Evidence-Based Series #16-3v2 IN REVIEW

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

Safe Handling of Cytotoxics


Report Date: December 16, 2013

An assessment conducted in May 2017 placed Evidence-based Series (EBS) 16-3 Version 2 IN REVIEW. This means that it is undergoing a review for currency and relevance. The Oncology Nursing Program has determined that it is still appropriate for this document to continue to be available while this updating process unfolds. The PEBC has a formal and standardized process to ensure the currency of each document (PEBC Assessment & Review Protocol)

Evidence-Based Series #16-3v2 is comprised of 3 sections:
Section 1: Guideline Recommendations
Section 2: Evidentiary Base
Section 3: Development Methods, Recommendations Development and External Review Process

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Evidence-Based Series #16-3

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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<tr>
<td>Version 2 2013</td>
<td>July 2006 to January 2013</td>
<td>New data added to original Full Report</td>
<td>Updated web publication. Peer review publication. Incorporated changes to include how cytotoxics should be handled throughout each step of the medication circuit. New recommendations have been added and previous recommendations have been expanded.</td>
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IN REVIEW
Evidence-Based Series #16-3: Section 1

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

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.e-laws.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.e-laws.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.e-laws.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.e-laws.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).

![Cytotoxic Symbol](image)

**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.

**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 respirator 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.

<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></td>
<td>(2 pairs)</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></td>
<td>(2 pairs)</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></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Preparing creams, ointments, oral</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>solutions and crushing tablets</td>
<td>(1 pair)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>(2 pairs)</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Routes of administration</td>
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<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>(intravenous, subcutaneous, intramuscular, intravesical, intraperitoneal, intrathecal, liquid oral)</td>
<td></td>
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<td></td>
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<tr>
<td></td>
<td>(1 pair)</td>
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<td></td>
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<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></td>
<td>(1 pair)</td>
<td></td>
<td></td>
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<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></td>
<td>(2 pairs)</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Aerosolized administration (e.g., ribavirin, pentamidine)*</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>(if risk of splashing)</td>
<td></td>
</tr>
<tr>
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<td></td>
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<tr>
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<td></td>
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<tr>
<td></td>
<td>(1 pair)</td>
<td></td>
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<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></td>
<td>(1 pair)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Handling of</td>
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<td></td>
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</tr>
<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>
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<tr>
<td>contaminated bedding on the wards</td>
<td></td>
<td></td>
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</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>(if suspicion of powder or aerosolization is generated)</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
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<td></td>
<td></td>
<td></td>
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<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>✓</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

### 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.

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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.

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 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).

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
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 manufacturers 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 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.
REFERENCES


RELATED GUIDELINES


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Evidence-Based Series #16-3: Section 2

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

Safe Handling of Cytotoxics: Evidentiary Base


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 (IRSST) (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 $\chi^2$ test for heterogeneity and the $I^2$ percentage. A probability level for the $\chi^2$ 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 Tevedapter 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 microbial 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. Yoshid 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 Queruau Lamerie did various contamination tests comparing six devices: Kis 1, Tevadaptor, PhaSeal, Codan Connect Z, Pchmx, 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 Pchmx 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>
</tr>
<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>
</tr>
<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>
</tr>
<tr>
<td>Reference</td>
<td>Purpose/Scope</td>
<td>Product(s) Tested</td>
<td>Method</td>
<td>Results</td>
<td>Disclosures re: Conflicts of Interest</td>
<td>Test Environment</td>
</tr>
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</tr>
<tr>
<td>al (2008) (9)</td>
<td>handling system for spill and leakage of chemotherapy during preparation.</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>
<td></td>
<td></td>
</tr>
<tr>
<td>Querua 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>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></td>
<td></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>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></td>
<td></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>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></td>
<td></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>Use of a closed system can reduce environmental contamination and exposure to chemotherapy.</td>
<td>No conflict of interest disclosed.</td>
<td></td>
<td></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>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></td>
<td></td>
</tr>
<tr>
<td>Reference</td>
<td>Purpose/Scope</td>
<td>Product(s) Tested</td>
<td>Method</td>
<td>Results</td>
<td>Disclosures re: Conflicts of Interest</td>
<td>Test Environment</td>
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</tr>
<tr>
<td>Carey et al (2011) (15)</td>
<td>Assess ability of the system to maintain product sterility</td>
<td>PhaSeal</td>
<td>Non-randomized, multicentre trial</td>
<td>99.7% probability of no microbial contamination.</td>
<td>No funding source. Peripheral author affiliation with sponsor.</td>
<td>Pharmacy</td>
</tr>
<tr>
<td>De Prijck et al (2008) (16)</td>
<td>Evaluate susceptibility to microbial contamination with use of closed systems.</td>
<td>PhaSeal, Chemo Protect Spike, Clave Connector, Securmix</td>
<td>Comparative/Observational</td>
<td>PhaSeal proved least susceptible to microbial contamination. Likely related to the thinness of the transfer needle.</td>
<td>Study supported by an unrestricted grant from Carmel Pharma (PhaSeal).</td>
<td>Laboratory</td>
</tr>
<tr>
<td>Jorgenson et al (2008) (17)</td>
<td>To validate systems against recommendations by NIOSH and ISOPP re: vapour leak and contamination</td>
<td>PhaSeal, Tevadaptor, Smart Site, Chemo protect spike, Chemo mini-spike</td>
<td>Comparative observational</td>
<td>Only the PhaSeal device met the criteria for a closed system.</td>
<td>Two of the authors are members of Carmel (PhaSeal) Advisory Board.</td>
<td>Laboratory</td>
</tr>
<tr>
<td>McMichael et al (2011) (18)</td>
<td>Assess ability of system to prevent microbial contamination.</td>
<td>PhaSeal</td>
<td>Observational</td>
<td>At the 168-hour mark, 98.2% probability of no microbial contamination.</td>
<td>Study supported by an unrestricted grant from Carmel Pharma (PhaSeal).</td>
<td>Pharmacy/Laboratory</td>
</tr>
<tr>
<td>Odou (2010/11) (19)</td>
<td>Overview of device characteristics.</td>
<td>PhaSeal, Tevadaptor</td>
<td>Descriptive review.</td>
<td>PhaSeal the only closed-system device suitable for handling cytotoxic drugs, based on accepted criteria.</td>
<td>No conflict of interest disclosed.</td>
<td>N/A</td>
</tr>
<tr>
<td>Zock et al (2010) (20)</td>
<td>Evaluate and compare the effectiveness of two closed system products in preventing cytotoxic contamination.</td>
<td>PhaSeal, Chemo CLAVE</td>
<td>Comparative/Observational</td>
<td>Low levels of contamination detected after each trial. No statistical analysis done to compare the two systems.</td>
<td>Study supported by ICU Medical Inc. (Chemo CLAVE)</td>
<td>Laboratory</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: 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


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.


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

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

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

ASCO (US) - [http://www.asco.org/ASCO/Quality+Care+%26%23126%3B+Guidelines/Practice+Guidelines](http://www.asco.org/ASCO/Quality+Care+%26%23126%3B+Guidelines/Practice+Guidelines)

NCCN (US) - [http://www.nccn.org/](http://www.nccn.org/) (consensus-based)


In addition, the websites of several, known, high-quality guideline developers were searched:
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 ISOPP” (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 ISOPP, Quapos4 and the Alberta Health 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 of 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>
<thead>
<tr>
<th>Question</th>
<th>Lowest Quality (1)</th>
<th>(2)</th>
<th>(3)</th>
<th>(4)</th>
<th>Highest Quality (5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Rate the guideline development methods.</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Rate the guideline presentation.</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Rate the guideline recommendations.</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Rate the completeness of reporting.</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Does this document provide sufficient information to inform your decisions? If not, what areas are missing?</td>
<td></td>
<td></td>
<td></td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>6. Rate the overall quality of the guideline report.</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. I would make use of this guideline in my professional decisions.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>8. I would recommend this guideline for use in practice.</td>
<td></td>
<td></td>
<td></td>
<td>2</td>
<td></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 to 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>Number (%)</th>
<th>General Questions: Overall Guideline Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lowest Quality (1)</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/18-24
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, an, ui]
17. pharmacist.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, ps, an, ui]
18. pharmacy technician.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, ps, an, ui]
19. pharmacy technician.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, dv, kw, nm, kf, ps, 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, <em>Handling of waste materials in health care facilities and veterinary health care facilities.</em></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><strong>Scope and Purpose</strong></td>
<td>1. The overall objective(s) of the guideline is (are) specifically described.</td>
<td>70% 86% 94% 60% 80%</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% 49% 86% 14% 47%</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% 27% 70% 7% 44%</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>
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<td></td>
<td>13. The guideline has been externally reviewed by experts prior to its publication.</td>
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<td>14. A procedure for updating the guideline is provided.</td>
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<tr>
<td><strong>Clarity of Presentation</strong></td>
<td>15. The recommendations are specific and unambiguous.</td>
<td>48% 56% 88% 43% 53%</td>
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<td>16. The different options for management of the condition or health issue are clearly presented.</td>
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<td></td>
<td>17. Key recommendations are easily identifiable.</td>
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<tr>
<td><strong>Applicability</strong></td>
<td>18. The guideline describes facilitators and barriers to its application.</td>
<td>33% 67% 67% 22% 44%</td>
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<td></td>
<td>19. The guideline provides advice and/or tools on how the recommendations can be put into practice.</td>
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<td></td>
<td>20. The potential resource implications of applying the recommendations have been considered.</td>
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<td></td>
<td>21. The guideline presents monitoring and/or auditing criteria.</td>
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<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% 33% 54% 10% 35%</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% 57% 71% 38% 58%</td>
</tr>
</tbody>
</table>
## Appendix D: Guideline Comparison and Assessment Checklist

- Each colour represents a different working group member

<table>
<thead>
<tr>
<th>Policies and Procedures</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 - guidelines/recommendations</td>
<td>• Yes - actually P&amp;P not standards last revised in 2000! Spill policy revised 2009</td>
<td>• Speaks specifically to Pharmacy staff - very much like Quapos4 Considers them to be standards of practice 1 1/8 page on administering medications</td>
<td>• More Standards and recommendations Basically for Pharmacy and those that support Pharmacy - housekeeping, receiving and transportation</td>
<td>• No- Only for Pharmacy some areas are vague and give the reader options</td>
<td>• Yes for pharmacy</td>
</tr>
<tr>
<td>• Institutional action plan defined with recommendations included.</td>
<td>• Written as policies in the entire document. Relatively little detail given.</td>
<td>• Wording use indicates that certain sections are obligatory or voluntary by using “must” and “should”.</td>
<td></td>
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<tr>
<td>• Yes</td>
<td>• Yes</td>
<td>• Most pertain to pharmacy staff</td>
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<tr>
<td>• Section 4: Establishing a hazardous drug committee...etc.</td>
<td>• V-10: Section C outlined the responsibilities of various staff members Module 1, Section A - written policies and procedures must be developed</td>
<td>• Section 21.8: A paragraph about the requirement of procedure manual with description of what should be in the manuals.</td>
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<tr>
<td>Policies and Procedures</td>
<td>Quebec</td>
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<td>ISOPP</td>
<td>Quapos4</td>
<td>Alberta Health</td>
</tr>
<tr>
<td>PPE</td>
<td>• Yes - very clear for all individuals in the medication circuit</td>
<td>• Yes, for preparing and administration</td>
<td>• 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</td>
<td>• 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</td>
<td>• Only for pharmacy not clear for RNs</td>
</tr>
<tr>
<td>• Defined in detail in Table 4.</td>
<td>• Defined in detail.</td>
<td>• 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</td>
<td></td>
<td>• Yes for pharmacy</td>
<td></td>
</tr>
<tr>
<td>• Very clear</td>
<td>• V-10: Section A, “Personal protective equipment” (no references cited) V-10: Table 2 (again, no sources cited)</td>
<td>• Good, clear descriptions of</td>
<td></td>
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<tr>
<td>• 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</td>
<td>• V-10: Section D, “Personal protective equipment” (no references cited)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• 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</td>
<td></td>
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<td></td>
<td></td>
<td>• Good, clear descriptions of</td>
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Section 3: Development Methods, Recommendations Development & External Review
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<tbody>
<tr>
<td>the recommendations are tailored to the different levels of exposure depending on the role (e.g., drug preparation vs., drug transport...etc.)</td>
<td>Module 1, section E (other guidelines cited, no primary literature)</td>
<td>certain types of PPE.</td>
<td>for the preparation of drugs</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>• Yes - for pharmacy not for nursing</td>
<td>• Very detailed description of PPE requirements with a clear indication of when each component should be used, changed, etc.</td>
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<td></td>
<td></td>
<td>• Section 6. Referenced other guidelines and standards.</td>
<td>• Section 3.2, 3.2.1, 3.2.2, 3.2.3: Very detailed discussion with primary literature support.</td>
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</tbody>
</table>

**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.

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<tbody>
<tr>
<td>Yes</td>
<td>Yes - not detailed refers to another policy</td>
<td>Yes</td>
<td>Yes - very detailed pharmacy working area dimensions etc</td>
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<tr>
<td>Yes</td>
<td>Defined in detail.</td>
<td>Yes - detailed not sure if not more textbook then recommendations</td>
<td>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.</td>
<td></td>
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<tr>
<td>Yes</td>
<td>Yes</td>
<td>Yes - detailed</td>
<td>Yes very detailed</td>
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<tr>
<td>Section 7: Different types of BSC discussed as well as its suitability.</td>
<td>Section 8: Very detail discussion re: different type of biological safety cabinets, testing and monitoring.</td>
<td>Section 2.2. European classification of BSC different from US?</td>
<td>Section II B. Clear policy stated regarding BSC standard.</td>
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<tr>
<td>Section 8: Cleaning procedures of ventilated cabinets.</td>
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<td>- Section IV: Working within a BSC.</td>
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**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
- 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

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<td></td>
<td>No</td>
<td>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</td>
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<td>Speaks to them from a Pharmacy perspective yet - however not clear as to whether best practice recommendation -</td>
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<td></td>
<td></td>
<td>No</td>
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<td>Section III H. Discussed Spiros. Focus is on the proper</td>
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<td></td>
<td>closed systems discussion. Studies cited to support the relative</td>
<td></td>
<td>great detail, but as far as I can tell, no specific guidance is</td>
<td>with respect to preparation</td>
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<td></td>
<td>effectiveness of different close systems.</td>
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<td>given regarding their use.</td>
<td>Detailed descriptions and illustrations of the common closed drug</td>
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<td>• A bit but no guidelines</td>
<td>transfer systems are provided, but specific guidance on the use of</td>
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<td></td>
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<td></td>
<td>• Section 7. Some primary literature cited.</td>
<td>these products is not provided, which is unfortunate, because it</td>
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<td></td>
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<td>• Section 10.3: Provides a description of closed systems, but did</td>
<td>leaves the reader unclear as to how best to proceed.</td>
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<td></td>
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<td>not include its effectiveness</td>
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<tr>
<td>Syringes and IV</td>
<td>Yes</td>
<td>Yes</td>
<td>Not really - speaks in general about a contained system versus</td>
<td>Yes - speaks to type of syringes eg. Single use, leur lock clear</td>
</tr>
<tr>
<td>sets</td>
<td>This topic is covered but just at a high level with no specifics given.</td>
<td>Yes</td>
<td>closed system • This topic is briefly mentioned.</td>
<td>scale etc. Nothing really specific about admin sets</td>
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<td>Yes - a bit</td>
<td></td>
<td>• No</td>
<td>A very detailed description of all the components required for</td>
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<td>Section 10.3</td>
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<td>• Section 12</td>
<td>chemotherapy delivery is provided.</td>
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<td>• Yes - detailed</td>
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<tr>
<td>Transport and</td>
<td>Yes - some information about labeling High-level guidance is provided.</td>
<td>Yes</td>
<td>Yes - quite general Both topics are clearly discussed.</td>
<td>Transportation and storage to and within the pharmacy - not clear</td>
</tr>
<tr>
<td>Labeling</td>
<td>Transport processes are defined in detail. Labeling recommendations are</td>
<td></td>
<td>• Yes Section 2. Good discussion about transportation and labeling</td>
<td>about to administration areas</td>
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<tr>
<td></td>
<td>included.</td>
<td></td>
<td>for external and internal transportation of chemo.</td>
<td>Labeling -yes to dispensed medication minimum requirements - not</td>
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<td></td>
<td>Yes</td>
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<td>necessarily based on best practice per se?</td>
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<td></td>
<td>Yes</td>
<td></td>
<td></td>
<td>Also labeling as per law in transporting out of building</td>
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<td></td>
<td>V-10 Section D, Table 1</td>
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<td>preparation: Clear guidelines provided</td>
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<td>or receiving Detailed information is provided on the details required for safe drug acceptance into the facility and for proper labeling. Yes - detailed Section 3.7: No clear distinction between internal and external transportation.</td>
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<td><strong>Education and Training</strong></td>
<td>Yes Well-documented and embedded in recommendations. Yes - some 4.1.4. Listed the content of continuing education and orientation program.</td>
<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>Yes - should have education and annual review. Re educate for new drugs etc, every 2-3 years. Detailed outline for pharmacy - includes outline of content, skill set of f 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>Yes -Described in great detail regarding when, and methods - but very specific to pharmacy and supporting staff to pharmacy. Described in detail Yes - lot and detailed Section 1.6, 1.6.1, 1.6.2: Good discussion. It also included the format of training (e.g., e-learning)</td>
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<tr>
<td><strong>Pregnancy</strong></td>
<td>Yes - recommend precautionary reassignment Recommendations re drug-specific exposure of health care workers. Allows reassignment of duties. Yes Section 2.3.2: Addressed heath effects of</td>
<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, breast feeding, or planning to “reproduce”</td>
<td>Yes -“Family Planning” 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</td>
<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</td>
</tr>
<tr>
<td>Section 15: Precautionary reassignment.</td>
<td>Section 3: A short discussion about family planning.</td>
<td>Other jurisdictions, but 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.</td>
<td>Yes</td>
<td>Section XIII: One paragraph describing policy.</td>
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### Surveillance

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<tbody>
<tr>
<td>Yes - for surfaces in admin and prep areas</td>
<td>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>administering States that pregnant workers should be permitted to avoid working with cytotoxics during their pregnancy. Not much V-20 section B</td>
<td>other jurisdictions, but 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.</td>
<td>Section 1.3: “Protection of working mothers and working young persons</td>
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### Medical Surveillance

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<tbody>
<tr>
<td>Speak to it - not recommended unless research study</td>
<td>Employees will have access to employee health/occupational health and safety</td>
<td>Implies “no” as state no direct measures to detect total exposure to cytotoxics - it is</td>
<td>Yes - Physical before employment - offered 12 -24 months after employment and prn - random bio-</td>
<td>No</td>
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<tr>
<td>no specific recommendations are given. Yes, but no recs Section 15.</td>
<td>services for the purpose 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. 3. Annually, employees are encouraged to arrange a routine medical examination with his/her family physician. 4. 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 actually yes... 1. persons with abnormal pathology should not be preparing Chemo until pathology has been investigated 2. As a baseline - then offered every six months Hospitals should have policies Regular monitoring is promoted with periodic blood tests. Yes</td>
<td></td>
<td>monitoring recommended 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</td>
<td>Section 2.1: Discussion surveillance of work area (bacterial contamination)</td>
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<td>training occurred (WCB Regulations Oct 99) These are covered in some detail under the Worksafe 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>
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<tr>
<td>Spills</td>
<td>Yes</td>
<td>Yes - revised 2009 Like 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>
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<tr>
<td><strong>Home Care</strong></td>
<td>Yes This topic is discussed in detail. Yes 11.3.3.</td>
<td>No not that I could see/find - No</td>
<td>Yes A descriptive section on home care is provided, and some specific issues of concern are addressed. Yes Section 18: Good discussion of various aspects of home care chemotherapy administration</td>
<td>Yes - fairly specific to pump and venous access education to patients A very detailed section on home care is provided. Yes Section 4.7</td>
<td>Vague - more inference No</td>
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<tr>
<td><strong>Nursing Administration</strong></td>
<td>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.</td>
<td>Yes very basic The responsibilities of a series of staff are spelled out. Yes V-10: Section D, E</td>
<td>Yes - 1 1/8 pages - No Section 12: Not a complete discussion, only highlighted some points of interest.</td>
<td>Mentions P&amp;P are important for admin of drugs fro 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</td>
<td>Virtually little to none - not helpful in my opinion for nursing at all. No</td>
</tr>
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<td>the immunosuppressed patient from nosocomial infections by staff and hence the protection of the patient”</td>
<td>Not really</td>
<td></td>
</tr>
<tr>
<td>New: Handling of Waste Materials &amp; Human Waste</td>
<td>Detailed section on this topic. yes</td>
<td>Described in detail in this document. yes</td>
<td>Described in detail. yes</td>
<td>Very detailed sections with good background. yes</td>
<td>No</td>
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</table>
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 (9).

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>
<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>
</table>

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>
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<tr>
<td>Unpacking and cleaning</td>
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<td>✓</td>
<td></td>
<td></td>
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<tr>
<td>Sterile preparations</td>
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<td>✓</td>
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<td>✓</td>
<td>✓</td>
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<tr>
<td>Non-sterile preparations: - Counting of solid oral forms - Preparing creams, ointments, oral solutions and crushing tablets</td>
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<td>✓</td>
<td>✓</td>
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<td>✓</td>
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<tr>
<td>Routes of administration (intravenous, subcutaneous, intramuscular, vesical, intraperitoneal, intrathecal, liquid oral)</td>
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<td>Topical administration (creams, ointments)</td>
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<td>Aerosolized administration (e.g., ribavirin, pentamidine)</td>
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<td>✓</td>
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<tr>
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<td>Spill or damaged or broken container</td>
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<td></td>
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<td></td>
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<td>✓</td>
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<td>(1 pair)</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
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.

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.
**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 polices 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 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 manufacturers 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 ENVIROMENTAL 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

Source: http://www.who.int/gpsc/5may/Glove_Use_Information_Leaflet.pdf
Appendix G: Technique for donning and doffing two pairs of gloves (4).

2) To remove the inner pair of gloves (under the cuff of the gown)

- Pull on the gloves to free them from the cuffs of the gown. Touch only the outside of the gloves.
- With gloved hand 1, remove the glove on hand 2, by grasping it on the outside.
- With bare hand 2, insert the fingers under the cuff of the remaining glove and remove it.

**FIGURE 6**
Procedure for removing gloves if the gown is kept on and two pairs of gloves are worn.