must provide protection at the side and be capable of being worn over any personal aids to vision. Overshoes must be liquid repelling and cover the entire foot as far as possible.

**Applying the PPE**

The proper applying of Personal Protective Equipment (PPE) is fundamental for safely and aseptically working with cytostatics; in doing so, the quality of the product is ensured and the greatest possible degree of safety is provided for all persons involved.

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**National Association of Pharmacy Regulatory Authorities (Nov 2016)**

The same PPE that is worn for the compounding of hazardous sterile preparations must be worn for any type of facility and equipment maintenance, including changing filters and pre-filters that have potentially been contaminated by hazardous products, even if the filters are accessible from outside controlled areas (anteroom and clean room).

Facility maintenance activities must be recorded in the general maintenance log.

PPE adapted and approved for the compounding of hazardous sterile preparations must be worn during such compounding activities.

**Gloves**

Gloves used in the clean room, in the clean area of the anteroom and during aseptic processes in all C-PECs (including isolators) must be

- non-powdered;
compliant with standard D-6978-05 of ASTM International (formerly the American Society for Testing and Materials);
sterile (outer glove only).
Non-sterile gloves that meet the ASTM International standard can be used in unpacking areas, the “dirty” area of the anteroom and storage areas and can be worn under sterile gloves for aseptic processes.
For the following activities, personnel must wear two pairs of gloves meeting the ASTM International standard:
• unpacking;
• cleaning and disinfecting the clean room;
• disinfecting the C-PEC;
• compounding of hazardous preparations;
• managing a spill;
• disposing of hazardous products.
Glove changes
Both pairs of gloves must be discarded and replaced at the earliest of the manufacturer’s limit for permeation of the gloves, every 30 minutes or immediately if a tear, puncture or contamination has occurred or is suspected.

Gown
The gown must have been tested by the manufacturer for resistance to permeability by hazardous Drugs. It must close in the back (i.e., no open front), and it must have long sleeves with fitted cuffs at the wrists.
The gown must be discarded and replaced at the earliest of the manufacturer’s time limit for permeation of the gown or after 2-3 hours of continuous compounding work or after each removal or after a contamination has occurred or is suspected.
A gown is required for unpacking a damaged hazardous drug or if a spill of hazardous material has occurred.

Hair cover
A disposable hair cover must be worn during the compounding of hazardous sterile preparations. It must be changed after each removal or if it becomes contaminated.

Mask
Table 5 outlines the uses for and limitations of different types of masks.
No mask is needed for unpacking hazardous drugs that have been received from the supplier in impervious plastic. However, if a hazardous drug shipment has been damaged before receipt, a chemical cartridge respirator is required during unpacking.

Surgical masks do not provide respiratory protection against drug exposure and therefore should not be used when respiratory protection from hazardous drug exposure is required.
For most activities, an N95 or N100 mask (NIOSH-approved) will protect against airborne particles. However, N95 or N100 masks offer no protection from vapours, gases and little protection from direct liquid splashes.
A chemical cartridge respirator with a pre-filter must be worn in the presence of vapours, gas and particles (e.g., dust) or if there has been a spill. A cartridge that protects against the chlorine found in chlorinated disinfectants used for cleaning the C-PEC or for chemical decontamination after a spill may also be considered, to help prevent irritation of airways.
A chemical cartridge respirator with a pre-filter must be worn in the presence of vapours, gas and particles (e.g., dust) or if there has been a spill. A cartridge that protects against the chlorine found in chlorinated disinfectants used for cleaning the C-PEC or for chemical decontamination after a spill may also be considered, to help prevent irritation of airways.
Any mask (including N95 or N100 masks and chemical cartridge respirators) must first be fit-tested. The mask must be changed at the earliest of the following: after 3.5 hours of continuous
compounding work, after each removal or if contamination has occurred or is suspected.

Goggles and face shield or full face-piece respirator
Goggles and a face shield or full face-piece respirator must be worn when working at or above eye level, when deactivating, decontaminating and cleaning underneath the work surface of a C-PEC, when cleaning up a spill, when there is risk of splashes to the face and eyes and when unpacking suspected damaged drugs.

Shoe covers
Shoe covers prevent the contamination of shoes and subsequent spread of contamination to other areas of the facility. Two pairs of disposable shoe covers are required at all times in the clean area of the anteroom and in the clean room, even if dedicated shoes are worn. The shoe covers must be changed after each removal or in the event of contamination, spill or breakage. Shoe covers worn in hazardous drug compounding areas are not to be worn outside the controlled area.

Beard cover
If the compounder has facial hair, a disposable beard cover must be worn while compounding hazardous sterile preparations. The beard cover must be changed at the earliest of the following: after 3.5 hours of continuous work, after each removal or if contamination occurs or is suspected.

Uniform
Compounding personnel shall wear clean room scrubs, not street clothes. Use of clean room scrubs reduces the risk of contaminating the environment through clothing.

Manitoba (Oct 2015)
Appropriate PPE, Cytotoxic Spill Kits, and Cytotoxic Waste Containers shall be available wherever Handling of Cytotoxic Medications occurs. Risk of Exposure is greatest when Handling Cytotoxic Hazardous Medications and Cytotoxic Medication Waste and to a lesser extent when Handling Human Waste of Patients known to have received a Cytotoxic Hazardous Medication in the last 48 hours. The appropriate PPE shall be worn when Handling Hazardous Medications and Medication Waste and when Handling Cytotoxic Human Waste for the 48 hour time period following Cytotoxic Hazardous Medication administration.

Gloves shall be changed at a minimum of every 30 minutes of continuous work with Hazardous Medications and immediately if contaminated or if the integrity of the glove is compromised.

BC Cancer Agency (Sep 2016)
Workers must follow protective guidelines to minimize the release of particles into the aseptic preparation environment leading to possible contamination of the final product(s) and to decrease the possibility of personal exposure to hazardous drugs. There must be procedures and directives available for safe and aseptic handling of hazardous drugs. There must be strict adherence to safe handling procedures and directives.

Protective equipment and clothing must be provided and used to minimize or prevent healthcare workers exposure to hazardous drugs. Prior to entering the cleanroom, proper ‘gowning’ of the healthcare worker is required (e.g., hair cover, mask, gown, chemotherapy gloves, and shoe covers).
Scrubs
A buttoned lab coat must be donned over scrubs upon exiting the cleanroom/anteroom.

Footwear
Each facility must be in compliance with WorkSafe BC regulations to help reduce preventable injuries due to inappropriate footwear.
WorkSafe BC Regulation 8.22 states:
1. “A worker’s footwear must be of a design, construction and material appropriate to the protection required.”
2. “To determine appropriate protection, the following factors must be considered; slipping, uneven terrain, abrasion, ankle protection and foot support, crushing potential, temperature extremes, corrosive substances, puncture hazards, electrical shock and any other recognizable hazard.”

Shoe Covers
Shoe covers must be put on by all workers before stepping inside the cleanroom and must be removed with gloved hands at the doorway/demarcation line upon exiting. Shoe covers worn inside the HD cleanroom must be disposed of in hazardous waste containers and not saved for re-entry into the cleanroom.

Hair Covers
A disposable hair cover (covering hair and ears completely) must be worn by all personnel working in the BSC and/or present in the cleanroom.

Masks
Surgical masks must be worn by all personnel working in the BSC and/or present in the cleanroom. Masks worn in the cleanroom must cover from the bridge of the nose down to include the chin.

Respirators
A NIOSH-approved respirator must be worn when cleaning up HD spills outside of the BSC and when decontaminating or cleaning the BSC.
Staff wearing a NIOSH-approved respirator (e.g., N95, P100) must be fit-tested prior to initial use and retested at least once a year, when there is a change in the respirator face piece, or when a user’s physical condition changes affecting the fit.
WorkSafe BC Regulation 8.41 states:
“Before each use of a respirator which requires an effective seal with the face for proper functioning, a worker must perform a positive or negative pressure user seal check in accordance with CSA Standard CAN/CSA-Z94.4-02, Selection, Use, and Care of Respirators.

Chemotherapy Gowns
To decrease particulate levels in the preparation area and to decrease the risk of direct skin contact with the hazardous drugs, workers must wear non-linting, impermeable, disposable chemotherapy gowns with long sleeves and tightly-fitting cuffs, a closed front, and tied in the back. Chemotherapy gowns must be worn for all activities that may result in the worker’s direct exposure to hazardous drugs.
Chemotherapy gowns worn in the HD cleanroom must be removed for storage or disposal while still in the cleanroom to prevent the spread of HD contamination from one area to another.
Lab coats or isolation gowns must not be worn in the hazardous drug cleanroom by staff working in the biological safety cabinet in place of chemotherapy gowns.

Chemotherapy Gloves
Chemotherapy approved gloves must pass permeation testing with nine chemotherapy agents as required by the American Society for Testing and Materials (ASTM) Standard 6978-05 (Standard Practice for Assessment of Resistance of Medical Gloves to Permeation by Chemotherapy Gloves). Gloves worn to handle hazardous drugs must be made of made of latex, nitrile, neoprene, or polyurethane, powder-free, and long enough to cover the cuff of the chemotherapy gown. If powder-free gloves are not available, powdered gloves must be wiped with a towel moistened with 70% alcohol prior to entering the cleanroom. Alcohol must not be sprayed to remove powder. Gloves made
of material other than latex, nitrile, neoprene, or polyurethane may be used if documentation of approved testing for impermeability to chemotherapy can be provided. Latex-free ‘chemotherapy-approved’ gloves must be made available to staff. Two pairs of disposable chemotherapy gloves must be worn for all activities that may result in hazardous drug exposure including handling all hazardous drugs and hazardous drug waste and must be disposed of as hazardous waste. Two pairs of disposable chemotherapy gloves must be worn at all times by all personnel working in the HD cleanroom. Both pairs of disposable chemotherapy gloves must be changed every 30 minutes or immediately if a tear, puncture or contamination is known or suspected. Hands must be washed with soap and water every time gloves are removed.

**Eye Protection**

Eye shields or safety goggles with side shields must be worn for splash protection when cleaning or decontaminating a BSC with the viewing window raised or when cleaning up a hazardous drug spill outside the BSC.

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**Work safe BC (2015)**

**Chemotherapy-tested gloves** Chemotherapy-tested gloves must be worn whenever hazardous drugs or potentially contaminated objects are handled. Chemotherapy gloves should meet the requirements of ASTM Standard 6978-05 Standard Practice for Assessment of Resistance of Medical Gloves to Permeation by Chemotherapy Gloves. Chemotherapy-tested gloves should:

- Not be powdered, as the powder can be contaminated and then fall off the gloves during removal and contribute to contamination
- Be compatible with cleaning and decontaminating agents used in the workplace
- Be latex free (acceptable alternatives include neoprene, nitrile, and polyurethane)
- Be able to maintain their resistance to permeation by hazardous drugs when disinfected with alcohol

When following best practices for the use of gloves during handling of hazardous drugs, workers should:

- Wear double gloves when the risk for dermal contamination with hazardous drugs is high (this is determined as part of your workplace risk assessment)
- Follow steps to avoid contamination when putting on gloves and during removal, including washing hands before and after wearing gloves
- Change gloves after 30 minutes of continuous compounding or if they have been contaminated or compromised
- Remove outer gloves before taking them out of a biological safety cabinet

**Chemotherapy-tested gowns** Chemotherapy-tested gowns used for handling hazardous drugs must be worn when there is risk of bodily contact with hazardous drugs or contaminated patient body fluids and waste during the precautionary period. Gowns should:

- Be identified by the manufacturer as gowns for handling hazardous drugs
- Be moisture resistant with long sleeves and tight-fitting cuffs
- Have a closed front that covers the worker from shoulders to knees and fastens in the back
- Be disposable

When following best practice for the use of chemotherapy gowns with hazardous drugs, workers should:

- Change the gown every 3.5 hours or immediately when contaminated or compromised
- Wash hands immediately after removing a gown

Chemotherapy gowns should meet the requirements of ASTM Standard F739-99a Standard Test Method for Resistance of Protective Clothing Materials to Permeation by Liquids or Gases under Conditions of Continuous Contact or a comparable standard.

**Respirators** An approved and fit-tested respirator must be worn when there is a risk of exposure to airborne particulates, aerosols, or vapours from hazardous drugs. The respirator selected must
provide protection from particulates as well as gases or vapours that can be generated from solid or liquid forms of hazardous drugs, depending on the activity. This could include a half-or full-face air-purifying respirator that has a particulate filter (such as P100) and a chemical cartridge that removes vapour contaminants from air as it is inhaled. The choice of respirator must be made as part of the risk assessment based on the potential exposure to airborne particulates, aerosols, or vapours from hazardous drugs for each task in the workplace. Fit tests must also be carried out before a respirator is issued to a worker. The worker must perform a seal check before each use. Refer to the WorkSafeBC publication Breathe Safer: How to Use Respirators Safely and Start a Respirator Program for more information on how to select an appropriate respirator.

**Face and eye protection** Face protection, such as full or partial face shields and goggles, should be worn when there is a risk of splashing, which may occur when handling liquid forms of hazardous drugs or contaminated body fluids and waste. When following best practice for wearing face protection for hazardous drugs, workers should:
- Wear full face shields
- Use disposable face protection whenever practicable
- Clean non-disposable face protection immediately after use

**Footwear and shoe covers** Workers must ensure their footwear is in a condition to provide protection against exposure to hazardous drugs, such as by wearing closed shoes that are made of a material that prevents liquids from soaking through. Refer to section 8.22 of the Regulation for more information on the requirements for footwear. Shoe covers are part of sterile preparation procedures but also help reduce exposure by preventing contamination being spread to other areas of the workplace on workers' shoes. Best practices for footwear and shoe covers include, but are not limited to:
- Having a dedicated set of footwear that is only used in the preparation area
- Having all workers wear shoe covers when entering a sterile preparation room
- Removing shoe covers with gloved hands and disposing as hazardous waste upon exiting the preparation room
- Wearing shoe covers when cleaning up spills or broken containers on the floor

Alberta Health Services (June 2017)
PPE must not be worn outside the preparation, dispensing, receiving or administration area to avoid spreading contamination and possibly exposing non-protected staff.
PPE must be worn when dismantling and disposing equipment used in the administration of these drugs.
Disposable PPE should be used whenever possible.
Used disposable PPE must be handled as cytotoxic waste.

**Gloves**
Suitable gloves are powder-free, made of nitrile, latex, polyurethane or neoprene and comply with American Society of Testing and Materials (ASTM) standard D-6978-05 for chemotherapy gloves or have been tested with cytotoxic drugs.
- Latex gloves should be avoided if possible due to the risk of latex sensitivity (allergies).
- Sterile procedures require sterile gloves.
- Inspect gloves for defects prior to use.
- Gloves must be changed within 60 minutes or in accordance with manufacturer’s recommendations or in the event of contamination, spillage, breakage or puncture.
- Do not touch other equipment with gloves that you have handled cytotoxic drugs with. Remove outer glove and use inner glove to manipulate equipment if needed. Gloves must not be reused.
Hands must be washed with soap and water after removal of gloves.

**GOWNS**
- Disposable, lint-free, moisture-resistant, made of low permeability fabric with a closed front, a back closure and long sleeves that can be enclosed with gloves such as sleeves with elastic or knit closed cuffs (hereafter referred to as the DMR gown) is required when handling cytotoxic drugs that may spill / splash/ emit or form liquid aerosolized droplets/solid particles.
- Gowns must be proven to protect against cytotoxic drugs.
- Gowns must be changed daily or whenever contamination is suspected. Gowns must be removed when leaving the treatment setting/unit. Gowns must not be shared.
- Yellow isolation gowns may be worn if there is no risk of spillage, splash or aerosolization of solid/liquid particles. (i.e. when handling of tablets or capsules) at the discretion of qualified staff.

**EYE PROTECTION**
- Eye/face protection consisting of face sealing chemical splash goggles with or without side vents or a full face shield must be worn when there is any hazard of eye contact (i.e. if risk of splashing or aerosolization of liquid/solid particles).
- Goggles are particularly appropriate for contact lens wearers (a potential additional hazard if contaminated).
- Eyeglasses do not provide sufficient eye protection.
- If goggles are not visibly or only minimally contaminated, they may be reused. Wash thoroughly with household detergent and water after use. Wear gloves and gown when washing goggles. If overtly contaminated, discard goggles into cytotoxic waste container.
- Adequate Workplace Safety and Health approved eyewash facilities must be provided.

**RESPIRATORY PROTECTION**
- Fit tested N-95 mask is required for protection whenever there is a possibility of aerosolized particles (solid or liquid).
- A surgical mask is not suitable as it does not provide adequate protection.

**HEAD AND SHOE PROTECTION** Appropriate head and shoe covers are recommended for spill cleanup and for the preparation and/or administration of any cytotoxic drugs that may splash or spill or aerosolize. Apparel may not be worn out of the area. Closed toe footwear recommended.

Table 2: WHEN and WHAT Equipment to Wear

<table>
<thead>
<tr>
<th>ACTIVITY</th>
<th>GLOVES</th>
<th>GOWN</th>
<th>EYE PROTECTION</th>
<th>RESPIRATORY PROTECTION</th>
<th>HEAD AND SHOE PROTECTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preparation crushing or splitting tablets, opening capsules and preparing oral liquid preparations or</td>
<td>Yes TWO pairs of gloves</td>
<td>Yes Disposable moisture-resistant, long-sleeved gown (DMR-gown)</td>
<td>Yes Goggles or Face Shield</td>
<td>Yes N-95 mask</td>
<td>Yes If potential for splash, spill or aerosolization</td>
</tr>
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</table>

Section 4: Document Review Summary
<table>
<thead>
<tr>
<th>IV admixtures1</th>
<th>Administration</th>
<th>Spill Clean-Up</th>
<th>Waste Disposal</th>
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<tr>
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<td>Yes</td>
<td>Yes</td>
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<td>TWO pairs of</td>
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<td></td>
<td>gloves</td>
<td>DMR-gown</td>
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<td></td>
<td>Goggles or Face Shield</td>
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<td>N-95 mask</td>
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<td>No</td>
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<td>N-95 mask</td>
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<td>spill.</td>
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</table>

1. should be completed in pharmacy whenever possible, but if necessary to do outside of pharmacy, follow chart

**United States Pharmacopeial Convention** (Chapter to become official July 1, 2018.)

**PERSONAL PROTECTIVE EQUIPMENT**

Personal Protective Equipment (PPE) provides worker protection to reduce exposure to HD aerosols and residues. Additional PPE may be required to handle the HDs outside of a C-PEC, such as treating a patient or cleaning a spill. The NIOSH list of antineoplastic and other HDs provides general guidance on PPE for possible scenarios that may be encountered in healthcare settings. Disposable PPE must not be re-used. Reusable PPE must be decontaminated and cleaned after use. Gowns, head, hair, shoe covers, and two pairs of chemotherapy gloves are required for compounding sterile and nonsterile HDs. Two pairs of chemotherapy gloves are required for administering antineoplastic HDs. Gowns shown to resist permeability by HDs are required when administering injectable antineoplastic HDs. For all other activities, the entity’s SOP must describe the appropriate PPE to be worn based on its occupational safety plan and assessment of risk (if used). The entity must develop SOPs for PPE based on the risk of exposure (see Types of Exposure) and activities performed.

Appropriate PPE must be worn when handling HDs including during:

- Receipt
- Storage
- Transport
- Compounding (sterile and nonsterile)
- Administration
- Deactivation/decontamination, cleaning, and disinfecting
- Spill control
- Waste disposal

**Gloves** When chemotherapy gloves are required, they must meet American Society for Testing and Materials (ASTM) standard D6978 (or its successor). Chemotherapy gloves should be worn for handling all HDs including non-antineoplastics and for re-productive risk only HDs. Chemotherapy gloves must be powder-free because powder can contaminate the work area and can adsorb and retain HDs. Gloves must be inspected for physical defects before use. Do not use gloves with pin holes or weak spots.
When used for sterile compounding, the outer chemotherapy gloves must be sterile. Chemotherapy gloves should be changed every 30 minutes unless otherwise recommended by the manufacturer’s documentation and must be changed when torn, punctured, or contaminated. Hands must be washed with soap and water after removing gloves.

**Gowns** When gowns are required, they must be disposable and shown to resist permeability by HDs. Gowns must be selected based on the HDs handled. Disposable gowns made of polyethylene-coated polypropylene or other laminate materials offer better protection than those made of uncoated materials. Gowns must close in the back (i.e., no open front), be long sleeved, and have closed cuffs that are elastic or knit. Gowns must not have seams or closures that could allow HDs to pass through. Cloth laboratory coats, surgical scrubs, isolation gowns, or other absorbent materials are not appropriate protective outer-wear when handling HDs because they permit the permeation of HDs and can hold spilled drugs against the skin, thereby increasing exposure. Clothing may also retain HD residue from contact, and may transfer to other healthcare workers or various surfaces. Washing of non-disposable clothing contaminated with HD residue should only be done according to facility policy as drug residue may be transferred to other clothing. Potentially contaminated clothing must not be taken home under any circumstances. Gowns must be changed per the manufacturer’s information for permeation of the gown. If no permeation information is available for the gowns used, change them every 2-3 hours or immediately after a spill or splash. Gowns worn in HD handling areas must not be worn to other areas in order to avoid spreading HD contamination and exposing other healthcare workers.

**Head, Hair, Shoe, and Sleeve Covers** Head and hair covers (including beard and moustache, if applicable), shoe covers, and sleeve covers provide protection from contact with HD residue. When compounding HDs, a second pair of shoe covers must be donned before entering the C-SEC and doffed when exiting the C-SEC. Shoe covers worn in HD handling areas must not be worn to other areas to avoid spreading HD contamination and exposing other healthcare workers. Disposable sleeve covers may be used to protect areas of the arm that may come in contact with HDs. Disposable sleeve covers made of polyethylene-coated polypropylene or other laminate materials offer better protection than those made of un-coated materials.

**Eye and Face Protection** Many HDs are irritating to the eyes and mucous membranes. Appropriate eye and face protection must be worn when there is a risk for spills or splashes of HDs or HD waste materials when working outside of a C-PEC (e.g., administration in the surgical suite, working at or above eye level, or cleaning a spill). A full-facepiece respirator provides eye and face protection. Goggles must be used when eye protection is needed. Eye glasses alone or safety glasses with side shields do not protect the eyes adequately from splashes. Face shields in combination with goggles provide a full range of protection against splashes to the face and eyes. Face shields alone do not provide full eye and face protection.

**Respiratory Protection** Personnel who are unpacking HDs that are not contained in plastic should wear an elastomeric half-mask with a multi-gas cartridge and P100-filter until assessment of the packaging integrity can be made to ensure no breakage or spillage occurred during transport. If the type of drug can be better defined, a more targeted cartridge can be used. Surgical masks do not provide respiratory protection from drug exposure and must not be used when respiratory protection from HD exposure is required. A surgical N95 respirator provides the respiratory protection of an N95 respirator, and like a surgical mask, provides a barrier to splashes, droplets, and sprays around the nose and mouth. For most activities requiring respiratory protection, a fit-tested NIOSH-certified N95 or more protective respirator is
sufficient to protect against airborne particles. However, N95 respirators offer no protection against gases and vapors and little protection against direct liquid splashes (see the Centers for Disease Control and Prevention's (CDC's) Respirator Trusted-Source Information). Fit the respirator and train workers to use respiratory protection. Follow all requirements in the Occupational Safety and Health Administration (OSHA) respiratory protection standard (29 CFR 1910.134). An appropriate full-facepiece, chemical cartridge-type respirator or powered air-purifying respirator (PAPR) should be worn when there is a risk of respiratory exposure to HDs, including when:
- Attending to HD spills larger than what can be contained with a spill kit
- Deactivating, decontaminating, and cleaning underneath the work surface of a C-PEC
- There is a known or suspected airborne exposure to powders or vapors.

Routes of unintentional entry of HDs into the body include dermal and mucosal absorption, inhalation, injection, and ingestion (e.g., contaminated foodstuffs, spills, or mouth contact with contaminated hands). Containers of HDs have been shown to be contaminated upon receipt. Both clinical and nonclinical personnel may be exposed to HDs when they handle HDs or touch contaminated surfaces. Table 1 lists examples of potential routes of exposure based on activity.

<table>
<thead>
<tr>
<th>Examples of Potential Opportunities of Exposure Based on Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Receipt</strong></td>
</tr>
<tr>
<td>• Contacting HD residues present on drug containers, individual dosage units, outer containers, work surfaces, or floors</td>
</tr>
<tr>
<td><strong>Dispensing</strong></td>
</tr>
<tr>
<td>• Counting or repackaging tablets and capsules</td>
</tr>
<tr>
<td><strong>Compounding and other manipulations</strong></td>
</tr>
<tr>
<td>• Crushing or splitting tablets or opening capsules</td>
</tr>
<tr>
<td>• Pouring oral or topical liquids from one container to another</td>
</tr>
<tr>
<td>• Weighing or mixing components</td>
</tr>
<tr>
<td>• Constituting or reconstituting powdered or lyophilized HDs</td>
</tr>
<tr>
<td>• Withdrawing or diluting injectable HDs from parenteral containers</td>
</tr>
<tr>
<td>• Expelling air or HDs from syringes</td>
</tr>
<tr>
<td>• Contacting HD residue present on PPE or other garments</td>
</tr>
<tr>
<td>• Deactivating, decontaminating, cleaning, and disinfecting areas contaminated with or suspected to be contaminated with HDs</td>
</tr>
<tr>
<td>• Maintenance activities for potentially contaminated equipment and devices</td>
</tr>
<tr>
<td><strong>Administration</strong></td>
</tr>
<tr>
<td>• Generating aerosols during administration of HDs by various routes (e.g., injection, irrigation, oral, inhalation, or topical application)</td>
</tr>
<tr>
<td>• Performing certain specialized procedures (e.g., intraoperative intraperitoneal injection or bladder instillation)</td>
</tr>
<tr>
<td>• Priming an IV administration set</td>
</tr>
<tr>
<td><strong>Patient-care activities</strong></td>
</tr>
<tr>
<td>• Handling body fluids (e.g., urine, feces, sweat, or vomit) or body-fluid-contaminated clothing, dressings, linens, and other materials</td>
</tr>
<tr>
<td><strong>Spills</strong></td>
</tr>
<tr>
<td>• Spill generation, management, and</td>
</tr>
<tr>
<td><strong>Transport</strong></td>
</tr>
<tr>
<td>• Moving HDs within a healthcare setting</td>
</tr>
<tr>
<td><strong>Waste</strong></td>
</tr>
<tr>
<td>• Collection and disposal of hazardous waste and trace contaminated waste</td>
</tr>
</tbody>
</table>

**RECOMMENDATION 3: RECEIVING AND TRANSPORT**

**Handling Cytotoxic Drug Delivery Containers**

It is strongly recommended that all receiving-dock workers receive training in the proper handling of cytotoxic drugs. It is strongly recommended that the receiving-dock workers check the integrity of the external packaging upon receipt; in the event of breakage or a damaged parcel likely to cause a spill, apply the Spill Protocol from your institution.

It is strongly recommended that delivery containers be taken immediately to the Pharmacy Department by the receiving-dock workers or the distributor.
It is strongly recommended that the receiving-dock or storeroom workers not open the delivery containers. It is strongly recommended that the delivery containers be handled with care to avoid breakage of the cytotoxic drug containers and not be left unattended in a corridor. Only trained workers (e.g., pharmacy technicians) are to proceed with the unpacking and subsequent steps.

**Damaged Containers/Spill**

It is strongly recommended that damaged containers be handled like spills. It is strongly recommended that the manufacturer or distributor be notified if the container is received in a damaged state. To limit exposure, it is strongly recommended that a damaged container never be returned to the manufacturer or distributor. Notify the pharmacy if any damaged containers are suspected.

See recommendation 10: Management of Waste, Accidental Exposure, Spills and Returns

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**National Association of Pharmacy Regulatory Authorities (Nov 2016)**

If a shipping container for hazardous drugs appears damaged upon receipt, there are two options:

- Seal the package without opening it. Contact the supplier. If the package is to be returned to the supplier, place inside an impervious container and label the impervious container as hazardous. If the supplier declines the return, then dispose of as hazardous waste.
- Seal the container in an impervious container. Unpack the shipping container in a C-PEC used for compounding of non-sterile hazardous preparations. Place a plastic-backed preparation mat on the work surface of the C-PEC. Open the package and remove any usable items. Wipe the outside of these items with a disposable wipe. Place the damaged item(s) in an impervious container. Label the impervious container as hazardous. Contact the supplier for instructions on returning the damaged items. (See also section 6.11.2.) If the supplier declines the return, dispose of as hazardous waste. Deactivate, decontaminate and clean the C-PEC. Discard the mat and cleaning disposables as hazardous waste.

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**Work safe BC (2015)**

Drug suppliers and shipping companies handling hazardous drugs should ensure that there are appropriate procedures in place to protect their workers from exposure to hazardous drugs. Best practices for purchasing and shipping of hazardous drugs include:

- Sealing hazardous drugs in plastic bags or shrink wrap during transport
- Ensuring there are warning labels on the outside of shipping or transport containers containing hazardous drugs
- Using packages and packaging methods that will minimize breakage

PPE must be consistent with the worker’s potential exposure and may include:

- Chemotherapy-tested gloves
- A chemotherapy-tested gown

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**Alberta Health Services (June 2017)**

**Receiving /Transport of Unprocessed Cytotoxic Drugs**

A cytotoxic spill kit should be available in receiving areas whenever possible. Alternatively, staff can be educated as to the location of the nearest spill kit or where to obtain a spill kit. Cytotoxic drugs from suppliers may arrive at the receiving /loading dock or may be delivered directly to the pharmacy. Regular receiving procedures will be used at the loading dock. The
package should remain intact and only quantity needs to be checked. The unpacking and storage will be completed in the pharmacy.

If a cytotoxic package is leaking, clear the area, and initiate cytotoxic spill cleanup procedures.

A small spill is a spill which can be contained using a cytotoxic spill kit and a large spill is a spill which cannot be contained with a cytotoxic spill kit. (See definitions section 1. C). For spills in public areas and/or those that cannot be managed with a cytotoxic spill kit by existing staff at site of spill, Environmental Services or a CODE BROWN can be called as per site policies/procedures.

To minimize exposure, a damaged package should never be returned to the manufacturer or distributor. The manufacturer or distributor must however, be notified.

United States Pharmacopeial Convention (Chapter to become official July 1, 2018)

RECEIVING

The entity must establish SOPs for receiving HDs. HDs should be received from the supplier in impervious plastic to segregate them from other drugs and to allow for safety in the receiving and internal transfer process. HDs must be delivered to the HD storage area immediately after unpacking.

PPE, including chemotherapy gloves, must be worn when unpacking HDs (see Personal Protective Equipment). A spill kit must be accessible in the receiving area.

The entity must enforce policies that include a tiered approach, starting with visual examination of the shipping container for signs of damage or breakage (e.g., visible stains from leakage, sounds of broken glass).

Table 4 summarizes the steps for receiving and handling of damaged shipping containers.

| If the shipping container appears damaged | • Seal container without opening and contact the supplier  
| | • If the unopened package is to be returned to the supplier, enclose the package in an impervious container and label the outer container "Hazardous"  
| | • If the supplier declines return, dispose of as hazardous waste |
| If a damaged shipping container must be opened | • Seal the container in plastic or an impervious container  
| | • Transport it to a C-PEC and place on a plastic-backed preparation mat  
| | • Open the package and remove undamaged items  
| | • Wipe the outside of the undamaged items with a disposable wipe  
| | • Enclose the damaged item(s) in an impervious container and label the outer container "Hazardous"  
| | • If the supplier declines return, dispose of as hazardous waste  
| | • Deactivate, decontaminate, and clean the C-PEC (see Deactivating, Decontaminating, Cleaning, and Disinfecting) and discard the mat and cleaning disposables as hazardous waste |

When opening damaged shipping containers, they should preferably be transported to a C-PEC designated for nonsterile compounding. If a C-PEC designated for sterile compounding is the only one available, it must be disinfected after the decontamination, deactivation, and cleaning step before returning to any sterile compounding activity. Damaged packages or shipping cartons must be considered spills that must be reported to the designated person and man-aged according to the entity’s SOPs. Segregate HDs waiting to be returned to the supplier in a designated negative pressure area. Clean-up must comply with established SOPs.

RECOMMENDATION 5: CYOTOXIC DRUG PREPARATION
Planning the Oncology Pharmacy

It is strongly recommended that the oncology pharmacy be in compliance with relevant guidelines from the Canadian Society of Hospital Pharmacists (CSHP) and Accreditation Canada standards. While the specific details of oncology pharmacy planning is beyond the scope of this document, details and some important considerations may be found in the Canadian Standard Association document CSA Z8000-11 (19).

It is strongly recommended that special requirements for heating, ventilation and air-conditioning (HVAC) systems in health care facilities be taken into consideration (18).

A class II type B biological safety cabinet is required with preference for the type B2, because it ensures that there is no recirculation of air within the cabinet (5).

There is emerging evidence suggesting some robotic devices that prepare cytotoxics improve the accuracy of medication preparation and reduce potentially harmful staff safety events. Further studies are required to establish the cost effectiveness of these robotic implementations. Each health care facility will need to assess the need for such devices in their environment (20).

It is strongly recommended that all mixing, and preparation of administration sets with a cytotoxic drug be performed in one centralized area in a specially designated class II type B biological safety cabinet that (18):
(a) is exhausted through a HEPA filter to the outside atmosphere in a manner that prevents recirculation into any inside area;
(b) has exhaust and ventilation systems that remain in operation for a sufficient period of time to ensure that no contaminants escape from the biological safety cabinet into the workplace; and
(c) is equipped with a continuous monitoring device to permit confirmation of adequate airflow and cabinet performance.

It is recommended that airlocks be considered if there are particular concerns about the propagation of airborne cytotoxic drugs.

It is strongly recommended that priming of administration sets be prepared in the manner mentioned above.

It is strongly recommended that the layout allow and facilitate the unimpeded cleaning of all surfaces (walls, floors, ceilings, doors, diffusers, windows). It is strongly recommended that the furniture and equipment in the sterile preparation room be kept to a bare minimum. It is strongly recommended that there be a visual link, for example, a window and a way to communicate between the sterile preparation room and the pharmacy, in order to view the work in progress. It is strongly recommended that access to the sterile room be limited to trained and authorized workers.

Limit worker traffic, particularly near unpacking and storage areas (to avoid accidental breakage) and near preparation cabinets (to avoid interfering with their proper operation).

It is legislated that the facilities include an emergency eyewash that may or may not be hooked up to the airlock sink (2). As a minimum, it is strongly recommended that emergency eyewash be able to provide 15 minutes of flushing to both eyes (21). It is strongly recommended that a full shower be accessible nearby (e.g., in the oncology units/clinics).

Closed-drug transfer systems (e.g., PhaSeal®) are not a substitute for class II type B biological
safety cabinets. There is evidence from studies (22-27) that closed-drug transfer-systems can reduce contamination during preparation. Further emerging evidence suggests that when these devices are not used as specified, they could become open to the environment. Further research is needed to evaluate this possibility.

It is strongly recommended that the biological safety cabinets remain in operation 24 hours a day, 7 days a week, as recommended by the manufacturers.

In the non-sterile drug preparation process (e.g., oral preparations), it is strongly recommended that the same level of worker protection be adhered to.

**Pharmacy Policies and Procedures**

Establish policies and procedures regarding preventive maintenance, monitoring, certification and the optimal use of facilities and equipment (28).

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**Saskatchewan (Regina, Feb 2016)**

1. PPE as per Appendix A
2. Administration equipment as indicated by route (IV tubing, injection needle, medication cup, etc.)
3. IV administration - closed administration equipment (i.e. EquaShield® or PhaSealTM) as available and required if hanging more than one medication. (See Appendix D)

**Quapos 5 (2016)**

Preparation takes place in a separate, clearly designated cleanroom work area, which is separated from the remaining areas by one or more air-locks. The classification of the cleanrooms with regard to particle and microbial counts should be performed on the basis of the EU GMP guideline (attachment 1). Cross-contamination must be avoided by means of organizational and spatial measures.

The rooms used must not be combined with the remaining pharmacy rooms.

The configuration and fixtures of the rooms must be designed such that contamination by microorganisms and particles is reduced to a minimum. Along with technical fixtures, the rooms should be set up in connection with preparation, production and documentation.

The entire equipment of the preparation room must be defined in a fixtures plan and reduced to the necessary minimum.

**Room air equipment**

A cytostatics workbench of type H (or “other design, e.g. with isolated work room”) must be used, type tested in accordance with DIN 12980 as laminar airflow (SWFC). SFWCs [safety workbenches for cytostatics] are equipped with an additional main filter that can be replaced free of contamination.

An exhaust air system as an additional security measure must always be installed.

Should an exhaust air system not be realizable for technical reasons, it is mandatory to use an SWFC with two HEPA filter stages. If a workbench is operated with recirculated air, and all regulations to the method recognized by regulatory and professional liability bodies to the chosen method need to be met.

In any case, a ventilation system must be installed that leads adequately conditioned and purified fresh air complying with DIN 1946 into the room for compensating the flow of exhaust air in accordance with the currently valid GMP recommendations, without impairing the protective function of the safety workbench. The velocity of the input air must not exceed 0.2 m/s.
Cytostatics preparation in a cytostatics hood (SWFC) is an aseptic drug preparation process that must be validated. Compliance with the requirements of the Ph. Eur. for parenteralia is fundamental. Simulations procedures instead of in general prepared products have to be tested for the absence of reproduction-competent germs, using appropriate microbiological procedures. A testing plan must be compiled. Number and frequency depend on the possibilities of the individual pharmacy.

National Association of Pharmacy Regulatory Authorities (Nov 2016)

Facilities for the compounding of hazardous sterile preparations must be designed and built in accordance with these Model Standards, with provincial/territorial and local regulations and, for health system facilities, with other applicable standards regulating the construction of buildings http://napra.ca/sites/default/files/2017-09/Mdl_Stnds_Pharmacy_Compounding_Hazardous_Sterile_Preparations_Nov2016_Revised_b.pdf

The air in controlled rooms must be “clean,” and levels of airborne particulates must be controlled. Thus, the facility’s heating, ventilation and air conditioning (HVAC) system must be designed both to minimize the risk of airborne contamination in controlled rooms used for the compounding of hazardous sterile preparations and to minimize the exposure of personnel to hazardous products in the work environment. It must also be designed to achieve and maintain ISO Class 7 air quality for clean rooms and anterooms used for the compounding of hazardous sterile preparations.

The air supplied to areas used for compounding hazardous sterile preparations must pass through a high-efficiency particulate air (HEPA) filter to ensure a very high level of cleanliness. The intake air must come from the ceiling via diffusers, each fitted with a terminal HEPA filter.

All sources that generate particles must be controlled to achieve and maintain the ISO class for clean rooms and anterooms used to compound hazardous sterile preparations.

The air quality in controlled rooms must comply with ISO 14644-1, according to the specifications listed in Table 1, under dynamic operating conditions, as follows: the number of particles ≥ 0.5 μm diameter per cubic metre of air must be verified while compounding personnel perform or simulate a typical hazardous sterile-product preparation (e.g., media fill). The particle count must be performed by trained, qualified personnel at least every 6 months as part of an internal quality control program for facilities and containment primary engineering controls (C-PECs) (e.g., biological safety cabinets [BSCs] or compounding aseptic containment isolators [CACIs]). The particle count may also be measured by a qualified certifier (see Appendices 5 and 6).

The return air from the clean room must be exhausted to the exterior of the building. Return air exhausts should be installed at the bottom of walls, forcing the particles to flow downward.

In older facilities, an airflow analysis must be performed under dynamic operating conditions (using the air speed achieved at the front of the C-PEC) to ensure that the location of the return air exhausts does not hinder the compounding process. An air conditioning system must be included in the HVAC system to help ensure the comfort of personnel wearing personal protective equipment (PPE).

Controlled rooms must not have windows or doors opening directly to the exterior of the building. If any windows are present, they must be sealed. If any doors lead to the outside or to a non-controlled area (other than the doors designated for accessing the room), they must be sealed. An
environmental control procedure and a housekeeping procedure, including the cleaning of sealed windows and doors, must be implemented by cleaning and disinfecting personnel.

Compounding areas must have at least two separate controlled rooms, enclosed and physically separated by a wall: a clean room, where the C-PEC (e.g., BSC or CACI) is located, and an anteroom, located next to the clean room.

Functional parameters of the clean room and anteroom for the compounding of hazardous sterile preparations

General principles:

- Maintain negative pressure to prevent air that might be contaminated by hazardous products from leaving the clean room (principle of containment).
- Ensure that construction quality is sufficient to guarantee that controlled rooms (i.e., rooms responsible for containment) are airtight.
- Notwithstanding the two preceding principles, do not depressurize the clean room too much, so as to minimize penetration of non-filtered air through gaps in the construction (since no room will be perfectly airtight).
- Maintain ISO Class 7 air quality (to prevent particles from entering the clean room).
- Protect pharmacy personnel (by means of air exhausts).

To adhere to these principles, the following functional parameters must be met:

- The clean room must be kept under negative pressure relative to the anteroom.
- The pressure of the clean room must be -2.5 Pa (equivalent to 0.01 inch water column) relative to surrounding areas (pharmacy or other).
- The pressure differential between the anteroom and the clean room (PB - PC; see Figure 1) must be at least 2.5 Pa to maintain unidirectional airflow from the anteroom to the clean room.
- The pressure in the anteroom must be positive. The pressure differential must be at least 5.0 Pa relative to the pharmacy adjacent to the anteroom.
- ISO Class 7 air quality must be maintained in the clean room and the anteroom under dynamic operating conditions.
- There must be at least 30 air changes per hour (ACPH) in the clean room and the anteroom.

Depending on the size of the rooms and the number of people working in them, a greater number of ACPH may be required.

- The return air from the clean room must be externally vented.
- The temperature in the controlled rooms must be less than or equal to 20°C, taking into account employees’ comfort once all clean room garb (including PPE) has been donned. Medication storage temperatures must not exceed 25°C. Note: There is no requirement for relative humidity; refer to the recommendations of the Canadian Society of Hospital Pharmacists

Compounding personnel must adhere to the following requirements when working inside the C-PEC:

- When diluting powder or withdrawing liquids, use a ventilated system equipped with a 0.22-μm hydrophobic filter.
- When withdrawing a hazardous solution, comply with the maximum fill limit of the syringe, i.e., 75% (3/4) of total syringe capacity.
- When dispensing a hazardous preparation in a syringe, use a protective Luer-Lok safety tip system.
- If possible, use a closed-transfer system (since the steps described above do not completely eliminate the risk of exposure to the hazardous preparation).
- Discard all materials used during compounding into a marked waste container specifically designated for hazardous products.
- Before removing a container holding a final hazardous compounded sterile preparation from the C-PEC, follow the surface decontamination procedure on all surfaces of the container.
• While the final container is still inside the C-PEC, compounding personnel must label it and place it in a sealable plastic bag. All final hazardous compounded sterile preparations must be marked “cytotoxic.”

Manitoba (Oct 2015)
All Injectable Cytotoxic Hazardous Medications shall be prepared by Pharmacy in a Class II Type B biological safety cabinet (BSC) or a negative pressure isolator.
Exception: Injectable Cytotoxic Hazardous Medications doses may be prepared on patient care areas when demonstrating preparation and administration to patients and their care givers. All Handling instructions outlined in the Safe Handling of Medications Chart (Appendix A) for Cytotoxic Hazardous Medications shall be followed.

• Each BSC shall be inspected and recertified on an annual basis.

Parenteral Cytotoxic Hazardous Medications shall be stored in pharmacy separately from all other medications in compliance with provincial standards.

BC Cancer Agency (Sep 2016)
Hand Hygiene
Hand hygiene must be performed by all staff prior to entry into the clean room to minimize microbial contamination of sterile products. After handling hazardous drugs and removing chemotherapy gloves, hand washing is performed to remove possible drug contamination.

Compounding personnel
Personnel handling hazardous drugs, performing activities other than compounding, must wash their hands immediately after removal of chemotherapy gloves.
Personnel compounding sterile HD preparations must wash their hands before donning chemotherapy glove. Prior to hand washing, all jewellery including bracelets, rings and watches must be removed to prevent material from being trapped around or underneath them. Hands must be dried with a clean, low lint towel.
Personnel compounding sterile hazardous drugs must wash their hands immediately after removal of chemotherapy gloves with soap and water.

Non-compounding personnel
Non-compounding personnel working in the clean room may apply ABHR prior to donning chemotherapy gloves in place of washing hands with soap and water. All personnel must wash hands with soap and water immediately after removal of chemotherapy gloves.
All personnel handling hazardous drugs, performing activities other than compounding outside the SPR are not required to wash their hands before donning chemotherapy gloves, but must wash their hands immediately after removal of chemotherapy gloves using soap and water.

Nails and Nail Polish
Wearing of artificial nails or nail extenders is prohibited while working in the sterile compounding environment. Natural nails should be kept neat and trimmed and must be free of nail polish.

Safety Stations
Eyewash stations and emergency showers must be easily accessible. The location of each emergency shower or eyewash station must be identified with a highly visible sign.
For potential exposure to high risk materials: WorkSafe BC Occupational Health and Safety (OHS) Regulation 5.89 states:
“Eye Equipment: Tempered continuous flow eyewash facility with a minimum duration of 15 minutes (or more if required by the nature of the material)
**Location:** Within 5 seconds walking distance of the hazard area, but no further than 6 meters (20 feet).

**Skin Equipment:** Tempered, continuous flow emergency shower facility with a minimum duration of 15 minutes (or more if required by the nature of the material).

Location: Same location criteria as for high risk eyewash facility except that the shower may be located further than 6 meters, and
(a) a supplementary emergency washing facility such as a non-tempered drench hose is located within 5 seconds walking distance of the hazard area but no further than 6 meters, and
(b) a tempered shower facility is available within the building to start emergency washing within 5 minutes of the contact”

**Eyewash Stations**

**Hand Held Portable**
Portable eyewash stations must be capable of delivering a minimum flush duration of 15 minutes.

**Emergency Showers**
Emergency showers must not be used to flush the user's eyes because the high rate or pressure of water flow could possibly damage the eye.

**Safety Stations Maintenance**
Inspecting and operating (activating) the emergency shower and mounted eyewash station must be performed and documented by an employee monthly.
Hand held portable eyewash equipment must be inspected and maintained according to the manufacturer's instructions.

Single use, individually packaged sterile 70% isopropyl alcohol swabs must be used to disinfect a critical site prior to accessing. 70% alcohol-soaked gauze pads or other particle-generating material must not be used to disinfect critical sites of containers prior to accessing.
Partially emptied containers of alcohol (including spray bottles) must not be topped up.

**Devices**
Devices used in the safe and accurate reconstitution and withdrawal of hazardous drug in a vial must support minimizing the production and release of HD aerosols and vapours, maintaining the sterility of hazardous drugs, and preventing HD leaks/spills.
Staff must be trained to use the proper aseptic technique required with each device utilized in the safe preparation of hazardous drugs.
The following criteria may be considered when deciding which devices are most suitable for the preparation of hazardous drugs.
- Venting devices must have filters
- Luer-lock fittings must be used for all hazardous drug connections made during manipulation and dispensing

**Syringes**
An appropriate size syringe must be selected so that no more than three-quarters (75%) of the syringe’s maximum calibrated volume is filled with hazardous drug solution at any time during the compounding process.
A syringe must not be used more than five times for a single compounding procedure (e.g., reconstitution).

**Syringe Tip Caps**
Care must be taken to avoid touch-contaminating the end of the multi-function tip cap that will be luer-locked to either the syringe or the chemotherapy dispensing pin (critical site).

**Needles**
All parts of a needle are critical sites. Needles must be manipulated by handling their paper over-wrap and/or needle caps. Paper-covered needles must be unwrapped by peeling apart the sides of
the package just enough to expose the needle’s luer-lock hub. Airflow to the hub must be maintained as the needle is un-wrapped and luer-locked onto a syringe. The needle cap must be left in place until the needle is ready to be used.

Aluminum-free needles and devices must be used in the preparation and administration of CISplatin, CARBOplatin and oxaliplatin.

Safety Engineered Needles (SEN) must not be used in the preparation of hazardous drugs. There is a risk that the HD will spray droplets off of the needle point when the SEN cap is engaged.

**Needle Caps**

Placing the open end of the needle cap directly on the work surface of the BSC must be avoided.

**Filters**

Solutions prepared for parenteral administration must be filtered when there is a possibility that glass particles or particulate matter (e.g., core from a vial stopper) may be present and the solution is filterable.

**Filter Needles**

The same filter needle must not be used for both withdrawing and expelling solution.

**Filter Discs**

A filter disc used for hazardous drugs must be equipped with proximal and distal luer-locking connections.

**Filter Venting Devices**

Negative pressure technique must not be used for hazardous drug reconstitution or withdrawal if filter venting devices or closed system drug transfer devices are available.

**Chemotherapy Dispensing Pins**

Chemotherapy dispensing pins or similar devices with spikes must not be used with vials of TAXOL® since they can cause the stopper to collapse resulting in loss of the sterile integrity and the possible release of hazardous drug.

**Note:**

- Chemotherapy dispensing pins must be inspected for cracks prior to use. A cracked chemotherapy dispensing pin must be replaced prior to manipulation of HD solution
- Chemotherapy dispensing pins must be disposed of in a HD sharps waste container if removed from a HD vial
- A new chemotherapy dispensing pin must be used for each vial. Spraying of the solution or touch contamination can occur upon removal of the pin

**Chemotherapy Vents**

A new chemotherapy vent must be inserted prior to removal of a plugged venting device.

A HD vial stopper must be disinfected with sterile 70% IPA prior to each puncture when multiple punctures are necessary.

**Syringe Fluid Dispensing Connectors/Syringe Tip Connectors**

Both ends of the individually packaged fluid dispensing connector used with hazardous drugs must have luer-lock connections which allow transfer of solution from one syringe to another without leakage.

**Closed System Drug Transfer Devices**

Closed System Drug Transfer Devices must be used within the ISO Class 5 environment of a biological safety cabinet. Protective clothing must be worn and best practice safety measures must be adhered to when using a Closed System Drug Transfer Device to prepare, administer and dispose of hazardous drugs.

**Containers**

**Ampoules**

The length of time between opening the ampoule and transferring the solution into a closed-system (e.g., syringe) must be minimized.
The neck of the ampoule must be wiped with an alcohol swab before breaking and must not be touch-contaminated after being swabbed. Glass particles in solutions must be filtered prior to administration unless the manufacturer indicates the solution cannot be filtered. Solution must not be withdrawn and injected using the same filtration equipment. All parts of an opened ampoule must be discarded into a sharps container.

**Vials**

Removal of a flip top cap from a hazardous drug vial must be performed carefully inside the BSC to ‘contain’ and avoid spreading HD contamination to areas outside of the BSC. Hazardous drug vials must be wiped to disinfect (not sprayed) using a low-lint towel or gauze moistened with 70% alcohol prior to placement inside the BSC. The date and time of puncture or the expiry date and time must be written directly onto reconstituted and partial vials that will be saved for future use with ink that will not smudge or wipe off.

**Non-Polvinyl Chloride (Non-PVC) Bags**

PACLitaxel, DOCEtaxel, temsirolimus, teniposide, etoposide, cycloSPORINE and ixabepilone must be prepared in non-PVC containers and administered using non-PVC tubing.

**Empty Sterile Infusion Bags**

Infusion bags used for HD solution waste must be disposed of as hazardous drug waste.

**Ambulatory Drug Delivery Infusion Devices**

**Elastomeric Infusion Devices**

**INFUSOR™ Flow Rates**

The correct size of elastomeric INFUSOR™ with the correct infusion rate must be selected when preparing hazardous drug medication. To decrease the risk of accidental exposure to HD, the delivery tubing of the INFUSOR™ must be primed with HD-free solution.

**Hazardous Drug Medication Infusion Device Labels**

The intended infusion rate must be stated in millilitres per hour (mL/hour) on the medication label when hazardous drug is administrated via an infusion device.

**Computerized Ambulatory Drug Delivery (CADD®) Pump and Medication Cassette Reservoir**

To decrease the risk of exposure to HD, the tubing of a CADD® medication cassette reservoir must be primed with hazardous drug-free solution.

**Section E**

**Operational Standards for Sterile Hazardous Drug Preparation**

Hazardous drugs shall be prepared only under conditions that protect the healthcare workers and other personnel in the preparation and storage areas. Operational standards must be adhered to when preparing sterile HD admixtures.

**Personnel Hygiene in the Cleanroom and BSC**

- Eating, drinking, smoking, chewing gum, storing food, or applying cosmetics in the vicinity of the BSC, in the cleanroom and in the anteroom are strictly prohibited.
- Personnel with rashes, severe sunburn, weeping sores, conjunctivitis, cold sores, active respiratory infection and wearing cosmetics are prohibited from preparing sterile admixtures.
- The wearing of artificial nails or extenders is prohibited while working in the BSC. Natural nails shall be kept neat and trimmed and must be free of nail polish.
- Compounding personnel must remove cosmetics and all jewelry including any visible body piercing above the neck before entering the cleanroom.
- Before entering the cleanroom, compounding personnel must remove personal outer garments (e.g., bandanas, coats, hats, jackets, scarves, sweaters, vests) because they shed flakes and particles.
Personal Protective Equipment
- Appropriate PPE (including hair cover, mask, gown, 2 pairs of chemotherapy gloves and shoe covers) must be donned prior to entering the cleanroom and/or working in the BSC.
- Hair covers (covering hair and ears completely) and masks must be worn by all personnel working in the BSC and/or present in the cleanroom.
- Shoe covers must be put on by all workers before stepping inside the cleanroom and must be removed with gloved hands at the doorway/demarcation line upon exiting.
- Chemotherapy gowns worn when preparing hazardous drugs must be non-linting, impermeable and disposable with long sleeves, tightly-fitting cuffs, a closed front, and tied in the back.
- Chemotherapy gowns worn in the cleanroom must be removed for storage or disposal while still in the HD preparation area, to prevent the spread of HD contamination from one area to another.
- Lab coats must not be worn in the cleanroom in place of chemotherapy gowns.
- Two pairs of disposable chemotherapy gloves must be worn at all times by all personnel working in the cleanroom. Both pairs of chemotherapy gloves must be inspected for visible defects.

- Gloves should be powder-free. If powder-free gloves are not available, the powder must be removed using a towel moistened with 70% alcohol prior to entering the cleanroom - alcohol must not be sprayed to remove powder.
- Gloves must be disinfected with 70% alcohol before performing aseptic compounding activities inside the BSC.
- Gloves worn during chemotherapy preparation must be changed every 30 minutes or when torn, punctured or in the event of suspected contamination. Hands must be washed every time gloves are removed.
- Pharmacy personnel who must be present in the cleanroom or in the area of the biological safety cabinet must wear an N95 or better respirator mask in addition to all other PPE if the viewing window is raised.

Biological Safety Cabinet
- The UV light may cause eye damage and must not be turned on when personnel are working in the cleanroom.
- All interior surfaces of the BSC (except under the work surface) must be cleaned and disinfected prior to commencing daily compounding. The BSC must purge for 15 minutes after cleaning.
- The viewing window must be kept at the manufacturer’s recommended level during HD preparation.
- Unnecessary items must not be taken into the BSC since airflow is disrupted in an overcrowded BSC.
- While working in the BSC, a path of first air must be maintained to critical sites at all times.
- Rapid arm movements that could disrupt the air curtain must be minimized.
- The front air intake grill and the rear air exhaust route must not be blocked.
- Manipulations must be performed at least six inches in from the front opening and side walls of the BSC.

General Procedures
- HD vials must be wiped with low-lint towels or gauze moistened with 70% alcohol to physically remove HD contamination prior to placement inside the BSC.
- Prior to placement inside the BSC, the outer wrapping of unopened supplies (e.g., syringes) must be disinfected with 70% alcohol.
- Best practice standards for aseptic technique in vertical airflow must be adhered to when preparing sterile hazardous drug admixtures.
- To decrease particle generation inside the BSC, paper coverings must be peeled away from
needle hubs (critical sites) rather than pushing them through

- Critical sites must be protected as soon as possible after being exposed and must not be touch contaminated
- Infusion solution bag ports and vial stoppers must be disinfected with sterile 70% alcohol prior to accessing
- A new sterile alcohol swab must be used to disinfect each critical site
- When reconstituting, the drug must be completely dissolved before withdrawing a dose or storing for future use
- The date and time of puncture/reconstitution or the expiry date and time must be written directly on the vials for future reference
- Syringes must not be overfilled with hazardous drug. In most cases, syringes should not be more than three-quarters (75%) full, although some preparations require accurate volume measurements that necessitate the use of a smaller volume syringe
- Negative pressure technique must not be used for hazardous drug reconstitution or withdrawal if filter venting devices or closed system drug transfer devices are available
- A puncture-proof sharps container must be used for disposal of all sharp objects including needles, chemotherapy dispensing pins, and chemotherapy vents
- All non-sharp waste generated during compounding must be placed inside a HD waste container (e.g., zip lock bag or sharps container) in the BSC for later removal and disposal.

Products from the BSC

- Infusion solution bag ports that have been accessed must be wiped with an alcohol swab prior to removal from the BSC to remove possible HD residue
- Outer gloves worn when compounding hazardous drugs must be removed, discarded within the BSC and replaced or wiped with a clean soap-moistened towel prior to touching items for removal from the BSC
- Surfaces of final preparation(s) may be contaminated with HD and must be wiped with a new soap-moistened towel (not previously used on gloves) before removal from the BSC
- To remove a vial of HD that will be saved for reuse from the BSC:
  - the vial stopper must be wiped with a sterile 70% alcohol swab to remove possible HD residue (if there is not a chemotherapy dispensing pin or CSDTD inserted)
  - the puncture date and time or expiry date and time must be written directly on the vial with a thin-tipped permanent marker
  - the vial must be wiped with a new soap-moistened towel
  - the vial must be placed inside a zip lock bag sealed above the front grill upon removal from the BSC

- Containers used for HD waste (sharp and non-sharp) must be sealed and wiped with a new soap-moistened towel inside the BSC before removal from the cabinet

Warning Labels

- All hazardous drugs and hazardous drug preparations must be easily identifiable by personnel involved in their handling
- The HD warning label must display a ‘Cytotoxic’ hazard symbol and/or the words CAUTION – Cytotoxic/Antineoplastic/Chemotherapy/Hazardous to indicate that HD safe practices must be followed while handling

Exiting the Cleanroom

- PPE must be removed upon exiting the cleanroom:
  - Removal of chemotherapy gowns for storage or disposal must be done with care to avoid
spreading HD contamination to other non-contaminated garments
- Outer gloves must be discarded in a hazardous waste container (inside or outside of the BSC) prior to exiting the cleanroom - outer gloves must NOT be worn outside the cleanroom once compounding hazardous drugs in the BSC has occurred
- Used shoe covers must be removed with gloved hands at the door leading out of the cleanroom and must be discarded as hazardous waste
- Mask and hair cover(s) must be removed outside of the cleanroom while wearing inner gloves
- Mask, hair cover(s) and inner gloves must be discarded in a hazardous waste container outside of the cleanroom
- Hands must be washed immediately with soap and water every time gloves are removed
- A buttoned lab coat (or isolation gown) must be donned over scrubs upon exiting the anteroom

Critical Sites
Critical sites must be protected as much as possible and must not be touch-contaminated. Critical sites of supplies or devices must not contact the work surface of the BSC. Protection of critical sites by precluding physical contact and airborne contamination must be given the highest priority in aseptic compounding practice.

First Air
While working in the BSC, a path of first air must be maintained to critical sites at all times. It is vital to avoid reaching over or working directly above or in front of exposed or previously swabbed critical sites

Swabbing
The stopper on a vial or the port on an infusion solution bag must be disinfected with a sterile 70% alcohol swab just prior to penetration. At least 10 seconds must be allowed for the alcohol to dry (act) before manipulations begin.
The correct swabbing technique is to make several firm strokes in the same direction over the rubber closure. A new sterile swab must be used on each new surface. The surface of sterile 70% IPA swabs used to disinfect entry points on infusion solution bags and vials shall not contact any other object before contacting the surface of the entry point.
Prior to removal from the BSC, the stopper of a vial or the port of an infusion solution bag that has had drug added must be wiped with an alcohol swab to remove possible HD residue.

Capping Needles Safely
Needles are a critical site and therefore must be capped when not being used for injection or withdrawal. Prior to manipulation of a hazardous drug-filled syringe, the needle must be capped to reduce aerosol release and prevent splashes from the needle tip.
For worker safety, two-handed recapping of a needle used for HD preparation is never an acceptable practice.

Safe Handling Aseptic Techniques
Transfer of Hazardous Drug Solution from a Syringe
If too much hazardous drug solution has been drawn into a syringe, care must be taken to minimize aerosol and vapour production, and to contain hazardous drug solution while removing the excess volume.

Note:
- Excess hazardous drug must NOT be ejected into the needle cap, sharps container, or any other open container as this could cause HD aerosolization, vaporization or contamination.

Removal of Bubbles/Air from a Syringe
Bubbles and air must be removed carefully in a manner that prevents the release of HD solution and minimizes the production of HD aerosols in the BSC.

Attaching and Priming Solution / Administration Sets
Priming any intravenous administration set with hazardous drug solution in an uncontrolled

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environment must be avoided. To minimize exposure to HD, the administration tubing/line must be primed with HD-free solution.

**Clean Up and Waste Disposal**

**Biological Safety Cabinet Waste Cleanup**
The entire aseptic preparation area must be kept clean so that aseptically prepared products remain as free from potential microbial and hazardous drug contamination as possible.

**Hazardous Drug Cleanroom and Anteroom**
Access to the hazardous drug cleanroom must be limited to authorized personnel who are assigned to work there. A warning sign must clearly identify the hazard and state that access to the cleanroom is controlled and limited to authorized personnel only. Door(s) leading into the cleanroom must not be left open. Appropriate personal protective equipment must be donned by all personnel prior to entering the cleanroom as the first major step in preventing microbial contamination of compounded sterile preparations and to minimize healthcare workers’ exposure to hazardous drugs.

**Biological Safety Cabinets**
WorkSafe BC Occupational Health and Safety (OH&S) Regulation 6.53(1) states: “All mixing, preparation and priming of administration sets with a cytotoxic (hazardous) drug must be performed in one centralized area in a specially designated Class II Type B biological safety cabinet that:
- is exhausted to the outside atmosphere in a manner that prevents recirculation into any work area;
- has exhaust and ventilation systems that remain in operation for a sufficient period of time to ensure that no contaminants escape from the biological safety cabinet into the workplace; and
- is equipped with a continuous monitoring device to permit confirmation of adequate airflow and cabinet performance”.

**Class I BSC**
Class I BSCs are used when there is a need for containment, but not aseptic product protection and therefore must not be used for sterile hazardous drug preparations.

**Class II BSC**
Class II Type A cabinets must not be used for preparing hazardous drugs. A minimum Class II Type B BSC must be used for the preparation of sterile hazardous drugs.

**HEPA Filter**
HEPA filters must be present in BSCs used for the preparation of hazardous drug sterile admixtures. Air that flows towards the work surface inside the cabinet and air that is expelled out to the environment must first pass through at least one HEPA filter.

**Airflow**
Manipulations must be performed at least six inches in from the front opening of the cabinet, behind the air ‘split’. Contaminated air must be able to escape via the rear grill, not via the front opening.
In order for the BSC to help protect the operator, paths of airflow must remain clear.

**Note:**
- Horizontal laminar airflow hoods must not be used for the preparation of hazardous drugs

**Ultraviolet Lights**
The ultraviolet light may cause eye damage and must not be turned on when personnel are working in or near the BSC, or in the cleanroom.

**Viewing Window**
To protect the upper body and face from any splashes or aerosols produced inside a BSC; the
viewing window must be kept at the manufacturers’ recommended height during hazardous drug preparation.

Location
A biological safety cabinet used for hazardous drug preparations must be located away from doorways, traffic corridors, and air conditioning and heating vents inside a restricted access ISO Class 7 cleanroom. Monitoring
The BSC must be operated continuously with the blower turned on 24 hours a day, seven days a week unless being serviced. It must be equipped with a continuous monitoring device to allow confirmation of adequate airflow and cabinet performance. For the safety of the patient and the operator, hazardous drug compounding must not take place when a BSC alarm is sounding or the lights and/or gauges indicate the cabinet is not functioning within the manufacturer’s specifications. Site specific procedures must be created and posted for workers so that when the gauges, lights or alarms indicate that the BSC is not working properly or there is a power interruption, the safety of personnel, the environment and the aseptic condition of the product (if possible) will be maintained.

Testing and Certifying Biological Safety Cabinets
Testing and certifying the biological safety cabinet must be completed by a qualified National Sanitation Foundation (NSF) certified technician when installed. The BSC must be re-certified to industry standards every six months and when the cabinet is altered, repaired or moved. Testing and certifying the biological safety cabinet must occur during simulated operating conditions. Certification procedures used must meet the requirements of the NSF and American National Standards Institute (ANSI) NSF/ANSI 49-2002, Class II (Laminar Flow) Biohazard Cabintery. Prior to servicing a biological safety cabinet, service technicians or maintenance workers must be informed that the BSC may be contaminated with hazardous drugs. Appropriate personal protective equipment must be worn when testing, certifying or servicing the BSC. After field certification, the BSC must have certification information posted on the front of the cabinet housing in a readily visible location.

Replacing HEPA Filters
Only NSF certified technicians informed of the hazardous nature of the admixtures prepared in the biological safety cabinet shall replace HEPA and charcoal (if present) filters. Appropriate personal protective equipment must be worn when replacing HEPA filters and the contaminated filters must be handled and disposed of as hazardous waste.

Turning off a Biological Safety Cabinet
If it is necessary to turn off a BSC for testing and certifying or for maintenance, the entire inner cabinet must be decontaminated first. If the internal blower and external exhaust fan of a BSC are both turned off, the work-access opening and the HEPA exhaust area must be covered with impermeable plastic and sealed with tape to prevent any remaining hazardous drug contamination from inadvertently escaping from the BSC until maintenance work begins. The BSC must be sealed with plastic whenever it is moved or left inoperative for a period of time.

Cleaning Biological Safety Cabinets
To maintain an aseptic environment and to protect against possible contact with hazardous drug particles, surfaces of the BSC must be cleaned and disinfected regularly throughout the day using aqueous antibacterial solution (e.g., chlorhexidine 0.05%) followed by 70% alcohol. Prior to cleaning a BSC, proper hand washing procedures must be followed and full personal protective equipment (PPE) must be donned.

Cleaning All Interior Biological Safety Cabinet Surfaces
Prior to commencing daily compounding, all interior surfaces of the biological safety cabinet (except under the work surface) must be cleaned and disinfected with an aqueous antibacterial
solution followed by 70% alcohol. If the viewing window has been raised during cleaning and disinfecting, it must be lowered to the manufacturers recommended operating level and the BSC must purge for at least fifteen minutes afterwards.

Following hazardous drug compounding, the BSC must purge for five minutes and then all interior surfaces (except under the work surface) must be cleaned and disinfected:
- after preparations within the BSC are completed for the day
- prior to compounding ‘latex-free’ preparations
- prior to compounding sterile HD preparations in a BSC once it has been used to compound non-sterile HD preparations
- prior to resuming compounding in a BSC that is turned off between aseptic processes for any reason (e.g., power interruption, maintenance)

If cleaning interior surfaces of a BSC with the viewing window raised, additional PPE is required including a NIOSH-approved respirator (e.g., N95) appropriately fit-tested for the operator and safety goggles with side shields to prevent splashing into the eyes.

To protect others from potential exposure to hazardous drugs, pharmacy personnel who must be present in the cleanroom or in the area of the biological safety cabinet must wear an N95 or better respirator mask in addition to all other PPE if the viewing window is raised.

**Cleaning the Work Surface of the BSC**

The work surface of the BSC must be cleaned and disinfected using an aqueous antibacterial solution (e.g., chlorhexidine or Wet Ones®) followed by 70% alcohol:
- after a completed preparation has been cleaned and removed from the BSC
- before leaving the BSC for an extended period of time (e.g., for a break)
- upon returning to the BSC after an extended period of time
- after a minor spill involving the working surface

At least 30 seconds of surface contact time must be allowed for the alcohol to act before beginning the next sterile preparation.

**Decontaminating Biological Safety Cabinets**

Decontamination of the BSC must occur once a week, after a HD spill in the BSC, and before maintenance/certification/servicing if shutdown of the BSC is required.

Prior to decontaminating the BSC, proper hand washing procedures must be followed and full personal protective equipment (PPE) must be donned.

When decontaminating interior surfaces of the BSC with the viewing window raised, additional PPE is required, including a NIOSH-approved respirator (e.g., N95) appropriately fit-tested for the operator and safety goggles with side shields to prevent splashing into the eyes.

To protect others from potential exposure to hazardous drugs, pharmacy personnel who must be present in the cleanroom or in the area of the biological safety cabinet must wear an N95 or better respirator mask in addition to all other PPE when the viewing window has been raised.

After decontamination is completed, the viewing window is lowered to the manufacturers recommended operating level and the BSC must purge for at least thirty minutes prior to sterile preparation.

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**Work safe BC (2015)**

**Work area design** Preparation rooms can be sterile or non-sterile, depending on the conditions that are required for the task being performed. A sterile preparation room (which may also be called a clean room) should not be used for compounding non-sterile preparations. Refer to the following resources for detailed information on clean room specifications:
- NAPRA “Model Standards for Pharmacy Compounding of Hazardous Sterile Products”
- USP Chapter <797> “Pharmaceutical Compounding - Sterile Preparations”
USP Chapter <800> “Hazardous Drugs - Handling in Healthcare Settings”

Sterile preparation rooms should:
- Be an ISO Class 7 environment, if the room contains a biological safety cabinet for sterile preparations
- Exhaust all air through at least one high efficiency particulate air (HEPA) filter before being exhausted externally from the building
- Have an ISO Class 7 anteroom through which personnel enter, with interlocking doors that cannot be opened at the same time
- Use pass-through hatches for the transfer of preparations out of the room
- Have a viewing window and an intercom system so workers can communicate with workers outside the room
- Have furniture and equipment made of materials that are easily cleaned and decontaminated, such as stainless steel

Non-sterile preparation rooms are where hazardous drugs can be prepared in non-sterile conditions, such as splitting or crushing oral medications, repackaging medications into dosettes, preparing oral solutions, or preparing topical creams. Non-sterile preparation rooms should:
- Be kept under negative pressure with respect to surrounding rooms
- Be a separate room that is dedicated for non-sterile hazardous drug preparations
- Exhaust all air externally
- Use furniture and equipment made of materials that are easily cleaned and decontaminated, such as stainless steel

A biological safety cabinet (BSC) is a ventilated containment cabinet that is designed to provide personnel, product, and environmental protection. Not all BSCs are appropriate for use with hazardous drugs. BSCs that are used for preparing hazardous drugs should:
- Be exhausted to the outside atmosphere to prevent recirculation into the preparation room
- Have exhaust and ventilation systems that operate continuously to ensure that no contaminants escape from the biological safety cabinet into the workplace

BSCs are divided into three classes (Class I, Class II, and Class III) that are each designed to meet different needs depending on their intended use. In workplaces where both sterile and non-sterile preparations take place, it is best practice to have a separate BSC dedicated for each purpose. Type A1 and A2 cabinets must not be used for the preparation of cytotoxic drugs. A minimum Class II Type B must be used when preparing cytotoxic drugs.

Performance testing of BSCs Performance testing of the preparation room equipment should take place regularly. All BSCs used for hazardous drugs should be equipped with a continuous airflow monitoring device to ensure adequate airflow and performance of the BSC before it is used to prepare hazardous drugs. Workers who use the BSC should regularly document the readings on the monitoring device and be able to recognize when the readings indicate a malfunctioning BSC, as well as appropriate procedures to follow if this occurs. Safe work procedures must be developed to ensure worker protection when a BSC is turned off. BSCs must be regularly tested and certified to ensure that they are performing properly following the manufacturer’s specifications and the requirements of the Regulation.

Closed-system transfer devices Closed-system transfer devices (CSTDs) are designed to contain hazardous drugs and minimize potential exposure when transferring hazardous drugs between containers or pieces of equipment. It is important to note that a CSTD is not a substitute for compounding preparations inside a BSC. When a CSTD is used during the preparation of hazardous drugs, it should always be inside a BSC. Several studies have demonstrated that the use of a CSTD in addition to a BSC reduces surface contamination of hazardous drugs in the workplace. Strong
consideration should be made to using a CSTD for transferring hazardous drugs between containers whenever practicable.

**Additional equipment** Many different types of equipment and supplies are used in the preparation of hazardous drugs. Further examples include:
- Fittings that prevent accidental disconnection, such as luer lock fittings
- Appropriate needleless systems or safety engineered needles that reduce the risk of workers getting a percutaneous exposure
- Filtered venting devices, such as chemotherapy dispensing pins and chemotherapy vents, which can minimize the accidental release of hazardous drugs when reconstituting or withdrawing from a vial Refer to Appendix 6 for information on medical equipment that may be appropriate for use with hazardous drugs.

Best practices for the preparation of hazardous drugs include:
- Obtaining hazardous drugs from the supplier in a form that is ready to administer
- Using safety-engineered needles that do not produce spray when activated
- Using CSTDs
- Using disposable plastic syringes
- Using an approved BSC for preparations of hazardous drugs (where possible, the BSC should be designated for either sterile or non-sterile compounding)
- Planning tasks to avoid unnecessary leaving and re-entering the preparation room
- Limiting access to the preparation room to workers trained to work in the room (such as pharmacy and housekeeping staff)
- Limiting equipment and materials in a BSC to those required to prepare one dose for one patient, to avoid overcrowding and mixing up drugs
- Implementing procedures for priming equipment with a hazardous drug solution in a BSC (see the next chapter for priming with a non-hazardous drug solution)
- Implementing procedures to have all alterations of hazardous drug tablets or capsules (such as cutting, splitting, and crushing) inside an approved BSC
- Not using automated unit-dose packaging machines or automated counting machines with tablet or capsule forms of hazardous drugs
- Implementing procedures to reduce contamination of containers and IV bags after they leave the BSC, such as cleaning with a soap-moistened towel and placing the product in a clear resealable bag

**Cleaning** The preparation room should also be cleaned regularly as part of regular housekeeping and throughout the work day. This includes:
- Regular cleaning of the interior of the BSC
- Cleaning and decontaminating of the preparation room, from cleanest areas to the most contaminated (for example, from the walls and then inwards to the BSC)
- Cleaning, disinfecting, and decontaminating the entire interior of the cabinet after a non-sterile preparation (this should be done before a sterile preparation can be performed in the same BSC)

PPE must be consistent with the worker’s potential exposure and may include:
- Chemotherapy-tested gloves
- A chemotherapy-tested gown
- Shoe covers
- Eye and face protection
- An approved and fit-tested respirator

**United States Pharmacopeial Convention (Chapter to become official July 1, 2018)**

**Compounding**
Engineering controls are required to protect the preparation from cross-contamination and microbial contamination (if preparation is intended to be sterile) during all phases of the compounding process. Engineering controls for containment are divided into three categories representing primary, secondary, and supplementary levels of control. A containment primary engineering control (C-PEC) is a ventilated device designed to minimize worker and environmental HD exposure when directly handling HDs. The containment secondary engineering control (C-SEC) is the room in which the C-PEC is placed. Supplemental engineering controls [e.g., closed-system drug-transfer device (CSTD)] are adjunct controls to offer additional levels of protection. Appendix 2 provides examples for designs of HD compounding areas.

Sterile and nonsterile HDs must be compounded within a C-PEC located in a C-SEC. The C-SEC used for sterile and nonsterile compounding must:

- Be externally vented
- Be physically separated (i.e., a different room from other preparation areas)
- Have an appropriate air exchange (e.g., ACPH)
- Have a negative pressure between 0.01 and 0.03 inches of water column relative to all adjacent areas

The C-PEC must operate continuously if it supplies some or all of the negative pressure in the C-SEC or if it is used for sterile compounding. If there is any loss of power to the C-PEC, or if repair or moving occurs, all activities occurring in the C-PEC must be suspended immediately. If necessary, protect the unit by covering it appropriately per the manufacturer's recommendations. Once the C-PEC can be powered on, decontaminate, clean, and disinfect (if used for sterile compounding) all surfaces and wait the manufacturer-specified recovery time before resuming compounding.

A sink must be available for hand washing. An eyewash station and/or other emergency or safety precautions that meet applicable laws and regulations must be readily available. Care must be taken to locate water sources and drains in areas where their presence will not interfere with required ISO classifications. Water sources and drains must be located at least 1 meter away from the C-PEC.

For entities that compound both nonsterile and sterile HDs, the respective C-PECs must be placed in separate rooms, unless those C-PECs used for nonsterile compounding are sufficiently effective that the room can continuously maintain ISO 7 classification throughout the nonsterile compounding activity. If the C-PECs used for sterile and nonsterile compounding are placed in the same room, they must be placed at least 1 meter apart and particle-generating activity must not be performed when sterile compounding is in process.

NONSTERILE COMPOUNDING

In addition to this chapter, nonsterile compounding must follow standards in *Pharmaceutical Compounding—Nonsterile Preparations* (795). A C-PEC is not required if manipulations are limited to handling of final dosage forms (e.g., counting or repack-aging of tablets and capsules) that do not produce particles, aerosols, or gasses.

The C-PECs used for manipulation of nonsterile HDs must be either externally vented (preferred) or have redundant HEPA filters in series. Nonsterile HD compounding must be performed in a C-PEC that provides personnel and environmental protection, such as a Class I Biological Safety Cabinet (BSC) or Containment Ventilated Enclosure (CVE). A Class II BSC or a compounding aseptic containment isolator (CACI) may also be used. For occasional nonsterile HD compounding, a C-PEC used for sterile compounding (e.g., Class II BSC or CACI) may be used but must be decontaminated, cleaned, and disinfected before resuming sterile compounding in that C-PEC. A C-PEC used only for nonsterile compounding does not require unidirectional airflow because the critical environment does not need to be ISO classified.

The C-PEC must be placed in a C-SEC that has at least 12 ACPH.
Due to the difficulty of cleaning HD contamination, surfaces of ceilings, walls, floors, fixtures, shelving, counters, and cabinets in the nonsterile compounding area must be smooth, impervious, free from cracks and crevices, and non-shedding.

STERILE COMPOUNDING

In addition to this chapter, sterile compounding must follow standards in (797). All C-PECs used for manipulation of sterile HDs must be externally vented. Sterile HD compounding must be performed in a C-PEC that provides an ISO Class 5 or better air quality, such as a Class II or III BSC or CACI. Class II BSC types A2, B1, or B2 are acceptable. For most known HDs, type A2 cabinets offer a simple and reliable integration with the ventilation and pressurization requirements of the C-SEC. Class II type B2 BSCs are typically reserved for use with volatile components. Appendix 3 describes the different types of BSCs. A laminar airflow workbench (LAFW) or compounding aseptic isolator (CAI) must not be used for the compounding of an antineoplastic HD. A BSC or CACI used for the preparation of HDs must not be used for the preparation of a non-HD unless the non-HD preparation is placed into a protective outer wrapper during removal from the C-PEC and is labeled to require PPE handling precautions. The C-PEC must be located in a C-SEC, which may either be an ISO Class 7 buffer room with an ISO Class 7 ante-room (preferred) or an unclassified containment segregated compounding area (C-SCA). If the C-PEC is placed in a C-SCA, the beyond-use date (BUD) of all compounded sterile preparations (CSPs) prepared must be limited as described in á797ñ for CSPs prepared in a segregated compounding area. Table 3 summarizes the engineering controls required for sterile HD compounding.

ISO Class 7 buffer room with an ISO class 7 ante-room:
The C-PEC is placed in an ISO Class 7 buffer room that has fixed walls, HEPA-filtered supply air, a negative pressure between 0.01 and 0.03 inches of water column relative to all adjacent areas and a minimum of 30 ACPH. The buffer room must be externally vented. Because the room through which entry into the HD buffer room (e.g., ante-room or non-HD buffer room) plays an important role in terms of total contamination control, the following is required:
- Minimum of 30 ACPH of HEPA-filtered supply air
- Maintain a positive pressure of at least 0.02 inches of water column relative to all adjacent unclassified areas
- Maintain an air quality of ISO Class 7 or better

An ISO Class 7 ante-room with fixed walls is necessary to provide inward air migration of equal cleanliness classified air into the negative pressure buffer room to contain any airborne HD. A hand-washing sink must be placed in the ante-room at least 1 meter from the entrance to the HD buffer room to avoid contamination migration into the negative pressure HD buffer room. Although not a recommended facility design, if the negative-pressure HD buffer room is entered though the positive-pressure non-HD buffer room, the following is also required:
- A line of demarcation must be defined within the negative-pressure buffer room for donning and doffing PPE
- A method to transport HDs, HD CSPs, and HD waste into and out of the negative pressure buffer room to minimize the spread of HD contamination. This may be accomplished by use of a pass-through chamber between the negative-pressure buffer area and adjacent space. The pass-through chamber must be included in the facility’s certification to ensure that particles are not compromising the air quality of the negative-pressure buffer room. A refrigerator pass-through must not be used. Other methods of containment (such as sealed containers) may be used.

HD CSPs prepared in an ISO Class 7 buffer room with an ISO Class 7 ante-room may use the BUDs described in (797) based on the categories of CSP, sterility testing, and storage temperature.
Containment segregated compounding area (C-SCA): The C-PEC is placed in an unclassified C-SCA that has fixed walls, a negative pressure between 0.01 and 0.03 inches of water column relative to all adjacent areas, and a minimum of 12 ACPH. The C-SCA must be externally vented. A hand-washing sink must be placed at least 1 meter from C-PEC and may be either inside the C-SCA or directly outside the C-SCA. Only low- and medium-risk HD CSPs may be prepared in a C-SCA. HD CSPs prepared in the C-SCA must not exceed the BUDs described in ñ797ñ for CSPs prepared in a segregated compounding area.

COMPOUNDING
Entities and personnel involved in compounding HDs must be compliant with the appropriate USP standards for compounding including (795) and (797). Compounding must be done in proper engineering controls as described in Compounding. When compounding HD preparations in a C-PEC, a plastic-backed preparation mat should be placed on the work surface of the C-PEC. The mat should be changed immediately if a spill occurs and regularly during use, and should be discarded at the end of the daily compounding activity. Disposable or clean equipment for compounding (such as mortars and pestles, and spatulas) must be dedicated for use with HDs. Bulk containers of liquid and API HD must be handled carefully to avoid spills. If used, APIs or other powdered HDs must be handled in a C-PEC to protect against occupational exposure, especially during particle-generating activities (such as crushing tablets, opening capsules, and weighing powder).

RECOMMENDATION 6: DRUG PREPARATION
The following recommendations apply to the preparation of all cytotoxic medications including parenteral, oral and topical, both sterile and non-sterile preparations. It is strongly recommended that policies and procedures include the use of appropriate personal protective equipment, the equipment for preparation including appropriate ventilation, and other automated equipment for packaging and a dedicated work area.

Personal Protective Equipment
It is strongly recommended that workers (pharmacists or pharmacy technicians) wear a cap, surgical/procedure mask, shoe covers, a protective gown and two (2) pairs of gloves (see Table 1) to make sterile preparations of cytotoxic drugs in preparation cabinets.

Organization of the Work
Organize the work to limit microbial and environmental contamination.

For both sterile and non-sterile preparations, it is strongly recommended that workers cover the work surface with a disposable, absorbent, sterile, plastic-backed pad to absorb any liquid contamination that may occur during handling. It is strongly recommended that the pad not cover the front and rear grilles of the preparation cabinet. It is strongly recommended that it be changed after 3.5 hours of continuous work or for a new batch of preparations (e.g., a set of vials of a given drug) or in the event of a spill or contamination. It is legislated that the pad be disposed of in a cytotoxic waste receptacle (10).

Limit the quantity of supplies and cytotoxic drugs in the cabinet, to avoid adversely affecting the laminar flow and to facilitate regular cleaning of the work surface; place the sterile products in the centre and the non-sterile products (e.g., waste receptacle) along the sides of the cabinet.

Removal of Packaging
Remove the packaging, when applicable, and clean all of the drug containers before taking them into the preparation cabinet. For sterile preparations, adhere to aseptic technique for sterility.

**Handling Techniques**
Use handling techniques that limit the risk of injury or accidental exposure.

It is strongly recommended that spiking of bags and priming of tubing occur before the addition of the cytotoxic drug unless the clinical protocol requires otherwise.

**Preparation, Priming and Removing Air from the Tubing**
It is strongly recommended that cytotoxic drugs be reconstituted in the pharmacy environment as described above. It is strongly recommended that the drug containers not be overfilled to avoid compromising the integrity of the container. It is strongly recommended that the techniques used for priming and removal of air minimize the exposure risks. It is strongly recommended that air never be removed from the IV tubing with a solution containing the drug. It is strongly recommended that IV tubing is primed and air removed in the pharmacy, prior to adding the cytotoxic drug(s) to the infusion solution. Glass containers are not recommended due to increased risk of breakage and exposure.

**Labeling and final packaging**
It is legislated that cytotoxic drugs be labeled to inform those handling these preparations of the nature of the drugs and the precautions to be taken. It is legislated that cytotoxic drugs display the “Cytotoxic” hazard symbol or the word “Cytotoxic” (9, 10).

It is strongly recommended that the outside surface of the cytotoxic drug containers (e.g., syringes, infusion bags, tubing) in the preparation cabinet be cleaned in the cabinet.

Place each cytotoxic drug container (e.g., syringe, bag) as well as the administration supplies (e.g., tubing) in a clear, leak-proof plastic bag (e.g., Ziploc® type) to facilitate identification by the nurse without having to remove the container from the bag.

Following final verification, it is strongly recommended that the plastic bags containing the cytotoxic drugs be placed in a rigid transport container (ideally opaque), properly identified with the “Cytotoxic” hazard symbol.

**Waste**
It is strongly recommended that everything that comes out of the cabinet be wiped clean.

It is strongly recommended that all contaminated waste be disposed of in the chemotherapy waste stream.

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**Saskatchewan (Sask health Nov 2014)**
All hazardous drugs will be dispensed in its final dosage form (i.e. IV solutions, tablets, opened capsules)

Solutions/suspensions will be packaged using standard volumes. Nursing may be required to discard excess solution/suspension in the appropriate biohazard receptacle.

Pharmacy will prepare injectable hazardous drugs in a biological safety cabinet.
The IV bag containing the hazardous drug will be spiked with a closed system secondary tubing set and primed with neutral solution by pharmacy. IV and injectable hazardous drugs will be delivered in a sealed transport bag. See Appendix B Closed Male Luer Connector: Spiros.

All hazardous infusions will be administered via designated IV tubing with a closed male luer connector attached to the end of the primary IV tubing closest to the patient.

Pharmacy will prepare compromised oral formulations.

If a patient is unable to swallow or requires medication administration via a PEG or nasogastric tube, contact the pharmacist for advice on alternative dose formulations. If required, the physician may need to be contacted for a new medical order. In the rare instance that Pharmacy is unable to make an oral formulation (stability issues, no recipe for formulation, etc.) refer to the dissolve-a-dose, and crushing notes below.

Note: To dissolve a tablet or capsule, place the medication in a capped “Dissolve-a-Dose” tube and add diluent (warm water or saline). Securely attach cap and mix gently until medication is dissolved. Open the small outer cap and attach an oral syringe and withdraw the entire contents of the tube. To crush a dose that can't be dissolved (i.e. enteric coated tablet), place the tablet(s) into an oral syringe and replace the plunger. Draw 0.5 – 1 ml of water into the syringe to ‘wet’ the tablet. Place a cap on the syringe and turn the plunger with a grinding motion to create a coarse powder. Draw several mls of water into the syringe and let the medication dissolve for several minutes. Shake periodically. Administer the suspension orally or via feeding tube.

National Association of Pharmacy Regulatory Authorities (Nov 2016)
Any of the following conditions will affect preparation quality. Personnel afflicted with any of these conditions shall be excluded from sterile compounding activities and sterile compounding areas until the condition has been remedied:

- uncontrolled weeping skin condition
- burns to the skin, including sunburns
- cold sores (active herpes simplex viral infection)
- conjunctivitis (viral or bacterial)
- active respiratory infection with coughing, sneezing or runny nose
- fresh piercings
- other fresh wounds

A person with permanent tattoos may compound sterile products. However, a recent tattoo on the face, neck or arms is considered a fresh skin wound, and the individual must cease sterile compounding activities and wait until the skin is completely healed before resuming such activities.

Before entering the anteroom, compounding personnel must:

- remove personal outer garments (e.g., coat, hat, jacket, scarf, sweater, vest, boots and outdoor shoes);
- remove jewelry, studs and other accessories from fingers, wrists, forearms, face, tongue, ears and neck (this includes personal electronic devices or accessories, such as cell phone, iPod and earbuds, which are not permitted in the anteroom or clean room);
- remove all cosmetics, including makeup, false eyelashes, perfume, hair products such as hairspray, henna tattoos and paper tattoos, as these products can generate particles that are possible sources of contamination;
- tie up long hair;
- remove nail polish and other nail applications (nail extensions and other synthetic nail-lengthening products are prohibited);
- ensure that natural nails are kept short and trimmed (0.6 cm);
• ensure that skin of hands and forearms is undamaged;
• change into dedicated, low-shedding apparel suitable for the controlled area (e.g., scrubs);
• wear pants that fully cover the legs;
• wear closed shoes and socks;
• wash hands.

Conduct in controlled areas (clean room and anteroom)
In controlled areas, the following measures should be taken:
• Food items, drinks, chewing gum, candy and cigarettes (or other smoking products) are prohibited.
• All access doors to controlled areas must be kept closed.
• Access to the controlled areas is restricted to personnel with specific responsibilities in the controlled areas.
• All personnel in the controlled area must follow specified hand hygiene and garbing procedures.
• Only essential conversations are allowed, to minimize the risk of particulate contamination. Coughing, sneezing and talking in the direction of the BSC should also be avoided.

After donning head and facial hair covers, face masks and shoe covers, personnel must wash and disinfect hands and forearms in the following sequence:
• Under warm running water, use a nail pick to remove debris from underneath fingernails.
• Wash hands and forearms up to the elbows with soap and water, for at least 30 seconds. Do not use brushes.
• Rinse with water.
• Dry hands and forearms with disposable, lint-free towel.
• Dispense alcohol-based hand rub (ABHR) with persistent activity onto one palm.
• Immerse fingertips of the other hand into the ABHR.
• Cover the forearm of the other hand with ABHR until the ABHR evaporates.
• Repeat with other hand and other forearm.
• Don gown.
• Enter the clean room. Dispense ABHR onto palm of one hand. Rub both hands with ABHR, making sure that all surfaces of the hands are covered. Continue to rub until the ABHR has evaporated.
• Allow hands to dry.
• For compounding hazardous preparations, don two pairs of gloves. The first (inner) pair of gloves goes under the sleeves of the gown, while the second (outer) pair must be pulled up over the gown cuffs. The outer gloves must be sterile.

This hand-washing sequence must be documented in the policies and procedures and updated as appropriate.

Garbing
PPE must be worn during the compounding of hazardous sterile preparations, regardless of the type of C-PEC that is used.
Compounding personnel must don and remove garb in the sequence described in the policies and procedures. The selected sequence must be documented and reviewed regularly.
The following general garbing sequence is recommended:
• While standing on the “dirty” side of the demarcation line in the anteroom, don hair net, then beard cover (if required) and then face mask.
• While stepping over the demarcation line, don two pairs of shoe covers.
• Under warm running water, use a nail pick to remove debris from underneath fingernails, and then wash hands and forearms (up to the elbows) with warm water and soap for at least 30 seconds, rinse with warm water and dry with disposable, lint-free towel (see also section 6.6.2.1).
• Apply ABHR with persistent activity.
• Don gown, closed at the neck and elastic cuffs.
• Apply ABHR with persistent activity to hands and allow hands to dry.
• Don gloves and routinely disinfect them with sterile 70% isopropyl alcohol or equivalent agent during the compounding process.

All compounding personnel must wear two pairs of gloves. The first (inner) pair of gloves goes under the sleeves of the gown, while the second (outer) pair must be pulled up over the gown cuffs. The outer gloves must be sterile.

Two pairs of shoe covers are required at all times in the clean area of the anteroom and the clean room. When the compounding of hazardous sterile preparations is complete, personnel must remove the PPE following an established technique and sequence, to minimize the risk of chemical contamination, as set out in a detailed procedure developed by the facility. Personnel must dispose of soiled PPE in a container for cytotoxic waste and must then wash their hands before exiting the compounding area and performing any other activity.

Manitoba (Oct 2015)
Preparation
• All Staff shall don appropriate PPE prior to Hazardous Medication preparation.
• Refer to Safe Handling of Medications Chart (Appendix A) and consult appropriate chart: Cytotoxic Hazardous Medications or Non-cytotoxic Hazardous Medications.
• All Hazardous Medications prepared by pharmacy shall be labeled and packaged to reflect the hazardous nature of these medications.
• All Cytotoxic Hazardous Medications shall be labeled as “Cytotoxic”.
• All Cytotoxic Hazardous Medications shall be transported in sealable plastic bags (e.g. Ziploc\ bag).
• Parenteral Cytotoxic Hazardous Medications shall be packaged for transport individually in double sealable plastic bags (e.g. Ziploc\ bags).
• Non-cytotoxic Hazardous Medications shall be labeled with “Wear Gloves” and “Do Not Crush” (if appropriate to the dosage form).
• Parenteral infusion bags containing Cytotoxic Hazardous Medications shall have tubing sets attached and primed by pharmacy with a solution not containing the Cytotoxic Hazardous Medication and shall be sealed with a dead end device.
• Exception: Pediatric preparations
• Syringes containing Cytotoxic Hazardous Medications shall be sealed by pharmacy with a dead-end device.
• Waste generated from the preparation of Cytotoxic Hazardous Medication shall be discarded in the appropriate Cytotoxic Waste Container.
• If a vendor delivers damaged Cytotoxic Hazardous Medication packages, the receiver shall don PPE and segregate (may place into another container or in a separate area) or dispose of the damaged package and inform the vendor of the status of the damaged package.

Alberta Health Services (June 2017)
Preparation of Cytotoxic Drugs
□ Whenever possible, preparation of cytotoxic drugs shall take place in Pharmacy in a biologic safety cabinet.
□ Whenever possible, a suspension must be supplied or prepared by pharmacy for administration of any doses that require opening of capsules or crushing/splitting of tablets.
□ If impossible and preparation/manipulation/compounding of a cytotoxic drug is necessary on unit or outside of a biologic safety cabinet, recommendations are as follows:
□ Preparation should occur in an isolated area away from drafts and traffic.
□ Double gloves, DMR gown, and N-95 mask must be worn.
□ The work surface should be covered with a disposable plastic back pad.
Contaminated equipment/work surfaces should be cleaned with water saturated gauze first and clean again with household detergent and water and rinse.
Contaminated materials should be discarded in a cytotoxic waste container.

United States Pharmacopeial Convention (Chapter to become official July 1, 2018)

DISPENSING FINAL DOSAGE FORMS
HDs that do not require any further manipulation, other than counting or repackaging of final dosage forms, may be prepared for dispensing without any further requirements for containment unless required by the manufacturer or if visual indicators of HD exposure hazards are present (e.g., HD dust or leakage). Counting or repackaging of HDs must be done carefully. Clean equipment should be dedicated for use with HDs and should be decontaminated after every use. Tablet and capsule forms of antineoplastic HDs must not be placed in automated counting or packaging machines, which subject them to stress and may create powdered contaminants.

RECOMMENDATION 7: TRANSPORT AND STORAGE FOLLOWING PREPARATION

On-site Transport of Cytotoxic Drugs
Transport cytotoxic drugs using a method that will prevent contamination of the environment in the event of breakage.

It is strongly recommended that cytotoxic drugs be placed in a closed, leak-proof plastic bag (e.g., Ziploc® type).
It is strongly recommended that transport of the cytotoxic drug in a closed, leak-proof plastic bag from the pharmacy to an area not adjacent to the preparation area (e.g., care unit, outpatient clinic), be done in a rigid, shock-resistant, leak-proof container made of a material that can be easily cleaned and decontaminated in the event of a drug leak. It is strongly recommended that the bottom be covered with an absorbent, plastic-backed cloth.
It is legislated that the transport container be identified with the “Cytotoxic” hazard symbol and be cleaned regularly (9, 10).
It is strongly recommended that mechanical transport systems, such as pneumatic tubes, not be used because of the stress they put on the contents, and the whole transport system would be compromised if a leak occurred.

It is strongly recommended that prepared medications be stored in a designated area prior to administration. It is strongly recommended that this area be cleaned regularly.

Off-site Shipping and Transport of Cytotoxic Drugs
Establish policies and procedures regarding the shipping of cytotoxic drugs (29).

In the event that cytotoxic drugs are shipped off-site (e.g., from one institution to another), it is strongly recommended that they be packed separately from other drugs, according to the recommendations from the manufacturer and distributor. It is strongly recommended that pharmacy be consulted in the packaging of cytotoxic drugs.

It is strongly recommended that Cytotoxic drugs be packed in a double plastic bag and placed in a box that is properly identified with the "Cytotoxic" hazard symbol. If necessary, immobilize the drug with packing material (30). It is legislated that the "Cytotoxic" hazard symbol be visible on the outside of the delivery container (30). It is strongly recommended that reusable delivery containers be cleaned regularly.
Ensure that the courier company will handle cytotoxic drugs.

Quapos 5 (2016)
Delivery of the finished products to the entity providing oncological therapy
For “In-house” transport the finished products are delivered in unbreakable, liquid tight, closable containers labelled with the inscription ”Caution Cytostatics”. (TRGS 525 5.6) ”
If the finished product will be transported out of the institution it needs to comply with hazardous freight regulations (Gefahrgutverordnung GGVS).
Cytostatic compounds partially belong to the group of hazardous freights. They have the UN number 1851 and need to be arranged under ‘drug, liquid, toxic’.

National Association of Pharmacy Regulatory Authorities (Nov 2016) (NAPRA)
Alternative storage must be provided if the storage temperature exceeds acceptable variations and when refrigerators and freezers are being cleaned.

Verification of stored products
Products that have been stored must be inspected before use, for evidence of deterioration.
Preparations that have exceeded their BUDs must be discarded promptly.

Transport and delivery of hazardous compounded sterile preparations
Policies and procedures must be developed and implemented for the transport of hazardous compounded sterile preparations and their delivery to patient care units, pharmacists and patients (See Appendix 4). A policy for return of expired or unused hazardous compounded sterile preparations from the patient’s home or the patient care unit in a health care facility must also be developed.
The transport and delivery procedures must identify the delivery person and the times when the min/max thermometer must be checked during transport. The steps to be followed in the event of non-maintenance of target storage temperature during transport must be indicated in the procedure.
The transport and delivery procedures must include any precautions to be taken by the delivery person, especially during delivery (e.g., personal delivery of the hazardous compounded sterile preparation, rather than delegation to another person) and during return of medications, waste, and sharp or pointed items.
For community pharmacies and health care facility pharmacies making deliveries outside the facility, the delivery container should be lockable or sealed.
The sterile compounding supervisor must ensure that personnel involved in preparation and delivery of products (pharmacist, pharmacy technician, pharmacy assistant and driver) receive training on the transport and delivery procedures, including the procedure for dealing with accidental exposure or spills.
The pharmacist or pharmacy technician must dispose of any unused hazardous compounded sterile preparations returned from a patient’s home.
In health care facilities, unused preparations returned from the patient care unit to the pharmacy may be reused if it can be shown that they have been properly stored (at the correct temperature, with protection from light, etc.) and there is no evidence of tampering

. Hazardous compounded sterile preparations must be transported in rigid containers marked “Cytotoxic” and designed to minimize the risk of cracking or failure of the preparation containers. They should not be transported via pneumatic tube systems.
When a private carrier is used, the sterile compounding supervisor must verify the steps taken to ensure maintenance of the cold chain throughout transport and storage of hazardous compounded sterile preparations.
The sterile compounding supervisor must also ensure that the private carrier knows the procedures to be followed in the event of a spill, that a spill kit is available and that transport personnel have received
appropriate training.
Where compounding is undertaken by another pharmacy, as permitted by provincial/territorial legislation, the compounding personnel must ensure that the preparation is transported to the dispensing pharmacy under conditions that maintain stability of the preparation. The receiving pharmacy must then ensure that transport conditions are maintained until delivery to the patient.
All personnel involved in transporting hazardous compounded sterile preparations must be trained in the procedures for such transport and for spills or accidental exposure.

During packaging, compounding personnel must
• put each final hazardous compounded sterile preparation in a clear plastic bag (or an amber bag, if the preparation must be protected from light);
• place items with an attached needle in a second rigid container;
• indicate storage requirements on the final package (e.g., temperature, protection from light);
• indicate additional precautions on the final packaging (e.g., pictogram indicating cytotoxicity);
• indicate transport precautions (e.g., temperature, fragility, safety) and instructions (name and address of the patient) on the outside packaging of each item.

Packaging procedure
To maintain the integrity of hazardous compounded sterile preparations and the safety of patients and delivery personnel, the sterile compounding supervisor must develop and implement a packaging procedure for final hazardous compounded sterile preparations. Appendix 4 presents a model for writing such procedures. The packaging procedure must specify the following details:
• equipment to be used to prevent breakage, contamination, spills or degradation of the hazardous compounded sterile preparation during transport and to protect the carrier;
• equipment to be used to ensure that packaging protects hazardous compounded sterile preparations against freezing and excessive heat (for hazardous compounded sterile preparations requiring refrigeration, the packaging must maintain a temperature between 2°C and 8°C and for hazardous compounded sterile preparations to be kept at room temperature, the packaging must maintain a temperature between 19°C and 25°C);
• method to be used to confirm whether the temperature of hazardous compounded sterile preparations has been maintained during transport (e.g., temperature maintenance indicator, min/max thermometer, certified cooler);
• packaging to be used to protect against extreme temperatures (i.e., excessive heat or freezing) during transport of hazardous compounded sterile preparations, unless information is available demonstrating the product’s stability at these temperatures.

Manitoba (Oct 2015)
All liquid preparations of Cytotoxic Hazardous Medications shall be hand-delivered to Patient care areas (includes all dosage forms; e.g. parenteral, oral, topical, etc.). Delivery via pneumatic tube systems and dietary lifts is not permitted. Solid dosage forms (tablets or capsules) of Cytotoxic Hazardous Medications may be transported via pneumatic tube systems but shall be appropriately packaged in a sealable plastic bag (e.g. Ziploc\ bag).

Designated pharmacy lifts may be used to transport all dosage forms of Cytotoxic Hazardous Medications but shall be appropriately packaged in sealable plastic bag(s) (e.g. Ziploc\ bag).

BC Cancer Agency (Sept 2016)
Hazardous drugs must be packaged and transported in a manner which minimizes the risk of HD exposure due to a spill or breakage during transit.

Work safe BC (2015)
Equipment
The equipment used for transporting hazardous drugs throughout a facility should be designed to minimize exposure to workers handling hazardous drug products. This includes:
• Equipment that reduces spills, such as carts with lipped edges and closed, hard-sided transport boxes
• Using equipment that is easy to clean

Guidelines for safe work practice
Best practices for transporting hazardous drugs include:
• Using resealable clear plastic bags to place hazardous drug products in before transport
• Using closed, hard-sided boxes to be used for transport throughout the facility
• Implementing procedures for safe handling of products during transport

Personal protective equipment (PPE)
PPE must be consistent with the worker’s potential exposure and may include:
• Double chemotherapy-tested gloves
• A chemotherapy-tested gown

Alberta Health Services (June 2017)
Deliveries (from the Pharmacy to the Patient Care Area)
1. Precautions shall be followed to prevent breakage, minimize exposure, and contain spills when transporting cytotoxic drugs.

2. Cytotoxic medications must be HAND DELIVERED to minimize the possibility of medication falling or breakage during delivery. Mechanical transportation devices such as the pneumatic tube system and the telelift system MUST NOT be used due to the stress these devices place on their contents and risk of breakage.

3. Cytotoxic medications shall be placed into two sealable plastic bags or one sealable bag placed into a rigid container and labeled with a warning label identifying the contents as cytotoxic. See below for examples:

4. Luer lock syringes should be used to contain injectable cytotoxic medications and these syringes should be transported with the luer lock end capped. Do not transport syringes with needles attached. A luer-lock syringe should NOT be used for oral preparations to avoid accidental parenteral administration. Cytotoxic medications will be packaged from pharmacy in safety engineered devices (SED) whenever possible and appropriate.

5. All pharmacy compounded IV, oral or topical formulations of cytotoxic medications must be handled with a single pair of disposable gloves during transportation and delivery as well as receiving and retrieving from storage on the patient care units.

6. Upon delivery/arrival, the cytotoxic medication should be checked to ensure it is delivered intact to the correct area, and is stored appropriately under refrigeration or at room temperature segregated from food and other drugs.

7. All individuals involved in the transportation shall be educated in spill management.

8. Intrathecal preparations must be placed in a designated intrathecal box, which is kept separate from other drugs.

9. Vinca alkaloids must be kept separate from intrathecal medications during delivery and storage on the patient care unit.
B. Returns
1. Unused/unopened cytotoxic medications
Unused/unopened cytotoxic medications may be returned to the pharmacy enclosed in two sealable plastic bags or one sealable bag placed into a rigid container and labeled with a warning label identifying the contents as cytotoxic. They must be HAND DELIVERED. The pharmacy must be notified when an unused/unopened cytotoxic medication is being returned.

2. Used/partially used/opened cytotoxic medications
Used/partially used/opened cytotoxic medications shall not be returned to pharmacy and must be disposed of as cytotoxic waste in a cytotoxic waste container on unit.

RECOMMENDATION 8: DRUG ADMINISTRATION

It is strongly recommended that safe handling and administration techniques be used to minimize possible exposure to individuals and the environment when administering cytotoxic drugs.

- It is legislated that appropriate personal protective equipment be made available to all healthcare workers and be worn as prescribed by the employer, please refer to Table 1 (2).
- It is strongly recommended that Luer-Lock connectors and needleless administration systems be used to administer any intravenous medications.
- Closed systems may offer additional protection.
- It is strongly recommended that disposable plastic-backed absorbent pads be used over work surfaces and placed under tubing or bag connections and ports when attaching any tubing, bag or syringe that have been exposed to a cytotoxic drug.
- Unless a closed system is used, never disconnect tubing from cytotoxic drug bags. Discard bag with attached tubing into an appropriate waste container as a single unit.
- It is legislated that safety engineered needles be used as per Needle Safety Regulation 474/07 made under the Occupation Health and Safety Act Labour, 2010 (31). Do not purge air from the needle before administration.
- It is strongly recommended that oral cytotoxics be handled in a manner that avoids skin contact, liberation of aerosols or powdered medicine into the air, and cross-contamination with other medicines (32).
- It is strongly recommended that solid oral preparations (tablets) of cytotoxic drugs be crushed or cut within the biological safety cabinet. If patients are unable to take in the solid format, it is strongly recommended that the pharmacy provide these drugs in an oral syringe, in a ready-to-administer, liquid oral form.
- It is strongly recommended that application of topical cytotoxic drugs be done using appropriate personal protective equipment and in a way that prevents contamination of the environment. Between applications, it is strongly recommended that the cytotoxic medication (i.e., tube or jar) be kept in a safe container (i.e., Ziploc) and in a secure place that prevents contamination of the surrounding environment.
- With any intravesical administration, e.g., bladder instillation, ensure there are detailed procedures in place to avoid risks of splashing.
- Use caution when administering intrathecal cytotoxic drugs, as there is risk of splashing due to increased intrathecal pressures.

Saskatchewan (Sask health Nov 2014)
RNs who are competent and certified in chemotherapy administration will independently calculate the
infusion rate, and check the settings on the infusion pump at initial set-up, change of bag and/or change in infusion rate. Document on the MAR and include both RNs initials and time of double-check.

All chemotherapy infusions will be administered via designated IV tubing with a closed male luer connector attached to the end of the primary IV tubing closest to the patient. 
Note: Pediatrics - use IV micro pump tubing.

All intravenous chemotherapy drugs must be infused via an infusion pump with the exception of vesicants administered peripherally and drugs ordered IV push. 
Pediatric Patients: All intravenous chemotherapy administration will be administered via a central venous catheter.

All chemotherapy infusions will be administered via the secondary function or Line B on the infusion pump.

To verify patency of the line, blood return must be confirmed prior to administration of any chemotherapy drug.

The primary IV line minimum flush volume will be 25mls of compatible IV solution prior to disconnection and 10 mls between drugs, unless otherwise required for a clinical trial. The IV site, rate and volume of infusion must be assessed hourly during administration of the chemotherapy drug.

Continuous Intravenous Drug Administration
Continuous Infusions must not be interrupted for more than 72 minutes in total over 24 hours. (equivalent to 5% of a 24-hour period).
Note: It is not acceptable to interrupt continuous chemotherapy infusions for tests, patient showers or personal preference. Interruptions should only occur when it is unavoidable (e.g delay from pharmacy, extravasations, chemotherapy spill).

Continuous infusions must be infused at a constant rate over 24 hours. Minor adjustments to hourly infusion rates may be made. The total 24 hour rate increase is not to exceed 5% of the initial rate. These adjustments must be documented on the MAR.

Each 24-hour dose of a continuous infusion must be infused within a 24-hour period and no longer than 72 minutes exceeding or falling short of this time. Any contents remaining after that time may be safely infused over 10 minutes providing the volume remaining does not exceed 5% of the original total volume.
Note: Pharmacy & the ordering physician are to be consulted in cases where the Above principles cannot be applied.

Blood return must be verified every 12 hours when infusing vesicants by continuous infusion

Registered Nurses (RNs), Graduate Nurses (GNs), Registered Psychiatric Nurses (RPNs) Licensed Practical Nurses (LPNs) and Graduate Practical Nurses (GLPNs) may administer hazardous drugs by all routes working within their scopes of practice

Hazardous Drug Precaution labels must be placed on the chart or in the equivalent record and intravenous tubing. See Appendix C Hazardous Drug Precaution labels.

A Hazardous Drug Handling sign must be placed above the patient bed or on the room door.
Care exempt) See Appendix D Hazardous Drug Handling sign.

A Chemotherapy/Hazardous Drug Spill Kit must be readily available on the unit, when injectable and/or liquid hazardous drugs are administered.

**Subcutaneous/Intramuscular Administration**

Do NOT expel air out of syringe. Tap air to the plunger end of the syringe before administering medication.

**Intravenous Administration**

Protect work area with a plastic backed absorbent pad.

Prime the primary IV tubing with a compatible solution that does not contain any additives.

At the bedside, verify the following information before opening the sealed transport bag:

- the patient’s identity with patient’s client identification band and/or picture identification and the label on the drug
- the secondary tubing is securely connected to the IV bag
- the secondary tubing is clamped
- there is absence of moisture within the transport bag (i.e., drug leakage)
- the red cap is on the end of the tubing to indicate sterility

Infuse the hazardous drug through the secondary port.

**When drug administration is complete:**

- If disconnecting the secondary line/administering other drugs - flush the secondary port with 10 mls neutral solution prior to disconnection from primary line
- If disconnecting the primary IV line from patient - flush primary IV tubing with 25 mls of neutral solution (Pediatrics: 10-20mls) prior to disconnection from patient

Wipe the port(s) after disconnection with a 2x2 gauze.

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**Saskatchewan (Regina, Feb 2016)**

Two RNs or an RN and physician must check dose of drug against physician’s written order and both must sign on Chemotherapy Administration Record (CAR).

- Work below eye level for administration of all hazardous drugs. All units handling hazardous drugs should have cytotoxic waste disposal set up

**Do not cut, crush, break or open tablets or capsules** for administration. Any drug preparation required must be done in pharmacy.

Closed administration system does not offer protection for administration of subcutaneous or intramuscular delivery, therefore N95 respirator is required. DO NOT expel air from needle. Pharmacy will send syringe with a closed administration system.

Label all IV tubing cytotoxic.

- All hazardous drug infusions will be administered via secondary medication line, except where drug requires specially tubing that must run on primary line.
- Do not remove spike from infusion bag. Do not disconnect any IV administration set in which exposure to hazardous medications may occur. Ensure line is flushed before disconnecting and dispose of entire administration set in cytotoxic waste.

Drug instillation into bladder is performed by physician in operating room.

- Catheter bag and chart should be labeled with a “Cytotoxic Label” – Stock #200083.
- Label must be clearly visible to receiving unit.
Hand off communication from OR to receiving unit is to include:
- Time of instillation
- Amount of time medication has been in bladder (refer to physician orders/OR notes)
- Time medication was drained from bladder

Do not empty chemotherapy agent with urine from drainage bag.
If catheter is to remain in place, use appropriate PPE, clamp catheter, disconnect catheter bag with chemotherapy agent, attach a new catheter bag and unclamp catheter. Apply cytotoxic label to catheter bag. Empty contents using appropriate PPE for 48 hours following installation.

Handling of oral Cytostatic

Oral cytostatics are only available in most cases as capsules or tablets. If there is a pediatric oncology department in a hospital, the question of other dose or pharmaceutical forms - in general, suspensions or solutions are desired since these are the easiest to handle during application and enable flexible dosing.

To produce such formulations, special precautions must be taken since the process may result in dusts from highly toxic substances. Employee protection is a key priority and must be ensured through appropriate measures and environmental conditions. Since this concerns oral preparations, product protection plays a less important role and thus aseptic production does not need to be ensured in most cases.

If drugs are turned into a new pharmaceutical form, it should additionally be ensured that the therapeutic effect is not impaired either through a lack of stability and incompatibility or through significantly altered pharmacokinetics, if drugs are turned into a new pharmaceutical form.

Administration in Patient Care Area

All Staff shall don appropriate PPE prior to Hazardous Medication administration.
- Refer to Safe Handling of Medications Chart (Appendix A) and consult appropriate chart: Cytotoxic Hazardous Medications or Non-cytotoxic Hazardous Medications.

A Cytotoxic Symbol shall be posted in the administration area and on the Patient chart and kardex or care plan during the administration and for 48 hours after the end of administration of Cytotoxic Hazardous Medications (includes all routes; e.g. parenteral, oral, inhalation, topical, etc.).

Once a Cytotoxic Hazardous Medication is removed from the sealable plastic bags (e.g. Ziploc bags) all manipulations of infusion bags/tubing/syringes shall take place on a plastic-lined absorbent pad with the absorbent side up.

Infusion bags containing Cytotoxic Hazardous Medications shall not be spiked at the Patient bedside. Following an infusion of Cytotoxic Hazardous Medication using a secondary set, the infusion line shall be flushed with a plain IV solution to ensure it is clear of all Cytotoxic Hazardous Medication before disconnecting.

When disconnecting syringe/IV line, a 2X2 inch gauze/alcohol pad shall be used to absorb any droplets of Cytotoxic Hazardous Medication and then disposed of in a Cytotoxic Waste Container.
Transport of Patients:
Transport Staff and the receiving department shall be notified when a Patient is under Cytotoxic precautions.

Transport of Patients with Cytotoxic Hazardous Medications infusing out of their Patient care area should be avoided. If the reason for transport is essential, a Cytotoxic Spill Kit and Staff trained in Cytotoxic Spill management shall accompany the Patient.

Patients should not be transferred between facilities with Cytotoxic Hazardous Medications infusing. If the need for inter-facility transport is essential, the Cytotoxic Hazardous Medication should be interrupted or discontinued.

Cytotoxic Hazardous Medications that are discontinued or temporarily stopped partway through administration shall have the tubing clamped and/or a dead-end device applied. Storage of interrupted Cytotoxic Hazardous Medication infusions should be discussed with the pharmacy if necessary.

- Cytotoxic Hazardous Medication infusions that are not resumed shall be sealed (e.g. dead-end capped, sealable plastic bag, etc.) and discarded in a Cytotoxic Waste Container. Hazardous Medication tablets or capsules shall not be split or crushed in a Patient care area prior to administration due to the risk of Exposure and environmental contamination. Contact pharmacy for assistance and recommendations.

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**BC Cancer Agency (Sept 2016) Safe Handling of Oral, Topical and Pre-Packaged Hazardous Drug Dosage Forms**

All drugs listed on the facility’s hazardous drug list must be handled according to hazardous drug safe handling guidelines. Oral, topical and pre-packaged hazardous drug dosage forms must be handled in a manner that prevents skin contact and minimizes the liberation of powdered or aerosolized HD into the air and cross contamination with other drugs.

**Oral Preparations**
- Two pairs of chemotherapy gloves must be worn when handling hazardous drug tablets and capsules and when pouring HD oral solutions or suspensions in a designated area of the pharmacy dispensary
- Dedicated ‘chemotherapy’ counting trays and spatulas must be used to count loose HD tablets and capsules
- Hands must be washed immediately after removing chemotherapy gloves
- Gloves worn when handling hazardous drugs must be discarded in HD waste
- Automated counting machines must not be used to count hazardous drug tablets and capsules

**Topical Preparations**
- Two pairs of chemotherapy gloves must be worn when handling hazardous drug topical preparations that have been removed from the original packaging

**Note:**
- All interior surfaces of a BSC (except under the work surface) used for both sterile and non-sterile HD preparations must be cleaned following non-sterile HD preparations. Once cleaned, the BSC must purge for 15 minutes prior to compounding sterile HD products
Hazardous drugs are administered in treatment areas in a number of different settings. The design of treatment areas should reflect the findings of the risk assessment. Treatment areas where hazardous drugs are administered:

- Should be kept under neutral or negative air pressure to the surrounding rooms, where possible
- Should use surfaces that are easy to clean, such as stainless steel, where possible
- Should keep any rest areas for workers or visitors isolated from any administration areas

**Drug administration equipment** The selection of appropriate equipment for the administration of hazardous drugs can help minimize the risk of exposure to workers. All activities involving the administration of medication to a person must be done with safety-engineered medical sharps or a needleless system, where clinically appropriate. Equipment used for the administration of hazardous drugs includes:

- Closed-system transfer devices (CSTDs) designed for the administration of hazardous drugs
- Safety-engineered needles
- Filtered venting devices, such as chemotherapy-dispensing pins and chemotherapy vents
- Administration equipment, such as IV pumps and CADD pumps

Refer to Appendix 6 for information on how to select medical equipment that is appropriate for use with hazardous drugs.

**Guidelines for safe work practice** Best practices for the administration of hazardous drugs include:

- Avoiding priming IVs with a hazardous drug solution at the point of administration (this should be done as part of the preparation step in an approved BSC)
- Avoiding altering oral medications, such as crushing or cutting, at the point of administration (this should be done as part of the preparation step in an approved BSC)
- Where possible, avoiding contact with oral medications during administration by using medication cups, unit-dose packaging from the manufacturer, or having patients administer their own medication
- If priming of administration sets cannot be done as part of the preparation step, implementing procedures so that priming is performed with compatible dilutant and the drug is added afterwards
- Using CSTDs for administration activities, including withdrawing and injecting hazardous drugs from syringes and IV systems
- Using disposable, absorbent pads to be placed under the patient where administration is occurring
- Using bandages that can be applied over an area where a topical medication has been applied to avoid spreading contamination to clothing or bedsheets
- Limiting access to administration areas (this is extremely important for some administration forms, particularly aerosolization therapy, and only the patient should be in the room where treatment is taking place)
- Implementing procedures for proper disposal of administration equipment, such as flushing IV tubing with a dilutant before disconnecting or discarding tubing immediately after use as hazardous waste

**Cleaning** There should be regular cleaning of administration areas. The administration area should have a set of cleaning equipment dedicated for that area.
Work areas, such as trays, carts, tabletops, chairs, and beds where hazardous drugs are administered, should be cleaned daily. Refer to Appendix 7 for more information on the selection of cleaning agents.

Considerations for home care Administering hazardous drugs in home care settings poses additional challenges because there is less ability to change the physical work environment. Where possible, an initial assessment of the home should be done to determine that there are appropriate facilities for the activities that will take place in the home. This may include:

- Running water to allow for hand washing
- A properly functioning toilet
- Windows that can be opened to provide ventilation

The guidelines for safe work practice in administration settings discussed in the previous sections may also be applied in the home care setting, where relevant. Additional best practices for administration in the home include:

- As much as possible, avoiding any alteration of hazardous drugs in the home (activities such as cutting or crushing oral medications and dissolving powders into solution should be done by pharmacy staff in a BSC)
- Providing the patient with instructions on:  
  - How to use administration equipment, such as electronic diffusion devices
  - Safe handling precautions for bodily fluids during the precautionary period for their treatment, including recommendations for the equipment and PPE required
  - How to safely dispose of hazardous drug waste and contaminated medical sharps

The precautionary period is the period of time that a patient excretes hazardous drugs after their treatment. For most treatment protocols this is 48 hours but may be up to seven days. Refer to the treatment protocol to determine the precautionary period for each patient.

PPE must be consistent with the worker’s potential exposure and may include:

- Chemotherapy-tested gloves
- A chemotherapy-tested gown
- Face and eye protection

Patient care area The design of the patient care area must reflect the results of a risk assessment to reduce exposure to hazardous drugs. In general, care areas where patients are receiving or have received hazardous drugs should:

- Be isolated from other patient care areas, where possible
- Have dedicated washroom facilities for patients who have received hazardous drugs
- Have appropriate laundry services

Equipment Equipment used for caring for patients within the precautionary period includes:

- Bed pans that are disposable, when possible
- Carts and trays that are easy to clean and dedicated for use with patients who have received hazardous drugs

Refer to Appendix 6 for information on how to select medical equipment that is appropriate for use with hazardous drugs.

Best practices for the care of patients receiving or who have received hazardous drugs include:

- Implementing safe handling procedures for handling body fluids of patients within the precautionary period, such as covering toilets and double flushing
- Implementing safe handling procedures for handling laundry from patients within the precautionary period, such as avoiding shaking, folding the bedding so any contamination is trapped in the centre, and placing laundry in a plastic bag
• Where possible, discarding laundry or bedding that is heavily contaminated by body fluids, or alternatively washing separately once before being added to other facility laundry
• On top of regular charting requirements, documenting the length of the precautionary period for the patient as per the treatment protocol
• Ensuring workers review patient history before providing care. When patients are being cared for after treatment at home, either by a health care worker or their family, they should be provided with the instructions described in Chapter 15.

Cleaning Patient care areas should be cleaned and decontaminated regularly. This includes:
• Cleaning washrooms of patients receiving hazardous drugs regularly
• Cleaning up spills of patient body fluids immediately

Personal protective equipment (PPE) PPE must be consistent with the worker’s potential exposure and may include:
• Chemotherapy-tested gloves
• A chemotherapy-tested gown, if there is a risk of splashing of body fluids
• Face and eye protection, if there is a risk of splashing of body fluids
• An approved and fit-tested respirator, if there is a risk of inhaling aerosols or particulates

Alberta Health Services (June 2017)
Routes of Administration and Who May Give: Non-Antineoplastic and Antineoplastic Cytotoxic Drugs
The administration of any these drugs by any route must be performed by qualified staff. It is the responsibility of the qualified staff to be aware of their qualifications / limitations based on their scope of practice, training, legislation and site/unit policies. The parenteral manual can be consulted to determine who and what qualifications are required for administration of parenteral and intravesical cytotoxic drugs.

General Administration Guidelines - All Routes
1. Qualified staff shall follow the AHS - Edmonton Zone Corporate Administrative Directive 2.3.5 / CH Medication Administration Policy on Drug Administration when administering cytotoxic drugs.
2. All drugs must be checked against the written order prior to administration for verification of drug, dose and schedule.
3. The expiry date/stability of the drug must be checked prior to administration to ensure medication has not expired.
4. The calculated body surface area (BSA) must be verify and be congruent with body shape of patient.
5. Ensure the SEVEN rights of drug administration are followed: Right drug, Right dose, Right time, Right route, Right patient, Right reason and Right documentation. In addition, other safety checks that may apply include ensuring the Right rate, Right protocol, Right site and Right frequency.
6. TWO qualified staff must independently co-check/co-sign all administration records for all antineoplastic cytotoxic drugs by all routes. Please refer to the AHS - Edmonton Zone Corporate Administrative Directive 2.3.5 / CH Medication Administration Policy for the Procedure on Medication Administration Independent Double Checks.
7. Explain procedure to patient, along with the side effects of drug administration. Ensure the information is understood.
8. Gather supplies.
9. Ensure a cytotoxic waste container is available where cytotoxic medications are prepared/poured/manipulated or administered and the patient-care unit has a cytotoxic spill kit

Section 4: Document Review Summary
on hand or is aware of the location of the nearest spill kit. A cytotoxic waste container may be kept in the patient’s room but away from the bedside or in another predetermined designated area. Cytotoxic containers shall be safely closed or fastened while in patient’s room. When the cytotoxic container is full or no longer required, the container should be stored with the lid securely sealed in a designated area (usually the dirty utility room) until picked up by environmental services for incineration.

10. Store cytotoxic medications in designated/segregated areas in bins that have high fronts and on shelves that have guards. Store at or below eye level.

11. Personnel shall wash their hands with soap and water thoroughly before putting on and after removing gloves when preparing, administering, or disposing of cytotoxic drugs or contaminated materials. Alcohol based hand sanitizer may be used before putting on gloves to eliminate bacterial contamination but as these products do not eliminate chemical contamination, they must not be used after removing gloves. Hands must be washed with soap and water after removing gloves.

12. Refer to Personal Protective Equipment (Table 2), to determine when PPEs are required.

13. Dispose of needles and syringes intact. Do NOT break or recap needles after use. Immediately discard into a rigid puncture proof cytotoxic waste container.

14. Whenever possible, use safety engineered or closed devices (SEDs) for the preparation and administration of cytotoxic drugs.

15. Use household detergent and water to wash surfaces that come into contact with cytotoxic drugs. PPE must be worn.

Intravenous (IV) Administration Also refer to General Administration Guidelines.

For personal protective equipment and when to wear it, see table 1 and 2.

Review your parenteral drug manual for specific drug information prior to administration. An extravasation kit shall be available on the patient care unit prior to administration of a vesicant drug.

Patient Monitoring: Frequency is determined by the patient’s condition/age, prescribed therapy, and Vascular Access Device (VAD) used. It includes, but is not limited to assessment of the VAD insertion site and surrounding area, infusion flow rate, patient’s response/compliance, and side effects. Patency must be assessed prior to the administration of cytotoxic drug via blood withdrawal from VAD.

1. Direct IV Administration General Procedure
   a. Appropriate dilutions of the drug should be administered into an IV catheter with a compatible primary IV solution infusing concurrently over a minimum of two to four minutes, or as recommended in the AHS-Edmonton Zone / Covenant Health Services Regional Parenteral Manual (or site based parenteral manual if regional monograph not available). The patient must be observed for changes in vital signs or other untoward reactions.
   b. The IV tubing must be flushed after each drug with at least 25 mL of compatible solution such as NS or D5W. Post-administration, monitor the IV site at least once per hour until satisfied that drug has cleared the administration site to ensure that tissue damage has not occurred.

   EXCEPTION: outpatients may be instructed on what to report and then sent home

   EXCEPTION: For Pediatrics refer to direct IV administration guidelines as per site/program policy

2. IV Infusion Administration General Procedure (Continuous or Intermittent, Peripheral or Central Vein)
   a. Prime IV administration set (primary and secondary) with compatible isotonic solution
(e.g., NS or D5W) that does not contain cytotoxic drug. The secondary IV administration set must be primed with the solution from the primary bag to ensure a closed system and decrease the risk of a spill. Calculate administration times/rates based on amount of flush used and desired rate.

b. It is recommended that cytotoxic drugs be infused via a secondary IV administration set using a needle-lock device attached to the primary IV administration set. IV administration sets must be secured and leak-proof. Use luer locks or safety engineered devices (SED) as required.

c. Ensure patency of the IV catheter prior to attaching cytotoxic drug. Patency of catheter must be checked each time that the catheter is accessed. Contact physician if patency is questionable. To determine patency, the following three must occur:
   i. Exit site is without signs of inflammation and infiltration such as redness, pain or swelling. Consider patient’s statements about comfort around site.
   ii. Blood return is brisk and consistent. If unable to aspirate blood from central line, obtain chest X-ray to confirm correct line placement (for vesicant drugs - dye studies are required).
   iii. IV fluid must run freely by gravity.

d. Attach the cytotoxic drug and begin infusion according to rate ordered.

e. The IV line must be dedicated to the cytotoxic drug only during administration.

f. Monitor the patient and the patient’s IV site at least hourly (q1h) or according to the cytotoxic drug protocol for any signs/symptoms of adverse reactions, extravasation, or phlebitis.
   i. If an adverse reaction is noted, stop the infusion, initiate emergency measures (e.g., Airway, Breathing, and Circulation) and notify the physician.
   ii. If extravasation is suspected with drug therapy, follow extravasation procedures (see section 10).
   iii. If phlebitis is suspected, discontinue infusion.

g. After drug administration, flush the IV administration set with 25 to 35 mL of compatible priming solution to ensure that the patient has received the full dose.

h. For consecutive administration of different cytotoxic drugs, remove the entire secondary drug administration set, prime a new secondary administration set from the primary infusion bag and, follow general administration procedure as outlined above.

i. All tubing /lines, including buretrols or similar devices must be changed for consecutive administration of drugs that are incompatible as there may be residual drug in the primary line.

j. Tubing/lines must be discarded into a cytotoxic waste container immediately upon completion of each dose or refer to site/program specific guidelines.

k. All IV administration sets used to deliver these drugs must be disposed of as cytotoxic waste, even if it has been flushed prior to disconnection.

l. When treatment is complete, a peripheral IV site may be left in place if needed. If no
longer needed, remove the peripheral IV catheter and apply pressure for at least 5 minutes. Apply dressing as needed.

m. Discard all contaminated waste (e.g., bags, bottles, syringes, administration sets, gloves, disposable gowns, incontinence pads, disposable diapers, gauze dressings) as per the Cytotoxic Waste Handling - section 12.

n. Never remove tubing from an IV bag containing these drugs. Discard infusions bags with tubing attached. Do not disconnect tubing at other points in the system until the tubing has been thoroughly flushed.

Additional requirements for PERIPHERAL IV Infusions and CENTRAL VENOUS CATHETER (CVC) Infusions, Additional Requirements for IV administration (Peripheral or Central) of Vesicants, Intramuscular and Subcutaneous Administration, Bladder Instillations and Intrathecal Administration can be found in the manual As well as Extravasation

Topical Administration
Also refer to General Administration Guidelines.
For personal protective equipment and when to wear it, see tables in section 2 (Protection of Employees and Patients).
1. Sterile double gloves suitable for handling cytotoxic drugs must be worn if the drug is being applied to an open skin lesion.

2. The drug shall be applied directly to the patient. A disposable plastic back lined pad shall be used to prevent contamination of the patient’s environment.

3. If the patient’s linens or gown become contaminated, they must be contained and secured. (See Cytotoxic Waste Handling - section 12).

4. All items used in dermal applications must be disposable. Dispose of these items into the cytotoxic waste container immediately after use.

5. The application process shall be carried out in a private area/treatment room away from other patients and in an area where all items can be disposed of immediately.

6. All multi-dose cytotoxic dermal solution/ointment/cream containers must be placed in double zip-lock bags labeled “cytotoxic” for storage. To avoid contamination of container, remove outer glove prior to placing container back in zip-lock bags.

7. Cytotoxic Dermal Solution Administration - Additional Guidelines
a. Soak a sterile gauze pad with the solution and apply directly to the skin surface using forceps.

8. Cytotoxic Dermal Ointments/Creams - Additional Guidelines
a. Remove the ointment/cream from the container using a sterile Q-Tip or tongue blade and apply directly to the skin. Use a new tongue blade or Q-Tip for each application.

b. Spread the ointment/cream over the designated surface. Double gloves, suitable for
handling cytotoxic drugs, must be worn (see section 2 C Personal Protective Equipment)

c. To prevent contamination of the environment, patient movement must be restricted after applications of dermal cytotoxics until the ointment or cream is fully absorbed

**Oral Formulation Administration**

1. Administering oral cytotoxic dosage forms present minimal risk unless the capsules are opened or the tablets are crushed or split. Capsule opening and tablet crushing/splitting on patient care units is generally not permitted due to the risk of aerosolized particles.

Pharmacy must be contacted to prepare a suspension formulation or to split tablets in a biologic safety cabinet whenever possible. Pharmacy shall provide suspensions /solutions of these drugs in an oral syringe, in a ready to administer form whenever possible. A luer-lock syringe must NOT be used for oral preparations to avoid accidental parenteral administration. In the event that Pharmacy Services are unavailable or unable to provide this service and tablets must be crushed /split or capsules opened or liquids prepared on the patient care unit, measures as listed below must be taken to protect staff. Preparation should occur in an area away from drafts and traffic. Double gloves, DMR gown and N-95 mask must be worn.

The work surface should be covered with a **disposable plastic back pad**. Tablets may be dissolved in water in a medication cup for immediate use. If a tablet requires crushing or splitting, place tablet and designated pill crusher/splitter, into a sealable plastic bag (i.e. Zip lock bag) and crush/split. Capsule contents may be placed in water in a medication cup for immediate use. Open capsules slowly into a small amount of water to minimize aerosolization. To crush cytotoxic drugs in unit-dose packaging, place the intact unit dose package and designated pill crusher in a small sealable plastic bag, and crush in sealed plastic bag without breaking the packaging. Clean contaminated equipment/surfaces with water saturated gauze first and clean again with household detergent and water and rinse. Discard contaminated materials in a cytotoxic waste container.

2. Double gloves must be worn when administering oral cytotoxic medications.

3. Discard used drug cups into a cytotoxic waste container.

4. If any powder has fallen on any surface (e.g., floor, counter), wash that area immediately with disposable paper towels, household detergent and water. Appropriate PPE must be worn (See Table 2)

5. Place paper towels, gloves and waste in a cytotoxic waste container.

6. If the spill is significant, use a cytotoxic spill kit (see section 13- Spills and/or Personnel Contamination).

7. When administering these drugs via enteral feeding tubes (i.e. PEG or NG tubes), follow required practices for each tubing system to minimize risk of spill or contamination via leakage. Full personal protective equipment should be worn if there is a risk of aerosolization, leakage, splash or spill.
If solution requires transfer to a syringe (i.e. 60 cc catheter tip) for administration, any manipulation should occur at the patient’s bedside using appropriate spill precautions and a plastic back absorbent pad. PPEs should be worn.

A plastic back absorbent pad should be place by site of administration to contain any leakage or spills.
Dispose of all cytotoxic waste generated in the manipulation and administration of the drug in a cytotoxic waste container immediately.

United States Pharmacopeial Convention (Chapter to become official July 1, 2018)
ADMINISTERING
HDs must be administered safely using protective medical devices and techniques. Examples of protective medical devices include needleless and closed systems. Examples of protective techniques include spiking or priming of IV tubing with a non-HD solution in a C-PEC and crushing tablets in a plastic pouch.
Appropriate PPE must be worn when administering HDs. After use, PPE must be removed and disposed of in a waste container approved for trace-contaminated HD waste at the site of drug administration. Equipment (such as tubing and needles) and packaging materials must be disposed of properly, such as in HD waste containers, after administration. CSTDs must be used for administration of antineoplastic HDs when the dosage form allows. Techniques and ancillary devices that minimize the risk posed by open systems must be used when administering HDs through certain routes. Administration into certain organs or body cavities (e.g., the bladder, eye, peritoneal cavity, or chest cavity) often requires equipment for which locking connections may not be readily available or possible. Healthcare personnel should avoid manipulating HDs such as crushing tablets or opening capsules if possible. Liquid formulations are preferred if solid oral dosage forms are not appropriate for the patient. If HD dosage forms do require manipulation such as crushing tablet(s) or opening capsule(s) for a single dose, personnel must don appropriate PPE and use a plastic pouch to contain any dust or particles generated.

Containment Supplemental Engineering Controls Containment supplemental engineering controls, such as CSTDs, provide adjunct controls to offer an additional level of protection during compounding or administration. Some CSTDs have been shown to limit the potential of generating aerosols during compounding. However, there is no certainty that all CSTDs will perform adequately. Until a published universal performance standard for evaluation of CSTD containment is available, users should carefully evaluate the performance claims associated with available CSTDs based on independent, peer-reviewed studies and demonstrated containment reduction. A CSTD must not be used as a substitute for a C-PEC when compounding. CSTDs should be used when compounding HDs when the dosage form allows. CSTDs must be used when administering antineoplastic HDs when the dosage form allows. CSTDs known to be physically or chemically incompatible with a specific HD must not be used for that HD.

RECOMMENDATION 9: HOME CARE
Home Care of Patients who Have Received Cytotoxic Drugs
It is strongly recommended that all cytotoxic drugs preparations be compounded in pharmacies meeting the requirements for cytotoxic drug preparation.
It is strongly recommended that cytotoxic drugs be transported, administered and disposed of...
by individuals who have received appropriate training. It is strongly recommended that cytotoxic drug transport containers are not reused by patients for domestic purposes, which may expose the family to cytotoxic drugs (e.g., toy box, sewing basket, etc.).

It is legislated that the health care provider who administers cytotoxic drugs in the home wear Personal Protective Equipment as outlined in Table 1 (2).

It is strongly recommended that health care providers follow the same recommendations outlined in Recommendation 8 - Drug Administration.

It is strongly recommended that a spill kit be readily available in the home in case of accidental spills.

It is strongly recommended that patients be informed of and be provided with written instructions for the safe handling of cytotoxic drugs.

It is strongly recommended that contact information be provided for home care patients who require assistance with safe handling of cytotoxics.

Cytotoxic Drug Waste in the Home

It is strongly recommended that the institution have a clear process to address the issue of cytotoxic waste from patients in their homes, in compliance with municipal or local cytotoxic waste rules. It is strongly recommended that this process include patient and caregiver education.

It is strongly recommended that caregiving staff provide the patients/caregivers involved in administering cytotoxic drugs in the home with a process for appropriate disposal of cytotoxic waste, including left-over drugs.

Quapos 5 (2016)
Patients, family members and personnel working in the home care setting need to be trained in the handling of cytostatics in this environment. The following points should be specifically stressed during their training:

- Special handling of cytostatics
- Handling of application devices
- Management of spilling or other incidents
- Management of paravasation
- Handling patient’s excretions
- Cytostatic waste disposal

An individual care plan should be established in cooperation with the responsible pharmacist (see chapter 5.1).

Alberta Health Services (June 2017)
Home Care
1. Administration of Cytotoxic Drugs by Home Care Staff
   Home Care staff will administer cytotoxic drugs in accordance with the Continuing Care Clinical Resource:
   i. Cytotoxic Medication Administration & Spill Management (located under Medication > Cytotoxic http://insite.albertahealthservices.ca/15965.asp)
2. Disposal of Cytotoxic Drugs by Home Care Clients
   a. Patients/caregivers shall be instructed in the appropriate handling and disposal of cytotoxic waste.
      i. Refer to Appendix D for “Safety Measures for Cytotoxic Drugs” for waste handling instructions.
      ii. Home care clients shall be instructed to dispose of all cytotoxic waste in an appropriate “cytotoxic container”. Staff shall ensure that the client is aware of how to seal the container & where to take it for disposal. Waste disposal containers are available for purchase at some community pharmacies and there are community pharmacies and AHS sites which accept them for disposal.
      iii. A cytotoxic spill kit must also be available in a client’s home. Cytotoxic Spill kits may be available for purchase at some community pharmacies or the outpatient pharmacy.

B. Home Care Client Self-administration
   1. Education
      Patients shall be instructed in proper handling, preparation, administration, and disposal of cytotoxic drugs.
      a. Refer to Appendix D - “Safety Measures for Cytotoxic Drugs”, for handling instructions for patients.
      b. Self-administration of subcutaneous methotrexate:
         a. For patient information on methotrexate use in pediatric rheumatic diseases and Crohn’s disease, refer to Appendix E.
         b. For information on administration of subcutaneous methotrexate, refer to Appendix F, titled “Patient Instructions for Methotrexate Subcutaneous Injections”.
         c. Complete the checklist found in Appendix G, titled “Methotrexate Subcutaneous Injection Teaching Record”, to ensure outpatients have received the required information for administering subcutaneous methotrexate.

2. Cytotoxic Preparation by Pharmacy
   a. Whenever possible, preparation of cytotoxic drugs for use in the patient’s home shall take place in Pharmacy.
   b. Patients should be advised to obtain injectable cytotoxic drugs in the unit of use (e.g. syringes) whenever possible. When injectable cytotoxic drugs cannot be obtained in the unit of use, patients/caregivers shall be instructed in proper techniques for withdrawing drug from vials/ampoules and safe handling during preparation.

3. Self-administration of Cytotoxic Drugs
   a. Patients/caregivers shall be instructed in the appropriate administration technique and safe handling precautions for the prescribed cytotoxic drug.
   b. When the patient/caregiver is not able to administer the cytotoxic drug, a referral may be made to the Home Care program.
   c. Patients/caregivers should be instructed not to crush/split tablets or open capsules of cytotoxic drugs. Oral cytotoxic that require opening crushing should be supplied by Pharmacy in a suspension or solution whenever possible. If this is not possible, patient should be instructed in the proper methods of preparation and safe handling during preparation.
4. Disposal of Cytotoxic Drugs used in the Patient’s Home

a. Patients/caregivers shall be instructed in the appropriate handling and disposal of cytotoxic waste.


RECOMMENDATION 10: MANAGEMENT OF WASTE

Bodily-Fluid Waste
It is strongly recommended that workers who handle the biological fluids, excreta, contaminated bedding and soiled equipment of patients who have received cytotoxic drugs wear one (1) pair of gloves and a protective gown. It is strongly recommended that face protection be worn when there is a risk of splashing.

Cytotoxic Drug Waste
Establish policies and procedures as per provincial legislation regarding cytotoxic waste management.

The term “cytotoxic waste” includes any material that comes into contact with cytotoxic drugs during their storage, handling, preparation, administration and disposal (e.g., packaging material, protective equipment, preparation supplies, such as syringes, tubing, drug bags), soiled disposable incontinent briefs of patients who have received cytotoxic drugs during the previous 48 hours or longer depending on the drug [e.g., it is known that cyclophosphamide may persist for several days], hood pre-filters and HEPA filters, etc.).

It is legislated that cytotoxic waste be placed in a waste container clearly identified with the “Cytotoxic” hazard symbol. It is legislated that cytotoxic waste be disposed of in the appropriate containers (10).

It is legislated that sharps be placed in rigid containers with a leakproof lid; CSA standard Z316.6-07 specifies the use of the colour red for the rigid containers (33). If the containers are another colour, follow the instructions of the company ensuring the final disposal (10).

It is strongly recommended that other waste (soft items, such as tubing, protective equipment, etc.) be placed in leak-proof and tear-resistant containers, identified with the “Cytotoxic” hazard symbol.

For final disposal outside the institution, it is legislated that all cytotoxic waste be in a rigid, leakproof, container identified with the “Cytotoxic” hazard symbol and scheduled for transport outside the institution (10).

It is legislated that any excess fluid from cytotoxic drugs (e.g., drug loss) be disposed of in a sealed container and placed in a rigid container, the bottom of which is to be covered with an absorbent pad. This rigid container will be handled like other cytotoxic waste (10).

It is recommended that disposable/incontinent briefs soiled by patients who have received cytotoxic drugs be placed in a cytotoxic waste container.
It is legislated that cytotoxic waste be incinerated at a high temperature (i.e., 800 °C to 1200 °C, depending on the product) (10).

It is legislated that cytotoxic waste not be disposed of in the receptacles used for infectious biomedical waste (which may be autoclaved and then sent to a landfill site) (10).

It is legislated that every area where cytotoxic drugs are handled will have an appropriate cytotoxic waste receptacle as close as possible to the work area (10).

The lids of cytotoxic drug receptacles must remain closed, except when depositing waste. Bins with foot pedals and lids, which lock automatically when full, are recommended to minimize exposure.

It is strongly recommended that workers be careful to avoid contaminating the outside of the receptacle when depositing waste.

It is legislated that the transport of cytotoxic waste receptacles be assigned to properly trained workers (2).

It is strongly recommended that workers who handle cytotoxic waste receptacles wear one pair of disposable gloves and have a spill kit at their disposal. It is strongly recommended that the waste go through as few care units, public areas and areas containing food or linens as possible.

It is legislated that the final storage areas for cytotoxic waste receptacles be secure. Refer to Ontario storage requirements (9, 10).

**Saskatchewan (Regina, Feb 2016)**

All body fluids are considered hazardous when a patient is receiving hazardous medication.

- Label all drainage collection devices with cytotoxic label.
- Discard all contaminated disposable material and disposable PPE in cytotoxic waste.
- PPE should always be worn when handling any body fluid (blood, vomitus, urine, saliva, sweat and stool) from patients treated with hazardous drugs and precautions continued for 48 hours following last dose.
- If a patient is incontinent, clean skin well with each change. Apply protective barrier ointment to skin as required. Physician may choose to order an indwelling catheter.
- Specimens do not require a cytotoxic label as universal precautions are used to handle all specimens.
- Prior to flushing hazardous body fluids down toilet, place plastic backed pad with absorbent side down over seat or put toilet lid down to reduce splash back.

**Quapos 5 (2016)**

Excretions of patients, who receive anticancer chemotherapy, may contain significant amounts of cytotoxic substances. Health protection measures should be provided to all persons handling these excretions. In addition applicable disposal rules and regulations need to be followed.

The principles of waste disposal are

- waste avoidance
• waste recycling
• waste disposal.

Disposal is to take place such that
- the health and well-being of persons
- the environment (air, water, ground, animals, plants and landscape) and
- public safety are not jeopardized.

Hazardous wastes and objects contaminated with these are collected
• separately from other wastes
• at the place they originate
• in appropriate, labelled collecting vessels.

In general, cytostatic waste is considered hazardous waste. It should be collected in specific containers, which can be hermetically sealed after filling. Cytostatic waste needs to comply with hazardous freight regulations (GGVS) and applicable national and regional statutory requirements.

Handling waste materials containing cytostatics should be defined in the operating instructions (where to find).

National Association of Pharmacy Regulatory Authorities (Nov 2016)

In the performance of assigned duties, the pharmacist or pharmacy technician must
• ensure that medications and sharp or pointed instruments are disposed of safely, in compliance with environmental protection laws in force in the jurisdiction;
• ensure that medications to be destroyed are safely stored in a location separate from other medications in inventory;
• develop and implement a procedure for destruction of pharmaceutical waste.

Pharmaceutical products that are expired or otherwise no longer usable are considered pharmaceutical waste. Hazardous products must be destroyed in accordance with regulations governing such products. A list of hazardous products in use must be available in the pharmacy. The NIOSH list can be used to determine whether a particular product is hazardous.

Policies and procedures for the management of hazardous waste must be developed and followed. These policies and procedures must comply with local, provincial/territorial and federal requirements and must include the following provisions:
• All personnel involved in the management of hazardous waste must receive appropriate training on destruction procedures to ensure their own protection and to prevent contamination of the premises or the environment.
• All equipment, products and vials used in the compounding of hazardous sterile preparations must be discarded in a hazardous waste container.
• Hazardous waste containers must be identified with a self-adhesive label marked “Hazardous waste - cytotoxic”.
• Containers should be filled to only three-quarters of their capacity.
• Once a bin is three-quarters full, it should be sealed. Personnel should never attempt to compress the contents of a hazardous waste bin.
• Sharps containers removed from the C-Pec must be decontaminated and then discarded into a hazardous waste container and sent for destruction.
• Non-sharps waste used in the compounding of hazardous sterile preparations must be placed in a
hazardous waste container inside the C-PEC or placed in a sealable plastic bag before removal from the C-PEC and then discarded in a hazardous waste container.

• Outer gloves must be removed inside the C-PEC. The gloves must be placed in a hazardous waste container inside the C-PEC or placed in a sealable plastic bag before removal from the C-PEC and then discarded in a hazardous waste container.

• All PPE must be discarded in a hazardous waste container.

• Bins used for hazardous waste must comply with local, provincial/territorial and federal requirements. These bins must be incinerated; decontamination by autoclave and subsequent burial is prohibited.

The efficiency of HEPA filters in the ventilation system must be tested during facility certification (at least every 6 months), and filters must be replaced periodically as recommended by the manufacturer.

Filters used to exhaust air from clean rooms or C-PECs must be considered contaminated and must be handled with a level of care appropriate to protecting personnel and the environment. Where applicable, “bag in/bag out” containment systems may be used to enhance the safety of such operations.

A sufficient number of hazardous waste containers of suitable size and made of materials resistant to damage from cleaning, disinfecting and decontamination products must be available. Waste containers must be closable, to limit the spread of vapours. The exterior of each waste container must be decontaminated before it is removed from the controlled area.

The waste shall be removed once a day, at a time when no compounding is occurring. Waste containers must be identified with appropriate hazardous materials symbols (e.g., pictogram indicating cytotoxicity).

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**Manitoba (Oct 2015)**

• All disposable items used while Handling Cytotoxic Hazardous Medications, regardless of route of administration (e.g. parenteral, oral, inhalation, topical, etc.), are considered Cytotoxic Medication Waste and shall be discarded in a Cytotoxic Waste Container.

• Cytotoxic Waste Containers should be located as close to point of care as possible (e.g. inside Patient room).

• Cytotoxic Waste Containers shall be prepared for disposal when three-quarters (3/4) full and not more than approximately 15 kg (35 lb) in weight. Cytotoxic Waste shall not be pushed down into the container to make more room. This practice may increase the risk of Exposure and environmental contamination.

• Cytotoxic Waste Containers shall have a Cytotoxic label and be sealed prior to collection.

• Exception: Home Care Program shall follow the Home Care Hazardous Medications Guidelines for disposal of Cytotoxic Waste. See [http://home.wrha.mb.ca/prog/homecare/manuals_hcguide.php](http://home.wrha.mb.ca/prog/homecare/manuals_hcguide.php)

• Disposable items used while Handling Cytotoxic Human Waste (including items used in Patient care (e.g. incontinence products, dressings, urinary catheters and bags) shall be discarded in a Cytotoxic Waste Container.

• Exception:

• Long Term Care facilities please see Procedure

• Home Care Program shall follow the Home Care Hazardous Medications Guidelines for disposal of Cytotoxic Human Waste. See [http://home.wrha.mb.ca/prog/homecare/manuals_hcguide.php](http://home.wrha.mb.ca/prog/homecare/manuals_hcguide.php)

• Site-specific procedures related to disposal of Cytotoxic Waste Containers shall be available at all facilities.
Hazardous Medications and Waste received and transported off site shall be packaged according to Transportation of Dangerous Goods Federal Regulations. See www.tc.gc.ca.


**Waste Handling**

Safe Handling precautions of Cytotoxic Human Waste shall be followed during administration period and for 48 hours after the last dose of Cytotoxic Hazardous Medication regardless of route of administration (e.g. parenteral, oral, inhalation, topical, etc.).

- Refer to Safe Handling of Medications Chart (Appendix A) and consult appropriate chart: Cytotoxic Hazardous Medications or Non-cytotoxic Hazardous Medications.

Contaminated laundry items shall be bagged at the point of care in a waterproof laundry bag (plastic bag) and sent to laundry service or home for cleaning as per site-specific practice.

- Laundry bags shall be sealed for transport to laundry service or home immediately after use to prevent access by other Staff or care givers.

Toilets shall be covered before flushing after use by Patients under Cytotoxic Hazardous Medications Handling precautions.

- In areas without toilet lids, the bowl shall be covered with a disposable plastic-lined pad prior to flushing. The pad shall be disposed in a Cytotoxic Waste Container. Long Term Care facilities please see Procedure 4.20.

Non-disposable items that come in contact with Cytotoxic Hazardous Medications, Cytotoxic Medication Waste or Cytotoxic Human Waste shall be washed with a non-antiseptic detergent or soap solution (e.g. dishwashing or hand soap) and rinsed with copious amounts of water while wearing Chemo Gloves. Electric equipment shall be wiped down thoroughly; first with a damp cloth and then disinfected using site-specific Routine Practices.

4.20

- Long Term Care facilities are regarded as Patients’ place of residence. The disposal of Patient Cytotoxic Human Waste, including disposable items used for Patient care (e.g. incontinence products, gloves) may be discarded in general waste.

**BC Cancer Agency (Sept 2016)**

Hazardous waste containers must be available in all areas where hazardous drugs are received, stored, prepared and administered.

All disposable items that may have come in contact with hazardous drugs during receipt, storage, preparation or administration must be treated as hazardous waste including PPE. Hazardous waste must be disposed of separately from general waste in hazardous waste containers with lids. The hazardous waste container must be distinctly different from other types of waste containers.

All disposable non-sharp HD waste must be disposed of in 4 mil thick plastic bags which are placed inside a rigid HD waste container or carton so that all waste is essentially ‘double-bagged’. The warning label must identify the contents as hazardous so that individuals transporting the waste are alerted to the need for special handling.

All sharps used for the preparation and administration of hazardous drug admixtures must be placed into a puncture-proof hazardous drug sharps container for disposal without being crushed or clipped. Chemotherapy dispensing pins and chemotherapy vents removed from HD vials must also be disposed of in a hazardous drug sharps container. The HD sharps container must be sealed when it is no more than three-quarters full or at the indicated maximum fill line.
HD waste containers must not be overfilled and the contents must not be pushed down to make more room due to the risk of HD exposure. Two pairs of chemotherapy gloves must be worn while handling hazardous waste.

While awaiting removal from the facility for disposal, hazardous waste must be stored in a secure area in securely sealed and properly labelled containers. Hazardous waste must be transported and disposed of according to Federal and Provincial regulations after leaving the facility.

**Work safe BC (2015)**

Hazardous drugs that are to be disposed of:
- Disposable equipment used to administer hazardous drugs, such as syringes, needles, or IV tubing
- Disposable PPE used for protection against exposure to hazardous drugs
- Bodily fluids, such as vomit, stool, urine, and sweat, from patients who have recently received hazardous drugs
- Disposable materials contaminated with body fluids from patients who are within the precautionary period

Potential activities that could result in exposure include:
- Disposing of hazardous drug-related waste, if it is contaminated or leaking
- Handling hazardous drug waste containers, which may have surface contamination

**Work area design**

If hazardous drug waste is stored at the workplace before it is taken to be disposed of, it should be stored with appropriate precautions, as determined by the risk assessment. This includes:
- Storing hazardous drug waste in a cool, locked, and ventilated area until it is transported out of the facility
- Isolating the storage area for hazardous drug waste from other areas of the workplace as much as possible
- Storing in a manner to prevent leaks and spills, such as by having shelves with lipped edges
- Using materials that are easy to clean, such as stainless steel

Hazardous drug waste should be collected in a hazardous drug waste container. A hazardous drug waste container:
- Must be leak-proof and puncture resistant
- Must be designated for use with hazardous drugs
- Should be easily identifiable as designated for hazardous drugs, such as by using a uniform colour throughout the workplace

A bag used for disposal of soft materials (for example, laundry, gloves, or gowns) contaminated with hazardous drugs:
- Should be leak-proof
- Should be made of thick, leak-proof plastic
- Should be easily identifiable
- Must be appropriately labelled with a hazardous drug warning

All areas where there is potential for hazardous drug waste should have a hazardous drug waste container. These areas can be determined as part of a risk assessment. Hazardous drug waste containers and bags should also be provided to patients and animal owners who are receiving hazardous drugs or being cared for at home.

**Guidelines for safe work practice**

Best practices for disposal of hazardous drug waste include:
- Coordinating of hazardous drug communication with external waste-collection companies to reduce worker exposure
- Sending hazardous drug waste for disposal by a certified hazardous waste organization and
in accordance with local regulations
• Having hazardous drug waste containers collected and transported throughout a facility only by workers trained to do so
• Arranging for the collection of hazardous drug waste containers from patients' homes
• Implementing procedures to reduce leaks from hazardous waste containers, such as by placing contaminated items in double plastic bags before placing in a hazardous drug waste container Refer to CSA Standard Z317.10-09 Handling of Waste Materials in Health Care Facilities and Veterinary Health Care Facilities for more information on hazardous drug waste.
PPE must be consistent with the worker's potential exposure and may include:
• Chemotherapy-tested gloves
• A chemotherapy-tested gown
• Face and eye protection, if there is a risk of splashing
• An approved and fit-tested respirator if there is a risk of inhaling aerosols or particulate

Alberta Health Services
Cytotoxic waste:
Cytotoxic waste is any material that has become contaminated with cytotoxic drugs. These items may include needles, syringes, IV bags and administration sets, IV tubing, vials, amps, disposable gowns, gloves, masks, hair covers, medication cups, goggles, shoe covers, paper towels, plastic liners and zip-lock bags.
Cytotoxic waste also includes urine, excreta, vomitus and other body fluids from patients who have received cytotoxic drugs **within the previous 48 hours, or 72 hours in the case of cyclophosphamide.** Please note, these are guidelines and some cytotoxic drugs may be present in bodily fluid for longer than 48 hours. Qualified staff should review the product monograph of any medications they do not know for any additional special handling requirements.

B. Procedure
1. It is the Pharmacy and patient care unit's responsibility to clean up spills that occur in their respective areas. In the event that the spill cannot be managed or in a public area, Environmental Services or a Code Brown can be called as per site policy/procedures.

2. All personnel involved in the preparation, delivery, and administration of cytotoxic drugs shall be made aware of the proper procedures for the safe handling, containment, and disposal of cytotoxic waste.

3. Cytotoxic waste must be disposed of in cytotoxic waste containers. Sharps must be discarded in rigid puncture-resistant plastic containers displaying a cytotoxic symbol. IV tubing sets and other waste should be placed **intact** into the cytotoxic waste containers to prevent aerosolization. Containers must be sealed after use.

4. A cytotoxic waste container must be brought to the patient's bedside for disposal of cytotoxic waste. The container with lid closed may be stored in the patient's room until completion of cytotoxic drug regimen if no safety issues have been identified. Full /used cytotoxic waste containers should be securely sealed with lid and stored in a secure designated area (usually the dirty utility room) until they are picked up by environmental services for incineration. Do not store in hallway or public access areas.

5. The cytotoxic disposal container must be checked for breaks or leaks before it is removed from the patient's room and transferred to a secure soiled utility room. Containers must not be
Section 4: Document Review Summary

filled to more than 2/3 of its capacity. Pressure must never be placed on the waste to push it into the container. Prior to storage (in soiled utility room) nursing staff will seal the container with the lid provided. A biomedical waste barcode label must be applied to the lid. Who applies the label varies by site. See Appendix B in resource guide at http://insite.albertahealthservices.ca/Files/hr-compulsory-education-ace-resource-guide.pdf

6. Environmental services or waste management staff shall pick up the sealed cytotoxic waste containers from the designated storage area or pharmacy and transport them to an on-site secured holding area (i.e. Biomedical Waste Cold room), until taken for incineration. Environmental services or waste management staff will not handle material improperly secured.

C. Linen
1. All reusable linen not visibly contaminated with cytotoxic waste is treated as per usual standard precautions.
   - Reusable linen products shall be placed into the laundry bags.
   - Laundry bags shall be secured by tying the bag with a knot.
   - Full laundry bags shall be stored in the soiled utility area for collection by environmental services staff.
2. Reusable linen that is grossly contaminated with body secretions or cytotoxic medication is disposed of into the yellow biohazard box. For additional information see Section 13 - Spills and/or Personnel Contamination - Contaminated Clothing/Linens procedure

3. DISPOSABLE LINENS SHOULD BE USED WHENEVER POSSIBLE.

D. Patient Waste
1. Personal protective equipment (approved double gloves, gown and a face mask/shield /goggles) must be worn if splashing/ aerosolization is possible when handling urine, excreta, vomitus, and other body fluids from patients receiving cytotoxic drugs within the previous 48 hours. Discard cytotoxic urine, excreta or vomitus waste into the toilet. Double flush when discarding cytotoxic waste in toilet. For toilets that splash when flushed, place a disposable pad over the seat before flushing and discard pad after use into a cytotoxic waste container. Certain drugs may require cytotoxic handling precautions for greater than 48 hours. It is the responsibility of the qualified staff to be aware of these exceptions and follow appropriate precautions. Qualified staff should review the product monograph of any medications they do not know, for any additional special handling requirements. Cytotoxic handling precautions are only required for the first 48 hours or as dictated by cytotoxic drug excretion patterns. Thereafter, usual handling of patient waste should be followed.

2. Diapers soiled with urine and/or excreta from patients receiving cytotoxic drugs within the previous 48 hours must be handled with disposable gloves suitable for handling cytotoxic drugs and discarded into a biohazard waste disposal box lined with a yellow biohazard waste labeled plastic bag. Certain drugs may require cytotoxic handling precautions for greater than 48 hours. It is the responsibility of the qualified personnel to be aware of these exceptions and follow appropriate precautions. Qualified staff should review the product monograph of any medications they do not know, for any additional special handling requirements. Cytotoxic handling precautions are only required for the first 48 hours or as dictated by cytotoxic drug excretion patterns. Thereafter, usual handling of patient waste should be followed.

3. Some EXCEPTIONS:
a. For waste handling of urine voided within 8 hours following BCG, mitomycin or thiotepa
bladder instillations, refer to Administration Guidelines - Bladder Instillations (section 8).
b. Cyclophosphamide is found in bodily fluids for longer periods; therefore precautions shall be followed for at least 72 hours after a dose.

Final Disposal
Cytotoxic waste is transported from the site of generation to a secured holding area where it will be removed and taken for incineration by a licensed waste transportation contractor. Cytotoxic waste is incinerated at a temperature of 1000º C or greater to ensure complete destruction.

Cleaning of Patient’s Room after Cytotoxic Drug Administration
Routine cleaning of room is recommended unless a spill has occurred. If a spill has occurred, follow procedure for a spill clean-up.

United States Pharmacopeial Convention (Chapter to become official July 1, 2018)
Disposal of Used Personal Protective Equipment Consider all PPE worn when handling HDs to be contaminated with, at minimum, trace quantities of HDs. PPE must be placed in an appropriate waste container and further disposed of per local, state, and federal regulations. PPE worn during compounding should be disposed of in the proper waste container before leaving the C-SEC. Chemotherapy gloves and sleeve covers (if used) worn during compounding must be carefully removed and discarded immediately into a waste container approved for trace contaminated waste inside the C-PEC or contained in a sealable bag for discarding outside the C-PEC.

Disposal All personnel who perform routine custodial waste removal and cleaning activities in HD handling areas must be trained in appropriate procedures to protect themselves and the environment to prevent HD contamination. Disposal of all HD waste, including, but not limited to, unused HDs and trace-contaminated PPE and other materials, must comply with all applicable federal, state, and local regulations.

RECOMMENDATION 11: ACCIDENTAL EXPOSURE

Be aware of any mandatory reporting requirements under the Occupational Health and Safety ACT and report requirements to WSIB (2).

Establish policies and procedures regarding accidental worker exposure.

If a cytotoxic drug accidentally comes into contact with a worker’s skin or clothing, it is strongly recommended that the worker immediately remove the contaminated clothing and thoroughly wash the skin of the affected area with soap and water and continue to rinse for 15 minutes. If appropriate, it is strongly recommended that the contaminated worker take a shower. It is strongly recommended that a deluge shower be made available in the vicinity (e.g., in the oncology clinics/units). It is strongly recommended that all contaminated clothing be discarded in cytotoxic waste.

If a cytotoxic drug comes into contact with a worker’s eyes, it is strongly recommended that the worker flush their eyes at an eye wash station. Alternatively, it is recommended that the workers use an isotonic solution to flush their eyes (e.g., sterile NaCl 0.9%). It is strongly recommended that eyes be flushed for at least 15 minutes (21). It is strongly
recommended that that if contact lenses are worn, they be removed immediately prior to flushing.

In the event of a needlestick or sharps injury, let the wound bleed freely. Under running water, gently and thoroughly wash the area with soap. Contact Occupational Health. Ensure that facility policies for needlestick or sharps injury are followed including completion of an incident report and reporting to WSIB if indicated.

Saskatchewan (Sask health Nov 2014)

Drug Exposure

Splash to eyes
Flush eyes immediately at eyewash station for at least 15 minutes (use entire contents of the eye wash station). If eyewash station unavailable, flush with copious amounts of water or normal saline for at least 15 minutes.
Report incident.

Splash to skin (intact or non-intact)
Remove contaminated clothing immediately.
Flush area with copious amounts of water for at least 15 minutes.
Follow with washing area with soap and water.
Report incident.
Launder contaminated clothing at home separately once, then re-wash with regular wash. Where available arrange for laundry services to launder your uniform for you; if a replacement uniform is not available on your unit, call SPD to arrange pick-up of a decontamination uniform.

Needle stick injury
Express blood from needle puncture site.
Flush puncture site with cool running water for at least 15 minutes.
Apply ice or heat to the injected site, as per SHR IV Medication Reference Manual. Treat skin punctures with vesicant or irritant drugs as if an extravasation has occurred.
Report incident

Mucosal Exposure:
- Flush affected membrane (i.e. eye) immediately with copious amounts of clean water for at least 15 minutes.
- If no eyewash station, use IV tubing and flush with normal saline.
- Do not administer anesthetic drops or ointment.

1.2 Skin Contact:
- Remove contaminated clothing.
- Wash affected area with copious amounts of clean water and soap.
- Do not administer anesthetic ointment.

1.3 Skin Puncture:
- Wash affected area with copious amounts of clean water and soap, encourage bleeding.
**NOTE:** Seek emergency medical attention as appropriate.
If skin puncture is contaminated with blood or body fluids see RHD Policy 1.5.3.02 - Protocol for RHD Employees Following Blood/Body Fluid Exposure - Non-Sexual.
**NOTE:** If vesicant, should be treated as per extravasation protocol see nursing procedure E.9.

2. Inform charge nurse or supervisor.

4. Complete RQHR Confidential Occurrence Report form if patient is involved and submit to manager.

5. Complete RQHR Employee Report of Incident Hazard and bring to Employee Health Office for Employee Health Nurse. Include in report:
   - Name of hazardous drug
   - Type of exposure/amount
   - If body fluid exposure, indicate treatment plan and chemo day

**National Association of Pharmacy Regulatory Authorities (Nov 2016)**
Policies and procedures to be followed in case of accidental exposure of personnel to hazardous products must be established (see Appendix 1). For products with material safety data sheets, those documents must be accessible in the workplace.

If a hazardous product comes into contact with skin or clothing, the person must immediately remove all PPE and contaminated clothing and wash the affected area with plenty of water and soap.

If a hazardous product comes into contact with the eyes, the eyes should be rinsed with water or saline for at least 15 minutes. An appropriate eyewash station must be available for this purpose. Persons wearing contact lenses must remove them promptly after exposure.

In the event of a needle-stick injury involving a hazardous product, bleeding should be induced by massaging toward the wound (without pinching). The area should then be rinsed abundantly with clear water for 5 minutes and then washed with plenty of water and soap. A physician should be consulted. The exposure must be documented in the appropriate logs.

**Manitoba (Oct 2015)**
- Staff shall report all Hazardous Medication/Waste Exposure (including Direct and Indirect Contact and skin puncture) to their immediate supervisor. Appropriate site-specific reporting documentation shall be completed (e.g. Patient Safety Event Report, work related injury near miss forms). Staff may also file a claim with the Worker’s Compensation Board (WCB) to document the Exposure incident in case of a future concern. Complete an Employee’s Report of Injury Form and send the information to the WCB.

Following all Hazardous Medication Exposures, Direct or Indirect, Staff shall immediately take the following precautions, as appropriate:

- **Eyes** - Flush affected eye(s) with copious amounts of clean water or normal saline for a minimum of 15 minutes.

- **Skin** - Remove contaminated clothing immediately. Wash affected area with soap and running water for a minimum of 15 minutes.

- **Skin Puncture** - Wash puncture site thoroughly with soap and running water for a minimum of 15 minutes. Squeeze puncture site to encourage bleeding.
In the event of Exposure with a Hazardous Medication that is a Vesicant; treat as an extravasation as per site specific policy.

**BC Cancer Agency (Sept 2016)**

**Accidental Exposure to Hazardous Drugs**
Healthcare workers must be made aware of how to manage accidental exposure to hazardous drugs.
Any accidental HD exposure as a result of a spill, needle stick or other accident must be reported immediately to the professional practice leader/department manager and by calling the Provincial Workplace Health Call Centre reporting line at 1-866-922-9464. Appropriate documentation must be completed.

**Ingestion**
Staff must not take food, gum, drinks, cigarettes or personal medication into an area where hazardous drugs are handled (e.g., received, stored, prepared, administered and disposed).

**Alberta Health Services (June 2017)**

**Accidental Exposures**

1. Accidental employee exposures are to be reported to the immediate supervisor, Patient Care Manager or designate and to the appropriate workplace, health and safety (WHS) service. An employee incident/injury reporting and investigation form must be completed.

2. The most responsible physician or designate shall be notified when patients are involved in accidental exposures. The incident shall be reported, as per current incident reporting guidelines.

3. Employees handling these drugs are encouraged to arrange a routine medical examination on an annual basis.

**RECOMMENDATION 12: SPILLS MANAGEMENT**

It is strongly recommended that the facility develop policies and procedures for spills management that take into account the types of spills (i.e., amount, location, concentration, powder vs. liquid, etc.).
It is strongly recommended that a spill management kit be readily available within the work area.
It is legislated that items from the clean-up of spills be placed in the cytotoxic waste receptacle (10).
Most spills can be contained and managed by the trained health care worker (e.g., leaking IV tubing).
When a spill is not contained or easily managed (e.g., exposure to large volume of fluid that is a risk to the environment or a large crate of vials filled with powder broken in the receiving area), it is strongly recommended that a Code Brown or equivalent be called.
Saskatchewan (Sask health Nov 2014)
**Drug Spill**
*Note: If the patient vomits immediately after ingestion treat vomit as a chemotherapy drug spill.*
Do NOT leave the area of the spill. Have a co-worker bring the Chemotherapy/ Hazardous Drug Spill Kit.
Alert persons in immediate area.
Put on PPE from the spill kit.
Immediately notify the manager/supervisor.
Attend to anyone who has been splashed with the drug.
Contain the spill from the outer edges to the center by placing absorbent towels over the contaminated area.
Wash area three times, first with the detergent (supplied in kit) followed by water. Dry well with absorbent towel. Follow these same guidelines to clean contaminated equipment.
Dispose of supplies and waste in appropriate waste containers
Remove PPE.
Report incident

Saskatchewan (Regina, Feb 2016)
Use spill kit to clean up any hazardous liquid medication that has been spilled or any large amount of body fluid not absorbed into linen. Smaller amounts of body fluid should be cleaned using same procedure with disposable absorbent material placed in hazardous waste container available on unit.

Quapos 5 (2016)
A decontamination kit must be permanently located in every area where cytostatics are dealt with. The responsibility for ensuring this is ideally carried by the pharmacy as a central unit.
The decontamination kit contains among other items:
- Instructions for the decontamination procedures
- Marking material
- Disposable gown
- Overshoes
- Breathing protection mask (P3)
- Protective gloves
- Additional pair of gloves providing adequate mechanical protection against glass splinters
- Protective eyewear with side protection, which can be worn over personal eyewear
- Disposable cloths or wadding
- Water and ethanol for dampening
- Aids for collecting up broken glass
- Adequate number of robust waste containers
- Form for documentation of an accident
The removal and disposal of spilled cytostatics may be performed only by properly instructed personnel.
The procedure to be followed after inadvertent release is part of the working rules and the annual instruction.

National Association of Pharmacy Regulatory Authorities (Nov 2016)
Policies and procedures for managing spills must be established.
Training and garb
Employees who clean up spills must have received adequate training, must wear appropriate garb while cleaning up a spill and must use a chemical cartridge respirator for organic vapours equipped with a pre-filter. The respirator must be properly fitted to provide maximum protection in the presence of aerosolized or powdered products.

Spill kits must be available in locations where hazardous products are handled and must be present on carts used for transporting hazardous products. The contents of spill kits should be verified regularly and their expiration dates checked. For additional information, please see the Prevention Guide — Safe Handling of Hazardous Drugs, published by the ASSTSAS, which describes the content and use of spill kits.

Incidents and accidents
When an incident or accident involving a hazardous compounded sterile preparation occurs, the compounding personnel must complete an event report and explanation form (see Appendix 11 for an example). In health care facilities or community pharmacies, a form developed or selected by the facility or pharmacy may be used. Complaints, accidents, incidents and reported side effects must be evaluated to determine their cause, and the necessary steps must be taken to prevent re-occurrence. Each organization must have a process for this activity and must maintain a log. The information in the log is used to investigate deviations from protocol and to improve processes.

Manitoba (Oct 2015)
Staff shall respond immediately to a Cytotoxic Spill and effectively control and minimize further contamination of the environment.

- Refer to the Cytotoxic Spill Management Algorithm (Appendix B).

Eyewash equipment shall be available in all areas involved in the Handling of Hazardous Medications

BC Cancer Agency (Sep 2016)
**Hazardous Drug Spills**
To minimize exposure of staff and patients to hazardous drugs, spills must be managed appropriately, according to established policies and procedures. Spill kits must be located in all areas where exposures may occur.

**Recommended Spill Kit Contents**
New employees must be advised of hazardous drug spill control procedures and be required to demonstrate competency in spill handling.
These procedures will be followed for any uncontained spill of a hazardous drug or body waste of a patient receiving hazardous drugs as part of their cancer treatment.
A contained hazardous drug spill (e.g. drug solution absorbed into bed linen) should be handled as disposable or non-disposable hazardous drug waste. A contained body waste spill (e.g. urine absorbed into bed linen) should be handled using standard body substance procedures.
New nursing and pharmacy employees will be advised of this directive and will be required to demonstrate competence in spill control. Training and competency assessment will be documented. Hazardous drug spill management re-familiarization for all nursing and pharmacy employees will be documented on the PHSA LearningHub as deemed appropriate.
Spill size will determine who is authorized to conduct the cleanup and decontamination and how the cleanup is managed. Spill kit stations will be located in all areas where exposures may occur. These
areas should include but are not limited to hazardous drug preparation, dispensing, storage, receiving, and administration areas.

SPILL KIT CONTENTS
Spill kits bought from a commercial source should be carefully reviewed to ensure they contain all items required under this directive. The contents of the kit should be, wherever possible, latex free.
Spill kits will contain NIOSH-approved respirators. All employees who work in areas where hazardous drug spills could potentially occur must participate in a respiratory protection program that includes fit-testing of respirators available in the workplace. Fit testing of all potential respirator users must be performed and recorded prior to initial use and retested once a year, when there is a change in the respirator face piece, or when a user’s physical condition changes the fit of the respirator (CSA standard Z94.4-02-Selection Care and Use of Respirators). Arrangements for fit-testing should be made through PHSA Workplace Health. Surgical masks do not provide adequate protection from hazardous drug exposure

PPE
1. Disposable gown, made of material that is sufficiently impermeable to hazardous drugs, with long sleeves and tight-fitting cuffs, closed-front, covers back and fastens/ties in the back
2. Two pair of chemotherapy gloves
3. Disposable safety eye goggles or face shield
4. Shoe covers
5. Hair bonnet
6. N95 (e.g. 3M 1870®Respirator Mask) or better disposable respirator mask

Supplies
1. Disposable scoop and scraper
2. Incinerable, absorbent material (gauze pads, spill towels, absorbent polymer, etc) in sufficient quantity
3. Two large plastic hazardous drug waste disposal bags (4 mil* or thicker) [*Note: 4 mil = 0.004 inches = 0.1 mm]
4. Decontaminating agent (detergent and water or commercial equivalent decontamination pads)
5. Warning sign and plastic “caution” tape (to quarantine spill area)
6. Puncture and leak resistant hazardous drug waste container (e.g. CHEMO GATOR®)

Documents
1. Laminated copy of BCCA Provincial Systemic Spill Management of Hazardous Drugs Policy V-30
2. Laminated copy of applicable site directives

PROCEDURES
Personnel Contamination
In the case of any spill, if there is, or potentially is, personnel contamination, either from the spilling or the clean-up of the spill, the following procedures should be followed:
1. Immediately remove contaminated PPE or clothing and discard or label for laundry according to Site Directive.

2. Immediately cleanse the affected skin with soap and water. Use shower if appropriate.

3. In the case of eye exposure, gently flush affected eye(s) at an eyewash station or with water or isotonic eyewash designated for that purpose for 15 minutes. Hold your eye(s) open with your thumb and finger and look directly into the water stream. Do not rub your eye(s).

4. Obtain medical attention according to Site Directive.

5. Contact the Workplace Health Call Centre at 1-866-922-9464

6. The employer will document the exposure in the employee’s exposure record. The employee will inform their family doctor or general practitioner of the exposure. Clean-up of spills within a BSC

1. Cease all compounding activity.

2. Inform supervisor that a spill has occurred.

3. If personnel contamination has occurred, follow Personnel Contamination Procedure. This procedure takes precedence over clean-up of the spill itself.

4. Restrict movement of personnel near the BSC to optimize proper airflow of the BSC and minimize the risk of air spillage, i.e. moving air out the front of the BSC and into the room.

5. If outer gloves have been contaminated by the spill, remove them immediately, within the BSC, and deposit them in the garbage container within the BSC. Remove arms from the BSC and don a new pair of outer gloves before proceeding further.

6. Obtain spill kit.

7. Don additional PPE that is required for spill cleanup (ie. respirator mask)

8. Use contents of spill kit, as appropriate, to clean the spill within the BSC. Liquids should be blotted with absorbent material (gauze pads, spill-control pads, pillows, etc.) Solids should be wiped with wetted absorbent material in such a way as to limit their spread.

9. Any broken glass fragments should be picked up using a scoop (never the hands) and placed in a sharps container. The container should then go into a hazardous drug disposal bag, along with all other contaminated waste.

10. If a biohazardous drug is spilled, specific disinfecting agents that are effective for the spilled biohazardous drug must be applied for the required contact time to disinfect the contaminated surfaces prior to the following surface decontamination step.

11. The spill area should be decontaminated by cleaning three times using a basic (i.e. pH 8-9) detergent solution followed by water (Detergent-Water-Detergent-Water-Detergent-Water).

12. If the HEPA filter has been contaminated, the BSC should be left running and labeled as contaminated, until the filter can be changed and disposed of properly by trained personnel wearing appropriate PPE.

13. All clean-up materials should be in sealed containers prior to removal from the BSC and ultimately contained in a rigid closed container labeled as hazardous drug waste. PPE used during the clean-up should at the completion of the job be contained in the same manner. Containers should be disposed of in an appropriate manner in accordance with all applicable federal, provincial and municipal regulations Spills within a BSC necessitate decontamination.
of all interior BSC surfaces after completion of the spill clean-up. Allow the BSC to purge for 5 minutes prior to decontaminating. Following decontamination, aseptic conditions should be re-established by cleaning with a disinfectant (70% alcohol) then purging circulating air for thirty minutes prior to use for compounding.

15. Following spill clean-up, wash hands with soap and water.
16. Contact the Workplace Health Call Centre at 1-866-922-9464.
17. Document incident in exposure records of employees involved in the spill and/or cleanup.
18. Replace all used items at Spill Kit station immediately following the clean-up.

II. Clean-up of spills outside of a BSC that may reasonably be contained and cleaned within the Centre’s capacity

1. Isolate the area and alert all individuals in the area of the spill so as to prevent spread of the spill.
2. Reasonably restrict the number of personnel involved in the clean-up. Never work alone.
3. Inform supervisor that a spill has occurred.
4. If personnel contamination has occurred, or potentially has occurred, follow Personnel Contamination Procedure. This procedure takes precedent over clean-up of the spill itself.
5. Obtain spill kit
6. Don PPE, as appropriate to the spill
7. Limit spread of the spill through use of absorbent sheets or spill control pads. If a powder is involved, damp cloths or towels should be used
8. Avoid aerosol generation and dispersal of powder or liquid spilled
9. Use contents of spill kit, as appropriate, to clean the spill. Liquids should be blotted with absorbent material (gauze pads, spill-control pads, pillows, etc.); solids should be wiped with wetted absorbent material in such a way as to limit their spread.
10. Any broken glass fragments should be picked up using a scoop (never the hands) and placed in a sharps container. The container should then go into an hazardous drug disposal bag, along with all other contaminated waste
11. If a biohazardous drug is spilled, specific disinfecting agents that are effective for the spilled biohazardous drug must be applied for the required contact time to disinfect the contaminated surfaces prior to the following surface decontamination step.
12. The spill area should be decontaminated by cleaning three times using a basic (i.e. pH 8-9) detergent solution followed by water (Detergent-Water-Detergent-Water). Refer to the “Biohazardous Drugs-Surface Disinfection Table” for recommendations regarding surface disinfection of biohazardous drugs. This process should be done by Pharmacy, Nursing or Housekeeping staff as has been delineated in site-specific Housekeeping contracts - refer to Site Directive.
13. All clean-up materials should be placed in sealed containers and ultimately contained in a rigid closed container labeled as hazardous drug waste. PPE used during the clean-up should at the completion of the job be disposed of in the same manner. Dispose of all spill cleanup materials in
a hazardous drug waste container in accordance with all applicable federal, provincial and municipal regulations.
14. Linen should be disposed of normally and any soiled patient clothing should be placed in a plastic bag to be taken home by the patient to be laundered (not dry cleaned)
15. Following spill clean-up, wash hands with soap and water.
16. Contact the Workplace Health Call Centre at 1-866-922-9464
17. Document incident in exposure records of employees involved in the spill and/or cleanup.
18. Replace all used items at Spill Kit station immediately following the clean-up

III. Clean-up of spills outside of a BSC that are of a size or extent large enough to be beyond a Centre’s capacity to contain and clean
1. Alert all individuals in the area of the spill so as to prevent spread of the spill and then isolate the area to prevent personnel exposure to the hazardous drug.
2. Avoid aerosol generation and dispersal of powder or liquid spilled
3. Inform supervisor that a spill has occurred.
4. If personnel contamination has occurred, or potentially has occurred, follow Personnel Contamination Procedure
5. Upon confirming the size of the spill, the supervisor will call for the external Hazardous Material (HazMat) Response Team according to the Site Directive e.g. Code Brown.
6. Remain available to the HazMat team to provide details as to the hazardous drug spilled, the quantity spilled and the circumstances and extent of contamination.
7. Contact the Workplace Health Call Centre at 1-866-922-9464
8. Document incident in exposure records of employees involved in the spill and/or cleanup.
9. Replace any used items at Spill Kit station immediately following the clean-up

Work safe BC (2015)
Employers must develop emergency procedures that address spills of hazardous drugs. Signs detailing spill response procedures should be posted in all relevant areas of the workplace. Potential activities that could result in exposure include:
• Contact with a leak or spill
• Inhalation of aerosols, vapours, or particulates released as the result of a spill
• Contact with contaminated cleaning supplies

Guidelines for safe work practice Best practices for hazardous drug spill response include:
• Supplying a spill kit in all areas where hazardous drugs are handled
• Placing personnel decontamination kits in all areas where hazardous drugs are handled
• Providing home care workers who are administering hazardous drugs with the tools they might need to safely clean up a spill
• Providing regular training on emergency spill procedures
• Allowing only workers trained and authorized to clean spills to do so
• Training workers not authorized to clean a large spill on how to notify other workers and block off an area
• Ensuring all spill cleanup supplies are discarded as hazardous waste Refer to Appendix 8 for an example of what should be included in a spill kit.

Personal protective equipment (PPE) PPE must be consistent with the worker’s potential
exposure and may include:
• Chemotherapy-tested gloves
• A chemotherapy-tested gown
• Face and eye protection, if there is a risk of splashing
• An approved and fit-tested respirator, if there is a risk of inhaling aerosols or particulate

Alberta Health Services (June 2017)
Cytotoxic Spill Kits
Patient care areas and departments (e.g. Environmental Services, Pharmacy) involved in preparation, handling and administration of cytotoxic drugs should have a cytotoxic spill kit on hand. Alternatively, spill kits can be supplied when cytotoxic medications are dispensed or staff can be educated as to the location of the nearest spill kit or where to obtain a spill kit. Staff will be aware of the location of kit, be familiar with the contents and follow instructions for the use of the kit as determined by site policies and procedures. Personal fit tested N-95 mask should be used in spill management. Do not use mask in kit if it is not a N-95 mask or if it is a N-95 mask which does not fit properly. Appropriate shoe covers and head bonnet may also be required and should be readily available in the event of a spill. Circumstances of and handling of spills should be documented as per site/agency policy. Spill kits should be inspected periodically to ensure that the contents have not expired and are suitable for use.

Cytotoxic SPILL KIT CONTENTS:
1 pair safety goggles
1 disposable moisture resistant long sleeved gown with cuffs - large
2 pairs of gloves approved for handling hazardous/chemotherapy drugs (non-latex preferred)
1 N-95 mask (use own fitted N-95 mask if one in kit does not fit)
2 yellow biohazard waste garbage bags (1 small & 1 large)
Kits may also contain:
Absorbent powder (e.g. Chemosorb®)
Plastic disposable scoop
2 absorbent towels
“Caution” sign

B. Accidental Exposure
All accidental exposures to employees are to be reported to immediate supervisor or designate and the appropriate WHS service. If a patient is directly involved, the most responsible physician must be notified, followed by completion of an adverse event report according to site policies.

1. Contaminated Clothing/Linens
a. Contaminated clothing/linens must be handled with double gloves. Proper personal equipment should be worn at the discretion of qualified staff based on the risk of contamination.
b. Remove contaminated clothing and/or bed linens as soon as possible. Ensure that the wet linen does not contaminate other surfaces.
c. Avoid shaking the linens as this may release contaminated particles.
d. Wrap linen to contain the spill.
e. Discard hospital linens and clothing into yellow biohazard waste bags (provided in the Cytotoxic Spill Kit). Seal the bag, and place in a large cytotoxic disposal container in the soiled utility area for pick up by environmental services or waste management staff.

f. Personal items may be placed in a plastic yellow biohazard waste bag and taken home to launder if desired. Patients should handle these items with double gloves. Wash separately, and then wash again. Do not dry clean contaminated items. Alternatively, if the patient does
not wish to keep their personal items, they can be placed into yellow biohazard waste bags and discarded in the same manner as hospital linens noted above.
g. Wash hands with soap and water after handling these items.

2. Eye/Skin Contact
a. Flush the affected eye(s) or skin with copious amounts of water or NS for at least 15 minutes.
b. For skin contact, wash with soap and water
c. Consult the MSDS sheet for further instructions.
d. If, after following steps as outlined above, the staff member is still experiencing symptoms of injury, seek medical attention as soon as possible for immediate assessment.
e. Report to incident to the appropriate WHS service and complete forms as required.
f. If contact lenses are involved, these must be removed immediately and discarded into cytotoxic disposal container.

3. Skin Punctures / Needle Stick Injury
a. Remove gloves and/or contaminated clothing.
b. Wash the puncture site thoroughly with soap and warm running water for 15 minutes. Allow wound to bleed freely. Puncture area may be squeezed to encourage bleeding to flush out any drug that may have been injected accidentally.
c. Treat as an extravasation if required, and follow guidelines outlined in the extravasation procedures (see section 10).
d. Report incident to the appropriate WHS service and complete forms as required

4. Inhalation
a. Medical attention must be sought for immediate assessment when cytotoxic drugs are inhaled.
b. Report incident to the appropriate WHS service and complete forms as required.

C. Environmental Contamination
Responsibility for cleanup of spills in Pharmacy and Patient Care Units rests with the staff in the area involved. In the event that the spill cannot be managed by existing staff at site of spill, Environmental Services or a CODE BROWN can be called as per site policies/procedures.
a. First attend to anyone who has been splashed with cytotoxic waste.
b. Inform the immediate supervisor. Inform the attending Resident or Staff Physician if a patient is directly involved.
c. After individual(s) requiring care for contamination has been assisted, next priority is spill containment.
d. Assess the size and scope of spill and request for trained help if required. More than 1 cytotoxic spill kit may be necessary. For spills that cannot be managed with existing staff or a spill in public areas, Environmental Services or a CODE BROWN can be called as per site policies/procedures.
e. Bring cytotoxic spill kit and a puncture-resistant cytotoxic disposal container to the area of the spill. One kit and container should be on-hand at all times in areas where cytotoxic drugs are administered, stored or prepared.
f. Identify and isolate the contaminated area to prevent people from approaching and spreading the contamination. Display “Caution” signage from Cytotoxic Spill Kit.
g. Alert other individuals in the area and the Pharmacy department of the spill if drug replacement is required. After hours, notify the pharmacist on call to remake the dose if therapy cannot be held until the next day.
h. DO NOT touch spill with unprotected hands. Put on personal protective equipment: double gloves, N-95 mask, goggles and disposable gown, head and shoe covers. See Table 1 for further details.
i. Once fully attired with appropriate PPEs, contain spill using cytotoxic spill kit. Spill cleanup should proceed from areas of lesser to greater contamination.
j. After absorbing/cleaning up spill using disposable towels, wash area with a household detergent and water. (Cavi wipes are not recommended) Rinse area with water. Wipe dry. Remove contaminated PPE according to Appendix B.
k. Call Environmental Services to thoroughly wash affected floor area.
l. Disposal – see “Cytotoxic Waste Handling” - section 12.
m. Document the nature and extent of all spills according to site policies/procedures.
n. Replace cytotoxic spill kit.

1. Liquid Spills
   a. If a patient receiving an oral cytotoxic drug vomits within 30 minutes after the dose, wearing appropriate PPEs clean spill with warm soapy water and a disposable cloth.
   b. Absorb spill with absorbent material (disposable towels or absorbent powder provided in cytotoxic spill kit).
   c. Apply the absorbent material gently, being careful not to touch the spill with your hand or to generate aerosols. If using powder, scoop up the moistened powder with disposable dustpan and brush or scraper.

2. Powder Spills
   If the spill is dry (in powder form) carefully pick up with disposable towels or absorbent pads moistened with water. Wipe up, being careful to avoid generating aerosols.

3. Sharps
   Sweep up sharp material (broken glass, needles, etc.) using a disposable dust pan and brush or scoop (available in cytotoxic spill kit). Place all sharps into puncture resistant cytotoxic disposal container.

4. Biologicals
   For spills of live concentrated mycobacteria (e.g., BCG), the contaminated surface must be covered with enough bleach (20 – 100% concentration) to allow the surface to remain wet for 10 – 15 minutes. Then remove the bleach with absorbent material.

5. Reusable Equipment
   a. Wash with household detergent and water. Rinse with water.
   b. Wipe dry.

6. Disposal
   a. Dispose of all contaminated material (absorbent pads, powder, dustpan etc.) in yellow biohazard waste garbage bag followed by outer pair of gloves.
   b. Tie yellow garbage bag for disposal and place in cytotoxic waste container.
   c. Remove personal protective equipment (gown, mask, contaminated goggles and inner pair of gloves) and place in second yellow biohazard waste bag. Place bag in cytotoxic waste container.
   d. Wash hands thoroughly after removing inner pair of gloves.
   e. Goggles, if only minimally or not contaminated, may be cleaned with soap and water.
Double gloves should be worn when washing goggles.

United States Pharmacopeial Convention (Chapter to become official July 1, 2018)

**SPILL CONTROL**

All personnel who may be required to clean up a spill of HDs must receive proper training in spill management and the use of PPE and NIOSH-certified respirators (see Personal Protective Equipment). Spills must be contained and cleaned immediately only by qualified personnel with appropriate PPE. Qualified personnel must be available at all times while HDs are being handled. Signs must be available for restricting access to the spill area. Spill kits containing all of the materials needed to clean HD spills must be readily available in all areas where HDs are routinely handled. If HDs are being prepared or administered in a non-routine healthcare area, a spill kit and respirator must be available. All spill materials must be disposed of as hazardous waste.

The circumstances and management of spills must be documented. Personnel who are potentially exposed during the spill or spill clean up or who have direct skin or eye contact with HDs require immediate evaluation. Non-employees exposed to an HD spill should follow entity policy, which may include reporting to the designated emergency service for initial evaluation and completion of an incident report or exposure form. SOPs must be developed to prevent spills and to direct the clean up of HD spills. SOPs must address the size and scope of the spill and specify who is responsible for spill management and the type of PPE required. The management of the spill (e.g., decontamination, deactivation, and cleaning) may be dependent on the size and type of spill. The SOP must address the location of spill kits and clean-up materials as well as the capacity of the spill kit. Written procedures should address use of appropriate full-facepiece, chemical cartridge-type respirators if the capacity of the spill kit is exceeded or if there is known or suspected airborne exposure to vapors or gases.

**RECOMMENDATION 13: ENVIRONMENTAL CLEANING**

Establish environmental cleaning policies and procedures for all surfaces where contact with cytotoxic drugs may occur. Examples may include: unpacking and storage, preparation, administration and disposal areas. Pharmacy counters are among the most contaminated surfaces.

It is strongly recommended that cleaning of the biological safety cabinets be performed by trained personnel following manufacturer’s guidelines (34).

**Use of Pumps to Administer Cytotoxic Drugs**

Make sure there is an appropriate policy to clean and inspect the equipment between uses.

**Laundry**

Ensure the facility complies with the Occupational Health and Safety Act - Ontario Regulation for Health Care and Residential Facilities (8).

National Association of Pharmacy Regulatory Authorities (Nov 2016)

Cleaning and disinfecting (housekeeping) in controlled areas must be performed to ensure the cleanliness required for the quality and integrity of final compounded sterile preparations. Cleaning and disinfecting procedures must be strictly adhered to in the clean room and the anteroom.
Policies and procedures for cleaning and disinfecting tasks must be developed, and cleaning and disinfecting personnel must be trained and assessed on correct application of these policies and procedures. Only trained and qualified cleaning and disinfecting personnel may be allowed to clean controlled areas.

Surface decontamination, deactivation and disinfection
When hazardous sterile preparations are compounded, cleaning of the premises and equipment must also eliminate chemical contamination from the hazardous products used. Methods used include decontamination, deactivation and disinfection.

Decontamination involves the transfer of a hazardous drug contaminant from a fixed surface (e.g., counter, bag of solution) to a disposable surface (e.g., wipe, cloth). The wipe is then contained and discarded as hazardous waste. Many solutions can be used for decontamination, for example, 70% isopropyl alcohol, sterile water, hydrogen peroxide and sodium hypochlorite.

Deactivation
Deactivation is the treatment of a hazardous drug to create a less hazardous agent, for example, by chemical deactivation. The material safety data sheets for some hazardous drugs recommend sodium hypochlorite for this purpose, usually as a 2% solution. This compound will corrode stainless steel surfaces, so it must then be neutralized with sodium thiosulphate or removed with a germicidal detergent. Surface Safe (Hospira) is a commercially available system of wipes containing both of these substances. Sodium hypochlorite also has an additional germicidal effect for disinfection.

Disinfection
Disinfection is the process of destroying microorganisms. Use of a germicidal disinfectant detergent is required to disinfect all surfaces in a clean room and anteroom. Many types of germicidal disinfectant detergents are acceptable.

The sterile compounding supervisor must
• select an appropriate disinfecting agent for controlled areas, considering mainly its effectiveness and compatibility with materials used for facilities and equipment;
• in health care facilities, take into account the organization’s disinfection policies and procedures, following the manufacturer’s directions to dilute the disinfectant properly;
• follow the manufacturer’s directions regarding required contact time between the disinfectant and the surface to be disinfected. Use of an alternative disinfectant in the rotation is unnecessary. However, the daily use of a germicidal disinfectant should be augmented with weekly (or monthly) use of a sporicidal agent. The material safety data sheets for disinfectants used in the facility must be available on site and easily accessible.

Equipment used for cleaning and disinfection and its storage
To avoid cross-contamination and to protect cleaning and disinfecting personnel, equipment must be specifically designated for cleaning areas used for the compounding of hazardous sterile preparations. Non-shedding equipment must be used for cleaning controlled areas. This equipment (mop, towels, etc.) should be disposable. Cleaning equipment and supplies (mop handle, outside of bottles, etc.) must be disinfected before each entry into a controlled area. A cabinet located in the anteroom or nearby must be provided for storing equipment (mop handle, etc.), refills (mop heads, towels) and cleaning products used for cleaning and disinfecting.

Garbing of cleaning and disinfecting personnel (housekeeping personnel) Cleaning and disinfecting personnel must comply with the pharmacy’s hand hygiene and garbing procedure before entering sterile compounding areas and performing housekeeping duties. Housekeeping personnel must also don two pairs of ASTM International approved gloves before starting work. The outer gloves must be sterile. Cleaning and disinfecting procedures must include surface decontamination followed by disinfection at regular intervals and at specific locations as described below. The minimum frequency of cleaning and disinfecting in clean rooms and anterooms will be either daily or monthly.

Daily cleaning, decontamination and disinfecting are required for the following surfaces and areas:
- C-PEC
- counters
- carts
- floors
- surfaces that are touched frequently (e.g., doorknobs, switches, chairs) In addition, waste and garbage must be removed daily. Monthly cleaning and disinfecting are required for the following surfaces and areas:
  - walls
  - ceiling
  - shelves
  - area outside the C-PEC (this area must be decontaminated along with cleaning and disinfecting)

Cleaning should be done from the “cleanest” area to the “dirtiest” area. Cleaning should also take into account the minimization of chemical contamination moving from less chemically contaminated areas to more chemically contaminated.

An environmental verification program must be established to ensure that facilities maintain established specifications and uphold the quality and safety standards set by the industry. The program should include verification for chemical contamination by hazardous materials on surfaces used for receipt, storage, preparation and verification of products and preparations, in addition to verification of microbiological contamination of controlled areas twice per year. A written sampling plan for controlled areas and the C-PEC must be established.

Sampling plan The plan for sampling air (for viable and non-viable particles) and surfaces must be established according to the specifications of a recognized standard, such as CETA application guide CAG-002, CAG-003 and CAG-008. Some laboratories offer testing for surface contamination with certain hazardous drugs. The level of hazardous drug contamination
should be measured at least every 6 months or more frequently if any major change is made in placement of furniture, aseptic processes, or cleaning and disinfecting practices. The sterile compounding supervisor or a delegate should sample the various sites, especially those most likely to be contaminated (e.g., outside the C-PEC, floor surrounding the C-PEC). The sites sampled and the frequency of monitoring should be established on the basis of results obtained on previous monitoring. A baseline assessment should precede any preventive measure (as described in the ASSTSAS guide), and monitoring should be repeated after implementation of such measures, to determine their effectiveness. Surface contamination by hazardous antineoplastic drugs, as determined by environmental monitoring, must be recorded in the general maintenance log.

Gloved fingertip sampling
GFS must include:

- a sample obtained after sterile gloves are put on (after aseptic washing of hands and forearms) but before application of sterile 70% isopropyl alcohol (disinfecting gloves with sterile 70% isopropyl alcohol immediately before sampling would lead to “false negatives”);
- a sample obtained after the media fill test (described in section 7.4.2), making sure that the employee has not applied sterile 70% isopropyl alcohol to his or her gloves in the minutes before sampling. Using tryptic soy agar contact plates with lecithin and polysorbate, the assessor obtains thumbprints and prints of gloved fingertips from both hands of the employee, asking the employee to gently press and roll each thumb and fingertip on the agar in the contact plate (one agar plate for each hand). When the sampling is complete, the gloves must be removed and discarded, and hand and forearm hygiene must then be performed. The samples must be incubated between 30°C and 35°C and must be read within 48 to 72 hours.

For each employee, a negative result (0 CFU) must be obtained three times for the first type of GFS sampling (after sterile gloves are put on) before the employee can be permitted to compound sterile preparations.

For each employee, GFS after the media fill test must be completed annually for low- and medium-risk sterile compounding and every 6 months for high-risk sterile compounding. For this test, the total CFU count for both hands must be no more than 3 CFUs. If the result on any GFS after a media fill test is more than 3 CFUs, the sterile compounding supervisor is prompted to investigate the employee’s work practices, procedures, use of disinfectants, etc.

The media fill test is a compounding simulation test conducted with nutrient media that promote bacterial growth. This test is used to verify the employee’s performance of aseptic processing.

### BC Cancer Agency (Sep 2016)

**Hazardous Drug Cleanroom and Anteroom**

All parenteral cytotoxic/hazardous drug admixtures must be prepared in a minimum Class II Type B Biological Safety Cabinet (BSC) that maintains an ISO Class 5 environment.

- The cleanroom or buffer room housing the BSC must be an ISO Class 7 environment physically separated from an adjacent ISO Class 7 or better ante-area
- A differential of at least 0.01 inch water column (negative pressure) must be maintained between the cleanroom and the pharmacy (anteroom)
- Floors, walls, ceilings and all exposed surfaces must be nonporous and washable
- Cleaning must take place in the cleanroom at a time when no aseptic operations are in progress
- Essential furniture in buffer rooms and cleanrooms must be nonporous, smooth, non-
shredding, impermeable, cleanable, and resistant to disinfectants
- Access to the cleanroom must be limited to authorized personnel who are assigned to work there.
- A warning sign must clearly identify the hazard and state that access to the cleanroom is controlled and limited to authorized personnel only.
- Doors must not be left open.
- Appropriate personal protective equipment (PPE) must be donned by all personnel prior to entering the cleanroom to minimize the spread of skin particles that may shed.
- Lab coats must not be worn in the cleanroom in place of chemotherapy gowns.
- No shipping or other external cartons may be taken into the cleanroom or the compounding area.
- Hazardous drugs must be stored separately from other inventory in a manner that prevents HD contamination and personnel exposure.

**Location of Biological Safety Cabinets**

A BSC used for HD compounding must be located away from doorways, traffic corridors, and air conditioning and heating vents inside a restricted access negative pressure ISO Class 7 cleanroom.

**Section B**

**B.1 Cleaning**

Staff must be instructed on how to safely carry out their cleaning responsibilities within the cleanroom, the anteroom and in the vicinity of the BSC in order to minimize HD exposure to themselves and the environment.

**Section C**

**C.1 Documentation**

Documentation records of routine BSC, cleanroom and anteroom cleaning must be completed and maintained.

**Work safe BC (2015)**

Guidelines for safe work practice. Best practices for cleaning activities in areas with hazardous drug contamination include:

- Providing training on hazardous drugs for workers, including potential routes of exposure and how to minimize exposure for themselves.
- Using cleaning supplies designated for areas known to have potentially high hazardous drug contamination, such as pharmacies.
- Changing routine cleaning practices to minimize hazardous drug contamination. Refer to Appendix 7 for information on how to select appropriate cleaning agents for use with hazardous drugs.

**Personal protective equipment (PPE)**

PPE must be consistent with the worker’s potential exposure and may include:

- Chemotherapy-tested gloves
- A chemotherapy-tested gown
- Face and eye protection,
- An approved and fit-tested respirator

Effective cleaning and decontamination is a key part of reducing hazardous drug surface contamination. Hazardous drug contamination has been detected on surfaces even after cleaning using conventional methods and cleaning products. Hazardous drug contamination may accumulate in porous materials. No single cleaning agent can be used in all situations.
The effectiveness of a cleaning or decontaminating agent depends on the chemical and physical properties of the drug, as well as the surface that is being cleaned. Workplaces should have multiple cleaning and decontaminating supplies that are effective on different drugs, or at least different types of drugs based on their chemical and physical properties. When selecting cleaning and decontamination supplies, workplaces should consider:

- Current research on the effectiveness of different procedures and agents on the types of hazardous drugs being used in the workplace
- Surfaces (e.g., stainless steel BSC) that may have specific cleaning requirements outlined by the manufacturer
- The characteristics of the surfaces that will be cleaned and decontaminated, such as porosity and texture
- The ease of use, such as having pre-packaged wipes soaked in solution
- The potential for hazardous by-products from cleaning and decontamination products, or products that are hazardous themselves

The table below compares some of the cleaning and decontaminating agents commonly used on surfaces that may have hazardous drug contamination.

United States Pharmacopeial Convention (Chapter to become official July 1, 2018)

DEACTIVATING, DECONTAMINATING, CLEANING, AND DISINFECTING

All areas where HDs are handled and all reusable equipment and devices must be deactivated, decontaminated, and cleaned. Additionally, sterile compounding areas and devices must be subsequently disinfected.

The entity must establish written procedures for decontamination, deactivation, and cleaning, and for sterile compounding areas disinfection. Additionally, cleaning of nonsterile compounding areas must comply with (795) and cleaning of sterile compounding areas must comply with (797). Written procedures for cleaning must include procedures, agents used, dilutions (if used), frequency, and documentation requirements.

All personnel who perform deactivation, decontamination, cleaning, and disinfection activities in HD handling areas must be trained in appropriate procedures to protect themselves and the environment from contamination. All personnel performing these activities must wear appropriate PPE resistant to the cleaning agents used, including two pairs of chemotherapy gloves and impermeable disposable gowns (see Personal Protective Equipment). Additionally, eye protection and face shields must be used if splashing is likely.

If warranted by the activity, respiratory protection must be used. The deactivating, decontaminating, cleaning, and disinfecting agents selected must be appropriate for the type of HD contaminant(s), location, and surface materials. The products used must be compatible with the surface material. Consult manufacturer or supplier information for compatibility with cleaning agents used. Agents used for deactivation, decontamination, and cleaning should be applied through the use of wipes wetted with appropriate solution and not delivered by a spray bottle to avoid spreading HD residue. All disposable materials must be discarded to meet EPA regulations and the entity's policies. Perform cleaning in areas that are sufficiently ventilated. Table 5 summarizes the purpose and example agents for each step.

<table>
<thead>
<tr>
<th>Cleaning Steps</th>
<th>Cleaning Step</th>
<th>Purpose</th>
<th>Example Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deactivation</td>
<td>Render compound inert or inactive</td>
<td>As listed in the HD labeling or other agents which may incorporate Environmental Protection Agency (EPA)-</td>
<td></td>
</tr>
<tr>
<td>Decontamination</td>
<td>Remove HD residue</td>
<td>Materials that have been validated to be effective for HD decontamination, or through other materials proven to be effective through testing, which may include alcohol, water, peroxide, or sodium hypochlorite</td>
<td></td>
</tr>
<tr>
<td>-----------------</td>
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<td>--------------------------------------------------------------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Cleaning</td>
<td>Remove organic and inorganic material</td>
<td>Germicidal detergent</td>
<td></td>
</tr>
<tr>
<td>Disinfection (for sterile manipulations)</td>
<td>Destroy microorganisms</td>
<td>EPA-registered disinfectant and/or sterile alcohol as appropriate for use</td>
<td></td>
</tr>
</tbody>
</table>

**Deactivation**
Deactivation renders a compound inert or inactive. Residue from deactivation must be removed by decontaminating the surface.

There is no one proven method for deactivating all compounds. The ultimate goal should be complete surface decontamination. Products that have known deactivation properties (EPA-registered oxidizing agents that are appropriate for the intended use) should be used when possible. Care should be taken when selecting materials for deactivation due to potential adverse effects (hazardous byproducts, respiratory effects, and caustic damage to surfaces). Damage to surfaces is exhibited by corrosion to stainless steel surfaces caused by sodium hypochlorite if left untreated. To prevent corrosion, sodium hypochlorite must be neutralized with sodium thiosulfate or by following with an agent to remove the sodium hypochlorite (e.g., sterile alcohol, sterile water, germicidal detergent, or sporicidal agent).

**Decontamination**
Decontamination occurs by inactivating, neutralizing, or physically removing HD residue from non-disposable surfaces and transferring it to absorbent, disposable materials (e.g., wipes, pads, or towels) appropriate to the area being cleaned. When choosing among various products available for decontaminating HDs, consideration should be given to surface compatibility and facility requirements. It is imperative to adhere to manufacturer’s use instructions. Because of the growing number of as-says available for HDs, additional surface wipe sampling is now possible and should be done to document the effectiveness of any agent used for decontamination of HD residue from work surfaces (see *Environmental Quality and Control*).

The amount of HD contamination introduced into the C-PEC may be reduced by wiping down HD containers. The solution used for wiping HD packaging must not alter the product label. The work surface of the C-PEC must be decontaminated be-tween compounding of different HDs. The C-PEC must be decontaminated at least daily (when used), any time a spill occurs, before and after certification, any time voluntary interruption occurs, and if the ventilation tool is moved.

C-PECs may have areas under the work tray where contamination can build up. These areas must be deactivated, decontaminated, and cleaned at least monthly to reduce the contamination level in the C-PEC. Accessing this area may be difficult. Deactivate, decontaminate, and clean as much as possible of the C-PEC surfaces before accessing the area under the work tray. When deactivating, decontaminating, and cleaning the area under the work tray of a C-PEC, the containment airflows are compromised by opening the cabinets.
To provide protection to the worker performing this task, respiratory protection may be required.

**Cleaning** Cleaning is a process that results in the removal of contaminants (e.g., soil, microbial contamination, HD residue) from objects and surfaces using water, detergents, surfactants, solvents, and/or other chemicals. Cleaning agents used on compounding equipment should not introduce microbial contamination. No cleaning step may be performed when compounding activities are occurring.

**Disinfection** Disinfection is a process of inhibiting or destroying microorganisms. Before disinfection can be adequately performed, surfaces must be cleaned. Disinfection must be done for areas intended to be sterile, including the sterile compounding areas.

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**RECOMMENDATION 14: MEDICAL SURVEILLANCE AND ENVIRONMENTAL MONITORING**

**Medical Surveillance**
Methods used to investigate potential health effects of exposure to cytotoxic drugs are inconclusive and difficult to interpret. The ideal test should meet several requirements — it should be sensitive, specific, quantitative, rapid, and reproducible. Importantly, the procedures for taking a sample should be non-invasive and should not cause unnecessary duress or anxiety to the individual. Unfortunately, there is currently no suitable test to meet these requirements. As a consequence, there is conflicting information and opinion about the value of routine biological monitoring for employees handling cytotoxic drugs.

Employers do have a responsibility to ensure that they remain aware of and apply any future developments for monitoring the health of employees in the handling of cytotoxic drugs.

The panel supports further research to determine if there are adverse health effects that result from exposure to cytotoxic drugs.

Adherence to agreed standard operating procedures with sufficient initial and regular on-going training in safe handling/administration is paramount to reducing potential for exposure and risk.

There is evidence in the literature of a higher rate of spontaneous abortion among women working in roles that expose them to cytotoxic drugs (35, 36). There are no other identified medical conditions known to result from chronic exposure of health care workers to cytotoxic drugs, no exposure limits set for cytotoxic drugs, and no standards for interpretation of test results of exposed health care workers to enable meaningful interpretation or action based on biological monitoring results.

**Environmental Monitoring**
It is recommended that the facility consider implementing an environmental monitoring program. Surface testing would audit contamination of the environment (e.g., pharmacy counters, patient bedside tables) and provide a quality indicator of cleaning effectiveness and adherence to recommended work practices.

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Quapos 5 (2016)
1.5. Occupational preventive medicine
Employees working in the area of cytostatics production in the pharmacy are dealing with potential carcinogenic, mutagenic and reprotoxic (CMR) drugs. They must be offered regular occupational medical check-ups taking into account all the relevant factors at the specific workplace. These check-ups include:
1. Initial examination before taking up employment.
2. Follow-up examinations during the employment at intervals of 1 to 2 years.
3. Examinations at the request of the employee if there is a suspicion of work-related impairment to health.

It is recommended that the follow-up examinations include biomonitoring to test the effectiveness of the existing protective measures.

Exposure to cytostatics must be documented by the employer in a suitable form. This documentation must include the types and amounts of cytostatics used and the frequency of their preparations for each employee handling these drugs. Furthermore, a continuous use of technical and personal protective measures has to be ensured by implementing standard operating procedures regarding compounding, disposal, and clean-up of cytostatics as well as cytostatics-related accidents and their acute management.

BC Cancer Agency (Sept 2016)
To ensure levels of hazardous drugs are at the low risk or non-detectable level, surface wipe sampling for cyclophosphamide levels (and other hazardous drugs as deemed appropriate) will occur in the pharmacy and the chemotherapy treatment areas.

PROCEDURES
Wipe samples will be taken 6 months after implementing a Closed System Drug Transfer Device (CSDTD) and then annually.
Surface wipe samples will be taken by two designated staff members (one each from pharmacy and nursing) (see BCCA Works Standard Wipe Sample Procedure located at H:\EVERYONE\Pharmacy\Surface Wipe Sampling). Samples are to be taken at the end of the workday before housekeeping and pharmacy have cleaned any surfaces (including the biological safety cabinet). Surface wipe samples will be performed on the same location and the same area of the location each time. Six samples will be taken in the pharmacy department and six in the chemotherapy treatment areas. Locations to be sampled are indicated in Appendix1.3. If levels are low or medium (see Table 1 BCCA risk Levels) the Pharmacy PPL or Clinical Nurse Leader will estimate the risk based on the affected surface. Steps will be taken to identify, document, and contain the source of contamination. Actions may include reevaluating work practices, re-training personnel, performing thorough deactivation, decontamination, cleaning and improving engineering controls.
Decontaminate and repeat wipe sampling as per Table 1.

Work safe BC (2015)
Environmental monitoring, when used, should be carried out: • Before implementing controls • After any changes (for example, new equipment, new drugs, or same drugs in a different format) that could affect hazardous drug contamination • After a major exposure event, such as a large spill • Periodically in areas of concern Environmental monitoring should also include the following: • Compare with records of past environmental measurements (suggested time period
is at least five years, but longer may be useful for research purposes). • Involve workers by asking for suggestions on where sampling should take place and informing them of the results of any monitoring activities.

United States Pharmacopeial Convention (Chapter to become official July 1, 2018)

ENVIRONMENTAL QUALITY AND CONTROL

Environmental wipe sampling for HD surface residue should be performed routinely (e.g., initially as a benchmark and at least every 6 months, or more often as needed, to verify containment). Surface wipe sampling should include: • Interior of the C-PEC and equipment contained in it
• Pass-through chambers • Surfaces in staging or work areas near the C-PEC
• Areas adjacent to C-PECs (e.g., floors directly under C-PEC, staging, and dispensing area) • Areas immediately outside the HD buffer room or the C-SCA
• Patient administration areas

There are currently no studies demonstrating the effectiveness of a specific number or size of wipe samples in determining levels of HD contamination. Wipe sampling kits should be verified before use to ensure the method and reagent used have been tested to recover a specific percentage of known marker drugs from various surface types found in the sampled area. There are currently no certifying agencies for vendors of wipe sample kits.

There is currently no standard for acceptable limits for HD surface contamination. Common marker HDs that can be assayed include cyclophosphamide, ifosfamide, methotrexate, fluorouracil, and platinum-containing drugs. An example of measurable contamination would be cyclophosphamide levels >1.00 ng/cm2, which were shown in some studies to result in uptake of the drug in exposed workers. If any measurable contamination is found, the designated person must identify, document, and contain the cause of contamination. Such action may include reevaluating work practices, re-training personnel, performing thorough deactivation, decontamination, cleaning, and improving engineering controls. Repeat the wipe sampling to validate that the deactivation/decontamination and cleaning steps have been effective.

MEDICAL SURVEILLANCE

Medical surveillance is part of a comprehensive exposure control program complementing engineering controls, safe work processes, and use of PPE. Healthcare workers who handle HDs as a regular part of their job assignment should be enrolled in a medical surveillance program. The general purpose of surveillance is to minimize adverse health effects in personnel potentially exposed to HDs. Medical surveillance programs involve assessment and documentation of symptom complaints, physical findings, and laboratory values (such as a blood count) to determine whether there is a deviation from the expected norms. Medical surveillance can also be viewed as a secondary prevention tool that may provide a means of early detection if a health problem develops. Tracking personnel through medical surveillance allows the comparison of health variables over time in individual workers, which may facilitate early detection of a change in a laboratory value or health condition. Medical surveillance programs also look for trends in populations of workers. Examining grouped data compared with data from unexposed workers may reveal a small alteration or increase in the frequency of a health effect that would be obscured if individual workers’ results alone were considered. Medical surveillance evaluates the protection afforded by engineering controls, other administrative controls, safe work processes, PPE, and worker education about the hazards of the materials they work with in the course of their duties. The data-gathering elements of a medical surveillance program are used to establish a baseline of workers’ health
and then to monitor their future health for any changes that may result from exposure to HDs.

Elements of a medical surveillance program should be consistent with the entity's Human Resource policies and should include:

- Development of an organized approach to identify workers who are potentially exposed to HDs on the basis of their job duties
- Use of an entity-based or contracted employee health service to perform the medical surveillance while protecting the confidentiality of the employees' personal medical information
- Initial baseline assessment (pre-placement) of a worker's health status and medical history. Data elements collected include a medical (including reproductive) history and work history to assess exposure to HDs, physical examination, and laboratory testing. Methods used to assess exposure history include a review of:
  - Records of HDs handled, with quantities and dosage forms
  - Estimated number of HDs handled per week
  - Estimates of hours spent handling HDs per week and/or per month
  - Performance of a physical assessment and laboratory studies linked to target organs of commonly used HDs, such as a baseline complete blood count. Biological monitoring to determine blood or urine levels of specific HDs is not currently recommended in surveillance protocols, but may have a role in the follow-up of acute spills with a specific agent.

- Medical records of surveillance should be maintained according to OSHA regulation concerning access to employee exposure and medical records
- Monitoring workers' health prospectively through periodic surveillance using the elements of data gathering described above (updated health and exposure history, physical assessment, and laboratory measures, if appropriate)
- Monitoring of the data to identify prevention failure leading to health effects; this monitoring may occur in collaboration with the employee health service
- Development of a follow-up plan for workers who have shown health changes suggesting toxicity or who have experienced an acute exposure. This follow-up should include evaluation of current engineering and administrative controls and equipment to ensure that all systems are appropriately and accurately implemented (see Follow-Up Plan)
- Completion of an exit examination when a worker's employment at the entity ends, to document the information on the employee's medical, reproductive, and exposure histories. Examination and laboratory evaluation should be guided by the individual's history of exposures and follow the outline of the periodic evaluation

**Follow-Up Plan**

The occurrence of exposure-related health changes should prompt immediate re-evaluation of primary preventive measures (e.g., administrative and engineering controls, PPE, and others). In this manner, medical surveillance acts as a check on the effectiveness of controls already in use.

The entity should take the following actions:

- Perform a post-exposure examination tailored to the type of exposure (e.g., spills or needle sticks from syringes containing HDs). An assessment of the extent of exposure should be conducted and included in a confidential database and in an incident report. The physical examination should focus on the involved area as well as other organ systems commonly affected (i.e., the skin and mucous membranes for direct contact or inhalation; the pulmonary system for aerosolized HDs). Treatment and laboratory studies will follow as indicated and be guided by emergency protocols
• Compare performance of controls with recommended standards; conduct environmental sampling when analytical methods are available
• Verify and document that all engineering controls are in proper operating condition
• Verify and document that the worker complied with existing policies. Review policies for the use of PPE and employee compliance with PPE use and policies. Review availability of appropriate PPE (see Personal Protective Equipment)
• Develop and document a plan of action that will prevent additional exposure of workers
• Ensure confidential, two-way communication between the worker and the employee health unit(s) regarding notification, discussions about a change in health condition, or detection of an adverse health effect
• Provide and document a follow-up medical survey to demonstrate that the plan implemented is effective
• Ensure that any exposed worker receives confidential notification of any adverse health effect. Offer alternative duty or temporary reassignment
Provide ongoing medical surveillance of all workers at risk for exposure to HDs to determine whether the plan implemented is effective
### Evidence Tables
**Closed system Transfer devices**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Purpose/Scope</th>
<th>Product(s)-tested</th>
<th>Method</th>
<th>Results</th>
<th>Disclosure of COI</th>
<th>Test Environment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lalande (2015)</td>
<td>To determine the ability of these systems to reduce cytotoxic exposure of nurses. The study also examined the ability of these systems to reduce the amount of cytotoxic drug not administered to the patient and evaluated the feasibility of these systems' integration into clinical practices</td>
<td>cytotoxic safe infusion systems (CSISs) Cair, Codan, and ICU Medical</td>
<td>Comparative</td>
<td>The average cytotoxic residual volume in the chemotherapy tubing and chemotherapy bags was to 4 mL (3-6 mL) for Codan, 1.5 mL (0-3 mL) for Cair, and 2.5 mL (1-5 mL) for ICU Medical. For all manufacturers, the residual volume was significantly decreased compared with traditional administration ($P &lt; 0.0001$). The average cytotoxic residual volume measured traditional administration was 13 mL (5-20 mL). The ultraviolet-visible spectroscopy analysis of the fluid volume collected at the end of the tubing did not find any cytotoxic residue.</td>
<td>The Authors have no conflicts to disclose</td>
<td>University teaching hospital in France</td>
</tr>
<tr>
<td>Savry 2014</td>
<td>The results of a media-fill test (MFT) study to validate processes for cytotoxic drug preparation inside and outside aseptic compounding isolators are presented. The team also tested alternative compounding systems, two closed-system transfer for use during power outages or other emergencies precluding drug preparation within isolators</td>
<td>a classical spike and two protective devices PhaSeal system and Spiros/Genie system</td>
<td>Comparative</td>
<td>Three operators did three MFTs (10 MFT units per test for a total of 30 units per operator) under simulated blackout conditions, each time with a different protective device. <em>Bacillus</em> species proliferated in only 1 unit of the 90 units produced; that incident involved the use of the Spiros/Genie system. When the test was redone by the same operator using the same device, with increased attention to the decontamination procedure, no microbiological contamination was observed.</td>
<td>The Authors have no conflicts to disclose</td>
<td>University teaching hospital in France</td>
</tr>
<tr>
<td>Vasseur 2017 (Abstract)</td>
<td>To describe the relative contribution of CSTD and the cleaning process in the control of occupational exposure inside isolators.</td>
<td>Spikes and needles were used in one isolator and a CSTD (BD-Phaseal) was used in the other one. A standard biocide (Surfa'safe, Anios, Lezennes, France) was used daily in both isolators</td>
<td>Comparative</td>
<td>For cyclophosphamide, cytarabine, ganciclovir and ifosfamide, the use of a CSTD was significantly associated with a risk reduction of contamination, either independently of other predictors or in interaction with time, leading to a risk reduction from about 70% for cytarabine to 98% for ganciclovir. For all drugs, except cyclophosphamide, the cleaning process alone or in interaction with time and/or localisation was significantly associated with a reduction in contamination by about 30% for gemcitabine to 80% for ifosfamide.</td>
<td>Not stated</td>
<td>Not stated (France)</td>
</tr>
<tr>
<td>González-</td>
<td>To compare the level</td>
<td>ChemoCLAVE</td>
<td>comparative</td>
<td>Splashes were produced in 7 preparations</td>
<td>Not stated</td>
<td>Hospital (Spain)</td>
</tr>
<tr>
<td>Haba Peña 2016</td>
<td>of environmental contamination generated during the preparation and administration of cytostatic drugs under actual working conditions using different valve closed-systems and their combinations</td>
<td>Spiros Connector vs without connector, Supporting vial spike vs anchoring spike, Clave Valve vs Fleboflex solution with Leur connection</td>
<td>without a connector (p = 0.015). No significant differences (p = 0.445) were detected in the use of a supporting vial spike vs an anchoring spike, or in the ChemoCLAVE vs valve systems with Fleboflex® solutions. Contamination at any critical point was produced in all preparations. The use of a supporting vial spike, syringe connector and bag solution with Luer connection was the most efficient modality. A syringe connector is needed to guarantee a closed system. Anchoring spikes do not show higher advantages compared with supporting vial spikes. Fleboflex® solutions with Luer bags are more efficient than ChemoCLAVE and show similar safety results.</td>
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<tr>
<td>Wakui 2013</td>
<td>To reduce the exposure to drug preparations, and develop drug preparation equipment without external drug leaks in a closed state for oral anticancer drugs</td>
<td>The closed drug preparation device was developed by connecting the 10mL disposable syringe that was attached to the projections for crushing the tablet and the no-processing 30mL disposable syringe to the three-way stopcock. In addition, the gasket of the plunger of the syringe was flattened using a hot plate to create a stable foundation for placing the tablet.</td>
<td>The experiment was performed 5 times. Cyclophosphamide was detected in trace amounts in two of the samples. It was confirmed that cyclophosphamide exposure of the preparer was reduced using the developed closed oral preparation device method.</td>
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<tr>
<td>Author</td>
<td>Study Details</td>
<td>Funder and Role</td>
<td>Institution</td>
<td></td>
<td></td>
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<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
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<td></td>
</tr>
<tr>
<td>Simon 2016</td>
<td>The objective of this randomized, prospective and controlled study was to investigate the ability of a closed-system transfer device (CSTD; BD-Phaseal) to reduce the occupational exposure of two isolators to 10 cytotoxic drugs and compare to standard compounding devices.</td>
<td>The study was funded by Becton-Dickinson laboratories, manufacturer of the tested device. The funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.</td>
<td>University Hospital (France)</td>
<td></td>
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</tr>
<tr>
<td>Schierl 2016</td>
<td>To compare environmental contamination of cyclophosphamide (CP) during 1 week of drug compounding by conventional manual procedure in a biological safety cabinet (BSC) with laminar airflow and a new robotic drug preparation system (APOTECAchemo).</td>
<td>None declared</td>
<td>Cancer research center in Italy</td>
<td></td>
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<tr>
<td>Vyas 2016</td>
<td>This study investigated the surface contamination arising from the preparation of five anticancer drug infusions (Epirubicin, Fluorouracil, Cisplatin, Oxaliplatin and Carboplatin) in a pharmaceutical isolator and compared use of a conventional syringe and needle technique with a closed-system drug transfer device (CSDTD).</td>
<td>None declared</td>
<td>University Hospital United Kingdom</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Authors</td>
<td>Methods</td>
<td>Results</td>
<td>Notes</td>
<td></td>
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<tr>
<td>Gómez-Álvarez 2016</td>
<td>Abstract in English only</td>
<td>to assess the impact of two closed-system drug transfer device on the local and environmental contamination and preparation times in the process of preparation of parenteral chemotherapy compared to the standard system</td>
<td>Care Fusion® and Icu Medical</td>
<td>Comparative</td>
<td>75 preparations were prepared. Local contamination was reduced 21% and 75% in closed-system Icu Medical® and Care Fusion® respectively. Care Fusion® closed system, local contamination was significantly lower than the standard system to the vial, syringe and final package, while Icu Medical® closed-systems only was significantly lower in the connection to the vial.</td>
<td>Unknown study in Spanish</td>
</tr>
<tr>
<td>Call 2017</td>
<td></td>
<td>This study’s aim was to determine how HD might spread through touch after handling contaminated vials in simulated pharmacy and nursing environments</td>
<td>ICU medical, Allison Medical (SEVA), BD PhaSeal, B. Braun Medical (Onguard) and CareFusion</td>
<td>Comparative</td>
<td>Transfer of the HD testing medium (Glo Germ) to IV sets, pharmacy PPE, and nursing PPE was observed in 4 of 5 CSTDs tested. The only CSTDs that showed no observable contamination was the Allison Medical Safety Enclosed Vial Adapter (SEVA) system (Littleton, CO).</td>
<td>No conflicts</td>
</tr>
<tr>
<td>Guillemette 2014</td>
<td></td>
<td>to evaluate the impact of two methods aiming at reducing hazardous drug environmental contamination: the centralization of the priming of IV tubing in the pharmacy and the use of a closed-system transfer device.</td>
<td>PhaSeal</td>
<td>Comparative</td>
<td>A total of 225 samples was quantified. After the centralization of priming in the pharmacy, no significant difference was found in the proportion of positive samples for cyclophosphamide, ifosfamide and methotrexate. Traces of cyclophosphamide found on the floor in patient care areas was significantly reduced (median[min-max]: 0.08[0.06-0.09]ng/cm² vs. 0.03[0.02-0.05], p&lt;0.0001). After using a closed-system transfer device, a significant difference was found for the proportion of cyclophosphamide positive samples (15/45(33%) vs. 0/45(0%), p&lt;0.0001), but no significant difference was found for ifosfamide (12/45(27%) vs. 5/45(11%), p=0.059) and methotrexate (1/45(2%) vs. 2/45(4%), p=0.557).</td>
<td>None declared</td>
</tr>
<tr>
<td>Miyake 2013</td>
<td></td>
<td>to compare surface contamination and personnel exposure to cyclophosphamide before and after the implementation of a closed system drug transfer device,</td>
<td>PhaSeal</td>
<td>Comparative</td>
<td>Four of 6 wipe samples collected before PhaSeal indicated a detectable level of cyclophosphamide. About 7 months after the initiation of PhaSeal, only one of 6 wipe samples indicated a detectable level of cyclophosphamide. Although all 4 employees who</td>
<td>None</td>
</tr>
</tbody>
</table>

Section 4: Document Review Summary
Pregnancy outcomes on health care workers handling cytotoxics

The literature search on pregnancy outcomes on health care workers yielded 27 articles, and one article by Zhang was retained.

The adverse health outcomes associated with antineoplastic agents exposure in nurses at two different hospitals in China were investigated. The main differences between the two hospitals are the way in which antineoplastic agents are prepared. Since 2013 Hospital A has a centralized location where the drugs are prepared with properly trained workers and Hospital B has intravenous chemotherapy preparation or reconstitution is carried out in an open-plan treatment area by nurses without an appropriate aspiration system. Before 2013 Hospital A had the same type of drug preparation plan as hospital B.

The nurses were categorized into the following four groups according to the probability of contact with antineoplastic agents: group I, comprising those in departments in hospital A in which antineoplastic agents are not handled; group II, comprising those in departments other than oncology departments in hospital A who handle antineoplastic agents; group III, comprising those in oncology departments in hospital A; group IV, comprising those in oncology departments in hospital B.

A questionnaire that contained 30 questions was designed to obtain relevant demographic, environmental, occupational, and health information from the nurses who had at least a 2-year occupational history in their staff position at the time of the investigation. All of the nurses recruited for this investigation were involved in the mixing and/or administration of antineoplastic agents; nurses in supervisory or coordinator positions were excluded from the survey. The survey was performed under anonymous conditions. Questions on reproductive history were included in the questionnaire. Given the one-child policy in China, and the fact...
that most women in China give birth before the age of 35 years, the age of participants studied in this regard was limited to married women aged less than 35 years old, and the incidence of self-reported adverse reproductive outcomes was calculated in that population. The reproductive toxicity of occupational exposure to antineoplastic agents was surveyed by evaluating adverse reproductive outcomes including impaired fertility (inability to conceive for more than 12 months) and spontaneous abortions (unintentional expulsion of an embryo or fetus before the 24th week of gestation) at both investigation time points (i.e., in 2011 and 2013). Pregnancies ending in an induced abortion, ectopic pregnancy, molar pregnancy, or multiple pregnancy were excluded.

The rate of full-term pregnancies in group III significantly increased from 15.9% in 2011 to 33.3% in 2013, which was markedly higher than 19.6% in group IV at the same time. While the reports of infertility were significantly higher in group III than in group I in both 2011 and 2013, no statistically significant increase of spontaneous abortion was found in group III as compared with group I at the same time. Application of the centralized preparation area led to significant decreases in both infertility and spontaneous abortion in group III (from 26.8% to 13.8% and from 14.6% to 4.6%, respectively, P<0.05). The reductions in adverse reproductive outcomes did not reach statistical significance in groups I and II. Meanwhile, the rates of infertility and spontaneous abortion were significantly higher in group IV than in group III in 2013 (30.4% vs. 13.8% and 22.3% vs. 4.6%, respectively, P<0.01).

### Effects of a centralized drug preparation area on the Number of Full-Term Pregnancies

<table>
<thead>
<tr>
<th>Group</th>
<th>2011-2013 n</th>
<th>Full-term pregnancy number</th>
<th>%</th>
<th>2013 After area n</th>
<th>Full-term pregnancy number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital A</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group I</td>
<td>106</td>
<td>25</td>
<td>23.6</td>
<td>108</td>
<td>31</td>
<td>28.7</td>
</tr>
<tr>
<td>Group II</td>
<td>30</td>
<td>5</td>
<td>16.7</td>
<td>29</td>
<td>9</td>
<td>31.0</td>
</tr>
<tr>
<td>Group III</td>
<td>82</td>
<td>13</td>
<td>15.9</td>
<td>87</td>
<td>29</td>
<td>33.3 P&lt;0.05 vs. before 2013</td>
</tr>
<tr>
<td>Hospital B</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group IV</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>112</td>
<td>22</td>
<td>19.6 P&lt;0.05 vs. group III</td>
</tr>
</tbody>
</table>

### Effects of a centralized drug preparation area on Adverse Infertility Outcomes

<table>
<thead>
<tr>
<th>Group</th>
<th>2011-2013 n</th>
<th>Infertility number</th>
<th>%</th>
<th>2013 After area n</th>
<th>Infertility number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital A</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group I</td>
<td>106</td>
<td>10</td>
<td>9.4</td>
<td>108</td>
<td>4</td>
<td>3.7</td>
</tr>
<tr>
<td>Group II</td>
<td>30</td>
<td>6</td>
<td>20.0</td>
<td>29</td>
<td>2</td>
<td>6.9</td>
</tr>
<tr>
<td>Group III</td>
<td>82</td>
<td>22 P&lt;0.01</td>
<td>28.8</td>
<td>87</td>
<td>12</td>
<td>13.8 P&lt;0.05 vs. group I and P&lt;0.05 vs. before</td>
</tr>
</tbody>
</table>
Effects of a centralized drug preparation area on Adverse Spontaneous Abortions Outcomes

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Spontaneous abortions number</th>
<th>%</th>
<th>n</th>
<th>Spontaneous abortions number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital A</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group I</td>
<td>106</td>
<td>10</td>
<td>9.4</td>
<td>108</td>
<td>3</td>
<td>2.8</td>
</tr>
<tr>
<td>Group II</td>
<td>30</td>
<td>6</td>
<td>20.0</td>
<td>29</td>
<td>2</td>
<td>6.9</td>
</tr>
<tr>
<td>Group III</td>
<td>82</td>
<td>12</td>
<td>14.6</td>
<td>87</td>
<td>4</td>
<td>4.6</td>
</tr>
<tr>
<td>Hospital B</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group IV</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td>112</td>
<td>25</td>
<td>22.3</td>
</tr>
</tbody>
</table>

P<0.05 versus before 2013

P<0.01 versus group III

General outcomes on health care workers handling cytotoxics

The literature search on general health outcomes in health care workers who handle cytotoxics yielded 1424 articles, of which three were relevant. As in the initial literature search for this topic, there were numerous studies that examined the DNA of health care workers and found DNA changes. However, these studies did not state what the results of the changes were and were therefore excluded.

The study by Fernandes evaluates the auditory and vestibular systems of nurses and pharmacy workers in a Brazilian hospital, who are exposed to chemotherapeutic agents. This study is a cross-sectional study using a quantitative method. Thirty three male and female workers, ranging from 21-60 years old, underwent conventional Audiologic Assessment; Transient Evoked Otoacoustic Emissions; and Computerized Vectoelectronystagmography. Most of the sample was female (90.9%). Individual protection equipment was used by 90.9% of the workers. Complaints of dizziness were reported by 56.25% of nursing workers and 52.94% of pharmacy workers. Audiological and vestibular assessment results were within normal limits, 96.97% and 74.20%, respectively. However, audiometric configuration of notch type was identified in 75.75% of all workers. Audiometric notches (76%) and altered caloric test (100%) were often associated with decreased use of coal masks.

The study by Poupeau recruited workers from the hematology-oncology department and control workers in a mother-child university health center in Quebec, Canada. An information period during that was aimed at enhancing the workers’ awareness and knowledge of the risks of occupational exposure was done before the study started. During the study participants filled out a journal containing activities performed and personal protective equipment worn. One urine sample was collected at the end of their shift and analyzed by for the presence of cyclophosphamide, ifosfamide, methotrexate, and alaphluoro-beta-alanine (5-fluorouracile’s main urinary metabolite).
The participation rate was 85.7% (102/119) and no urine samples had detectable concentrations of any of the four drugs evaluated (0/101; 0/74 nurses, 0/11 pharmacists, 0/9 pharmacy technicians, and 0/7 doctors). One activity with an antineoplastic agent was performed within 5 days of the sampling in 72.8% of the participants. Nurses wore all of the recommended protection for technical activities (86.2%), but rarely for non-technical activities (14.9%). Pharmacists and pharmacy technicians wore all of the recommended protection for all activities (100.0%).

The adverse health outcomes associated with antineoplastic agents exposure in nurses at two different hospitals in China were investigated by Zhang. The main differences between the two hospitals are the way in which antineoplastic agents are prepared. Since 2013 Hospital A has a centralized location where the drugs are prepared with properly trained workers and Hospital B has intravenous chemotherapy preparation or reconstitution is carried out in an open-plan treatment area by nurses without an appropriate aspiration system. Before 2013 Hospital A had the same type of drug preparation plan as hospital B.

The nurses were categorized into the following four groups according to the probability of contact with antineoplastic agents: group I, comprising those in departments in hospital A in which antineoplastic agents are not handled; group II, comprising those in departments other than oncology departments in hospital A who handle antineoplastic agents; group III, comprising those in oncology departments in hospital A; group IV, comprising those in oncology departments in hospital B.

The incidence of abnormal liver or kidney function was significantly higher in group III than in group I in both 2011 and 2013, reflecting the higher risk of organ damage with antineoplastic exposure in the oncology nurses. Although the centralized drug preparation location did not lead to statistically significant reductions in the incidence of organ function abnormalities in the three groups from hospital A (groups I-III), the markedly higher incidence of abnormal kidney function in group IV as compared to group III implies a protective role of the centralized drug preparation area.

<table>
<thead>
<tr>
<th></th>
<th>2011-2013</th>
<th>After 2013 of centralized drug preparation area</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Liver (n)</td>
</tr>
<tr>
<td>Hospital A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group I</td>
<td>138</td>
<td>3.6% (5)</td>
</tr>
<tr>
<td>Group II</td>
<td>39</td>
<td>0</td>
</tr>
<tr>
<td>Group III</td>
<td>118</td>
<td>10.2% (12)</td>
</tr>
<tr>
<td>Hospital B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group IV</td>
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<td></td>
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</tbody>
</table>
Hair loss was measured by self-reported tests. The results showed that hair loss in oncology nurses was markedly more serious than in their nonexposed counterparts both before and after initiation of a centralized drug preparation area. This implementation led to a significant alleviation of the symptoms of hair loss in all three groups from hospital A. However, no clear difference was found between groups III and IV in 2013.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>- (%)</th>
<th>+ (%)</th>
<th>++ (%)</th>
<th>P</th>
<th>n</th>
<th>- (%)</th>
<th>+ (%)</th>
<th>++ (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital A</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>182</td>
<td>81 (44.5)</td>
<td>54 (29.7)</td>
<td>47 (25.8)</td>
<td>P&lt;0.05 versus before 2013</td>
</tr>
<tr>
<td>Group I</td>
<td>179</td>
<td>55 (30.7)</td>
<td>77 (43.0)</td>
<td>47 (26.3)</td>
<td></td>
<td>55</td>
<td>26 (47.3)</td>
<td>18 (32.7)</td>
<td>11 (20.0)</td>
<td>P&lt;0.05 versus before 2013</td>
</tr>
<tr>
<td>Group II</td>
<td>46</td>
<td>8 (17.4)</td>
<td>25 (54.3)</td>
<td>13 (28.3)</td>
<td></td>
<td>148</td>
<td>19 (12.8)</td>
<td>59 (39.9)</td>
<td>70 (47.3)</td>
<td>P&lt;0.01, versus group I and before 2013</td>
</tr>
<tr>
<td>Group III</td>
<td>123</td>
<td>4 (3.3)</td>
<td>27 (22.0)</td>
<td>92 (74.8)</td>
<td>P&lt;0.01, versus group I</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital B</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Group IV</td>
<td>/</td>
<td>/</td>
<td>/</td>
<td></td>
<td></td>
<td>190</td>
<td>41 (21.6)</td>
<td>68 (35.8)</td>
<td>81 (42.6)</td>
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</table>
Hematotoxicity caused by antineoplastic agents were evaluated by blood cell counts, including White blood cell (WBC), platelet (Plt), and red blood cell (RBC) counts, and by the number of nurses with abnormal blood cell counts. The findings of these hematological examinations are given in the table below. In 2011, the mean WBC count was significantly lower in group III than in groups I and II, and there were significantly more nurses with WBC abnormalities in group III than in groups I and II. The mean Plt count was markedly higher in group II than in groups I and III, with no clear difference between groups I and III. Although the mean RBC counts did not differ significantly among groups I, II, and III, the number of nurses with an abnormal RBC count was markedly lower in group III than in group I. Application of a centralized drug preparation area in 2013 in hospital A resulted in significant increases in WBC, Plt, and RBC counts in group III, and marked decreases in the numbers of nurses with an abnormal WBC count in group III and an abnormal RBC count in group I. In contrast, none of the simultaneously slightly increased mean blood cell counts observed in groups I and II reached statistical significance. Thus, both Plt and RBC counts were significantly higher in groups II and III than in group I after centralized drug preparation area implementation. In addition, mean blood cell counts, including WBC, Plt, and RBC were significantly lower and the number of nurses with abnormal RBC and WBC counts was markedly higher in group IV than in group III in 2013. These results indicate that application of a centralized drug preparation area decreased the hematotoxicity associated with AD exposure in the nurses.

<table>
<thead>
<tr>
<th>Group</th>
<th>2011-2013</th>
<th>After 2013 of centralized drug preparation area</th>
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<tbody>
<tr>
<td></td>
<td>WBC (x10⁹/l)</td>
<td>Plt (x10⁹/l)</td>
</tr>
<tr>
<td></td>
<td>n (n of &lt;4)</td>
<td>n (n of &lt;100)</td>
</tr>
<tr>
<td>Hospital A</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group I</td>
<td>88</td>
<td>5.28±1.25 (11)</td>
</tr>
<tr>
<td>Group II</td>
<td>33</td>
<td>5.33±1.18 (7)</td>
</tr>
<tr>
<td>Group III</td>
<td>101</td>
<td>4.24±1.17 (48)</td>
</tr>
<tr>
<td>Hospital B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group IV</td>
<td>/</td>
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</tr>
</tbody>
</table>

These results indicate that application of a centralized drug preparation area decreased the hematotoxicity associated with AD exposure in the nurses.
References


10. Batka G. "It is in your hands" - How healthcare professionals can ensure their safety when handling hazardous drugs. Acta Pharm Hung. 2017;87 (3-4):100.


