



Safe handling of cytotoxics: guideline recommendations

A.C. Easty PhD PEng,† N. Coakley MLIS,‡§
R. Cheng RPh BScPhm PharmD,|| M. Cividino MD,##**
P. Savage RN MAEd,†† R. Tozer PhD MD,‡‡§
and R.E. White MA†*

ABSTRACT

Background

This evidence-based practice guideline was developed to update and address new issues in the handling of cytotoxics, including the use of oral cytotoxics; the selection and use of personal protective equipment; and treatment in diverse settings, including the home setting.

Methods

The guideline was developed primarily from an adaptation and endorsement of an existing guideline and from three systematic reviews. Before publication, the guideline underwent a series of peer and external reviews to gather feedback. All comments were addressed, and the guideline was amended when required. The guideline applies to health care workers who could come into contact with cytotoxic drugs at any point in the medication circuit. The intended users are hospital administrators, educators, and managers; occupational health and safety services; and pharmacy and health care workers.

Results

The recommendations represent a reasonable and practical set of procedures that the intended users of this guideline should implement to minimize opportunities for accidental exposure. They are not limited to just the point of care; they cover the entire chain of cytotoxics handling from the time such agents enter the institution until they leave in the patient or as waste.

Conclusions

Reducing the likelihood of accidental exposure to cytotoxic agents within the medication circuit is the main objective of this evidenced-based guideline.

The recommendations differ slightly from earlier guidelines because of the availability of new evidence.

KEY WORDS

Cytotoxic drugs, guidelines, hazardous waste, cytotoxic drug administration, personal protective equipment, cytotoxic drug preparation

1. INTRODUCTION

The objective of this guideline is to update and address new issues in the handling of cytotoxics that have developed since release of the previous guideline on this topic from the Program in Evidence-Based Care (PEBC), including the use of oral cytotoxics; the selection and use of personal protective equipment (PPE); and treatment in diverse settings, including the home setting.

1.1 Summary of Guideline Development Methods

The PEBC's 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 produces evidence-based and evidence-informed guidelines, known as Evidence-Based Series reports, using the methods of the practice guidelines development cycle^{1,2}. The PEBC is a provincial initiative of Cancer Care Ontario, supported by the Ontario Ministry of Health and Long-Term Care. All work produced by the PEBC is editorially independent from the Ontario Ministry of Health and Long-Term Care.

The complete methods and search strategies used for this guideline can be found online in *Safe Handling of Cytotoxics*, Section 2 (<https://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=293471>). A two-stage approach was used: a search process identified and ranked existing guidelines, and then a systemic review of the primary

literature focused on areas not covered by existing and accepted guidelines. This article summarizes the complete document, *Safe Handling of Cytotoxics*.

This guideline is an adaptation of an existing guideline, combined with three systematic reviews in the areas of closed-system transfer devices, pregnancy outcomes in health care workers who handle cytotoxic drugs, and general health outcomes in health care workers who handle cytotoxic drugs. The guideline *Prevention Guide: Safe Handling of Hazardous Drugs*³ was chosen because it was current, broad, and sufficiently detailed. It also addressed the safe handling of cytotoxic drugs from the point at which they enter the centre to the point at which they leave as either waste or in the patient. The original recommendations can be found in *Prevention Guide: Safe Handling of Hazardous Drugs*³. Note that, for the purposes of the present work, a cytotoxic is defined as “an agent that possesses 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.”

1.2 The Recommendations

In the recommendations presented here, the notations that appear in parentheses in the text aim to help the user determine the level of variation that might be expected in following the particular recommendation. The notation lies at the end of each sentence. Where a notation is provided at the end of a paragraph, it should be taken to apply to all parts of that paragraph. The notations are these:

- **Legislation or regulation requires (LR)** The recommendation is supported by law, regulation, or standard. All centres and users are expected to implement this recommendation with little variation.
- **Strongly recommend (SR)** The course of action or practice is recommended based on evidence in the medical literature or a strong consensus of the expert panel, or both. Variation from this course of action or practice should be based on a considered judgment of how local circumstances might vary from those typically found in practice.
- **Recommend (R)** This course of action or practice is, in the consensus of the expert panel, sound and worth considering, but implementation might vary according to local circumstances.

1.3 Hierarchy of Controls

In the National Institute for Occupational Health and Safety Engineering Controls Program Portfolio, the U.S. Centres for Disease Control and Prevention says “Controlling exposures to occupational hazards is the fundamental method of protecting workers.” The program describes the hierarchy of controls

used to implement feasible and effective control. In descending order, they are elimination, substitution, engineering controls, administrative controls, and use of PPE.

Engineering controls are used to remove the hazard or place a barrier between the worker and the hazard⁴. In health care, examples of engineering controls include the use of biosafety cabinets and safety-engineered medical devices—in particular, safety-engineered needles that help to protect workers from exposure to blood-borne pathogens. Administrative controls include policies and procedures and staff education and training.

Although PPE is the last control between a hazard and the worker, it is really the primary control on which workers rely. It is very important that health care workers be educated in the appropriate selection and use of PPE for protection against exposure to cytotoxic drugs. Appropriate PPE usually consists of gloves, gowns, and eye protection when necessary.

1.4 Target Population and Intended Users

The target population for this guideline is health care workers who could come into contact with cytotoxic drugs at any point in the medication circuit. The intended users of this guideline are hospital administrators, educators, and managers; occupational health and safety services; and pharmacy and health care workers.

2. RECOMMENDATIONS

2.1 Recommendation 1: General Measures

2.1.1 Committee Responsible for Policy and Procedures for Cytotoxic Drugs

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

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

The committee is responsible for implementation and follow-up of the risk prevention management program related to the use of cytotoxic drugs.

2.1.2 Continuing Education and Orientation Program

Initial and ongoing hospital-approved education should be provided to all staff involved with cytotoxic

drugs throughout the medication circuit, including education for safe handling and spill or leak management⁵ (LR). All staff should have initial and ongoing training to the best-practice standards in place at the time (SR).

There is documentation that annual training for safe handling of cytotoxic drugs has occurred⁵ (LR).

2.1.3 Identification and Safety

Each institution should maintain a list of cytotoxic drugs (SR).

Cytotoxic drugs and their waste should be properly identified with the capital “C” symbol and, under it, the words “CYTOTOXIC/CYTOTOXIQUE” in capital letters (Figure 1)^{6,7}. All cytotoxic waste under the Ministry of Environment regulation (guideline C4) should include bilingual wording, and both the words and the symbol should appear on a dark grey rectangle^{6,7} (LR).

2.1.4 Purchasing Cytotoxic 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 the volume of potential spills (SR).

2.1.5 Spills Kit

A spill management kit should be available in all areas where cytotoxic drugs are stored, transported, handled, and administered (SR).

2.1.6 Precautionary Reassignment

All staff should be fully informed of the potential reproductive hazards of cytotoxic drugs⁸ (SR).

The facility should consider alternative duties for women who are pregnant or breast-feeding (SR).

2.2 Recommendation 2: Personal and Protective Equipment

Workers should 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 used⁹ (LR).



FIGURE 1 Standard label for cytotoxic drugs or their waste.

The appropriate PPE for the task (as described in Table 1) should be worn throughout the medication circuit⁹. It is the employer's responsibility to provide the necessary PPE and training on how to use the equipment (LR).

2.2.1 Gloves

The gloves used to handle cytotoxic drugs should comply with ASTM standard D-6978-(05)-13 and be powder-free¹⁰. Gloves are recommended to be nitrile, polyurethane, neoprene, or latex¹⁰. Latex is a known allergen, a factor that should be taken into consideration for glove selection. Vinyl gloves should not be used. The frequency of glove changes can be adjusted according to the level of exposure at each step in the medication circuit. For example, when administering reconstituted medications, workers should change gloves immediately if the gloves become torn, punctured, or visibly contaminated with a cytotoxic drug, and should ensure to follow Routine Practices¹¹. Great care should be taken in the removal of gloves so as to not contaminate the skin. When two pairs of gloves are required, put on the first pair before putting on the gown (SR).

2.2.2 Gown

Gowns used for handling cytotoxic drugs should be disposable; should be made of lint-free, low-permeability fabric; should have long sleeves with tight-fitting cuffs; and should fasten in the back. Gowns have to be changed in the event of contamination, spillage, or rips, and at the end of the procedure (SR).

For medication preparation, gowns have to be changed halfway through a shift or every 3.5 hours¹². The supplier should be able to certify that the gown protects against cytotoxic drugs (SR). Care must be taken to avoid contamination of the hands by avoiding touching the outside of the gown when removing it (SR).

2.2.3 Facial Protection

Surgical or procedure masks are required when handling and preparing medications in a biological safety cabinet; in this instance, they are worn to prevent microbial contamination of the sterile field (SR).

Full-face protection should be worn whenever a risk of splashing is present (for example, during certain drug administration procedures). The use of a full face shield is preferred. If goggles are used, they have to be worn in conjunction with a fluid-resistant mask (SR). For further information, see Canadian Standards Association (CSA) standard Z94.3-07: *Eye and Face Protectors*¹³.

2.2.4 Respiratory Protection Apparatus

Fit-tested respirators such as those certified N95 or N100 by the U.S. National Institute for Occupational Health and Safety should be used when there is a risk that an airborne powder or aerosol will be generated (SR).

TABLE 1 Personal protective equipment to be worn throughout the medication circuit

<i>Circuit step</i>	<i>Gloves</i>	<i>Gown</i>	<i>Respiratory protection</i>	<i>Face protection</i>	<i>Cap</i>	<i>Shoe covers</i>
Unpacking and cleaning	Yes (2 pair)	Yes				
Sterile preparations	Yes (2 pair)	Yes		Yes	Yes	Yes
Nonsterile preparations						
Counting solid oral forms	Yes (1 pair)	Yes				
Preparing creams, ointments, and oral solutions, and crushing tablets	Yes (2 pair)	Yes				
Route of administration						
Liquid ^a	Yes (1 pair)	Yes		Yes ^{b,c}		
Solid oral (tablets) ^d	Yes (1 pair)					
Topical (creams, ointments) ^b	Yes (2 pair)	Yes		Yes		
Aerosolized ^e	Yes (1 pair)	Yes	Yes	Yes ^b		
Patient care	Yes (1 pair)	Yes		Yes ^{b,f}		
Management of						
Extravasation	Yes (1 pair)	Yes				
Contaminated bedding on the wards	Yes (1 pair)	Yes				
Waste collection and transport	Yes (1 pair)					
Spill or damaged or broken container	Yes (2 pair)	Yes	Yes ^g	Yes		Yes ^h
Cleaning of						
Sterile preparation room and airlock	Yes (1 pair)	Yes			Yes	Yes
Preparation cabinets (hoods)	Yes (2 pair)	Yes	Yes	Yes	Yes	Yes
Other oncology pharmacy rooms and care units or clinics	Yes (1 pair)					

^a Intravenous, subcutaneous, intramuscular, intravesical, intraperitoneal, intrathecal, liquid oral.

^b If risk of splashing.

^c For example, bladder installation or nasogastric, gastric, or jejunostomy tube.

^d 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.

^e For example, ribavirin, pentamidine (although cytotoxic, they are not neoplastic).

^f For example, disposal of bodily fluids.

^g If suspicion of powder or aerosolization is raised.

^h If on the floor.

Respirators should be used in accordance with a respiratory protection program such as that outlined in CSA standard Z94.4-11: *Selection, Use and Care of Respirators*¹⁴ (SR).

2.2.5 Cap

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

2.2.6 Shoe Covers

Disposable shoe covers are worn to prevent contamination of the health care workers' shoes, and covers should be worn when in the sterile preparation room or in the event of a spill. Shoe covers should be removed immediately when leaving the sterile prep room to avoid contamination of other areas (SR).

2.3 Recommendation 3: Receiving and Transport

2.3.1 Handling Delivery Containers of Cytotoxic Drugs

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 (SR).

Delivery containers should be taken immediately to the pharmacy department by the receiving-dock workers or the distributor (SR).

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 not be left unattended in a corridor. Only trained workers (for

example, pharmacy technicians) are to proceed with the unpacking and subsequent steps **(SR)**.

2.3.2 Damaged Containers or Spills

Damaged containers should be handled as if they were spills. The manufacturer or distributor should be notified if a 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 **(SR)**.

See also recommendation 10.

2.4 Recommendation 4: Unpacking and Storage

Packaging can have high levels of contamination. There should be an unpacking area in the pharmacy to limit exposure risks. The unpacking area should be a separate dedicated space, separate from eating areas and preferably a separate room **(SR)**. There should be adequate ventilation in the area, negative pressure, and preferably vented to the outside¹⁵ **(LR)**. A receptacle for cytotoxic waste should be available in the unpacking area for the disposal of secondary packaging^{5,16} **(SR)**.

Workers at risk of exposure should wear a protective gown and 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 (or both) 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 or secondary packaging (or both) should be cleaned before being placed in storage **(SR)**.

A regular cleaning protocol should be in place either at this stage or before storage in the clean room. All drug containers should be cleaned to reduce external contamination. One possible method is to use pre-moistened towelettes. It is important to ensure that the cleaning procedure does not damage the container or interfere with the reading of the label. It is also important to ensure that any product used in cleaning containers will not cause further contamination. The cleaning procedure should also not increase the risk of incidents or accidents resulting from damage to the cytotoxic drug container or label **(SR)**.

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

Establish a dedicated negative-pressure storage area for cytotoxic drugs that minimizes the risk of contamination¹⁶ **(SR)**.

When removing or transporting drugs out of the storage area, 1 pair of gloves and a gown should be worn **(SR)**.

2.5 Recommendation 5: Cytotoxic Drug Preparation

The oncology pharmacy should be in compliance with relevant guidelines from the Canadian Society of Hospital Pharmacists and with Accreditation Canada standards. Although the specific details of oncology pharmacy planning is beyond the scope of the present document, details and some important considerations can be found in the CSA Z8000-11 standard¹⁷ **(SR)**.

Special requirements for heating, ventilation, and air-conditioning systems in health care facilities should be taken into consideration¹⁵ **(SR)**.

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 cabinet¹⁸ **(SR)**.

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 environment¹⁹.

All mixing and preparation of administration sets with a cytotoxic drug should be performed in one centralized area in a specially designated class II, type B biological safety cabinet¹⁵ that **(SR)**

- is exhausted through a HEPA (high-efficiency particulate air) filter to the outside atmosphere in a manner that prevents recirculation into any inside area.
- has exhaust and ventilation systems that remain in operation for a sufficient period of time to ensure that no contaminants escape from the biological safety cabinet into the workplace.
- 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.

Priming of administration sets should be prepared in the manner mentioned above **(SR)**.

The layout should allow for 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. The sterile preparation room and the pharmacy should have a visual link (for example, a window and a way to communicate) so that the work in progress can be monitored. Access to the sterile room should be limited to trained and authorized workers **(SR)**.

Limit worker traffic, particularly near unpacking and storage areas (to avoid accidental breakage) and

near preparation cabinets (to avoid interfering with their proper operation) (SR).

Facilities should include an emergency eyewash station that may or may not be hooked up to the airlock sink⁹ (LR). At a minimum, emergency eye washing should be able to provide 15 minutes of flushing to both eyes²⁰. A full shower should be accessible nearby (for example, in the oncology units or clinics) (SR).

Closed-drug transfer systems [PhaSeal (Becton, Dickinson and Company, Franklin Lakes, NJ, U.S.A.), for instance] are not a substitute for class II, type B biological safety cabinets. There is evidence from studies^{21–26} 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.

Biological safety cabinets should remain in operation 24 hours per day, 7 days per week, as recommended by the manufacturers (SR).

In the non-sterile drug preparation process (for example, oral preparations), the same level of worker protection should be adhered to (SR).

2.5.1 Pharmacy Policies and Procedures

Establish policies and procedures regarding preventive maintenance, monitoring, certification, and the optimal use of facilities and equipment²⁷.

2.6 Recommendation 6: Drug Preparation

The following recommendations apply to the preparation of all cytotoxic medications, parenteral, oral, and topical, and both sterile and non-sterile. Policies and procedures should include appropriate PPE; equipment for preparation, including appropriate ventilation; other automated equipment for packaging; and a dedicated work area (SR).

2.6.1 Personal Protective Equipment

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

2.6.2 Organization of the Work

Organize the work to limit microbial and environmental contamination.

For both sterile and non-sterile preparations, workers should cover the work surface with a disposable absorbent plastic-backed sterile pad to absorb any liquid contamination that may occur during handling. The pad should 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 (for example, a set of vials

of a given drug) or in the event of a spill or contamination (SR). A cytotoxic waste receptacle should be used for pad disposal⁷ (LR).

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 (for example, the waste receptacle) along the sides of the cabinet (SR).

2.6.3 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 (SR).

2.6.4 Handling Techniques

Use handling techniques that limit the risk of injury or accidental exposure (SR).

The spiking of bags and priming of tubing should occur before the addition of the cytotoxic drug unless the clinical protocol requires otherwise (SR).

2.6.5 Preparation, Priming, and Removing Air from Tubing

Cytotoxic drugs should be reconstituted in the pharmacy environment as already described. The drug containers should 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 intravenous tubing with a solution containing the drug. Intravenous tubing should be primed and air removed in the pharmacy, before the cytotoxic drug or drugs are added to the infusion solution. Glass containers are not recommended because of the increased risk of breakage and exposure (SR).

2.6.6 Labelling and Final Packaging

Cytotoxic drugs should be labelled to inform those handling these preparations of the nature of the drugs and the precautions to be taken. Cytotoxic drugs should display the “Cytotoxic” hazard symbol (Figure 1) or the words “Cytotoxic/Cytotoxique”^{6,7} (LR).

The outside surface of cytotoxic drug containers (for example, syringes, infusion bags, tubing) in the preparation cabinet should be cleaned in the cabinet (SR).

Place each cytotoxic drug container (for example, syringe, bag) as well as the administration supplies (for example, tubing) in a clear, leak-proof plastic bag [Ziploc (SC Johnson, Racine, WI, U.S.A.) type, for instance] to facilitate identification by the nurse without having to remove the container from the bag (SR).

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

2.6.7 Waste

Everything that comes out of the cabinet should be wiped clean (SR). All contaminated waste should be disposed of in the chemotherapy waste stream (SR).

2.7 Recommendation 7: Transport and Storage After Preparation

2.7.1 On-Site Transport of Cytotoxic Drugs

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 (for example, Ziploc type) (SR).

Transport the cytotoxic drug in a closed, leak-proof plastic bag from the pharmacy to an area not adjacent to the preparation area (for example, care unit, outpatient clinic) 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 of the container should be covered with an absorbent plastic-backed cloth (SR).

The transport container should be identified with the “Cytotoxic/Cytotoxique” hazard symbol (Figure 1) and should be cleaned regularly^{6,7} (LR).

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

Prepared medications should be stored in a designated area before administration, and this area should be cleaned regularly (SR).

2.7.2 Off-Site Shipping and Transport of Cytotoxic Drugs

Establish policies and procedures regarding the shipping of cytotoxic drugs²⁸ (SR).

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

Cytotoxic drugs should be packed in double plastic bags and placed in a box that is properly identified with the “Cytotoxic/Cytotoxique” hazard symbol (Figure 1). If necessary, the drug should be immobilized with packing material²⁹ (SR). The “Cytotoxic/Cytotoxique” hazard symbol should be visible on the outside of the delivery container²⁹ (LR). Reusable delivery containers should be cleaned regularly (SR).

Ensure that the courier company will handle cytotoxic drugs.

2.8 Recommendation 8: Drug Administration

Safe handling and administration techniques should be used to minimize possible exposure to individuals and

the environment when cytotoxic drugs are administered⁵ (SR).

- Appropriate PPE should be made available to all health care workers and be worn as prescribed by the employer (see Table 1⁹) (LR).
- Luer-lock connectors and needleless administration systems should be used to administer intravenous medications (SR).
- Closed systems may offer additional protection.
- Disposable plastic-backed absorbent pads should be used over work surfaces and be placed under tubing or bag connections and ports when attaching any tubing, bag, or syringe that has been exposed to a cytotoxic drug (SR).
- Unless a closed system is used, never disconnect tubing from cytotoxic drug bags. Discard the bag with its attached tubing into an appropriate waste container as a single unit (SR).
- Safety-engineered needles should be used per Needle Safety Regulation 474/07 under the *Occupational Health and Safety Act, 2010*³⁰. Do not purge air from the needle before administration (LR).
- Oral cytotoxics should be handled in a manner that avoids skin contact, liberation of aerosols or powdered medicine into the air, and cross-contamination with other medicines³¹ (SR).
- Solid oral preparations (tablets) of cytotoxic drugs should be crushed or cut within the biological safety cabinet. If patients are unable to take in the solid format, the pharmacy should provide these drugs in an oral syringe, in a ready-to-administer liquid oral form (SR).
- Application of topical cytotoxic drugs should be done using appropriate PPE and in a way that prevents contamination of the environment. Between applications, the cytotoxic medication (that is, the tube or jar) should be kept in a safe container (that is, a Ziploc-type bag) and in a secure place that prevents contamination of the surrounding environment (SR).
- With any intravesical administration (for example, bladder instillation), ensure there are detailed procedures in place to avoid risks of splashing (SR).
- Use caution when administering intrathecal cytotoxic drugs, as there is a risk of splashing because of increased intrathecal pressures (SR).

2.9 Recommendation 9: Home Care

2.9.1 Home Care of Patients Who Have Received Cytotoxic Drugs

All cytotoxic drug preparations should be compounded in pharmacies meeting the requirements for cytotoxic drug preparation (SR).

Cytotoxic drugs should be transported, administered, and disposed of by individuals who have received appropriate training. Cytotoxic drug transport containers should not be reused by patients for domestic

purposes, which may expose the family to cytotoxic drugs (for example, toy box, sewing basket, etc.) (SR).

Health care providers who administer cytotoxic drugs in the home should wear PPE as outlined in Table 1⁹ (LR).

Health care providers should follow the same recommendations outlined in Recommendation 8, “Drug Administration” (SR).

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

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

Contact information should be provided for home care patients who require assistance with the safe handling of cytotoxic drugs (SR).

2.9.2 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 (SR).

Caregiving staff should provide patients and caregivers involved in administering cytotoxic drugs in the home with a process for the appropriate disposal of cytotoxic waste, including leftover drugs (SR).

2.10 Recommendation 10: Management of Waste

2.10.1 Bodily Fluids

Workers who handle the biologic fluids, excreta, contaminated bedding, and soiled equipment of patients who have received cytotoxic drugs should wear 1 pair of gloves and a protective gown. Face protection should be worn when there is a risk of splashing (SR).

2.10.2 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—for example, packaging material; protective equipment; preparation supplies such as syringes, tubing, drug bags, soiled disposable incontinence briefs of patients who have received cytotoxic drugs during the previous 48 hours [or longer, depending on the drug (for example, cyclophosphamide is known to persist for several days)]; hood pre-filters and HEPA filters; and so on.

Cytotoxic waste should be placed in a waste container clearly identified with the “Cytotoxic/Cytotoxique” hazard symbol (Figure 1). It should be disposed of in the appropriate containers⁷ (LR).

Sharps should be placed in a rigid container with a leak-proof lid; CSA standard Z316.6-07 specifies the use of the colour red for the rigid containers³². If the containers are another colour, follow the instructions of the company ensuring the final disposal⁷ (LR).

Other waste (soft items such as tubing, protective equipment, etc.) should be placed in leak-proof and tear-resistant containers identified with the “Cytotoxic/Cytotoxique” hazard symbol (SR).

For final disposal outside the institution, all cytotoxic waste should be in rigid leak-proof containers identified with the “Cytotoxic/Cytotoxique” hazard symbol and scheduled for transport outside the institution⁷ (LR).

Any excess fluid from cytotoxic drugs (for example, drug loss) should 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 waste⁷ (LR).

Disposable incontinence briefs soiled by patients who have received cytotoxic drugs should be placed in a cytotoxic waste container (R).

Cytotoxic waste should be incinerated at a high temperature (that is, 800–1200°C, depending on the product)⁷ (LR).

Cytotoxic waste should not be disposed of in the receptacles used for infectious biomedical waste (which is autoclaved and then sent to landfill)⁷ (LR).

Every area in which cytotoxic drugs are handled will have an appropriate cytotoxic waste receptacle as close as possible to the work area⁷ (LR).

The lids of cytotoxic drug receptacles must remain closed, except when depositing waste (SR).

Bins with foot pedals and lids, which lock automatically when full, are recommended to minimize exposure (R).

Workers should be careful to avoid contaminating the outside of the receptacle when depositing waste (SR).

The transport of cytotoxic waste receptacles should be assigned to properly trained workers⁹ (LR).

Workers who handle cytotoxic waste receptacles should wear 1 pair of disposable gloves and have a spill kit at their disposal. The waste should travel through as few care units, public areas, and areas containing food or linens as possible (SR).

The final storage areas for cytotoxic waste receptacles should be secure. Refer to Ontario storage requirements^{6,7} (LR).

2.11 Recommendation 11: Accidental Exposure

Be aware of any mandatory reporting requirements under the *Occupational Health and Safety Act* and requirements to report to the Workplace Safety and Insurance Board⁹.

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 should immediately remove the contaminated clothing, thoroughly wash the skin of the affected area with soap and water, and continue to rinse for 15

minutes. If appropriate, the contaminated worker should take a shower. A deluge shower should be made available in the vicinity (for example, in the oncology clinics or units). All contaminated clothing should be discarded in the cytotoxic waste (SR).

If a cytotoxic drug comes into contact with a worker's eyes, the worker should flush their eyes at an eyewash station (SR). Alternatively, workers can use an isotonic solution (for example, sterile NaCl 0.9%) to flush their eyes (R). Eyes should be flushed for at least 15 minutes²⁰ (SR). If contact lenses are worn, they should be removed immediately before flushing (SR).

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 (SR). Contact Occupational Health. Ensure that facility policies for needlestick or sharps injury are followed, including completion of an incident report and reporting to the Workplace Safety and Insurance Board, if indicated.

2.12 Recommendation 12: Spills Management

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

Items used during clean-up of a spill should be placed into the cytotoxic waste receptacle⁷ (LR).

Most spills (for example, leaking intravenous tubing) can be contained and managed by a trained health care worker.

When a spill is not contained or easily managed (for example, a 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 should be called (SR).

2.13 Recommendation 13: Environmental Cleaning

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

Cleaning of the biological safety cabinets should be performed by trained personnel following manufacturers' guidelines³³ (SR).

2.13.1 Use of Pumps to Administer Cytotoxic Drugs

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

2.13.2 Laundry

Ensure that the facility complies with the *Occupational Health and Safety Act*, Ontario Regulation for Health Care and Residential Facilities⁵ (LR).

2.14 Recommendation 14: Medical Surveillance and Environmental Monitoring

2.14.1 Medical Surveillance

Methods used to investigate the 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 noninvasive and should not cause unnecessary distress 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 handling of cytotoxic drugs.

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

Adherence to agreed standard operating procedures, with sufficient initial and regular ongoing training in safe handling and administration, is paramount in reducing the 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^{34,35}. 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.

2.14.2 Environmental Monitoring

The facility should consider implementing an environmental monitoring program (R). Surface testing would audit contamination of the environment (for example, pharmacy counters, patient bedside tables) and provide a quality indicator of cleaning effectiveness and adherence to recommended work.

3. ACKNOWLEDGMENTS

The Cytotoxic Handling Expert Panel and the Working Group 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 copyediting.

- Roxanne MacAskill, Project Coordinator, Princess Margaret Cancer Centre, University Health Network, for help with closed-system transfer devices.

The PEBC is a provincial initiative of Cancer Care Ontario supported by the Ontario Ministry of Health and Long-Term Care. All work produced by the PEBC is editorially independent of the Ontario Ministry of Health and Long-Term Care.

4. CONFLICT OF INTEREST DISCLOSURES

The guideline authors declared no conflicts of interest, except for ACE, who is president and owner of a medical consulting company. That company is not engaged in any work related to handling of cytotoxics.

5. REFERENCES

1. Browman GP, Levine MN, Mohide EA, *et al.* The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. *J Clin Oncol* 1995;13:502–12.
2. Browman GP, Newman TE, Mohide EA, *et al.* Progress of clinical oncology guidelines development using the practice guidelines development cycle: the role of practitioner feedback. *J Clin Oncol* 1998;16:1226–31.
3. Association paritaire pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS), Working Committee on the Safe Handling of Hazardous Drugs. *Prevention Guide: Safe Handling of Hazardous Drugs*. Montreal, QC: ASSTSAS; 2008. [Free download available at: <http://www.irsst.qc.ca/-publication-irsst-guide-de-prevention-manipulation-securitaire-des-medicaments-dangereux-cg-002.html>; cited July 13, 2013]
4. United States, Department of Health and Human Services, Centers for Disease Control and Prevention (CDC), National Institute for Occupational Health and Safety. Workplace Safety & Health Topics: Engineering Controls [Web page]. Atlanta, GA: CDC; 2014. [Available online at: <http://www.cdc.gov/niosh/topics/engcontrols/>; cited May 8, 2014]
5. Service Ontario, e-Laws. *Occupational Health and Safety Act*. Ontario Regulation 67/93: Health Care and Residential Facilities [Web page]. Toronto, ON: Government of Ontario; 2013. [Available at: http://www.e-laws.gov.on.ca/html/regs/english/elaws_regs_930067_e.htm; cited May 8, 2014]
6. CSA Group. *Handling of Waste Materials in Health Care Facilities and Veterinary Health Care Facilities*. CSA Z317.10-09. Toronto, ON: CSA Group; 2009: 60.
7. Ontario, Ministry of the Environment. *Guideline C-4: The Management of Biomedical Waste in Ontario*. Toronto, ON: Government of Ontario; 2009. [Available online at: <https://dr6j45jk9xcmk.cloudfront.net/documents/1761/197-bio-medical-waste-en.pdf>; cited July 30, 2013]
8. BC Cancer Agency. *Employee Health: Management of Risks Related to Hazardous Drugs*. Policy V-20. Vancouver, BC: BC Cancer Agency; 2012.
9. Service Ontario, e-Laws. *Occupational Health and Safety Act*. RSO 1990, Chapter O.1 [Web page]. Toronto, ON: Government of Ontario; 2011. [Available at: http://www.e-laws.gov.on.ca/html/statutes/english/elaws_statutes_90o01_e.htm; cited July 31, 2013]
10. ASTM International. *ASTM D6978-05(2013) Standard Practice for Assessment of Resistance of Medical Gloves to Permeation by Chemotherapy Drugs*. West Conshohocken, PA: ASTM International; 2013.
11. Ontario Agency for Health Protection and Promotion, Provincial Infectious Diseases Advisory Committee. *Routine Practices and Additional Precautions*. 3rd ed. Toronto, ON: Queen's Printer for Ontario; 2012. [Available online at: http://www.publichealthontario.ca/en/eRepository/RPAP_All_HealthCare_Settings_Eng2012.pdf; cited May 8, 2014]
12. ASTM International. *ASTM F739-12 Standard Test Method for Permeation of Liquids and Gases through Protective Clothing Materials under Conditions of Continuous Contact*. West Conshohocken, PA: ASTM International; 2012.
13. CSA Group. *Eye and Face Protectors*. CSA Z94.3-07. Toronto, ON: CSA Group; 2007.
14. CSA Group. *Selection, Use, and Care of Respirators*. CSA Z94.4-11. Toronto, ON: CSA Group; 2012.
15. CSA Group. *Special Requirements for Heating, Ventilation, and Air-Conditioning (HVAC) Systems in Health Care Facilities*. CSA Z317.2-10. Toronto, ON: CSA Group; 2010.
16. Accreditation Canada. *Medication Management Standards: For Surveys Starting After: January 01*. Ver. 8. Ottawa, ON: Accreditation Canada; 2013.
17. CSA Group. *Canadian Health Care Facilities*. CSA Z8000-11. Toronto, ON: CSA Group; 2011.
18. Public Health Agency of Canada (PHAC). *Laboratory Biosafety Guidelines*. 3rd ed. Ottawa, ON: PHAC; 2004.
19. Seger AC, Churchill WW, Keohane CA, *et al.* Impact of robotic antineoplastic preparation on safety, workflow and costs. *J Oncol Pract* 2012;8:344–50.
20. American National Standards Institute (ANSI). *American National Standard for Emergency Eyewash and Shower Equipment*. ANSI/ISEA Z358.1-2009. Washington, DC: ANSI; 2009.
21. Favier B, Labrosse H, Gilles-Afchain L, *et al.* The PhaSeal system: impact of its use on workplace contamination and duration of chemotherapy preparation. *J Oncol Pharm Pract* 2012;18:37–45.
22. Nyman HA, Jorgenson JA, Slawson MH. Workplace contamination with antineoplastic agents in a new cancer hospital using a closed-system drug transfer device. *Hosp Pharm* 2007;42:219–25.
23. Sessink PJM, Connor TH, Jorgenson JA, Tyler TG. Reduction in surface contamination with antineoplastic drugs in 22 hospital pharmacies in the US following implementation of a closed-system drug transfer device. *J Oncol Pharm Pract* 2011;17:39–48.
24. Siderov J, Kirsas S, McLauchlan R. Reducing workplace cytotoxic surface contamination using a closed-system drug transfer device. *J Oncol Pharm Pract* 2010;16:19–25.
25. Yoshida J, Koda S, Nishida S, Yoshida T, Miyajima K, Kumagai S. Association between occupational exposure levels of antineoplastic drugs and work environment in five hospitals in Japan. *J Oncol Pharm Pract* 2011;17:29–38.
26. Yoshida J, Tei G, Mochizuki C, Masu Y, Koda S, Kumagai S. Use of a closed system device to reduce occupational

- contamination and exposure to antineoplastic drugs in the hospital work environment. *Ann Occup Hyg* 2009;53:153–60.
27. NSF International. *Biosafety Cabinetry: Design, Construction, Performance, and Field Certification*. NSF/ANSI 49-2008. Ann Arbor, MI: NSF International; 2008. [Available online at: http://standards.nsf.org/apps/group_public/download.php/3604/NSF_49-08e-rep-watermarked.pdf; cited May 8, 2014]
 28. Transport Canada. Transportation of Dangerous Goods. [Web resource]. Ottawa, ON: Transport Canada; 2014. [Acts and regulations can be searched at: <http://www.tc.gc.ca/eng/tdg/safety-menu.htm>; cited May 8, 2014]
 29. International Society of Oncology Pharmacy Practitioners Standards Committee. ISOPP standards of practice. Safe handling of cytotoxics. Section 2—Transport of cytotoxics. *J Oncol Pharm Pract* 2007;13(suppl):7–9.
 30. Service Ontario, e-Laws. *Occupational Health and Safety Act*. Ontario Regulation 474/07: Needle Safety [Web page]. Toronto, ON: Government of Ontario; 2010. [Available at: http://www.e-laws.gov.on.ca/html/regs/english/elaws_regs_070474_e.htm; cited July 31, 2013]
 31. Roos I, Makela T. Human resource issues in cytotoxic drug dispensing. *J Oncol Pharm Pract* 1997;3:200–18.
 32. CSA Group. *Evaluation of Single Use Medical Sharps Containers for Biohazardous and Cytotoxic Waste—Second Edition*. CSA Z316.6-07. Toronto, ON: CSA Group; 2007.
 33. Canadian Association of Pharmacy in Oncology (CAPO). *Standards of Practice for Oncology Pharmacy in Canada*. Ver. 2. North Vancouver, BC: CAPO; 2009.
 34. Lawson CC, Rocheleau CM, Whelan EA, *et al*. Occupational exposures among nurses and risk of spontaneous abortion. *Am J Obstet Gynecol* 2012;206:327.e1–8
 35. Quansah R, Jaakkola JJ. Occupational exposures and adverse pregnancy outcomes among nurses: a systematic review and meta-analysis. *J Womens Health (Larchmt)* 2010;19:1851–62.

Correspondence to: Anthony C. Easty, HumanEra, Centre for Global eHealth Innovation, Toronto General Hospital, R. Fraser Elliott, 4th Floor, Room 4RFE423, 190 Elizabeth Street, Toronto, Ontario M5G 2C4.

E-mail: tony.easty@uhn.ca

- * Institute of Biomaterials and Biomedical Engineering, University of Toronto, Toronto, ON.
- † Centre for Global eHealth Innovation, University Health Network and University of Toronto, Toronto, ON.
- ‡ Cancer Care Ontario, Program in Evidence-Based Care, Hamilton, ON.
- § Department of Oncology, McMaster University, Hamilton, ON.
- || Institute for Safe Medication Practices Canada (ISMP Canada), Toronto, ON.
- # Public Health Ontario, Hamilton ON.
- ** St. Joseph's Healthcare, Hamilton, ON.
- †† Princess Margaret Cancer Centre, Toronto, ON.
- ‡‡ Juravinski Hospital, Hamilton, ON.