



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

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

Safe Handling of Cytotoxics

June 22, 2018

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

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

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| Section 3: | Development Methods, Recommendations Development and External Review Process |
| Section 4: | Document Assessment and Review |

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Phone: 905-527-4322 ext. 42822 Fax: 905-526-6775 E-mail: ccopgi@mcmaster.ca

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IN REVIEW

Evidence-Based Series #16-3 Version 2

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

Safe Handling of Cytotoxics

Guideline Report History

GUIDELINE VERSION	SYSTEMATIC REVIEW		PUBLICATIONS	NOTES and KEY CHANGES
	Search Dates	Data		
Original 2007	1966 to July 2006	Full Report	Peer review publication. Web publication.	Not applicable
Current Version 2 2013	July 2006 to January 2013	New data added to original Full Report	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.
Version 2 Reviewed June 2018	January 2013 - November 2017	New data found in Section 4	Updated web publication	2013 recommendations REQUIRE UPDATING

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

**Safe Handling of Cytotoxics:
Guideline Recommendations**

A. Easty, N. Coakley, R. Cheng, M. Cividino, P. Savage, R. Tozer, R. White, and the Safe
Handling of Cytotoxics Expert Panel

Report Date: December 16, 2013

The 2013 guideline recommendations

REQUIRE UPDATING

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

GUIDELINE OBJECTIVES

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

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

TARGET POPULATION

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

INTENDED USERS

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

SUMMARY OF GUIDELINE DEVELOPMENT METHODS

This guideline was developed primarily by adaptation and endorsement of the guideline "Prevention Guide: Safe Handling of Hazardous Drugs," developed by the Association paritaire

pour la santé et la sécurité du travail du secteur affaires sociales (ASSTSAS), and the Institut de recherche Robert-Sauvé en santé et en sécurité du travail (IRSST) (1), as described in Section 3 of this document. This adaptation/endorsement process was supplemented with additional searches for evidence in the medical literature on some specific topics as described in Section 2 of this document. The recommendations below reflect the consensus of the expert panel on how best to adapt and endorse the recommendations in the “Prevention Guide: Safe Handling of Hazardous Drugs,” as well as the assessment and interpretation of the identified evidence.

IN REVIEW

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

Closed-System Drug-Transfer Device (CSTD): A drug transfer device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of hazardous drug outside the system, and the escape of hazardous drug or vapour concentrations outside the system (6).

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

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

Extravasation: Passage or escape into tissue of (cytotoxic) drugs. Signs and symptoms may be sudden onset of localized pain at an injection site, sudden redness or extreme pallor at an

injection site, or loss of blood return in an IV needle. Tissue slough and necrosis may occur if the condition is severe. Treatment depends on the causative agent.

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

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

Packaging:

External packaging = outer cardboard box or shrink-wrap.

Secondary packaging = manufacturer's cardboard box. It directly contains the vials.

Primary packaging = the vials.

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

RECOMMENDATIONS

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

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

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

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

RECOMMENDATION 1: GENERAL MEASURES

Committee Responsible for Policy and Procedures for Cytotoxic Drugs

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

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

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

Continuing Education and Orientation Program

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

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

Identification and Safety

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

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



Purchasing of Drugs

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

Spills Kit

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

Precautionary Reassignment

It is strongly recommended that all staff be fully informed of the potential reproductive hazards of cytotoxic drugs (11).

It is strongly recommended that the facility consider alternative duties for women who are pregnant or breast feeding.

RECOMMENDATION 2: PERSONAL PROTECTIVE EQUIPMENT (PPE)

It is legislated that a worker work in compliance with the Occupational Health and Safety Act and regulations and use or wear the equipment, protective devices or clothing that the

employer requires to be used (2).

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

Gloves

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

Gown

It is strongly recommended that the gowns used for handling cytotoxic drugs be disposable, made of lint-free, low-permeability fabric, have long sleeves with tight-fitting cuffs and fasten in the back. Gowns need to be changed in the event of contamination, spillage, rips, and at the end of the procedure.

For medication preparation, gowns need to be changed halfway through a shift or every 3.5 hours (14). It is strongly recommended that the supplier be able to certify that the gown protects against cytotoxic drugs.

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

Facial Protection

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

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

Respiratory Protection Apparatus (RPA)

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

Cap

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

Shoe Covers

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

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

Medication circuit steps	Gloves	Gown	RPA	Face protection	Cap	Shoe covers
Unpacking and cleaning	✓ (2 pairs)	✓				
Sterile preparations	✓ (2 pairs)	✓		✓	✓	✓
Non-sterile preparations: - Counting of solid oral forms -Preparing creams, ointments, oral solutions and crushing tablets	✓ (1 pair) ✓ (2 pairs)	✓ ✓				
Routes of administration (intravenous, subcutaneous, intramuscular, intravesical, intraperitoneal, intrathecal, liquid oral)	✓ (1 pair)	✓		✓ (if risk of splashing, e.g., bladder installation or NG, G, or J tube)		
Solid oral administration (tablets)*	✓ (1 pair)					
Topical administration (creams, ointments)	✓ (2 pairs)	✓		✓ (if risk of splashing)		
Aerosolized administration (e.g., ribavirin, pentamidine) [†]	✓ (1 pair)	✓	✓	✓ (if risk of splashing)		
Patient care	✓ (1 pair)	✓		✓ (if risk of splashing, e.g., disposal of bodily fluids)		
Management of extravasation	✓ (1 pair)	✓				
Handling of	✓	✓				

Medication circuit steps	Gloves	Gown	RPA	Face protection	Cap	Shoe covers
contaminated bedding on the wards	(1 pair)					
Waste management (collection and transport)	✓ (1 pair)					
Spill or damaged or broken container	✓ (2 pairs)	✓	✓ (if suspicion of powder or aerosolization is generated)	✓		✓ (if on the floor)
Cleaning of sterile preparation room and airlock	✓ (1 pair)	✓			✓	✓
Cleaning of preparation cabinets (hoods)	✓ (2 pairs)	✓	✓	✓	✓	✓
Cleaning of other oncology pharmacy rooms and care units/clinics	✓ (1 pair)	✓				

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 that any product that is used will not further contaminate. However, it is strongly recommended that this procedure not increase the risk of incidents/accidents due to damage to the cytotoxic drug container or label.

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

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

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

RECOMMENDATION 5: CYOTOXIC DRUG PREPARATION

Planning the Oncology Pharmacy

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Pharmacy Policies and Procedures

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

RECOMMENDATION 6: DRUG PREPARATION

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

Personal Protective Equipment

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

Organization of the Work

Organize the work to limit microbial and environmental contamination.

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

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

Removal of Packaging

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

Handling Techniques

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

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

Preparation, Priming and Removing Air from the Tubing

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

Labeling and final packaging

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

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

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

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

Waste

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

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

RECOMMENDATION 7: TRANSPORT AND STORAGE FOLLOWING PREPARATION

On-site Transport of Cytotoxic Drugs

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

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

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

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

It is strongly recommended that mechanical transport systems, such as pneumatic tubes, not be used because of the stress they put on the contents, and the whole transport system would be compromised if a leak occurred.

It is strongly recommended that prepared medications be stored in a designated area prior to administration. It is strongly recommended that this area be cleaned regularly.

Off-site Shipping and Transport of Cytotoxic Drugs

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

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

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

Ensure that the courier company will handle cytotoxic drugs.

RECOMMENDATION 8: DRUG ADMINISTRATION

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

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

medication (i.e., tube or jar) be kept in a safe container (i.e., Ziploc) and in a secure place that prevents contamination of the surrounding environment.

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

RECOMMENDATION 9: HOME CARE

Home Care of Patients who Have Received Cytotoxic Drugs

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

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

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

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

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

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

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

Cytotoxic Drug Waste in the Home

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

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

RECOMMENDATION 10: MANAGEMENT OF WASTE

Bodily-Fluid Waste

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

Cytotoxic Drug Waste

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

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

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

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

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

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

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

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

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

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

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

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

It is strongly recommended that workers be careful to avoid contaminating the outside of the receptacle when depositing waste.

It is legislated that the transport of cytotoxic waste receptacles be assigned to properly trained workers (2).

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

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

RECOMMENDATION 11: ACCIDENTAL EXPOSURE

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

Establish policies and procedures regarding accidental worker exposure.

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

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

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

RECOMMENDATION 12: SPILLS MANAGEMENT

It is strongly recommended that the facility develop policies and procedures for spills management that take into account the types of spills (i.e., amount, location, concentration, powder vs. liquid, etc.).

It is strongly recommended that a spill management kit be readily available within the work area.

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

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

tubing).

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

RECOMMENDATION 13: ENVIRONMENTAL CLEANING

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

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

Use of Pumps to Administer Cytotoxic Drugs

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

Laundry

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

RECOMMENDATION 14: MEDICAL SURVEILLANCE AND ENVIRONMENTAL MONITORING

Medical Surveillance

Methods used to investigate potential health effects of exposure to cytotoxic drugs are inconclusive and difficult to interpret. The ideal test should meet several requirements – it should be sensitive, specific, quantitative, rapid, and reproducible. Importantly, the procedures for taking a sample should be non-invasive and should not cause unnecessary 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 in the handling of cytotoxic drugs.

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

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

There is evidence in the literature of a higher rate of spontaneous abortion among women working in roles that expose them to cytotoxic drugs (35, 36). There are no other identified medical conditions known to result from chronic exposure of health care workers to cytotoxic drugs, no exposure limits set for cytotoxic drugs, and no standards for interpretation of test results of exposed health care workers to enable meaningful interpretation or action based on biological monitoring results.

Environmental Monitoring

It is recommended that the facility consider implementing an environmental monitoring program. Surface testing would audit contamination of the environment (e.g., pharmacy counters, patient bedside tables) and provide a quality indicator of cleaning effectiveness and adherence to recommended work practices.

IN REVIEW

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Phone: 905-527-4322 ext. 42822 Fax: 905-526-6775 E-mail: ccopgi@mcmaster.ca

IN REVIEW